

TypeStreamTM Visual NGS Analysis Software User Manual

Version 2.x.x

Catalog #TSVPGR

For Research Use Only in US and Canada. Not for use in diagnostic procedures



In Vitro Diagnostic use in the European Union Only





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Table of Contents

| TypeStream Visu | al NGS Analysis Software | |
|--------------------|----------------------------|-----|
| | Introduction | |
| | Program Updates | 8 |
| | Supported Products | 8 |
| | Technical Support | 8 |
| | Scope of this Manual | 9 |
| | System Requirements | 9 |
| | Software Activation | 9 |
| | Installation | 14 |
| Application Setu | o | 22 |
| | Home Page | 22 |
| | Profile Management | 22 |
| Utilities and Supp | port Functions | 32 |
| | Toolbar Functions | 32 |
| | Main Menu Options | 34 |
| | Utilities | 37 |
| Automation | | 59 |
| | Automation (Auto-Analysis) | 59 |
| Create Session a | nd Analyze Data | 69 |
| | Open Create Session Page | 69 |
| | Create a session | 72 |
| | Create Session for PACBio | 77 |
| | ALLType FASTPlex | 78 |
| | Job Manager | 79 |
| | Navigator | 82 |
| View Analysis | | 83 |
| | Session Summary | 83 |
| | Analysis Panel | 100 |
| | Reads viewer | 113 |
| | Reads viewer in detail | 128 |
| Reports | | 135 |
| Data Manageme | nt | 149 |
| | Manage Data Window | 149 |
| | Sample Management | 157 |
| Patient Manager | nent | 161 |

| | Patient Information | 161 |
|------------------|---------------------|-----|
| Database Utility | | 171 |
| | Database Tasks | 173 |
| Appendix A | | 187 |
| Indev | | 101 |



TypeStream Visual NGS Analysis Software

Introduction

Intended Use: TypeStream Visual Software is an accessory for the evaluation of test results from One Lambda, Inc Next Generation Sequencing (NGS) products for molecular typing.

It is a standalone software solution that supports the analysis of both single read and pairedend sequencing data produced using AllType^{TM} NGS assays.

Upon completion of sequencing, TypeStream Visual automatically aligns unmapped barcode sequences to the IMGT reference library to generate individual allele assignments. In addition to genotyping, TypeStream Visual provides the analyst with a wide range of analytical tools, run statistics and quality metrics to facilitate examination and reinforce decision making.

NOTE: Make sure you have downloaded the most up to date Nomenclature and/or Serology Equivalent files before you import catalogs or attempt to analyze sessions/samples.

The first thing you may notice is a change in icon. The new look for TypeStream Visual makes it unique to TSV.



TypeStream Visual now leverages multi-processor CPU, effectively cutting in half, or better, your analysis time for any session with more than two samples. Engine and logical processor

use is as follows:

Total logical processors 8-23: 2 engines Total logical processors 24-31: 3 engines If the total logical processors >= 32: threads per engine 6, engine #= total processors / 6-1

Sessions with only single samples will not be able to take advantage of this increase in analysis speed.

Program Updates

You may also obtain updates of TypeStream Visual by request. Please contact your One Lambda, Inc. representative for a copy of the software, or see the Technical Support section below for more contact information. Product information updates, (catalog files, etc.) for TypeStream Visual are available through your One Lambda Inc. representative, or from the One Lambda website:

• www.onelambda.com

Supported Products

All One Lambda software products are designed to assist personnel experienced in analysis by suggesting typing results. However, results must be carefully reviewed by a person qualified in typing to assure correctness. This software may be used to aid in suggesting results but should not be used as the sole method for determining reportable results. This software is meant as a laboratory aid, not as a source of definitive results.

Catalog selection needs to match the SKU name for the assay used. For AllType NGS Amplification reagents, use catalog beginning with 'ALL.' Refer to the table below when analyzing using TypeStream Visual NGS Analysis Software (Cat. No. TSVPGR)

| Product Description | Catalog Number | Assay Regulatory Status | |
|---------------------------------------|----------------|--------------------------------|--|
| AllType NGS 11 Loci Amplification Kit | ALL-11L | CE-IVD | |
| AllType NGS 11 Loci Amplification Kit | ALL-11LX | For Research Use Only. Not for | |
| | | use in diagnostic procedures. | |
| AllType NGS 9 Loci Amplification Kit | ALL-9LX | For Research Use Only. Not for | |
| | | use in diagnostic procedures. | |
| AllType NGS 8 Loci Amplification Kit | ALL-8LX | For Research Use Only. Not for | |
| | | use in diagnostic procedures. | |
| AllType FASTplex NGS 11 Loci Assay | ALL-FAST11LFX | For Research Use Only. Not for | |
| for Illumina | | use in diagnostic procedures. | |

Technical Support

For technical support or to report software problems, contact your One Lambda representative. From the United States, call 800-822-8824, or in the Greater Los Angeles Area, call 747-494-1000. Contact us by e-mail at: lambda-techsupport@thermofisher.com

For system requirements, see the TypeStream Visual Installation Guide.

Scope of this Manual

This manual provides information on how to import raw data, make changes to configuration and control adjustments as necessary for analysis. It is very important to recognize that the defaults set in this program are based on One Lambda's experience with the product in a tightly-controlled research and development environment. A laboratory performing typing in another environment may need to reset parameters to meet specific laboratory requirements.

From the Main Menu of TypeStream Visual, you can access the four major components of the program:

- Analyze Data
- Create Reports
- Manage Records
- Manage Database

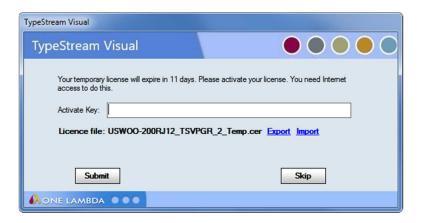
System Requirements

The minimum system requirements are as follows:

- Microsoft® Windows® 10.0, 64-bit OS
- 4-Core processor with 8 threads, 16 GB RAM
- 8-bit graphic adapter and display with 1920 x 1080 screen resolution
- Microsoft .NET 4.6.1 Framework (included in installation package)
- Microsoft Visual C++ 2005 SP1 Redistributable package (included in installation package)
- Microsoft SQL Express 2014 (included in installation package)
- Crystal Reports 13.0.17 Runtime for .Net 4.6.1 64-bit (included in installation package)
- WinZip (not included in installation package)

Software Activation

IMPORTANT: When you first install TypeStream Visual, you will receive this message. The software will expire in 11 days if you do not activate your license.



License Key Activation

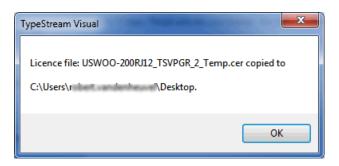
TypeStream Visual requires a license key to run the application. A temporary license is provided for the first 11 days of usage, after which the software will cease to function unless a permanent license is obtained. After the permanent license is activated, the software will display a warning message at 30 days before expiration of this license. Your license information for TypeStream Visual is stored in a certificate file on your local computer

Please convert your temporary license into a permanent license as soon as possible to avoid interruption of software operation. To convert your temporary license into a permanent software license, please do the following:

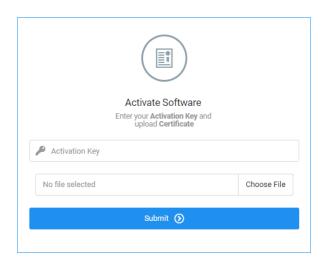
- 1. After the initial installation, when TypeStream Visual starts up, an 11-day license reminder screen will be displayed as shown above.
- 2. If you do not yet have a license key, you can click Skip to ignore the warning and continue to operate the software; however, please convert your license at the earliest opportunity to avoid interrupted software operation.
- 3. At the reminder screen, type in your Activation key and press Submit. Your activation key can be found on your order confirmation.
- **4.** If the activation of your license fails by using the Activate Key facility, proceed with the rest of these steps.
- 5. Export your certificate file to disk using the Export link. The Export for Folder box will appear and allow you to save the certificate file on your computer. Press OK when ready to save the file:



6. A message will then appear confirming successful saving of the file.



- 7. On a computer with Internet access, navigate to the **OLI License Renewal website** and do the following:
 - a. In a web browser, go to https://forms.onelambda.com/software/activation

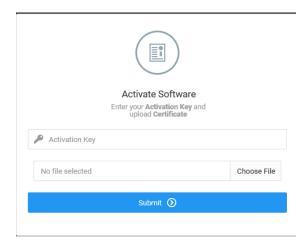


b. Copy your certificate from Step 4 to a folder on this computer.

c. Enter your activation key in the **Activation Key** box shown above, then click the **Choose File** button (your certificate file name and location will vary from the example shown).

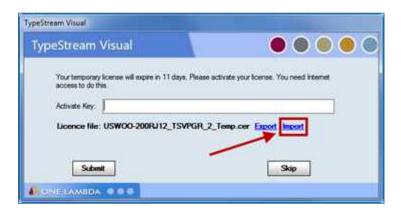


- d. Click on the certificate file you previously saved and click **Open** (above).
- **e.** The certificate file will be displayed in grey on the web form (shown below).



Click the blue Submit button, and observe the results:

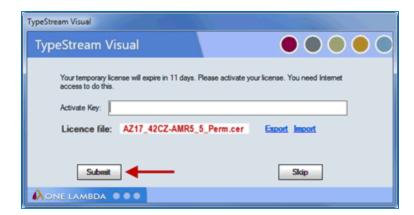
- If the operation was successful, your order information will be updated for TypeStream Visual and it will convert your temporary license into a permanent license.
- Click on the Download button to download your certificate with your permanent license
- Copy your certificate file with your permanent license, back to that the computer you are attempting to activate TypeStream Visual.
- **8.** Startup TypeStream Visual. If the program runs successfully, you are finished with the licensing procedure. Skip to Step 9.
- 9. Click the **Import link** on the reminder screen to install the certificate with permanent license that you obtained from the website:



10. A selection box will appear and allow you to choose the certificate file to import into TypeStream Visual:



11. Once the new certificate file has been selected, it will be displayed in the **License file field.** At this point, click **Submit**:



Installation

Proceed with the installation as described in the Installation Guide.

Launch Application

When installation is complete, select the check box for Launch TypeStream Visual 2.0, and then click the Finish button.

The installer automatically launches the TypeStream Visual application (This may take a few moments.) If TypeStream Visual does not start, double-click the TSV 2.0 icon on your computer desktop

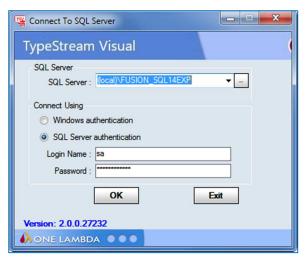
If the TypeStream Visual database connection is not yet set up when the program is launched, (as is the case the very first time it is launched) a System Initialization message is displayed to indicate this. Click the Continue button.



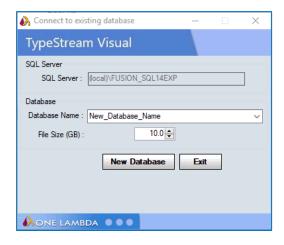


Select Server/Standalone installation type from the TypeStream Visual Database Utility window that displays after TypeStream Visual has been installed.

Connect to a SQL Server



- 12. Select a SQL Server by doing one of the following:
 - a. Type in the full path, directory, and server name.
 - b. Click the drop-down arrow in the SQL Server field to display a list of local SQL Servers.
 - c. Click the Browse button to display a list of SQL Servers available from your network.
- 13. Select a security connection type. SQL Server authentication is recommended.
- 14. For SQL Server authentication, enter Login Name and Password, (Windows authentication usually requires configuration by administrator).
- 15. Click the OK button.

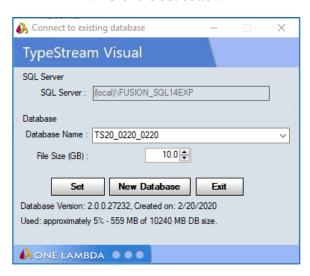


Note: The specified SQL Server must be allowed to receive remote connections and you must have the appropriate user ID and password to connect to it. If necessary, contact your system administrator to determine whether the specified SQL Server is configured for Windows, or for SQL Server authentication, or both.

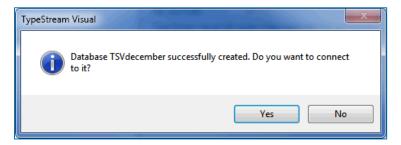
Connect to a Database

16. Create a new database and/or connect to an existing one

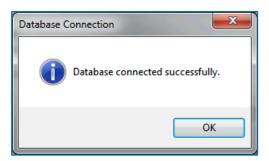
- a. Instructions for connecting to an existing database
 - i. Select existing database from dropdown menu.
 - ii. Click the Set button.



- b. Instructions for creating a new database
 - i. To create a new database, enter a unique name for the new database, and click the New Database button.
 - ii. It is highly recommended that database names contain no spaces or dashes.
 - iii. After the database has been created, click the Set button (above).



A confirmation message is displayed when you have successfully connected to a database:

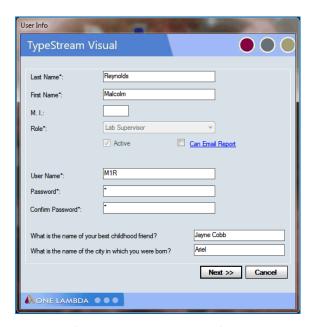


Click the OK button. The TypeStream Visual application should automatically launch. If it does not, double-click the TSV 2.0 icon located on your computer desktop.

17. Set Up the first user profile and lab information

When the software launches with a connection to a new database, the User Info

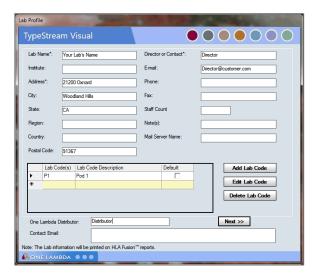
Screen appears. Fill in all required fields, (denoted with an asterisk*) to set up a User Profile and click the Next button.



Enter all necessary information on the Lab Profile Screen (an asterisk * denotes required fields)

Click the Next button. (See next chapter for more information.)

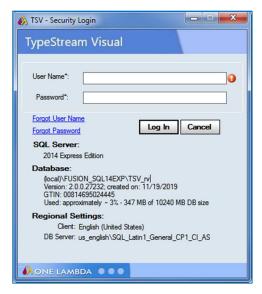
NOTE: The <u>first</u> user is always set to the Lab Supervisor Role. See more detail about Supervisor vs. Technician roles and permissions under "User Profile" in Chapter 2. Lab name and contact information will be displayed in the footer section of the TypeStream Visual reports.



NOTE: If you will be using TypeStream Visual to generate NMDP code reports, add a Lab Code to the Lab Profile.

Log in

Log in to TypeStream Visual using the credentials entered during installation/configuration.

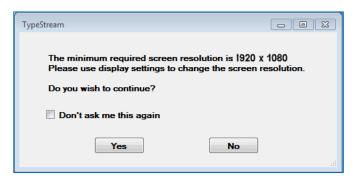


- 1. Version of SQL server used
- 2. Database which is currently active in TypeStream Visual
- 3. GTIN number: a number established in the GS1 database for Unique Device Identification (UDI).
- 4. Database Collation

Key System Settings

Screen Resolution

TypeStream Visual software requires a minimum screen resolution of 1920 x 1080. The software displays a message if your current resolution is less than the expected generals.



You can select 'Yes' to continue to start the application or No to exit the program.

In addition, if your computer is running Microsoft® Windows 10®, the text display size setting must be set to "Smaller - 100% (default)." Take these steps if you need to adjust this setting:

- 1. Right-click on the computer desktop. Select the Screen Resolution option.
- 2. Select Smaller sized text.

Software may not resize for full view of graphic user interface if the window is not maximized. This truncated view is eliminated by maximizing the screen.

File Permissions

All TypeStream Visual users must have read and write permissions to the following directories and files:

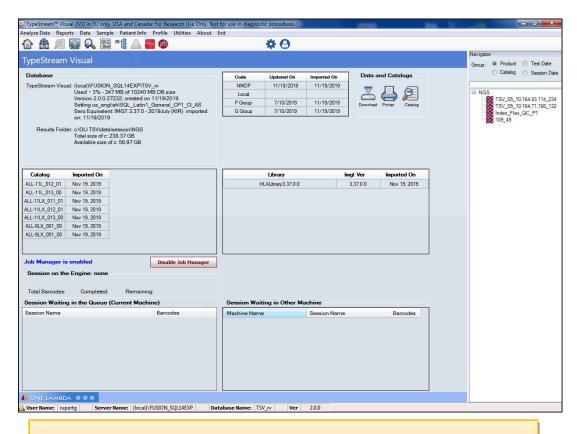
- C:\Program Files (x86)\One Lambda\
- OneLambda.Fusion.Interface.exe.config
- ReportMap.xml
- C:\OLI TSV\ (and all the sub directories and the files in these directories)
- C:\ProgramData\One Lambda folder (Note: C:\ProgramData is a hidden folder)



Application Setup

Home Page

Login will take you to the home page.



Important: TypeStream Visual is optimized for use with Microsoft Windows when set to 100% zoom.

Home page contains information on the following:

Database status

Active catalogs

Active library

Reference files

Job Manager - which session is currently on the engine and what is waiting in the queue

Toolbar and Menu Options

See the following chapter for more information on these topics.

Profile Management

TypeStream Visual tracks all changes to analysis data made by users and allows added data security with a two level analysis result confirmation (Save and Confirm). TypeStream Visual also stores general laboratory information to be used on reports including multiple contract lab codes.

User Profile

From the Profile main menu, you can:

Add new users
Edit existing user profiles
Change passwords
Reset passwords
Archive users

TypeStream Visual uses two user levels for added security and control of typing and screening results.

| Supervisor | Technician, if given specific permission |
|-----------------------------------|--|
| Modify all product configuration | Modify all product configuration settings—except to |
| settings | enable Auto Accept All |
| Save and Confirm analysis results | Analyze data and save analysis results |
| Update reference files, such as | (Only if authorized by the supervisor) - Update reference |
| catalogs and NMDP codes | files, such as catalogs and NMDP codes |
| Archive catalogs | Archive catalogs |
| Modify and delete session and | (Only if authorized by the supervisor) - Modify and delete |
| sample data | session and sample data |
| Modify own & other user accounts | Modify own account only |
| Change the Lab Profile | Manage sample and patient information |

Viewing the User List

The List User option displays a list of all users currently in the database, both active and retired. You can look up and select user profiles.

- 1. From the Main Menu, select Profile > List User.
- 2. Type in a name and click Search to search for current users.

- 3. Double-click to the left of a user entry to view the profile.
- 4. Click Close to return to the main menu.

Adding New Users

Supervisors can add new supervisor or technician level users. Technicians cannot add new users. Fields marked with an (*) are required.

- 1. From the Main Menu, select Profile > List User.
- 2. Click Add User to add a new user.
- 3. Enter new user information.
- 4. Select the Active check box under the Role field to activate the user account.
- 5. Click Save to save the new user information and return to the main menu or click Close to discard changes and return to the main menu without saving.

NOTE: If this is a lab tech profile and you want to allow reference file update and/or data management privileges for this user, select the appropriate check boxes

Editing User Profiles

Supervisors can edit the user profile of any user. Technicians can only edit their own profiles. Fields marked with an asterisk (*) are required.

- 1. To edit your own profile, select Profile > My Profile.
- 2. To select from a list of users to edit, select Profile > List User and double-click to the left of a user to select that profile.
- 3. Edit user information.
- 4. Click Save to save user information and return to the Main Menu.
- 5. Click Close to discard changes and return to the Main Menu without saving.
- 6. You will not be able to modify a username.

Changing Passwords

Supervisors can change passwords for any user, but they must have the user's old password. Technicians can change only their own passwords.

- 1. From the Main Menu, select Profile > My Profile.
- 2. In the user profile, click the Change Password button.
- 3. Enter the current and new passwords.
- 4. Click the Save Password button to change the password. Or, click Close to close and return to the main menu without changing the password.

Resetting Passwords

If a user loses or forgets their password, TypeStream Visual can reset the password. The new password is the same as the user's username. Only Supervisors can reset a user's password.

- 1. From the Main Menu, select Profile> List User and select a user.
- 2. In the user profile, click the Reset Password button.
- 3. Click Close to return to the main menu.

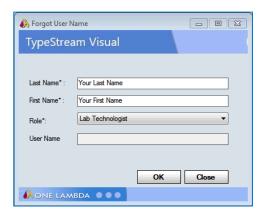
Changing User Privileges

Only Supervisors can modify a user's privilege level.

- 1. From the main menu, select Profile > List User
- 2. Double-click to the left of a user to open their profile.
- 3. In the user profile, select the check box next to either Manage Data or Update Reference Files, or both, to give the selected user privileges for those activities within the TypeStream application.
- 4. Click **Close** to return to the Main Menu.

Retrieving a Forgotten Username or Password

If you forget your Username, click the Forgot Username link, enter your first and last name, and select your lab role, (supervisor or technician). The system displays the username matching the data you provide.



If you forget your password, click the Forgot Password link and answer the two security questions you were asked when you set up your user profile.



The password is displayed when the questions are answered correctly.

Deactivating Users

Supervisors can deactivate users who are no longer using TypeStream Visual. User information is still stored in the database, but the user is not able to log into the program.

- 1. From the Main Menu, select Profiles > List User and select a user to edit.
- 2. Clear the Active check box to deactivate the user.
- 3. Click Save to save user information and return to the main menu or click Close to discard changes and return to the Main Menu without saving.

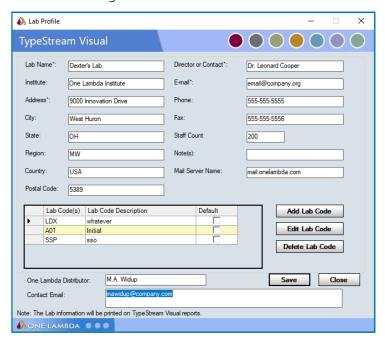
NOTE: If a User ID is still associated with analysis records, the User ID cannot be deleted.

Lab Profile

The Lab Profile menu displays the contact information for your lab, network information used by TypeStream Visual, and NMDP contract lab codes. Most of this information is entered during installation but can be updated at any time. Only supervisors can change the Lab Profile.

From the Lab Profile menu, you can:

- Edit the Lab Profile
- Add, edit and remove Lab Codes
- Change the Network Path
- Change the Email Server Name



Editing the Lab Profile

Laboratory information displays on most reports and includes contact information for your lab. This information is initially entered during installation and can be edited any time from the Lab

Profile menu. Fields marked with an asterisk are required.

- 1. From the main menu, select Profile > Lab Profile.
- 2. Edit lab profile information.
- 3. Click Save to save changes and return to the main menu or click Cancel to return to the main menu without saving any changes.

Managing Lab Codes

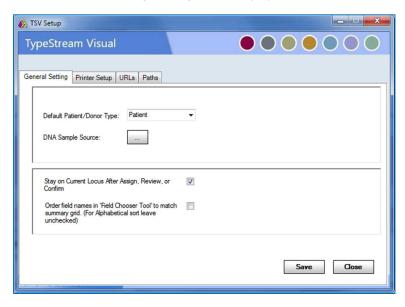
Lab codes are used on NMDP reports to identify contract labs. Multiple lab codes may be entered and stored in TypeStream Visual. You can select the lab code you wish to use when creating an NMDP report. Only the first three digits of a lab Code are used on NMDP reports; lab code descriptions are not included on reports.

- 1. From the main menu, select Profile > Lab Profile. Add, edit or delete Lab codes:
 - a. Click Add Lab Code to add a new lab code. Enter information into the new row.
 - b. Highlight a lab code to be edited. Click Edit Lab Code to edit the lab code.
- 2. Edit lab code information.
- 3. Highlight a lab code to be deleted.
- 4. Click Delete Lab Code to delete the lab code.
- 5. Click Save to save changes and return to the main menu or click Cancel to discard changes and return to the main menu without saving.

General Settings

You can set a number of general system settings, including printer defaults and URLs and Paths.

1. Select Utilities → General Settings from the TypeStream Visual main menu. The General Settings dialog box is displayed.



2. Use the drop-down menus or select check boxes as appropriate to make your selections on this dialog window.

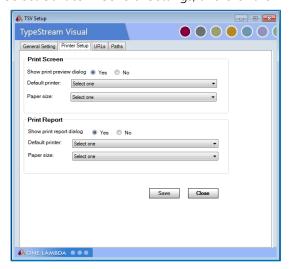
3. When you have made all of your selections, click Save.

| ltem | Definition | | | |
|---|---|--|--|--|
| Default Patient/Donor Type | The three options are Patient, Donor, or Both. This applies to the creation of new sessions. "Patient/Donor" column on the far right of the sample row will default to the selected option if there is no value already associated with the sample. | | | |
| DNA Sample Source | The four default options for sample source are Cord Blood, Whole Blood, Filter Paper, and Buccal Swab. User is able to additional sources. The software will not auto-fill source for samples where the source is not given, but a sample source cannot be input on the session import page if it is not on this list. | | | |
| Stay on Current Locus after Assign, Review or Confirm | When unchecked and the user Assigns (Reviews or Confirms) A locus, for example, the software will automatically move on to the next unassigned or unreviewed or unconfirmed locus. If there is no other locus in the current sample that meet the criteria the software advances to the next sample. When checked, the software will remain on the locus that was just assigned. | | | |
| Order field names in 'Field Chooser Tool" to match summary grid. (For Alphabetical sort leave unchecked.) | On session summary screen, clicking on the icon at the far left on either session or locus header row will bring up the 'Field Chooser' tool, allowing the user to select which fields to display in session summary. When unchecked, the selectable fields will display in alphabetical order. When checked, the fields will display in the order in which they will appear on the sample or locus header. See session detail section for more information. | | | |

Printer Defaults

From the Printer Setup tab on the General Settings dialog box, you can select settings such as default printer and paper size, which will be in place when you print reports or do a print screen.

1. Select Utilities > General Settings, and click the Printer Setup tab.+



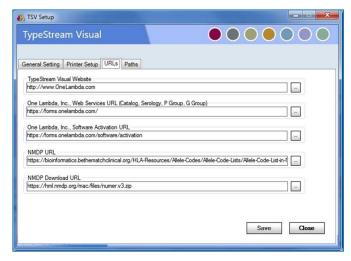
- 2. Select from the following options for both the Print Screen and Print Report panels of the dialog box:
 - a. If you want to see a print preview or print report dialog each time you print, make sure the Yes option is selected. Otherwise, select No.
 - b. If you do not want to select a printer each time you print, select the default printer and paper size from the drop-down menus.
 - c. This default printer configuration may be overwritten by the specific page properties of certain reports.
- 3. Click Save Save

Setting TypeStream Visual Default URLs and Directory Paths

The URLs & Paths option under the General Settings menu allows you to set the default URLs for OLI and NMDP websites to download reference and catalog files, and product updates. This option also allows you to set the directory path where TypeStream Visual, by default, stores catalogs, session/batch files, reports, etc.

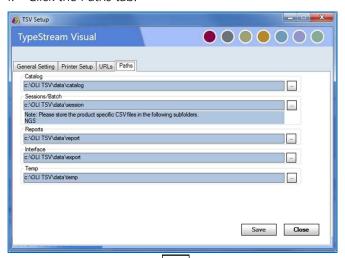
Modifying URLs or paths ahead of time allows you to avoid having to browse for files each time you need them.

- 1. From TypeStream Visual home page select Utilities > General Settings from the main menu.
- 2. Select the URLs tab.



3. Enter a URL and verify it works by clicking

4. Click the Paths tab.



- 5. Use the browse button to locate the directory you want to use for the specified purpose (e.g., where you want to store reports when they are generated).
- 6. Click Save

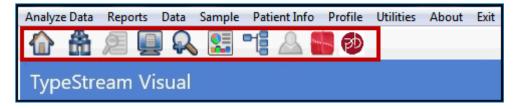
NOTE: In using the Restore Database function (see Chapter on databases), if the user restores a database .bak file from one machine to another, the NGS Session folder must also be copied to the destination machine and the path in General Settings must point to the folder path.



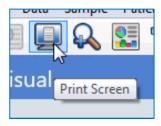
Utilities and Support Functions

Toolbar Functions

TypeStream Visual provides a toolbar, displayed just below the main menu bar options with access to commonly used functions.



When you hover your mouse over the buttons, a label will pop up with the name of each button.





Home

Clicking this icon from any other page returns the user to the Home screen. This can be especially useful after submitting sessions for analysis in order to check their progress.

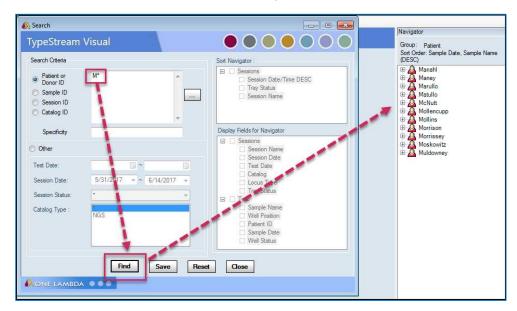


Find: Search

Click the Find ("Bino") button to open the TypeStream Visual Search Window to look for records using various criteria. The Find dialog box also allows you to modify the Navigator Session sort and display criteria.

To use this tool, do the following:

- Enter a search parameter into the area of interest. In the example below, user wants to find all sessions with a Patient ID beginning with 'M.'
- 2. Click Find.
- 3. The Navigator displays all sessions that fit the search parameter with the sort order described above the listing.



The date range set here, in the Session Date field, is used as the default date range throughout TypeStream Visual, such as in the Navigator and Reports windows. Each time you change it, and click the Find button, the default changes for the rest of the application.



Quick Reports (Print Preview)

This button allows the user to quickly create any of the following reports for the selected session without having to go to the reports page. When a session is selected which originated from Illumina or Ion Gene Studio S5, the following options will display:

- A. XML Report
- B. Genotype Summary (pdf)
- C. Genotype Summary Table (csv)
- D. Genotype Summary Health (csv)

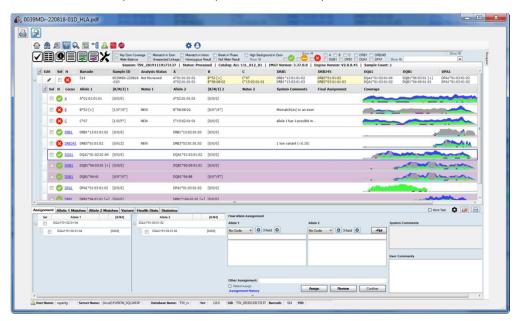
When a PACBio session is selected, only the following option will display:

E. PACBio Summary Health (pdf)

Reports created will adhere to default settings.

Print Screen

From any Analysis Screen, click the Print Screen button to open a new window containing a screen shot of the current analysis window. Click the Print 🗐 button, (top, left corner) to send the screen shot to the printer. The software will use the configuration selected for "Print Report" on the settings configuration page. The sample name will display on the top left corner in the format "[Samplename]_HLA_[patient first name_patient last name]."



To close this window, click the Exit X button or the Close Close button.

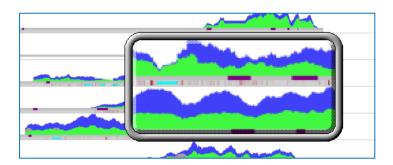
If more than one sample is selected in the summary, then the screenshot is labelled with the last sample that is selected.

Magnify

From any Analysis Window, click the Magnify button to activate the magnifying glass and enlarge any section of the window. Use your mouse to move the magnifier and use the arrow keys on your computer keyboard to increase or decrease the height and width of the magnified area.

Use the right and left arrow keys on the keyboard to increase and decrease the size of the magnified area.

Click anywhere on the screen to deactivate the magnifying glass.



Show Navigator

If the TypeStream Navigator, (normally displayed on the right side of the application window) is not visible, click the Show Navigator button on the toolbar. Once the Navigator tab is displayed, move your cursor over it to slide the Navigator panel open.

Patient/Donor Information

From any Analysis Screen, click the Patient button to display the Patient/Donor Information Screen where you can enter or edit information related to a patient or donor and associate it with the current sample.

You can also open the Patient/Donor Information screen at any time by clicking Patient Info on the TypeStream Menu Bar, followed by Manage Patient.

For detailed information on the operation of this screen and its tabs, please see the section entitled Patient Management.

NGS Session Builder

To create a session to analyze raw data from either Ion S5 sequencers or Illumina MiSeq or MiniSeq sequencers, click the "NGS Session Builder" icon. This opens the Create Session page in which the user may designate the path to the raw data and then select the analysis parameter set, IMGT library version, and catalog for analysis. (See next chapter for more detail.)

PACBio Session Builder

To create a session to analyze raw data from either PACBio sequencers, click the "NGS Session Builder" icon. This opens the Create Session page in which the user may designate the path to the raw data and then select the analysis parameter set, IMGT library version, and catalog for long amplicon analysis. (See next section for more detail.)

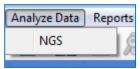
Main Menu Options

You can access TypeStream Visual functionality at any time from the toolbar's Main Menu, which is displayed at the top of all TypeStream Visual application windows. See the following

sections for a list of the options available under each main menu item.

Analyze Data

Raw data files can be analyzed coming from Ion S5 and Illumina sequencers using this file option.



TypeStream Visual is able to analyze data from for One Lambda's FastPlex. (See the next chapter for more detail.)

Reports

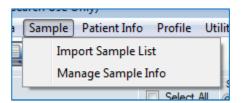
When you select this menu item, the Reports Page is displayed, allowing you to create standard or specialty reports for your analyzed data. (See Reports Section for detailed information.)

Data

When you select this menu item, a Data Window displays that allows you to manage, (i.e., search for, delete, archive or activate) sessions and samples. (See Data and Session Management for detailed information.)

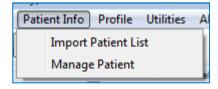
Sample

Options under this menu item pertain to importing, creating and managing sample information. (See Sample Management)



Patient Info

Options under this menu item pertain to importing patient/donor lists and managing individual patient/donor information. (See Patient Management)



Profile

There are options under this menu item for creating and managing your own user profile, lists of system users and privileges and lab information. There is also an option for switching between the home page options depending on your system and navigation preference. (See

profile management for more information.)

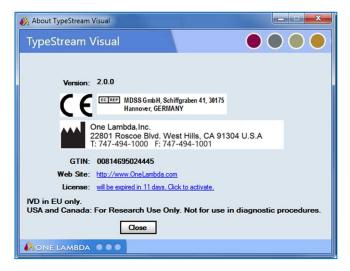


Utilities

See next section.

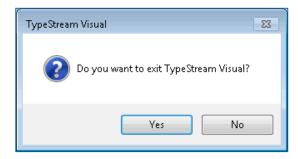
About

This menu item allows you to access the following TypeStream Visual Software information:



Exit

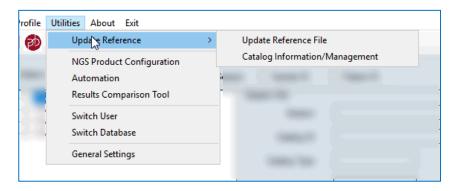
When you select this menu item, a dialog box displays that allows you either to select 'Yes' to exit and close the TypeStream Visual application or select No to keep the current session open.



Utilities

All the controls governing how your files are processed, from catalog and library import to serology settings or metrics to be flagged after analysis are all conveniently located under "Utilities."

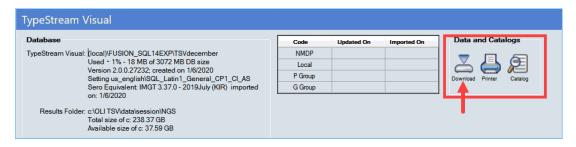
The options under this menu item pertain to importing catalog, code, and serology files, configuring the molecular products, and setting up your TypeStream Visual system. It also allows you to switch users, switch databases, and set up automatic analysis.



Update Reference Files

TypeStream Visual uses a variety of reference files for data analysis that need to be updated for new products, lots and revisions. You can also change many global product settings to customize analysis for your lab, and you can modify default system settings to reflect your personal or network file system.

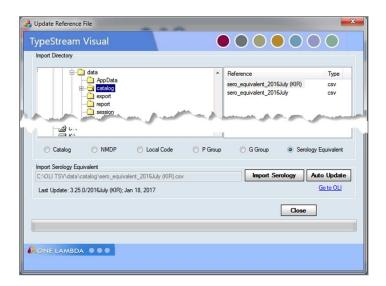
There are two way to access the screen for reference file selection. The first is to click the Download button under Data and Catalogs.



The second way is to navigate to Utilities → Update Reference → Update Reference File. Either method will open the Update Reference File window.

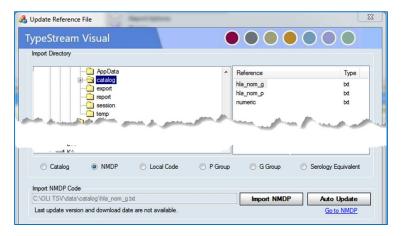
Prior to first analysis, a number of configuration steps will need to be taken. Follow the steps below.

- 1. Set Serology Reference File
 - a. Navigate to Utilities \rightarrow Update Reference \rightarrow Update Reference File.
 - b. Click 'Serology Equivalent' radio button and click on Auto Update button
 - c. Select sero_equivalent reference files from list, click 'Import Serology'



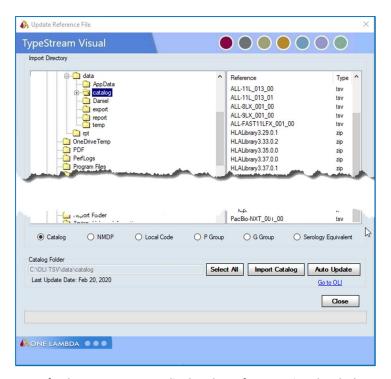
2. NMDP, P and G codes

- a. Navigate to Utilities \rightarrow Update Reference \rightarrow Update Reference File.
- Click the NMDP, P Group or G Group radio button and click on Auto Update button to update the database with the NMDP/P group / G group codes.



3. Select Catalog and library.

- a. Navigate to the folder containing the catalog and library files you wish to download.
 - i. Catalog is based on Alltype lot #, e.g. All-11LX_013
 - ii. PACBio catalogs are based on PACBio lot #, e.g. PACBio-NXT_001_00.
 - iii. FastPlex catalogs based on AllFAST lot #, e.g. ALL-FAST11LFX 001 00.
 - iv. IMGT catalogs are in zipped files labeled with "HLALibrary" and the particular library release, e.g. "HLALibrary3.37.0.1."
- b. Click on Import catalog.
- c. Users can alternately click on the "Auto Update" button to download the catalogs and HLALibrary.zip files directly from the One Lambda website.



4. Refresh Home Page to display the references just loaded.

NOTE: When a library file is imported, the application compares the IMGT release to that of the serology file loaded previously. If the two are not of the same release, the software will display a message to that affect and will ask the user whether to proceed with the download.

Managing Catalog Reference Files

Catalog reference files contain all of the reaction-specific information needed for analysis. Each new lot or revision of a product needs its own catalog file for analysis results to be accurate.

Catalog Management window may be accessed in one of two ways. The first is by using the 'Catalogs' icon under 'Data and Catalogs."



The second way is to navigate to Utilities → Update Reference → Catalog Information/Management. Both methods open the Catalog Management window where catalogs can be activated, archived, unarchived, or deleted.



A few things to note while working with catalog management:

The list includes both catalogs and IMGT libraries loaded into the current database.

Any catalog that has been used in an analysis cannot be deleted but can be Archived

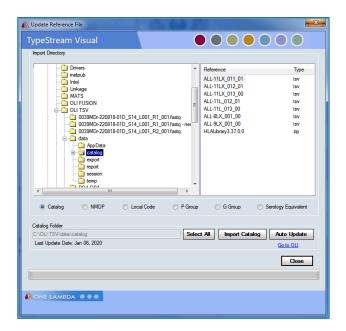
"A" in the 'Status' column indicates that the catalog has been archived.

Updating Catalog Files from a Local or Network Drive

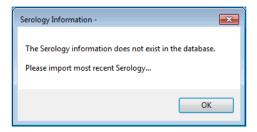
Lab supervisors can input new catalog files for use in analysis when new products, lots, or updates become available. Catalog files are also available on the One Lambda website.

From the main or any of the product home pages, click the download icon, or from the main menu, select Utilities > Update Reference > Update Reference File.

The Update Reference File dialog box displays.



If your serology information is outdated, or you have not yet imported it, the following message will be displayed"



If you see the message, click OK dismiss the message. Select the radio button to import serology first. If you do not see this type of message, go to the next step.

Using the file directory tree on the left, locate catalog files to be imported.

To determine which catalog is the most recent available, TypeStream Visual looks first at the lot number and then the revision number. An updated lot number gets flagged as the most recent version of a catalog, even if there is also an update to the revision number of the previous lot since you last downloaded catalogs.

Highlight the files you want to import or click Select All Select All to select all files listed.

Updating Catalog Files from the One Lambda Website

Product catalog files are available on the One Lambda website https://www.onelambda.com/en/product/typestream-visual-software.html

From the main or any of the product home pages, click the Download link, or from the main menu, select Utilities > Update Reference > Update Reference File. The Update Reference File dialog box displays.

1. Click Auto Update to open the One Lambda Catalog Updates Selection window.



- 2. Select the check box next to the files you want to import. Click the plus or minus signs on the file directory tree, to locate the catalog files for each product. You can also click Select All or Deselect All to select or clear all the check boxes at once.
- 3. Click Import to import the selected catalog files.
- 4. When the confirmation dialog box displays import results, click OK.
- 5. Click Close and then Yes to return to the Update Reference menu.
- 6. Imported catalog files can be used without restarting TypeStream.

You can also click Go to OLI, click the links for the products and catalog files you want to import, and follow the download instructions. If Auto Update does not respond, verify your network connectivity and that the Web Service URL you set for One Lambda in Utilities > URLs & Paths is correct.

When updating catalogs, user will not get message regarding serology files.

Updating Molecular Typing Reference Files

Reference files contain allele code and serology equivalent information used in analysis. It is important to update them regularly for accurate allele code and serology assignments.

From the Update Reference menu, you can download the necessary files:

- NMDP codes
- P-Group and G-Group codes
- Local codes
- Serology Equivalent files

Updating NMDP Codes from a Local or Network Drive

The National Marrow Donor Program (NMDP) provides a list of allele codes that can be used in molecular typing analysis. If you have a current list stored on your local or network drive, use

this procedure to import it so TypeStream Visual can access it. The most current NMDP code file is available on the NMDP download site.

- From the main or any of the product home pages, click the Download link, or from the main menu, select Utilities > Update Reference > Update Reference File.
- The Update Reference File dialog box displays.
- Select the NMDP option.
- Navigate to the NMDP file on a local or network drive, using the Import Directory tree.
- Click Import NMDP to import the selected file.
- Click Close to return to the Update Reference menu.

Updating NMDP Files from the NMDP Website

Follow this procedure to import the NMDP list from the NMDP website.

- 1. From the main or any of the product home pages, click the Download link, or from the main menu, select Utilities > Update Reference > Update Reference File.
- 2. The Update Reference File dialog box displays.
- 3. Select the NMDP option.
- 4. Click Auto Update, which automatically imports the current NMDP file for use with TypeStream Visual. Or, click Go to NMDP and follow the instructions for downloading an NMDP file from the website.

NOTE: If Auto Update does not respond, verify your network connectivity and that the URL you set for NMDP in Utilities > URLs & Paths is correct.

Creating a Local Code File

Local code files are created by individual labs; local codes are created to make ambiguous typing assignments easier to store and read. For example, ambiguities, such as B*1501/1501N/1502, can be condensed with a code to B*15AB for simpler record keeping.

- 1. Copy the local code template from the TypeStream Visual CD to a local drive.
- 2. Use a text editor to edit the template and add code definitions.
- 3. Follow the example format, using a **Tab** to separate each field, and a slash to separate multiple values within a field:
- 4. letter code <tab> numeric allele extension to which the code applies
- 5. Save the file as local_code.txt

Updating the Local Code File

After a Local Code file has been created, it must be updated in TypeStream Visual.

From the main or any of the product home pages, click the Download link, or from the main menu, select Utilities > Update Reference > Update Reference File.

The Update Reference File dialog box displays.

- 1. Select the Local Code option.
- 2. Use the Import Directory tree to locate and select the Local code file to be imported.
- 3. Click Import Local Code to import the selected file(s).
- 4. Click Close to return to the Update Reference menu.

Updating Serology Equivalent File from One Lambda Website

The Serology Equivalent file can be auto updated from the One Lambda website.

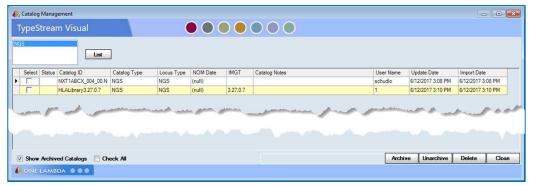
- 1. From the main or any of the product home pages, click the Download link, or from the main menu, select Utilities > Update Reference > Update Reference File.
- 2. Select the Serology Equivalent option.
- 3. Click Auto Update to open the One Lambda Catalog Updates Selection window.
- 4. Select the check box next to all files you want to import.
- 5. Click Import Serology to import the selected files. Catalog files are ready for use without restarting TypeStream Visual.
- 6. A confirmation dialog box displays import results, click OK.
- 7. Click Close and then Yes to return to the Update Reference menu.

If Auto Update does not respond, verify your network connectivity and that the URL you set for Serological in Utilities > URLs & Paths is correct.

Archive Catalogs

You can archive catalog files that are no longer used. The catalog information still exists in the database but is not included in the list of available catalog files for analysis. Catalog files can also be restored for use in analysis.

From the Main Menu, select Utilities > Update Reference > Catalog Information/Management.



- 1. Select the S (select) check box for the catalog files you want to archive and click Archive Archive.
- 2. When a pop-up message displays Data Saved, click OK.
- 3. Click Close to return to the main menu.

NOTE: When you import a new version of a catalog file, the system auto-archives the previous version.

Un-Archive Catalogs

Archived catalog files display an A in the Status column when you view the catalog list and the check box for Show Archived Catalogs is selected.

From the Archive Catalog window, select the check boxes next to the catalogs you want to unarchive, and click Unarchive.

Deleting Catalog File Information

You can delete a catalog file from the Catalog Management menu. Catalog files displayed with an 'A' in their Status column have been archived.

- From the Main Menu, select Utilities → Update Reference → Catalog Information/Management.
- 2. Select the check box next to any catalog you want to delete.
- 3. Click Delete to remove the catalog information.

NGS Product Configuration

All aspects of NGS Product Configuration are located all under the same window option. User will notice a number of elements that have been rearranged from previous versions of TypeStream Visual. Here you will now find the following:

Assignment Settings to choose codes and/or fields in which assignments display; enable KIR, Bw4/Bw6 and serology settings; select position notation style, and more.

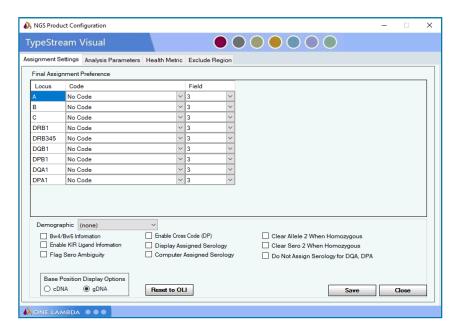
Analysis Parameters Health Metrics Exclusion Region tool

Setting Configuration

Setting overall configuration options in this screen applies to all session and samples analyzed. Many can be overridden on a per-sample basis as described in the chapter on creating sessions.

Analysis Parameters must be selected for each session created; therefore, a session in queue will not change if a new parameter set is created.

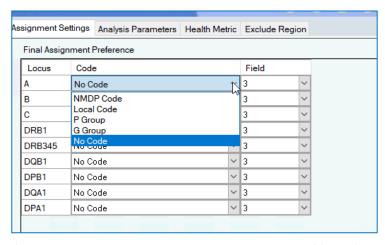
Assignment Settings



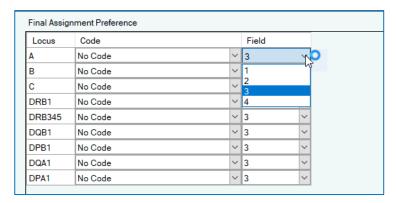
Note: Current assignment settings are applied when the session starts the processing of samples.

Final Assignment Preference

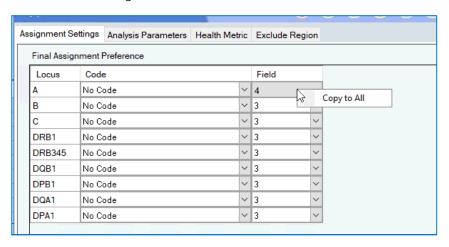
This section governs how final genotype is displayed, e.g. 3-field, P code, NMDP code, etc. For each locus user may select any of five settings: NMDP Code, Local Code, P Group, G Group, or No Code.



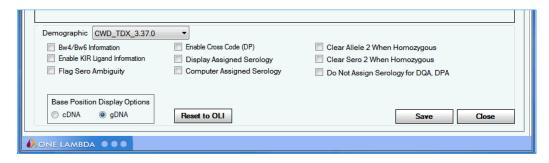
If No Code is selected, user may select the number of fields from 1 to 4.



For both code and field columns, the software enables user to right-click on the selected option and apply it to all the following loci. Note, however, that each locus can be configured with a different code setting if desired.



General Options for Configuration

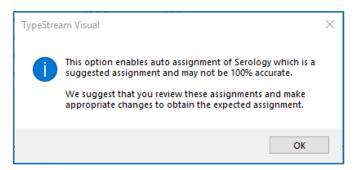


Setting any one of these checkbox options has the following effect:

1. Demographic Group Selection: This option allows you to organize alleles according to their frequency. Select a predefined Demographic Group using the drop-down control



- 2. Bw4/Bw6 Information: Includes Bw4/Bw6 information in serology results. These are serological epitopes that differ only at a specific region.
- 3. Enable Kir Ligand: Includes KIR Ligand information for the C locus in analysis results. The user should import the serological_equivalent file containing the KIR ligand information.
- 4. Flag Sero Ambiguity: When there is a Serological Ambiguity, it is identified in the System Comments.
- 5. Enable Cross Code (DP): Enables the utilization of NMDP codes that combine alleles with differing first-fields, using G Code associations.
- 6. Display Assigned Serology: Allows the user the option of having the assigned serology display on the analysis panel or not, as preferred.
- 7. Computer Assigned Serology: Automatically populates serology assignment fields while also storing results in the database. When this option is selected, TypeStream Visual will display the following warning message:

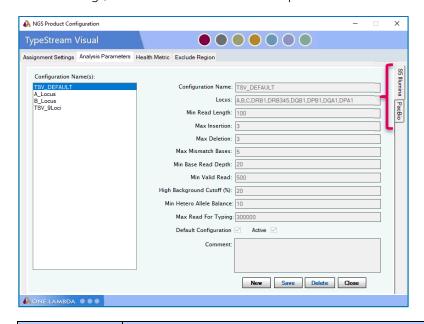


- 8. Clear Allele 2 When Homozygous: When checked, Allele 2 of a homozygous pair will not display in the Final Allele Assignment panel.
- 9. Clear Sero 2 When Homozygous: When checked, Sero 2 of a homozygous pair will not display in the Final Sero Assignment panel.
- 10. Do Not Assign Serology for DQA, DPA: When checked, the software will not assign serology for DQA and DPA loci.
- 11. Base Position Display Options: User may select between display cDNA and gDNA base positions on the nucleotide viewer.
 - cDNA Complementary DNA mirrors IMGT, in which all introns begin with position 1 and each exon continues from the previous exon
 - gDNA position count is continuous, starting with exon 1 (E1) through the remainder of the gene, including 3'UTR. The 5'UTR starts with -1, then continues with negative numbering upstream.
- 12. Reset to OLI: This button will reset all of the settings on this tab to the defaults established by One Lambda, Inc.

When you are done setting options, click Save save to save changes.

Analysis Parameters / S5 and Illumina

The Analysis Parameter tab has a second set of tabs at the right side to select either S5/Illumina or PACBio. Analysis Parameters are applied at the session level – the user selects one of the default settings, or creates more to fit his own specifications.



| Parameter | Definition | |
|------------------------|--|--|
| Configuration Name | The name of the configuration. There are two supplied by the software. "TSV_Default" analyzes 11 loci; "TSV_9Loci" analyzes 9 loci (no DQA1 or DPA1). When creating a new parameter set, user supplies the set name here. "TSV_Default" is not modifiable by the customer. | |
| Locus | User may enter text that represents a single or multiple loci in a comma-separated list. The engine will only analyze loci present in the library. | |
| Min. Read Length | User may enter the minimum length for valid reads. Reads less than this length will be filtered and not used for analysis. | |
| Max Insertion | User may enter the maximum number of insertions for a valid read. If a read has more insertions than the parameter when compared to the reference allele, it will be filtered and not used for consensus generation. | |
| Max Deletion | User may enter the maximum number of deletions for a valid read. If a read has more deletions than the parameter when compared to the reference allele it will be filtered and not used for consensus generation. | |
| Max Mismatch Bases | User may enter the maximum number of base mismatches for a valid read. If a read has more mismatches than the parameter when compared to the reference allele, it will be filtered and not used for consensus generation. | |
| Min Base Read Depth | User may enter the minimum number of valid reads for any base position for an allele. If the base depth is below the parameter, no consensus base will be added at that position and it will be treated as a wild card when comparing to database to find closest matching allele. | |

| Min Valid Read | User may enter the minimum number of valid reads for the software to make a typing call. If the number of reads found for a locus is less than the parameter, no typing call will be attempted for the locus. |
|------------------------------|---|
| Cutoff Value (%) | User may enter the minimum percentage of alternate bases at a position before the software will mark it with a high background flag. |
| Min Hetero Allele Balance | User may enter the minimum allele balance percentage used for the software to identify a position as variant (heterozygous). |
| Max Reads for Typing | User may enter the maximum number of reads used for the genotype call. If input file contains more than the specified number of reads, software will randomly select that many reads for analysis. |

Additionally, user may designate any of the analysis parameter sets as the default configuration and may make any of the Active or Inactive.

Analysis parameter sets may only be deleted if they have not been used in a session. If such parameter sets are no longer needed, they may be made inactive and will not appear as an option for selection.

Comments may be optionally added to new parameter sets. These comments will not appear on the analysis, but only on this configuration window.

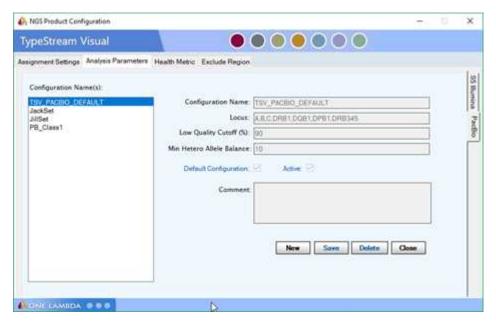
NOTE: If an expected locus is reported as a "NO CALL" and the "Total Read Count" value for the barcode is the same as the "Max Read for Typing" analysis parameter (or exactly double for paired end samples), it is recommended that the user rerun with an increased value for the "Max Read for Typing" parameter. This will allow the software to analyze more reads from the raw data and may detect enough for the locus to provide a typing.



New in v2.0

Analysis Parameters – PACBio

Long Amplicon Analysis data from PACBio has different default parameters.



| Parameter | Definition | |
|-------------------------------|---|--|
| Configuration Name | The name of the configuration. There is one supplied by the software. "TSV_PACBIO_Default" analyzes 9 loci. When creating a new parameter set, user supplies the set name here. | |
| Locus: | User may enter text that represents a single or multiple loci in a comma-separated list. The engine will only analyze loci present in the library. | |
| Low Quality Cutoff (%) | I Detaillt is 90% (DV score is taken from the PAC Bio nackage file on import | |
| Min. Hetero Allele Balance | | |

As with the S5/Illumina parameters, user may designate any of the analysis parameter sets as the default configuration and may make any of the Active or Inactive.

Analysis parameter sets may only be deleted if they have not been used in a session. If such parameter sets are no longer needed, they may be made inactive and will not appear as an option for selection.

Comments may be optionally added to new parameter sets. These comments will not appear on the analysis, but only on this configuration window.

Health Metric

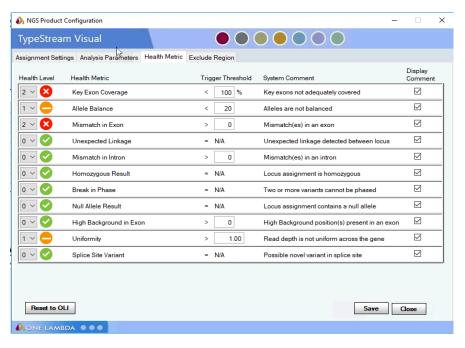
Users may configure the health metrics with respect to the following:

1. Health Level: For each of the health warning flags, the user may give it the weight appropriate to the task. Use the dropdown on the far left to select a numerical level, which is paired with an appropriate icon.

| Level | lcon | Meaning |
|-------|--|---|
| 0 | (| Least level of severity. If this level is chosen, the icon will display green even if the metric fails. The green icon also displays when no metrics for the locus fail. |
| 1 | | Failure of this metric is of medium concern. |
| 2 | Level two failures are considered unacceptable. Further investigation is required. | |

- 2. Trigger Threshold: The value at which the flag will be triggered. User is allowed to set the default threshold for each health metric, with the exception of Unexpected Linkage, Homozygous Result, Break in Phase, and Null Allele Result.
- 3. System Comment: the wording that will display in the system comments for the locus if metric is triggered.
- 4. Display comment: The user may decide for each metric whether it is necessary to display the comment in the locus system comments.

The current health metrics are used in the analysis when a session starts processing. However, the user may reset the health level and display choice at the locus level from the analysis panel. More will be given on this in chapter on creating sessions.



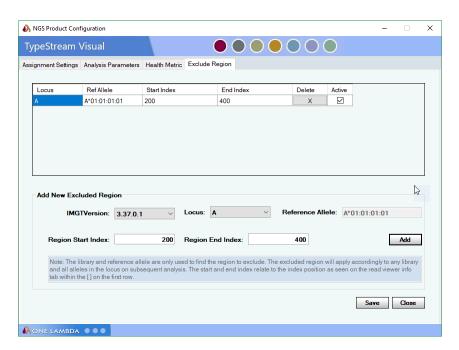
Results can be reset to the OLI factory settings. Be certain to save after changing. (See "Filters" section in View Analysis chapter for definitions of each of the metrics.)



New in v2.0

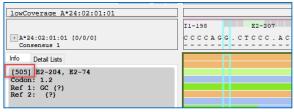
Exclude Region

The Exclude Region Tool allows a user to exclude any region – intron or exon – from analysis.



The Exclude Region window allows the user to select the locus and specify as many regions for exclusion as necessary. To use the tool, do the following:

- 1. Select IMGT Version. You may select any of the libraries in your active database.
- 2. Select Locus.
- 3. When locus is selected, the Reference Allele will populate in the Reference Allele text field.
- 4. Enter Region Start Index. This is the raw position number, irrespective of its cDNA or gDNA designation. Position number can be found by going to reads viewer. In this example you want to begin the exclusion at the beginning of Exon 2, E2-74 in cDNA. When that position is selected on the reads viewer, the info panel shows you that it is position '505'. So '505' is the Region start index. Determine Region End Index in the same manner.



- 5. Click Add.
- 6. Your region for exclusion displays in the grid.
- 7. You may add as many regions for exclusion as necessary. If any of them overlap, you will get a message to that effect and the software will not accept it.
- 8. When finished, click Save and Close.

Other things to note about the Exclude Region tool:

- 1. The current exclude region metrics are used in the analysis when a session starts processing. Any region exclusion can be deleted or de-activated. Note that those changes will not apply to sessions already analyzed.
- 2. An exclusion that has been made inactive still displays on the exclusion grid but will not be used in the analysis.
- 3. If the user wants to load a different library but keep the excluded regions, the

application will automatically adjust and exclude the correlated region using the new library.

4. Reference alleles were selected for the greatest homology for all locus alleles.

| Default Reference Alleles | | |
|---------------------------|------------------|------------------|
| A*01:01:01 | B*07:02:01 | C*01:02:01:01 |
| DRB1*01:02:01 | DRB3*02:02:01:02 | DQB1*02:01:01 |
| DPB1*01:01:01 | DQA1*01:01:01 | DPA1*01:03:01:01 |

Automation

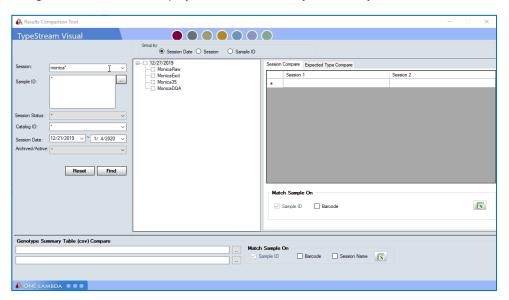
Please see next chapter for instructions on automatically analyzing sessions from Ion S5 or Illumina sequencers.

Results Comparison Tool

Users may employ this tool to make comparisons from session to session for samples of the same name for the purpose of establishing concordance or detecting discrepancies.

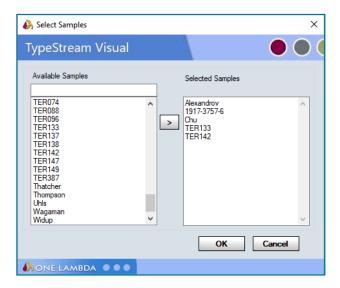
On the left side of the tool window is a search panel. Search can be conducted by Session name, Sample ID, Session status, Catalog ID, Session Data, or Archived/Active status. When the search criteria is ready, click 'Find' and display results in the center panel, grouped according to the method selected via radio buttons above.

In the example below, several sessions had been named beginning with 'Monica'. All sessions fitting the search criteria display under the date they were analyzed.

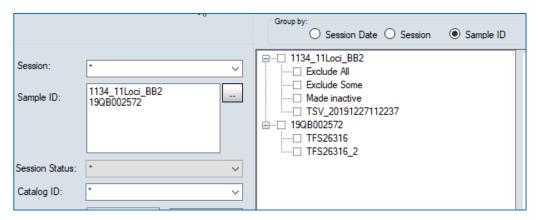


If sample names are unknown, clicking the search box will display a list of available samples from the sessions in the currently active database. Select the desired session names and use the right arrow to move them to the Selected Samples panel. When you have

completed sample selection, click OK.

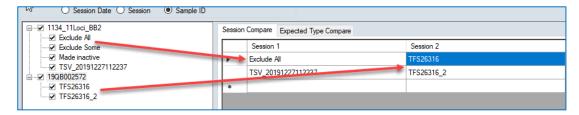


The selected sample names display in the sample ID panel on the tool window. Clicking 'find' will then show, with "Sample ID" radio button selected, which sessions contain those samples.



At this point, drag-and-drop the desired session names into the Session Compare window.

Known anomaly: when a session is checked, it has no affect on inclusion in the tool. The user must drag and drop sessions into their correct position.



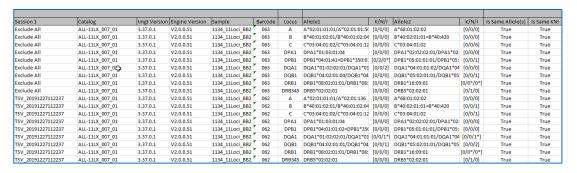
Make comparison type selection at the bottom of the session compare window.

- Compare by Sample compares the results of the two session by sample.
- Compare by Sample and Barcode compares the results of the two session by Sample and barcode.
- If there are more than one row of session pairs, the summary excel will output one session comparison followed by the next.
- The comparison of the results are exact string matches. Any differences will

be highlighted in yellow in the IsSameAllele(s) and IsSameKNI column.



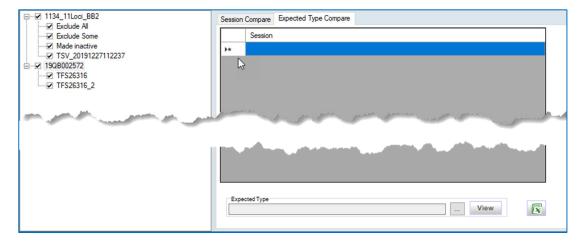
Click the Excel icon, and the software provides a spread sheet which compares each of the sessions for allele and K/N/I values, returning "True" if the values match.



Expected Type Compare

Expected type comparing allows the user to compare a selected session against an expected type file.

- Template "example_expected_types" for the expected type file is located in the Application install folder.
- View (Button) allows the user to view the contents of the expected type file.
 Note: If no expected type file is provided, the View button displays the template of the expected type file.
- Output file is in Excel format and displays the concordance at 3 field and 4 digit field level.
- When the sample is discordant at 3 field level the typing is highlighted red. When the sample is discordant at 4 field level, the typing is highlighted yellow.



Comparing Genotype Table reports

Compares the results from the export of two genotype summary report. Comparison of the two reports can be a combination of Sample, Barcode and/or Session.



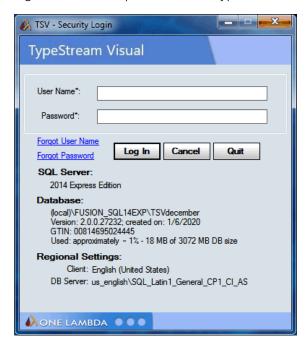
Use the ellipsis search buttons to navigate to and select two existing Genotype Summary Table (csv). Click the Excel icon and receive a comparison of the files. Results are exact string matches.

Any difference in Allele calls or K/N/I will be flagged with a yellow highlight. The comparison tool does an exact match string comparison.

Switch User

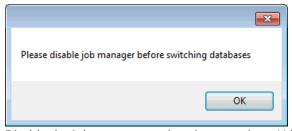
TypeStream Visual allows you to switch the active user. From the TypeStream Main Menu, select Utilities → Switch User. The following screen will now appear:

Supply the username and password of the desired user. If the login is successful, the system will log the user in and proceed to the TypeStream Home Screen.



Switch Database

TypeStream Visual allows you to switch the active database. From the TypeStream Main Menu, select Utilities → Switch Database. If job manager is currently enabled, the following message will appear:



Disable the job manager and navigate again to Utilities → Switch Database. The following screen will appear:



Use the drop down control to select the database name, then click the OK button. If the database choice is valid, the system will attach the database and proceed to the TypeStream Login Screen. Login as you would when first opening the application.

If you click Cancel on the login screen, the application will close but will retain the switched database as the one to which the user is connected.

NOTE: The database to which you are switching must be from the same release as the current. For example, if you are currently using TSV 2.0, you will not be able to switch to a database from a previous version, e.g., TSV 1.3, without upgrading it first. "Upgrade Database" functionality can be found in the Database Utility.

General Settings

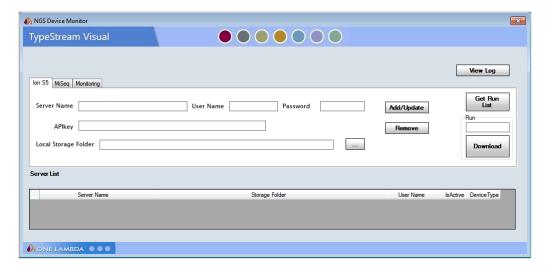
See previous chapters for general settings.



Automation

Automation (Auto-Analysis)

TypeStream Visual can be configured to automatically download and analyze data from Ion S5 and MiSeq sequencers. To do so select Utilities → Automation from the menu bar. The following NGS Device Monitor screen will display:



Ion S5 files will be downloaded to your local drive in order to analyze the data. MiSeq files will be analyzed from the MiSeq output folder. Folder names may include an underscore character.

NOTE: When using automatic analysis, the Automation functionality, it is essential to ensure the Local Storage folder has adequate capacity to hold all the .bam files to be downloaded from the lon S5.

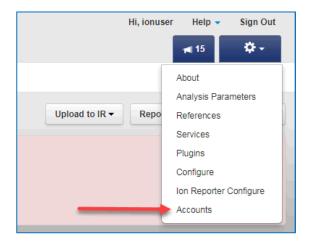
Downloading from Ion S5

Enter the server name, username, and password for the target server. The IP address may be used instead of server name if preferred. Designate a storage folder where the downloaded files will be kept. This folder may be local or in an available networked location.

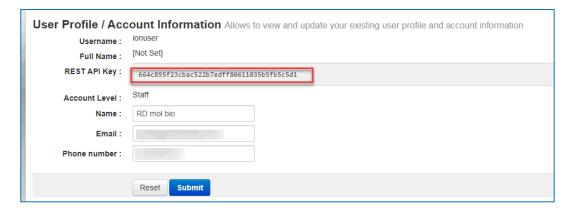
The steps shown here may differ slightly depending on the version of Torrent Server in use.

Obtaining API Key

To obtain the API key from your Ion S5 server, navigate to Accounts from the Torrent Suite web interface.



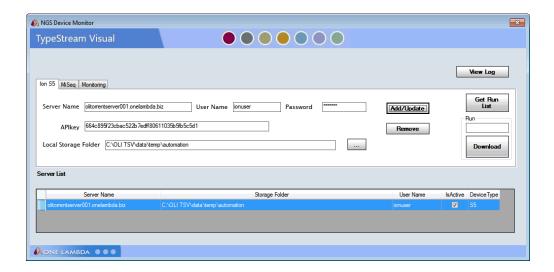
Copy the entire character line from "REST API Key" and paste it into the correct field on the NGS Device Monitor.



Add/Update

When you click Add/Update, your configured server will be displayed on the server list. All servers are checked 'IsActive' by default.

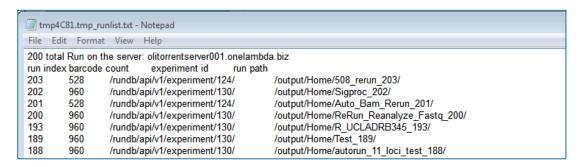
Clicking "Remove" will remove the selected server from the server list.



Get Run List

To get a list of all runs on an Ion S5 server, select the server from the server list. (Monitoring does not have to be on.) Click "Get Run List."

After several minutes (depending on the size of the server and the number of runs it holds) a text file will open, displaying the number of total runs on the selected server. Following that will be the list of available runs, including run index, barcode count, experiment ID, and run path.

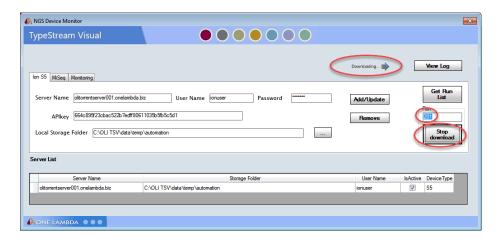


Download a Specific Run

To download and analyze a specific run, enter the run number (first column from the Run List above) into the 'Run' text box. Click 'Download.'

Download Indicator will begin to blink, signifying a download is in process. 'Download' button changes to 'Stop download.'

Download may be stopped at any time. When 'Download' is clicked again, the software will continue to download raw files, picking up where it had left off.

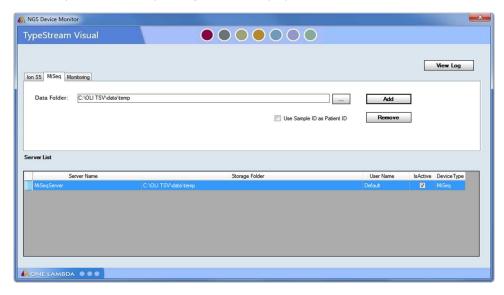


If monitoring is on (see section on Monitoring below), the session will automatically be sent to the engine for analysis when the download is complete. If monitoring is off, the session will begin analysis when 'Start Monitoring' is clicked.

See 'Monitoring' section below for more information on what happens during and after a download.

Downloading MiSeq Data

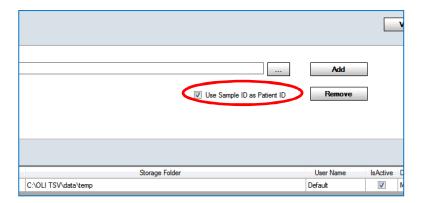
Click the "MiSeq" tab in the NGS Device Manager. The MiSeq window displays as illustrated here. Any servers already configured will display on the server list.



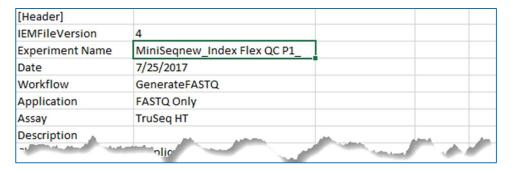
Use the search button (. . .) to navigate to the location of the output folder for MiSeq files. Select the correct folder and click 'Add.' The MiSeq output folder displays on the server list.



User may elect to have the software automatically use the Sample Id as the Patient ID by selecting the checkbox displayed under the Data Folder path.



On the open sample sheet below, the "Experiment Name" is "Index Flex QC P1". That name will be used as both the Sample ID and the Patient ID. If the checkbox "Use Sample ID as Patient ID" is NOT checked, "Index Flex QC P1". will still be used as the Sample ID.

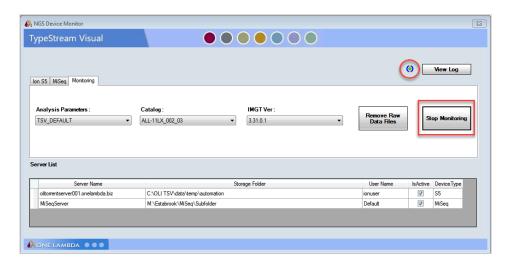


Follow folder structure for placement of Sample Sheet: ...\MiSeq\MiSeq_MiniSeq\MiSeq_MiniSeq\Mi90725_M01817_0045_000000000-B2L57\Data\Intensities\BaseCalls\Alignment.

NOTE: When using "Use Sample ID as Patient ID" the checkbox must be checked prior to loading the server path.

Monitoring

Click the 'Monitoring' tab in the NGS Device Monitor. All configured servers display in the server list. Select options for analysis parameters, catalog, and library version. Click 'Start Monitoring.'



Monitoring indicator begins to blink and 'Start Monitoring' button changes to 'Stop Monitoring.' Every 10 seconds, the software checks each of the active servers to detect new runs. If no new runs are detected when monitoring begins, software will download the most recent two runs that have not been analyzed already.

By default, the software will auto-apply a machine generated name for the session in the following format: "TSV_S5_[server name]_[run ID]."



New in v2.0

Using Run Name

Additionally, the user may enable the software to use the Planned Run Name from Gene Studio S5 by careful use of "-" when the session is named in the S5 sequencer. The software will look for the last "-" to extract the session name. For a run with the following name from the S5:

Auto_User_GSS5PL-0026-122-2019-9-26_ALL-LIBX_STAB_ACC_2106818_PH_467

The software will look for the final "-" and extract the name as such:

> LIBX_STAB_ACC_2106818_PH-467

It then drops the first and last name field in the name, which results in this session name:

> STAB ACC 2106818 PH

For a MiSeq session, session name will be taken from "Experiment name" on the SampleSheet.csv.

NOTE: When configuring servers for with the Automation functionality, user must be certain that the username and password are correct, as TSV software cannot verify these when entered. If incorrect, new data generated by the sequencer will be noted but not fully downloaded; a .tmp file will display in the folder in its place. The Auto Log will display entries per the following example:

[20180606161037] downloading from server: olitorrentserver001.onelambda.biz run: 203 barcode: IonXpress_021

[20180606161038] Can't download the file. Check web access permission or file path:

http://olitorrentserver001.onelambda.biz/output/Home/508_rerun_203/basecaller_results/lonXpress_021_rawlib.basecaller.bam. Failed to download C:\OLI

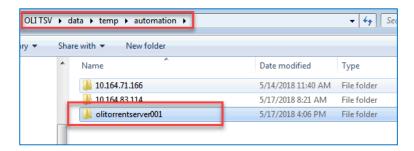
 $TSV \ data \ temp\ automation\ olitor rentser ver 001\ 203\ lon X press_021_9086_raw lib. base caller. bamber 1995\ data \ base caller. base caller. base caller. base caller. base caller. base caller. bamber 1995\ data \ base caller. base$

Option Selection

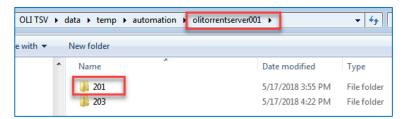
Options selected from 'Analysis Parameters,' 'Catalog,' and 'IMGT Vers' will apply to all sessions downloaded from any active server.

Folder structure

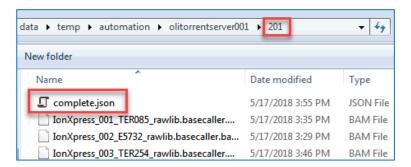
When the software detects a new Ion S5 server, it creates a folder in the storage location with the name of the server.



For each run detected on that server, the software creates a folder with the run ID.



Files continue to download into this folder. While in process, the file currently being downloaded has the extension ".tmp." When the download of all files is complete, the software creates the file "complete.json." This file contains a log of the download and save process.

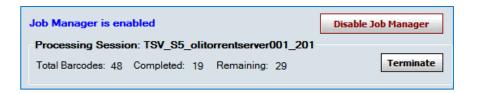


Folder structure is a little different for MiSeq sessions. There will not be a "completed" file, but the 'submitted.log' file can be found along a path like this:

...\MiSeq\Subfolder\170725_M11111_0045_000000000-B2L57\Alignment_1\12345-10293\fastq

Automatic Session

After completing the download, software sends the session to the Job Manager. When the session is submitted to the engine, the software creates the file "submitted.log" and places it into the folder.



NOTE: If there is inadequate space on the drive, the software will indicate this on the session summary page after the run cycle finishes, and there will be no genotyping. All sessions so affected will need to be rerun manually after adequate space becomes available.

Remove Raw Data Files

Because .bam files are large (typically 1.5 GB to 5 GB per file), user may find it necessary to delete the original raw data files for sessions that have finished analysis in TypeStream Visual in order to save space on the hard drive. To do so, make sure the server whose files you want to remove is *Active* on the server list. Click "Remove Raw Data Files."

NOTE: When using the "Remove Raw Data Files" button within the Automation functionality, software will delete completed sessions on the MiSeq output folder as well as the downloaded S5 files. If you do not want the MiSeq files deleted, simply make the MiSeq server inactive on the server list

Additionally, the software will only delete files for sessions in the current database. Those sessions in other databases will not be removed.

Software will check each of the subfolders for the selected server for the presence of the files "complete.json" and "submitted.log." It will also verify that the analysis has been performed by checking to see if the session name appears in the database and the run is complete. If these criteria are met, software will remove all raw data files from the folder, leaving in their place a small file "removed.txt." This file contains the time stamp for the removal of the files.

Reanalyzing after Deletion

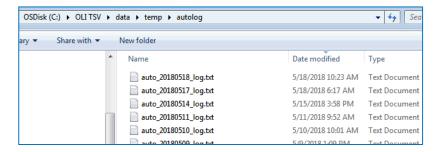
After deleting the raw data files, session can still be reanalyzed using the following process:

- 1. Go to Analyze Data → NGS on the menu bar to start a session the normal way.
- 2. Click Add Fastq/BAM File
- 3. Navigate to C:\OLI TSV\data\session\NGS\[session name]\[barcode output folder]
- 4. Select 'mappedReads.bam' and click Open
- 5. File displays on the create session page. User will have to supply a Sample ID.
- 6. Repeat this for each barcode to be reanalyzed.
- 7. Click 'Submit.'

View Log

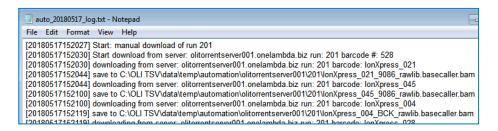
TypeStream Visual software creates a daily log for all activity on the NGS Device Monitor.

Clicking "View Log" brings up today's log file. To view log files from other days, navigate to C:\OLI TSV\data\temp\autolog and double-click on the desired date.



An automatic download will display download start, each of the files downloaded, and the submission to job manager.

A manual download will specify that it is a manual download and indicate the save location for the files.



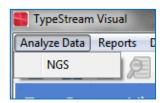
If a manual download is stopped while in progress, the log will display the log line "Abort: manual download of run [ID]." When started again, the download will pick up where it left off.



Create Session and Analyze Data

Open Create Session Page

From the top left corner of the screen, navigate to Analyze Data \rightarrow NGS.



Page displays for creating a new session.

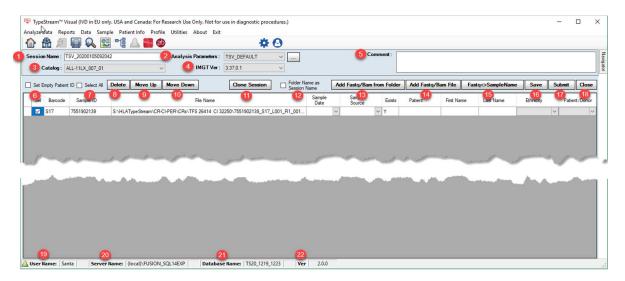
Optionally, clicking the NGS icon will bring up the same page.



Required Files

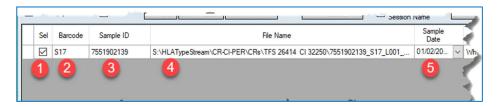
If either catalog files or an IMGT library have not yet been downloaded, the software will warn the user and not allow a session to be created until that task has been done.

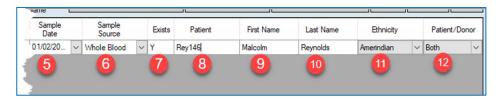
Session creation page displays as shown below. See end of this section for PACBio session creation page.



| | Item | Description |
|----|---------------------------|--|
| 1 | Session Name | Session name as entered on the session import page. User may overwrite the |
| | | session name automatically assigned by the software. |
| 2 | Analysis Parameters | The parameter set selected by the user. Software comes with default settings for |
| | | both 9-loci and 11-loci. User may also create new parameter sets to suit specific |
| | | needs. |
| 3 | Catalog dropdown selector | Select from any of the catalogs in the database |
| 4 | IMGT Ver | Select from any of the IMGT library versions in the database |
| 5 | Comment | Optional User comment field. Comments entered here will display on the session |
| | | summary. |
| 6 | Set Empty Patient ID | When checked, TSV will use the Sample ID to populate any Patient ID fields that |
| | | are blank. |
| 7 | Select All | Selects all the files in the session grid |
| 8 | Delete | Deletes all selected files |
| 9 | Move Up | When a sample is selected in the grid, use this button to move it up in the list. |
| | | (Software will analyze in the order displayed.) |
| 10 | Move Down | When a sample is selected in the grid, use this button to move it down in the list. |
| 11 | Clone Session | Clicking this button brings up a list of analyzed sessions in the database. User may |
| | | select sessions or individual samples for reanalysis. |
| 12 | Folder Name as Session | Checking this box prior to loading files will enable the software to use the folder |
| | Name | name as the session name. |
| 13 | Add Fastq/Bam from Folder | Will load multiple files by selecting the folder. |
| 14 | Add Fastq/Bam File | Opens a navigation window to load files. |
| 15 | Fastq<>Sample Name | Will load sample names from a .csv file |
| 16 | Save | Saves the session as entered to the Navigator; does not send to the engine |
| 17 | Submit | Send the session to the engine for analysis |
| 18 | Close | Closes the session in the import screen. Does not save any save on the grid. |
| 19 | Username | Name of logged in user |
| 20 | Server Name | Name of the SQL instance to which you are attached. |
| 21 | Database Name | Name of the database currently in use. |
| 22 | Ver | Version of TypeStream Visual |

Grid columns:



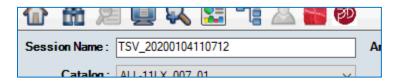


| | Item | Description |
|----|----------------|--|
| 1 | Sel (checkbox) | Selection checkbox – select samples for deletion or to move up or down in the grid. Selection does not affect submission to the engine; all samples on the grid are submitted. |
| 2 | Barcode | Barcode number automatically derived from the file name. |
| 3 | Sample ID | In most cases will be derived from sample name. If not, can be manually entered or modified. |
| 4 | File Name | Displays the path to the raw data files. |
| 5 | Sample Date | User may manually enter the date sample was collected |
| 6 | Samples Source | Source of collected sample |
| 7 | Exists | Will display 'Y' if the sample ID already exists in the active database. Will display 'N' if the sample ID does not exist in the active database. |
| 8 | Patient | Patient ID. If sample ID exists in the database and is associated to a patient, patient ID displays here. Can be manually entered. |
| 9 | First Name | Patient first name |
| 10 | Last Name | Patient last name |
| 11 | Ethnicity | Select ethnicity from dropdown list |
| 12 | Patient/Donor | Select from 'Patient', 'Donor', or 'Both' |

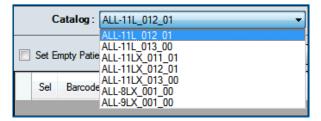
Create a session

1. Enter session name

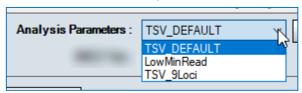
Software automatically enters a session name which includes date and time stamp, but user may type in any alpha-numeric up to 75 characters. If two sessions have the same user-supplied session name, the second session will overwrite the first. For that reason, if choosing not to use the system-generated session names, care must be taken to give unique names to all sessions.



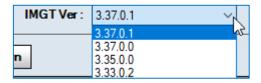
2. Select a catalog – Catalog selection needs to match the SKU name for the assay used. For AllType NGS 11 Loci Amplification reagents, use catalog beginning with 'ALL.' By default, the system will select the last catalog used in analysis.



- 3. Analysis parameters
 - a. select an existing parameter set
 - b. or create a new one by first clicking the ellipsis. (See "Utilities" for more information.)



4. Select library:



5. Enter comment (optional)

Comments entered here will appear on the session summary page of the analyzed session and on the Genotype Summary Report (.pdf). By default, the software will select the last library used in analysis.



Load Files

It is recommended that users follow standard naming conventions for input files for TypeStream Visual. Files coming from Ion Torrent, S5 should use one of the following:

IonXpress_barcode.samplename_otherinfo.bam IonXpress_barcode.samplename_otherinfo.fastq

MiSeq filenames (pairend files) should follow MiSeq filename convention, typically in one of the following forms:

```
Samplename_S#_L###_R1_###.fastq
Samplename_S#_L###_R2_###.fastq
```

There are three buttons which enable the loading of data files.

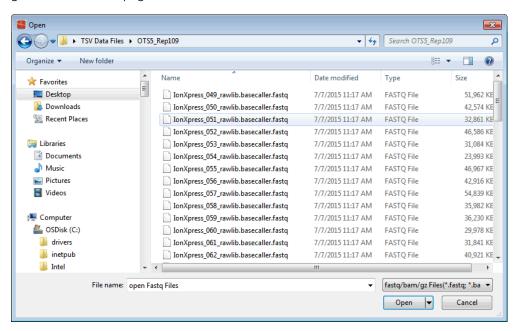


- 'Add Fastq/Bam File' is the most commonly used to load files from any source.
- 'Add Fastq/Bam from Folder' when files exist in separate folders. TypeStream Visual will create a separate file for each folder.
- 'Fastq<>Sample Name' is used to populate sample names when the name cannot be derived from the file or file name.

Add Fastq/Bam

To load most standard files for analysis, click button 'Add Fastq/BAM file'

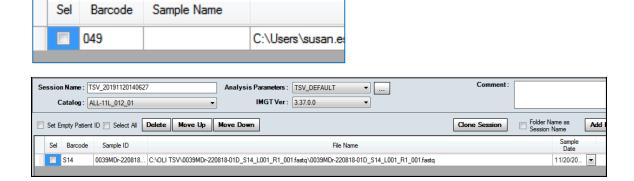
Navigation pane will display. Navigate to the location of the data files, select and click Open. System will accept .bam, .fastq, and .gz files. The path to the selected files will appear on the grid on the session page.



The software will automatically assign a time-stamped session name. This name can be changed to user's preference.



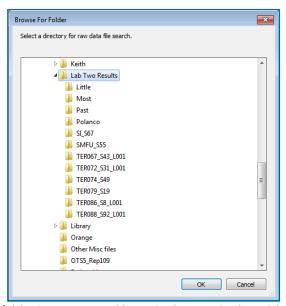
The system requires Sample Name to be populated. If the Sample Name column is blank, it can be manually entered. Please refrain from using blanks or dashes when naming.



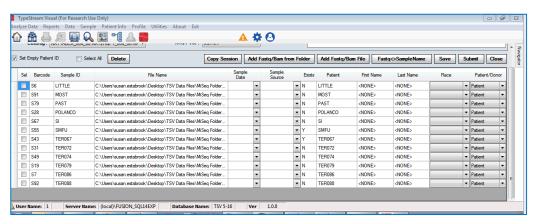
Click 'Submit' or 'Save' button. 'Submit' will send the session directly to the engine for analysis. 'Save' will keep session for later analysis.

Add Fastq/Bam from Folder

In the illustration below, one folder has multiple subfolders containing typing results. TypeStream Visual will load the contents of each of the subfolders by selecting the folder "Lab Two Results" below.



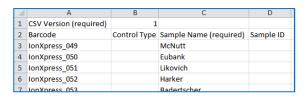
Each folder is represented by a single entry in the grid.



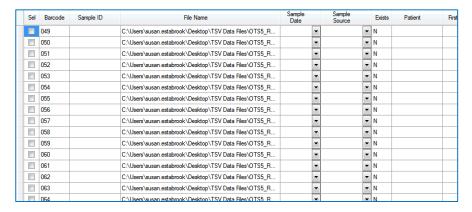
Click 'Save' or 'Submit.'

Fastq<>Sample Name

If the user has a large number of files to load but the sample names cannot be derived from the file or file name, they can be uploaded in bulk via a .csv file. User must construct the .csv file containing the barcode numbers and Sample Name, or optionally Sample ID.



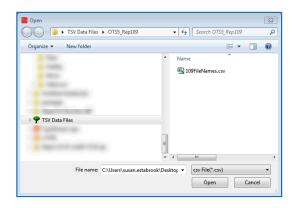
Load the files using the 'Add Fastq/Bam File' as described earlier. Files will display without sample names.



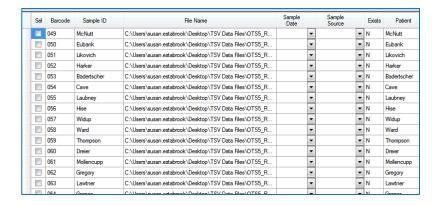
Click 'Fastq<>Sample Name' button. Select Sample Name or Sample ID.



Click Load. Navigate to location of the .csv file containing the sample names for the files.



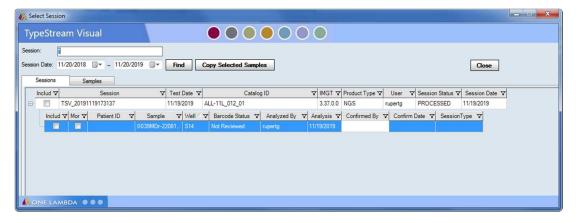
Click Open. The sample names are populated for each file.



Regardless of the method of loading, any file may be removed prior to submitting for analysis simply by check the check box in the first column and clicking 'Delete' button.

Clone Session

A previously-run session, or any combination of sessions or samples, can be run again to compare results. Sessions can be run using the same or a different analysis configuration. To clone a session, click "Clone Session" button at the top of the screen. The following screen displays, from which the user may select any or all of the sessions.



The session opens in the import screen as if it were a new session. Session Name, Analysis Parameters, Catalog, and IMGT version can all be modified for the new session. Users have more flexibility in analysis to obtain desired results.

NOTE: Although users are able to select sessions and samples that have been analyzed using different catalogs, the created session will use only the catalog selected. Some results may differ.

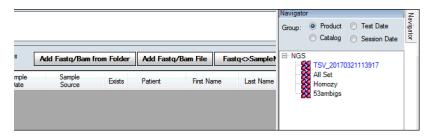
NOTE: After selecting sessions and/or samples for the new session you MUST CLICK 'Copy Selected Samples" in order to send them to the create session page.

Save a Session

The situation may arise where the user has loaded the path to the raw data files and selected

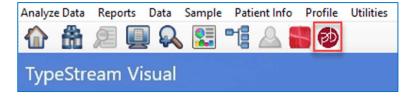
other variables but chooses not to analyze right away. Instead of submitting to the engine right away, clicking "Save" will put the session name into the navigator without submitting it to analysis.

For any file saved but not analyzed, the name of the file will display in the Navigator in Blue.

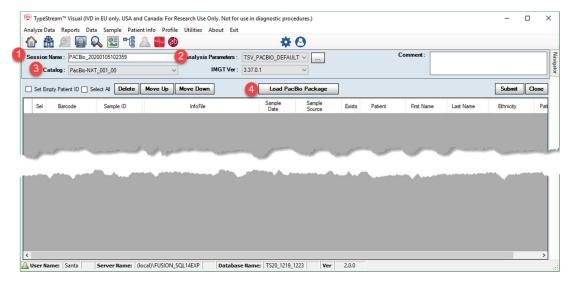


NOTE: This functionality is not available for PACBio sessions. Because of the input structure, the software is currently unable to save the path to the raw data.

Create Session for PACBio

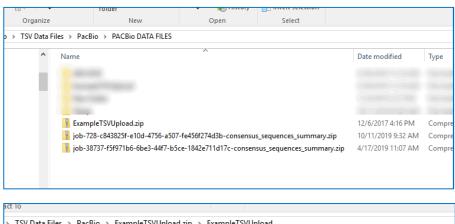


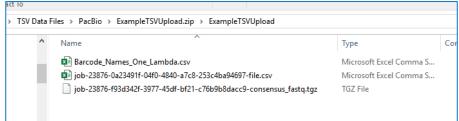
Clicking the icon for 'PACBio Session Builder' will bring up a screen which is largely the same as for Ion S5 and Illumina but differs in important ways. Those ways are highlighted below.



| | Item | Description | | | | | |
|---|---------------------------|---|--|--|--|--|--|
| 1 | Session Name | Session names are preceded by "PACBio_" followed by the time stamp. They can be modified or replaced prior to analysis | | | | | |
| 2 | Analysis Parameters | The software contains a separate set of default parameters for PACBio. See Utilities for more information. | | | | | |
| 3 | Catalog dropdown selector | Only PACBio catalogs may be used; only PACBio catalogs will display | | | | | |
| 4 | Load PACBio Package | This button will allow navigation to the PACBio data files. Only whole 'packages' can be downloaded. | | | | | |

PACBio packaged files are zipped files containing all data from the PACBio sequencer.





ALLType FASTPlex

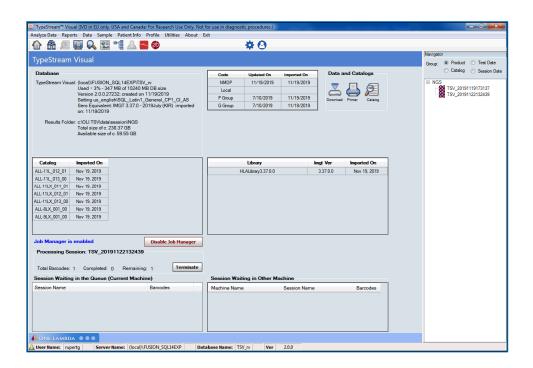
TypeStream Visual supports ALLType FASTPlex workflow, and is applicable to Illumina MiSeq, Illumina iSeq, and Illumina MiniSeq raw files.

Catalogs for FASTPlex begin with "ALL-FAST."

The software trims twenty (20) bases from the outside edge of both of the paired ends to reduce systematic sequence error from FASTplex workflow.

Job Manager

A session sent to the engine will appear in left column of the Job Manager under "Sessions Waiting in the Queue." Sessions submitted subsequent to this will appear in the right column under "Session Waiting in Other Machine."



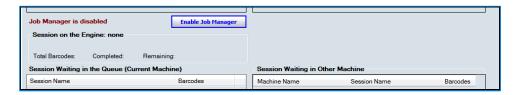
Job Manager displays the name of the session on the engine, total number of barcodes in the session, how many have been analyzed, and how many remain.



There is limited functionality with respect to the queue waiting on other machine. User on current machine cannot change the analysis order, remove from queue, or terminate sessions on the other machine. It is there for informational purposes only.

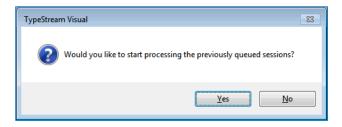
Disable/Enable Job Manager

"Disable Job Manager" will stop the engine and return the current session to the queue. The number of barcodes successfully analyzed will display. To continue processing, click "Enable Job Manager."



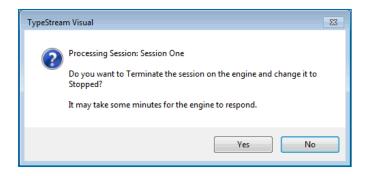
The Job Manager will automatically be disabled when the application is closed or the computer is shut down.

When the application is re-opened, user will be asked if the session running at last shutdown should be started again. If "No" is selected, sessions will remain in the queue and job manager will remain in 'disabled' state.



Terminate a session

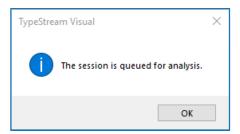
"Terminate" button will end the analysis process for the session on the engine. Software will confirm the termination.



That session will then appear in Navigator in red text. The engine will proceed with analysis on the next session in the queue.

A terminated session can be returned to the engine by doing the following:

- Click on the session name in the Navigator the session opens in summary screen.
 Each sample will display status of "Not Reviewed," "In Process," or "Not Submitted."
- Click the **Functions** button and select "Resubmit the Session". (See more information in Chapter 6.)
- Software will send the session back to the queue and give confirmation to the user.



Session Queue

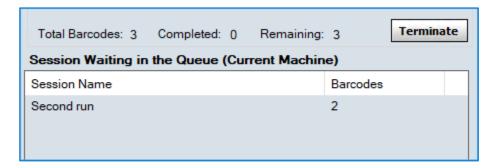
The session Queue consists of two separate panels:

- "Sessions Waiting in the Queue (Current Machine)" and
- "Session Waiting in Other Machine." This second panel enables multiple users connected to the same database to see what sessions the other user have waiting.

Sessions Waiting in the Queue (Current Machine)

Sessions in the queue display with Session Name, and the total number of barcodes.

The order of sessions waiting in the queue can be modified by dragging and dropping the session name to another position. This must be done while the engine is disabled.



Session Waiting in Other Machines.

Sessions in this queue display the session name, machine name, and number of barcodes for sessions connected to the same database where the sessions are running on a different machine.

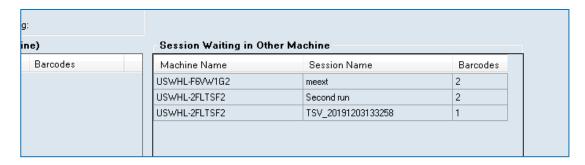
As with the current machine queue, when the session goes to the engine, it is removed from the queue list.



The other machine will display the reverse of this machine:

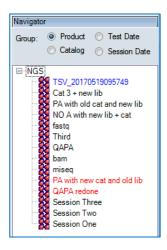


"Session Waiting in Other Machine" can accommodate multiple other machines and multiple sessions on the same machine.



Navigator

All sessions display in the Navigator. A session that was Saved but not Submitted on the Import page displays in **blue** font. A session terminated from the engine displays in **red** font.



Sessions in the Navigator can also be sorted by Test Date, Session Date, Product or Catalog.

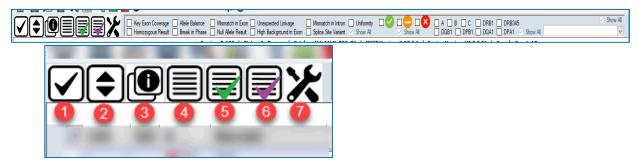


View Analysis

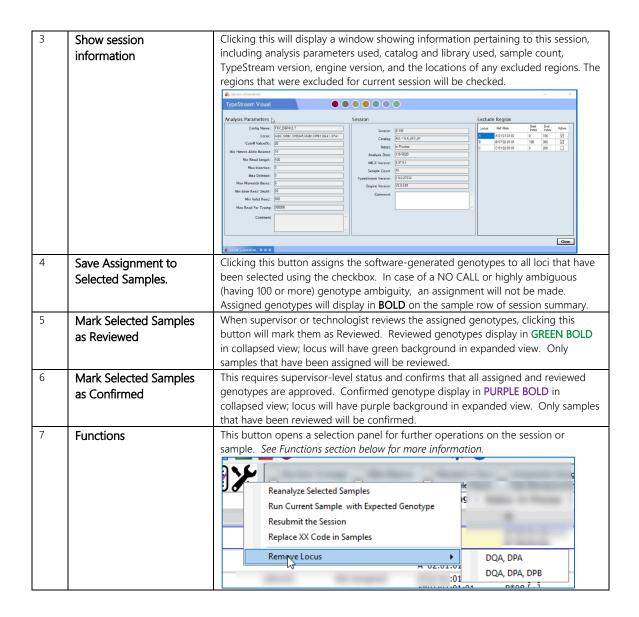
Session Summary

The Session Summary window displays the results of the TypeStream Visual analysis for all samples. This window can display in either 'collapsed' or 'expanded' view to show differing levels of detail.

At the top of the page, whether in collapsed or expanded view, are a set of functions and filters for use after analysis. What displays here is a high-level explanation. More detailed information follows later in the chapter.



| | Hover Tooltip | Description |
|---|---|---|
| 1 | Toggle Select All | Will select or de-select all samples in a session |
| | Session Detail View / Session Summary View | This button will toggle between 'collapsed' (session summary view) and 'expanded' (session detail view). The icon above indicates that the samples are currently in collapsed view and clicking this will expand them. The icon to go from expanded to collapsed looks like the following and will replace the icon at position 2. When moving from one session to another, the view will be in collapsed mode. |



Filtering for Health Metrics

The health metrics discussed in the 'Utilities' section of a previous chapter can be filtered here for easy viewing. Refer to that section and later in this chapter for information on the specifics of each filter.

| Key Exon Coverage Allele Balance | Mismatch in Exon Unexpected Linkage | ☐ Mismatch in Intron ☐ Uniformity |
|----------------------------------|--|-----------------------------------|
| Homozygous Result Break in Phase | Null Allele Result High Background in Exon | Splice Site Variant V Show All |

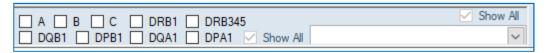
Filtering for Health Metric Level

In NGS Configuration, each of the health metrics above was weighted with the level of severity of the metric. Use the filters below for a quick view.

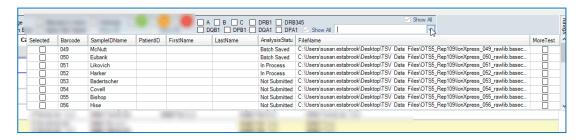


Filtering for Locus and Barcode

Loci may be filtered to view single loci or combinations (e.g. DRB1 + DRB345). Can also be used in combination with barcode, or any other filter option.



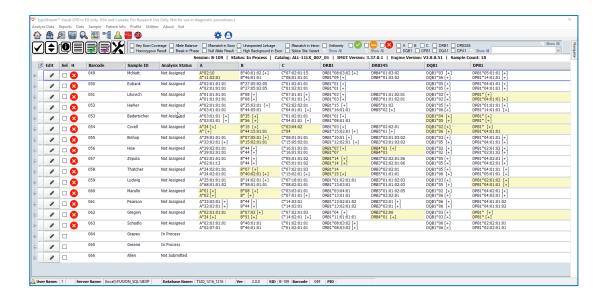
Clicking the dropdown for barcode display all barcodes in the session and includes related information as well as current analysis status.



Session Summary View - collapsed

When first selected from the Navigator, sessions open in Session Summary View. This is a high-level overview in which you see the following:

- Above the grid are listed the session name, session status, catalog used, IMGT library version used, engine version, and sample count.
- Each sample is shown on a separate summary row, displaying health level, Barcode, Sample ID, Analysis Status, and all loci represented in the data.
- Health level for the barcode represents the highest (most severe) rating from the individual samples.
- Software-derived genotyping displays for each locus.
- Any failure of a metric will be highlighted in yellow.



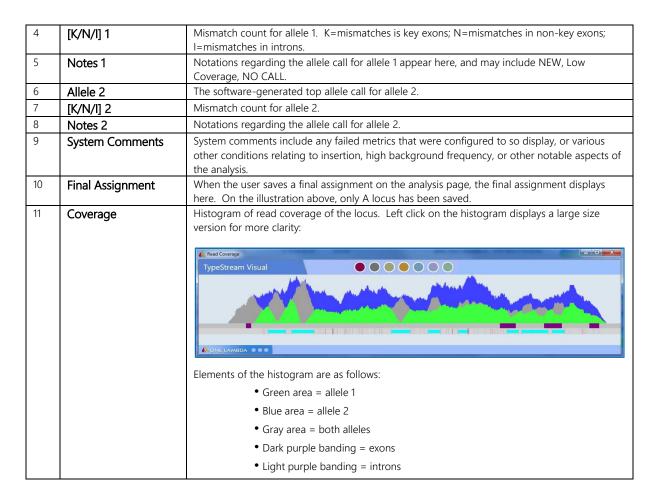
Session Detail View - expanded

To view the individual loci and get more detailed information click "Session Detailed View" button. This will expand all samples and all loci will be visible. Or click "+" on barcode to display individual loci for only one sample. The grid expands as shown below.



With all rows expanded, grid displays barcode list with the data columns listed below. Please note that the selection checkbox on the far left is for selecting loci for functions (e.g. 'Assign All') and has nothing to do with what displays in the analysis panel.

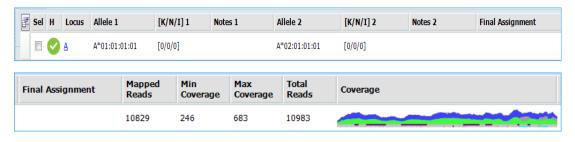
| | Item | Description | | | | | | | |
|---|-----------------------|---|--|--|--|--|--|--|--|
| 1 | Locus Health icon (H) | Health – health metric and severity as established in Utilities. Each locus will display the health | | | | | | | |
| | | con that represents the highest number (most severe) of all the failed metrics. | | | | | | | |
| 2 | Locus | All loci present in the sample display here. Locus field displays in green when the locus is | | | | | | | |
| | | saved on the analysis page and purple when it is confirmed on the analysis page. | | | | | | | |
| 3 | Allele 1 | Displays the software-determined genotyping. | | | | | | | |
| | | • [+] indicate there are ambiguous alleles. Hover over this indicator to view the allele list. | | | | | | | |
| | | "r" indicates a rare allele if the software has been configured to display allele frequency | | | | | | | |
| | | Cis/trans ambiguities are shown in purple with both genotypes displaying. | | | | | | | |



All column widths on the locus level can be resized by the user. To retain the resized columns, go to Home page before selecting another session to view.

Allele display

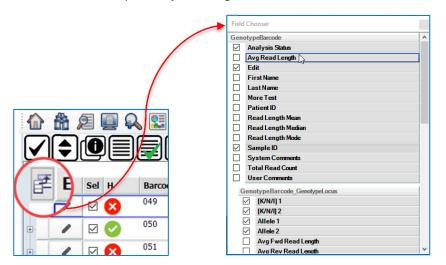
TypeStream visual will display locus results based on the latest IMGT library in the database. A typical heterozygous allele displays with top software-generated genotypes and accompanying data as described above. For a cis/trans ambiguity, the software will fully display both genotypes on the summary detail page, and the data will be shaded with a purple background.





Field Chooser

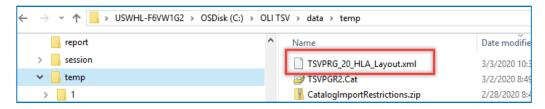
User may include more columns in the grid by clicking the icon in the top left corner of the grid. Field Chooser window displays. The top part of the chooser shows options available for the collapsed mode, the bottom part shows options for the expanded mode (locus level). Select the desired options by checking the checkbox and exit the field chooser to save them.



After making selections, use the 'x' in the upper right corner to remove the Field Chooser. A message will display confirming that the layout should be saved.



To clear all field selections and return to default settings, navigate to C:\OLI TSV\data\temp and remove the file "TSVPRG_20_HLA_Layout.xml."





Assign, Review, Confirm



Using these three buttons, it is possible to assign, review, or confirm genotyping for all samples or selected samples with the click of a button.



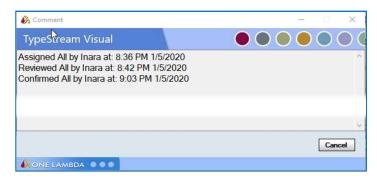
In the example above, barcode 58 has had all loci assigned using the Assign button. The genotypes display in bold and Analysis Status displays "Assigned."

Barcodes 56 and 57 were first Assigned, then Reviewed using the Review button. The genotypes display in bolded green and Analysis Status displays "Reviewed" and has a green background.

Barcodes 49 and 51 were first Assigned, then Reviewed, and then Confirmed using the Confirm button. The genotypes display in bolded purple and Analysis Status displays "Confirmed" and has a purple background.

By design, samples cannot be confirmed before they are reviewed and cannot be reviewed before they are assigned.

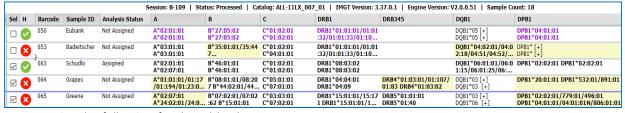
All assignments, reviews, and confirmations are tracked and can be accessed via "Assignment History" on the Analysis Panel.



There are several instances in which the assignments will not be made by the software.

In the case of a cis/trans ambiguity, the software will not select one genotype over the other

A highly ambiguous allele having 100 or more ambiguities A NO CALL allele



Notice the following for the table above:

Barcode 50 has been confirmed but has NO CALL for DRB345 and a highly ambiguous DQB1. Because of the high ambiguity, the software did not make an assignment for DQB1, and the alleles are neither bold nor in purple. Additionally, Analysis Status retains its "Not Assigned" value because the assignments are not complete.

Barcode 53 has a NO CALL for DRB345. DPB1 is a cis/trans ambiguity and was therefore not assigned by the software. Analysis Status again retained its "Not Assigned" value.

Barcode 63 has a NO CALL for DRB345. As this was expected due to linkage association, and all other loci have been assigned, the Analysis Status has been changed to "Assigned."

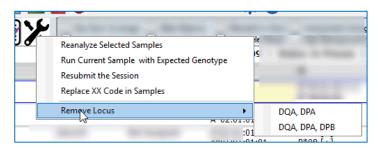
Barcode 64 and 65 both have highly ambiguous DQB1 alleles and have therefore not been assigned. Although the other loci have been assigned, and, for barcode 64, reviewed, the Analysis Status remains "Not Assigned."

Note that this process displays genotypes to the number of fields specified in Assignment Settings in NGS Configuration. (See "Utilities" for more information.)

Note also that using this process will not save genotypes to the patient record. That must be done manually on the Analysis Panel.

Functions

TypeStream Visual contains number of functions for further operations on analyzed data that are available directly from the Summary Page, whether in expanded or collapsed mode. Just click on the tools icon and select the option you wish to use.



Reanalyze Selected Samples

'Reanalysis' will open a new session for any selected barcode directly from the summary page. Select a single or multiple barcodes or the entire session, click 'Reanalysis,' and the application opens the selected barcode(s) in a new session. Session Name, Analysis Parameters, Catalog, and IMGT version can all be modified for the new session.

Run Current Sample with Expected Genotype

Formerly known as "Retype Current Barcode" this tool can help user who feel that the software may have not used the correct reference allele in its analysis.

In a regular run, the software first estimates candidate alleles based on the raw read sequences. The sequences from the candidate alleles are used to map reads. The mapped reads then are used to construct consensus sequence for genotyping.

When the estimated candidate alleles are too different from the target alleles, it causes a read mapping problem; the consensus sequence may then result in a wrong genotype or none.

By using this function, the user can provide an expected genotype, i.e., sample was previously typed by different method. With the expected genotype, the software does not need to use candidate alleles as a mapping reference. Instead, it uses the user-provided alleles as a

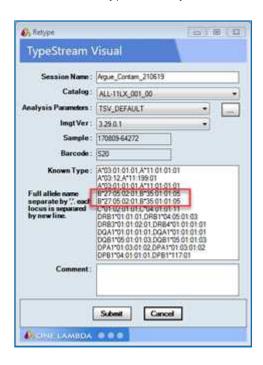
reference for downstream mapping and typing.

Usually, the resulting genotype should be close to the given genotype. If it is completely different, either the given genotype is not expected or the software is mis-mapping the reads.

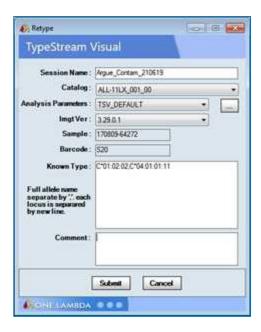
User may select the 'Rerun Current Barcode with Expected Typing' option, manually enter the correct type, and submit for reanalysis, which may use the same parameters and library or may change

The known type format is very restricted and the software will pre-fill the typings as determined in original analysis. The user needs only to edit the alleles for which the typing call is in question and leave the rest as is. The software does not verify if the allele name entered is valid; any invalid allele name will be ignored, i.e., using DRB1*04:01:01:01 and not DRB1*04:01,which may lead to a mistype.

In the example below, B locus has two genotypes. If the user clicks submit with the window as is, B locus will retype with only the first B locus genotype



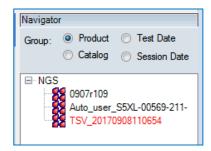
If user wants the software to leave B locus alone and only change, for example, the C locus, she will change it to the following and then hit submit:



Using this method, the B locus will still display as multiple genotypes as displayed above.

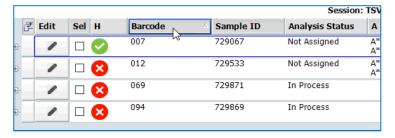
Resubmit the Session

Resubmit option is available only for a session that was only partly analyzed. When a session analysis has been terminated using the 'Terminate' button, the session displays in the Navigator in **red** text.



Selecting the session opens the session summary page. Go to Functions > Resubmit the Session.

Each of the samples and barcodes in the session displays with the status of 'Not Assigned,' 'In Process,' or 'Not Submitted.'



Selecting 'Resubmit the Session' will send the session back to the engine to continue analysis where it left off.

Replace XX Code

Following the upload of an updated NMDP file, clicking this button will replace any "XX" placeholders in final assignment with updated NMDP code. Status of the sample and locus is irrelevant when replacing XX Code.

Remove Locus

User has the option of removing DQA1, DPA1 and/or DPB1 analysis results from the session. This ability is most useful when 9-loci data has been analyzed with 11-loci settings. In this case DQA1 and DPA1 will display as NO CALL, when in actuality there is no data and therefore even NO CALL is a wrong call.

To rectify this situation, go to 'Functions \rightarrow Remove Locus \rightarrow DQA, DPA.' The two loci will be removed from the summary and will not display as a NO CALL.

Similarly, if 11-loci analysis was using for an 8-loci sample, go to 'Functions \rightarrow Remove Locus \rightarrow DQA, DPA, DPB. All three loci will be removed from all samples in the session.

Note: One the loci have been removed, they cannot be brought back.

Filters

The filter panel covers several categories of filters. Filters and filter types can be used in any combination the user wishes to see.

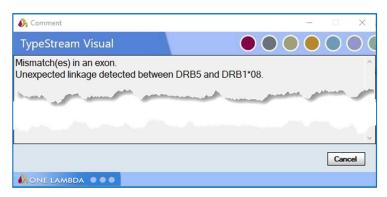
Health Metrics

Loci failing the named metrics display on the summary page. For more detail on any of these metrics, click the locus or the barcode to access the analysis page.

| Filter | Description |
|-------------------------|---|
| Key Exon Coverage | For exons 2 & 3 (Class I) and exon 2 (Class II), if the percentage of bases covered for a given exon drops below 100%, the test is flagged. |
| Homozygous Result | User may display only homozygous samples with this filter. |
| Allele Balance | The degree to which one allele is represented in the data compared to the other. If the allele balance ratio is \leq 0.3, the test is flagged. |
| Break in Phase | User may display only samples that contain at least two consecutive variants that couldn't be phased (or that don't have sufficient read coverage to determine phase) with this filter. |
| Mismatch in Exon | If a mismatch towards the reference sequence is present in an exon, the test is flagged. |
| Null Allele Result | User may display only samples that contain a novel position which indicates the new allele could have a null expression with this filter. |
| Unexpected Linkage | User may display only samples that contain DRB1/DRB345 or DRB1/DQB1 typings that do not match known association rules with this filter |
| High Background in Exon | User may display only samples with a high background position in a key exon with this filter. |
| Mismatch in Intron | User may display only samples that contain an intronic mismatch with this filter |

| Splice Site Variant | In the case of a possible splice site mutation, if an expressed intron (excluding UTR) does not start with "GT" or end with "AG" the software will consider the result as having a possible null expression, by including an 'N' at the end of the closest match defined allele name in the Session Summary. In this scenario, the software will not place a "Possible Null" warning in the System Comments pertaining to that test. Class I expressed introns are introns 1-4. Class II expressed introns are introns 1-3. |
|---------------------|--|
| Uniformity | The degree to which the read depth across a sequenced region remains consistent. When the CV for the uniformity calculation is ≥ 1 , the test is flagged. |

Notice of health metrics missed displays in system comments.



Locus Filters

Loci may be filtered by any single locus or a combination of loci.



Health Level

Referring to Health Metrics filters (following), the color-coded icons display the level of health metrics that do not meet the standard. User may alter the default severity standards in the NGS Configuration window, as well as whether it displays in system comments.

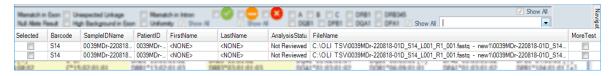


Hovering over a Health Metric icon for a locus will display the missed metrics in a tooltip.



Barcode Filter

Clicking the dropdown selector for Barcode displays all barcodes available in the session. Select any combination of barcodes, then click anywhere off the grid to examine the barcodes.



Elements of the Locus Row

Allele 1 and Allele 2

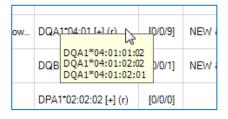
Allele 1 and Allele 2 display with the best typing to the highest level of homology. "[+]" indications the existence of ambiguities associated with the typing.

K/N/I values

K/N/I values display for each of the top possible genotypes and indicate the number and location of mismatches to the reference allele. K = mismatch in a key exon, N = mismatch in a non-key exon, and N = mismatch in an intron or UTR. The addition of a star (*) next to a number indicates that there are unknown bases present.

Ambiguities

The display of "[+]" next to the allele name indicates the presence of ambiguous alleles. Hovering over the "[+]" will display a tooltip listing the all the associated ambiguous alleles. This allele list is limited to 30, so for an allele with >30 ambiguities, you should refer to the ambiguities list on the Analysis page. (See next section)



Rare Alleles

A rare allele is indicated with "(r)" next to the allele name if the software has been configured to do so. On Analysis Panel, this designation will display for all rare alleles on the allele list.

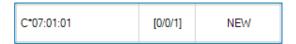


Notes

Notes fields display for each allele and are can display a number of important attributes about the results, including 'NEW,' 'Low Coverage,' 'NO CALL.'

NEW – Novel Allele Identifier

Due to the increased coverage of genes offered by NGS, users may run across scenarios in which the top results display is shown to contain mismatches in key exons, non-key exons, or intronic regions. When this occurs, the word **NEW** is tagged in the Notes field. The list of allele pairs listed under Allele 1 and Allele 2 columns represent the closest match allele.



While further investigation by the user into such samples is required for confirmation, such cases can represent a scenario in which a previously uncharacterized allele is present in the sample tested. In such cases, users should ensure they are working with the most up-to-date library.

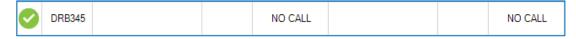
Low Coverage

When read coverage on a region is below a preset threshold (see Analysis Parameters), it may cause ambiguities in the genotype. When this occurs, **Low Coverage** displays in the Notes field.



NO CALL

When there are not enough reads of a particular locus to meet the minimum requirement (see Analysis Parameters), the software will not determine a genotype and instead will display the words "NO CALL."



In such a case, system comments will contain more specifics on the reads.

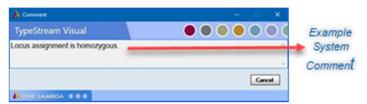




NOTE: If an expected locus is reported as a "NO CALL" and the "Total Read Count" value for the barcode is the same as the "Max Read for Typing" analysis parameter (or exactly double for paired end samples.) It is recommended that the user rerun with an increased value for the "Max Read for Typing" parameter. This will allow the software to analyze more reads from the raw data and may detect enough for the locus to provide a typing.

System Comments

This is an un-editable text field (and pop-up dialog box, if user clicks in the place within the System Comments area in the Analysis screen) where the software spells out the possible areas of interest for the user. The warnings and informative texts are comprised of both the user-selected messages from Health Metrics configuration and other warnings as described below.



| Message | Meaning | | | | | |
|---|--|--|--|--|--|--|
| High Insertion Count | The system comments will include insertion information, including location, if the software finds the insertion count is more than 20% of the total base count at a base location. Up to 5 such insertion locations can be listed. | | | | | |
| Low Variant Count | One or more variant positions have an Allele Balance of less than 10%. | | | | | |
| Key Exons Not Adequately Covered | Key exons are not adequately covered. | | | | | |
| Alleles Not Balanced | Software has detected that alleles are not balanced. | | | | | |
| Ruled Out Possible Cis-Trans Allele Pair | Software has ruled out a possible Cis-Trans allele pair. | | | | | |
| Possible Novel Variant | Possible novel variant is present in a splice site. | | | | | |
| High Background | High background positions are present in an exon. | | | | | |
| Mismatches | Mismatches are present in an exon | | | | | |
| No reads found for locus | No reads are found for a locus | | | | | |
| Two or more variants | Two or more variants cannot be phased. | | | | | |
| Locus Assignment Homozygous | Locus assignment is homozygous. | | | | | |
| No expected Linkage | When there is no genotyping call for a locus, and none is expected based on linkage disequilibrium data. See Linkage Table below for expected linkage between locus groups. | | | | | |

Linkage table

Following is a table of expected linkage between locus groups. When an allele from the lead group column appears in a genotype, the software will look for a corresponding allele from the expected group. If such is not found, the software displays a warning in system comments. The warning specifies what linkage was expected and not found.

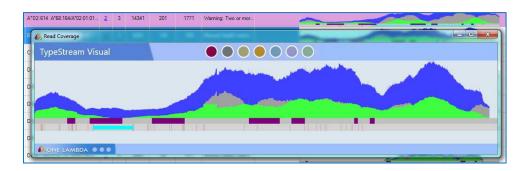
| DRB1 | Expected DRB345 | DRB1 | Expected DQB | DRB1 | | Expected DQA | | DQB1 | Expected DQA |
|---------|------------------|---------|--------------------------|------|------|---------------------|---|---------|---------------------|
| Group | group | Group | group | Grou | р | group | | Group | group |
| DRB1*01 | None - or - DRB5 | DRB1*01 | 03 - or - 05 | DRB1 | *01 | 01 - or - 05 | Г | DQB1*02 | 02 - or - 03 - or - |
| | | | | | | | | | 05 |
| DRB1*03 | DRB3 | DRB1*03 | 02 - or - 04 | DRB1 | *03 | 04 - or - 05 | | DQB1*03 | 02 - or - 03 - or - |
| | | | | | | | | | 04 - or - 05 - or - |
| | | | | | | | | | 06 |
| DRB1*04 | DRB4 | DRB1*04 | 03 - or - 04 - or - 05 | DRB1 | *04 | 01 - or - 03 | | DQB1*04 | 03 - or - 04 |
| | | | [02 rare] | | | | | | |
| DRB1*07 | DRB4 | DRB1*07 | 02 - or - 03 | DRB1 | .*07 | 02 | | DQB1*05 | 01 |
| DRB1*08 | None | DRB1*08 | 03 - or - 04 - or - 06 | DRB1 | *08 | 01 - or - 04 - or - | | DQB1*06 | 01 |
| | | | | | | 05 - or - 06 | | | |
| DRB1*09 | DRB4 | DRB1*09 | 02 - or - 03 | DRB1 | *09 | 03 | | | |
| DRB1*10 | None | DRB1*10 | 05 | DRB1 | *10 | 01 | | | |
| DRB1*11 | DRB3 | DRB1*11 | 02 - or - 03 - or - 06 | DRB1 | *11 | 01 - or - 05 | | | |
| DRB1*12 | DRB3 | DRB1*12 | 03 - or - 05 | DRB1 | *12 | 01 - or - 05 - or - | | | |
| | | | | | | 06 | | | |
| DRB1*13 | DRB3 | DRB1*13 | 02 - or - 03 - or - 05 - | DRB1 | *13 | 01 - or - 02 - or - | | | |
| | | | or - 06 | | | 05 | | | |
| DRB1*14 | DRB3 | DRB1*14 | 03 - or - 05 | DRB1 | *14 | 01 - or - 05 | | | |
| DRB1*15 | DRB5 | DRB1*15 | 02 - or - 05 - or - 06 | DRB1 | *15 | 01 | | | |
| DRB1*16 | DRB5 | DRB1*16 | 03 - or - 05 | DRB1 | *16 | 01 - or - 05 | | | |

Final Assignment

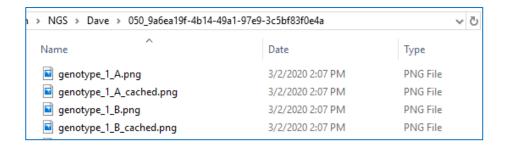
The final assignment will not display in the final assignments field until a user, technologist or supervisor, selects a final assignment and clicks "Assign" on the analysis panel. From that point, it will display in session detail mode, with or without the analysis panel in display. More information about Final Assignment in the next section.

Histogram

Clicking on the histogram in Session Detail View will bring up a larger-scale view.



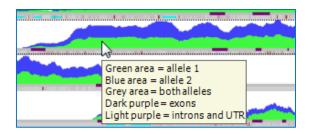
NOTE: in the interest of faster histogram display, the histogram files exist in two versions in the session directory: 1). The original .png file and 2). A 'cached' version which is smaller and quicker to load.



Elements of the histogram are as follows:

- Green area = allele 1
- Blue area = allele 2
- Gray area = both alleles
- Dark purple banding = exons
- Light purple banding = introns
- Light blue banding = unphased region between heterozygous positions
- Dark orange 'tick marks' = heterozygous positions

Hovering over a histogram on session summary will display a tooltip



Homozygous genotypes

Homozygous calls are immediately identifiable by their single-color shading in the histogram.



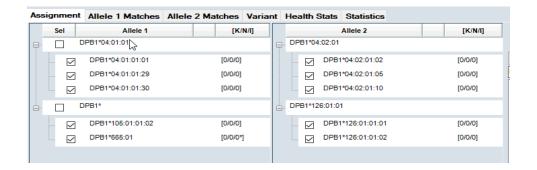
These alleles are also filterable using the warning flag functionality (see above).

Cis-Trans Ambiguities

If two positions required to resolve a cis-trans ambiguity span a distance that exceeds a kit's maximum read length, the specific cis-trans ambiguity will persist in the data. Both genotypes will display and background will be shaded purple.



The software will not assign a genotype to this allele if "Assign All" functionality is used to assign type. On the Analysis page, the two pairs of genotypes are displayed separately. The user may then select the final genotype.



NOTE: In cases where phase¹ cannot be established between key exons, and the phase break correlates to a known cis-trans pair, the software will report both pairs of alleles. An intronic or non-key exon mismatch in only one pair will not lead to elimination of the pair from the reported genotypes as a means of accounting for novel alleles where an understanding of the key-exon phase is required.

¹Phase: When there is at least one mapped read bridging the distance between two variant positions, the positions are known as "in phase." Phase breaks are caused when no mapped reads can be found which will bridge that distance.

Suffixes used with allele names

There are additional optional suffices that may be added to an allele to indicate its expression status. Alleles that have been shown not to be expressed, 'Null' alleles have been given the suffix 'N'. Those alleles that have been shown to be alternatively expressed which may have the suffix 'L', 'S', 'C', 'A', 'Q', or 'X'.

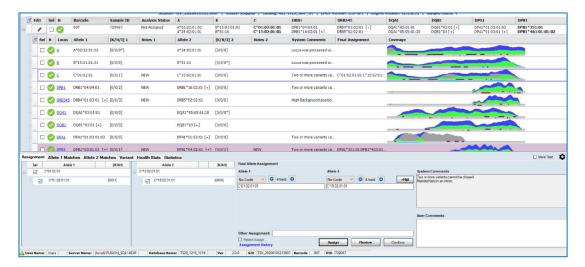
| Suffix | Definition |
|--------|--|
| N | An allele that has been shown not be expressed, or is 'Null'. |
| L | Indicates an allele which has been shown to have 'Low' cell surface expression when compared to normal levels. |
| S | Used to denote an allele specifying a protein which is expressed as a soluble 'Secreted' molecule but is not present on the cell surface |
| С | Indicates an allele product which is present in the 'Cytoplasm' but not on the cell surface. |
| Α | Indicates 'Aberrant' expression where there is some doubt as to whether a protein expressed. |
| Q | Used when the expression of an allele is 'Questionable' given that the mutation seen in the allele has previously been shown to affect normal expression levels. |
| | |

Analysis Panel

To view your analyzed files, you can do one of the following actions.

- 1. From collapsed mode, click on the locus genotypes for the locus you wish to view. Analysis panel opens for that locus.
- 2. From expanded view, click on the locus row anywhere except the locus itself or the histogram. The analysis panel opens on the bottom half of the page with the selected locus highlighted. It is subdivided into panels; the borders between the panels can be repositioned

so the user can focus on a chosen section. Here the C locus is highlighted in the top window, and the pertinent information is displayed below in the lower window.



The Analysis Panel consists of six tabs displaying different but related information for the user.

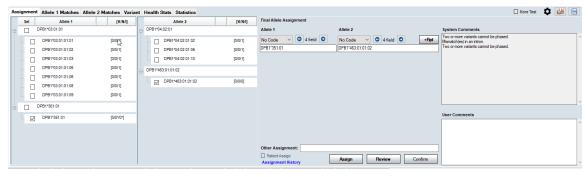
Assignments – displays possible and final allele assignments plus system and user comments

Allele 1 Matches and Allele 2 Matches – displays ambiguities, resolving positions, and close match list per allele.

Variant – shows all variant positions with consensus bases, counts and percentages of variation, and whether each variant is phased. Also show allele balance bar graph.

Health Stats – displays status and numerical values for all Health Metrics Statistics – displays values for Mapped Read Metrics and Locus Coverage

Assignments tab



The assignments tab provides the user with a complete list of all ambiguities. On the right-hand side, both allele 1 and allele 2 have top-level selection boxes for the user to choose the entire allele string in one stroke – when the Allele 1 top box is checked, all boxes on the right are automatically checked as well. Individual alleles can also be selected or de-selected. As each allele is checked, the resulting combination displays in the Final Allele Assignment text fields. Formatting of the fields is also variable.

Final Assignment

User has a lot of latitude in determining the final genotype assignment. TypeStream is highly versatile in allowing last-minute changes is use of codes or even the number of fields to display if no code is selected. Final assignments can be saved down to the 1-field level.

"Other Assignment" text field allows users to assign a different final assignment in free text.

Allele Codes

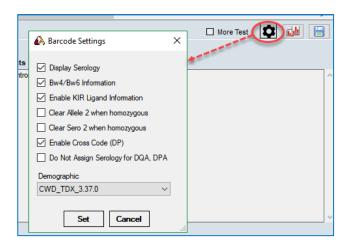
As defined earlier in this chapter, allele code will display based on the top genotype as selected by the software.



Serology

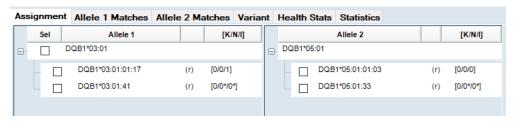
User may decide whether serology displays or not. There are two places to make this determination. To provide a global serology setting, from the file menu, navigate to Utilities → NGS Product Configuration. Selection of serology is on the lower half of the *Assignment Settings* tab. (See earlier section on product configuration.)

The second method is to click the small gear icon on the right side of the analysis panel. This will bring up a small configuration window where you can override global settings on a perlocus basis.

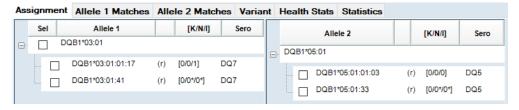


Bw4/Bw6, KIR/Ligand, and Demographics display can also be decided on a locus-by-locus basis.

Opting to display sero inserts a column into the allele lists.



1 Sero not displayed



2 Sero displayed

Assign, Review, Confirm

On the Analysis Panel, the user may Assign, Review, and Confirm genotypes individually at the locus level. The same rules pertain here as they do with the bulk assign on the summary page with respect to the order of carrying out assign \rightarrow review \rightarrow confirm. See earlier in this chapter.

Additionally, on a locus level the genotype can be un-confirmed and un-reviewed if changes are deemed to be necessary.

- Assign on clicking Assign, the final assignment displays in the Final Allele Assignment window and in the Final Assignment column on summary view.
- Review on clicking Review, the Review button text changes to 'Undo Review' and displays in green. User comments become un-editable.



- Lock icon displays to the left of the buttons, signifying that assignments cannot be changed and user comments not added until either the lock icon or the Undo Review is clicked. At that time, button will go back to saying "Review."
- Confirm this is a supervisor-only activity. On clicking Confirm, the Confirm button text changes to 'Undo Confirm' and displays in purple. The lock icon appears and Undo Review becomes disabled.
 - If Patient Assign checkbox has been checked, this is when the assignment is associated with the patient.
 - Lock icon here works the same as with Review.

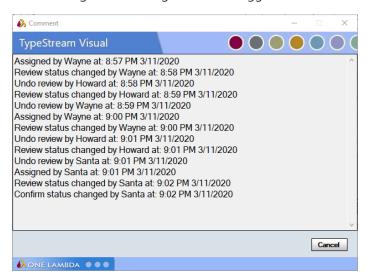
Patient Assign

When this box is checked prior to the Review/Confirm process, the saved genotyping, allele code, and/or serology will be saved to the patient associated with the analysis.

Patient must be assigned to the session prior to saving the results in order for them to appear on the patient information page.

Assignment History

All the changes to the assignments are logged



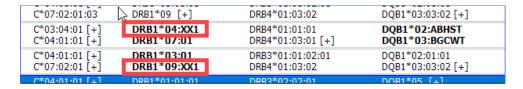
+Rpt

The +Rpt function allows you to look up and report unknown allele codes with the National Marrow Donor Program (NMDP).

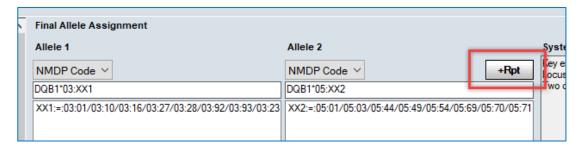
Unknown allele codes within Visual TypeStream analysis results are marked with XX followed by a sequential number. The numbers are reset to 1 for each sample and locus. For instance, DRB1*04:XX1 is an unknown allele code.

When you see unknown codes, you should first make certain you have imported the latest NMDP file. If you have the latest code file and are still seeing XX codes, you can store these unknowns for later submission to the NMDP. XX codes are stores in a ".txt" file named nmdp_code_report.txt, (by default stored in C:\OLI TSV\data\export). This location can be changed by modifying the path in Utilities->General Settings->Paths). Code information is appended to this text file as it is added; the newest additions are at the bottom.

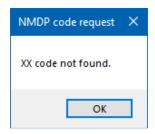
Unknown alleles appear like so in the Session Summary window:



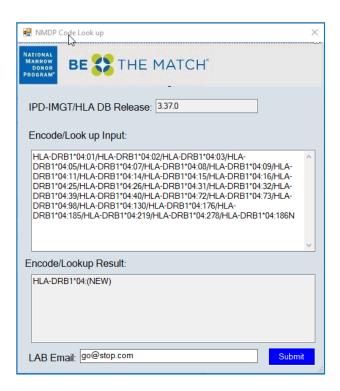
To send the unknown code information directly to NMDP, make a Final Assignment (1) of an allele that has incomplete information, then (2) click the +RPT button:



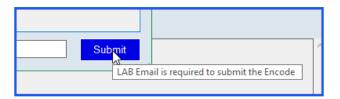
If an XX code is not found, you will receive the following message:



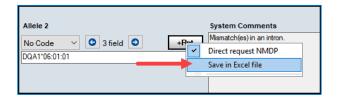
If an XX code is confirmed by the system, and you are connected to the Internet, TypeStream Visual will open the *Bioinformatics.NMDP.Org* webpage and allow you to look up the unknown allele:



To submit the unknown code to NMDP, you must type in your lab email address and click the Submit button. (Hovering your mouse over the Submit button will confirm this requirement).



To add the unknown code information to an Excel spreadsheet file, (by default stored in C:\OLI TSV\data\export) right-click on the +Rpt button and select Save in Excel file:



After the unknown code has been saved, TypeStream Visual displays a confirmation message that the text file has been saved (not shown).

When you are done, click the Close button, (on the right of the +Rpt button) to remove the buttons from the display.

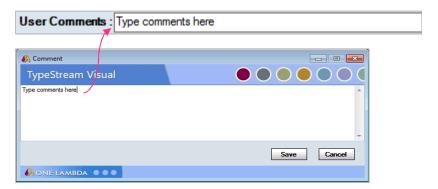
NOTE: The +Rpt button retains the last selection you made, (direct or Excel) so it can be used as a shortcut. Unless you want to change your selection, the next time you report XX code simply click +Rpt.

System Comments

This field is not editable by the user. System comments may include assignment information, saving and confirming by locus and by user. The system comments displayed in this panel should match those seen in the summary detail panel.

User Comments

Comments added by the user display here. Clicking in the user comment field brings up a comment text window. Comment may be saved or cancelled. Clicking "Cancel" will not remove comments entered on a different page.



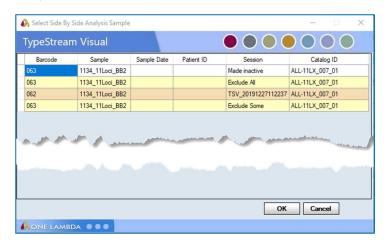
More Test

If "More Test" was selected on the session summary, it will display as checked here, too. If not check in session summary, More Test can still be check here on analysis page. More Test applies on a sample level, not a locus level, and when checked can be used as a search parameter in compiling a Clone Session or preparing reports.

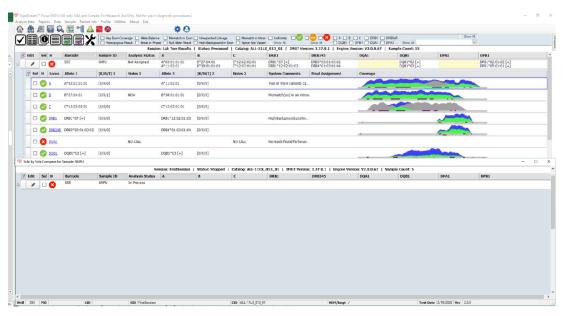
Side-by-Side Analysis



For users who wish to compare current run results to previous results for the same sample, clicking the Side-by-Side Analysis icon brings up a grid with every session containing the same sample and have the same patient ID. User selects the session to which he would like to compare results and clicks OK.



The selected session opens on a half screen on the lower half of the current session, enabling direct sample-to-sample comparison of data.



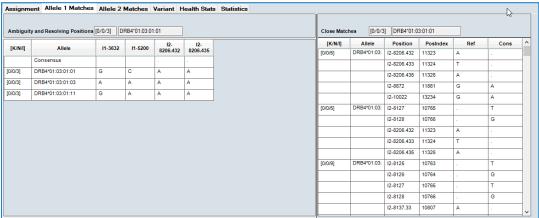
Windows may then be resized as required for a better look at the data of interest.

Save Locus Layout



On most of the tabs on the Analysis Panel, the boundaries between sections are movable. The user can maximize the space he uses most and save that layout. Text window will confirm that the layout has been saved. Every time a new locus or sample is opened, it will be formatted in the saved layout.

Allele 1 and 2 Matches tabs



Resolving Positions

For alleles that contain a mismatch to the reference, TypeStream Visual identifies the location of the mismatch, the reference base, and the consensus base. Double-clicking the consensus cell for a position opens the Reads Viewer to that position.

| [K/N/I] | Allele | UTR5-216 | UTR5-114 | I1-196 | I3-1081 | 16-2588 | UTR3- 3113 | | | UTR3- 3725 |
|----------|---------------|----------|----------|--------|---------|---------|---------------|---|---|---------------|
| | Consensus | Α | | С | С | G | С | А | С | |
| [0/0/1] | B*40:01:02:01 | А | Т | С | С | G | С | А | Т | Α |
| [0/0/0*] | B*40:01:02:09 | Α | С | c/3 | С | G | * | * | * | * |
| [0/0/1*] | B*40:01:02:02 | G | Т | С | С | G | * | ż | * | * |
| [0/0/1*] | B*40:01:02:03 | А | Т | Α | С | G | * | * | * | * |
| [0/0/1*] | B*40:01:02:04 | А | Т | С | С | G | С | Α | Т | G |
| [0/0/1*] | B*40:01:02:07 | * | * | С | С | Α | * | * | * | * |
| [0/0/1*] | B*40:01:02:08 | * | Т | С | Т | G | * | * | * | * |
| [0/0/1*] | B*40:01:02:10 | А | Т | С | С | G | Т | А | * | * |
| [0/0/1*] | B*40:01:02:11 | Α | Т | С | С | G | С | G | * | * |

The consensus base at each of the positions displays in the top row. The bases at the same positions are displayed for the three top ambiguous reference alleles. Notice that there is agreement between the positions and the K/N/I values – positions are correctly identified as intronic, and the presence of unknown bases is noted.

Close Match List

The Close Match list provides users with a list of perfect matches and close matches for the sample. Typing information is broken out by allele. For matches that contain a mismatch towards the reference, user may click the position, which will open the Reads Viewer to the position in question. For an ambiguous result, the software will identify the resolving position.

| [0/1*/0*] DRB4*0 |)1:06 E3-421 | 13559 | Т | С | |
|------------------|--------------|-------|---|---|--|
|------------------|--------------|-------|---|---|--|

The above can be read as "The DRB4*01:06 allele is a close match with a single mismatch in a non-key exon at position E3-421. The consensus base call at this position is a 'C' while the reference base at this position is a 'T'."

Variant tab

There are two parts to the Variant tab – the variant table and the bar chart which alternately displays base count and percentage at each position or allele balance.

Variant Table

| Position | Allele 1 | Allele 2 | Base Count 1 | Base Count 2 | Allele Balance | Phased With Previous | Bkgd | ^ |
|----------|----------|----------|-----------------|-----------------|-------------------|----------------------------|-------|---|
| 14-74 | Α | G | 49%(196) | 51%(202) | 0.97 | | 0%(0) | |
| E5-900 | G | Α | 48%(223) | 52%(239) | 0.93 | | 0%(0) | |
| E5-916 | G | Α | 48%(230) | 52%(254) | 0.90 | | 0%(1) | |
| E5-985 | G | Α | 49%(256) | 51%(265) | 0.96 | | 0%(1) | |
| E5-1008 | Т | С | 51%(250) | 49%(246) | 0.98 | | 0%(1) | |
| I5-102 | G | С | 55%(237) | 45%(194) | 0.81 | | 0%(0) | |
| 15-325 | С | Т | 51%(217) | 49%(212) | 0.97 | \square | 0%(0) | |
| 15-371 | Т | G | 50%(215) | 50%(218) | 0.98 | | 0%(0) | |
| 15-414 | G | С | 49%(214) | 51%(221) | 0.96 | | 0%(0) | |
| E7-1046 | G | С | 54%(201) | 46%(171) | 0.85 | | 0%(0) | |
| UTR3-579 | А | G | 50%(355) | 50%(359) | 0.98 | | 0%(0) | |
| UTR3-682 | Т | С | 53%(222) | 47%(194) | 0.87 | | 0%(0) | |
| UTR3-796 | С | Т | 53%(174) | 47%(156) | 0.89 | | 0%(0) | |
| UTR3-853 | Α | G | 50%(146) | 50%(146) | 1.00 | | 0%(0) | V |

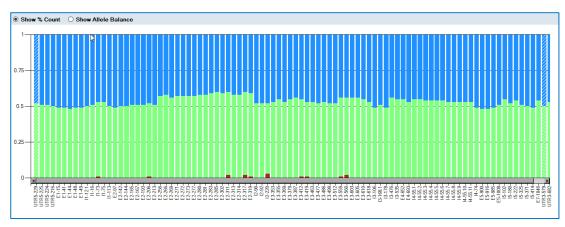
Variant tab displays a table of all the variants identified in the locus. A variant, also referred to a heterozygous position, is a position that has reads representing more than one base. The ratio to determine the variant positions is a user-defined parameter; the default is 0.3 or 30%.

| Column | Description | | |
|---------------------|--|--|--|
| Position | The cDNA or gDNA identification of the base position | | |
| Allele 1 / Allele 2 | The bases at the variant position | | |
| Base Count 1 / 2 | The Base count for allele 1 and allele 2 at each of the variant positions, showing | | |
| | in both hard count numbers and percentage of the total. | | |

| Allele Balance | Allele balance is calculated using the following formula: $ AlleleBalance = \frac{(A1/A2)i_1 + (A1/A2)i_2 + \cdots (A1/A2)i_N}{N} $ where A1=the allele with the lower number of reads; A2=the allele with the higher number of reads, i=a heterozygous position; and N=the total number of heterozygous positions. |
|----------------------|---|
| Phased with previous | Indicates if the phase was continued between current variant and the previous consecutive variant. |
| Bkgd | Background percentage |

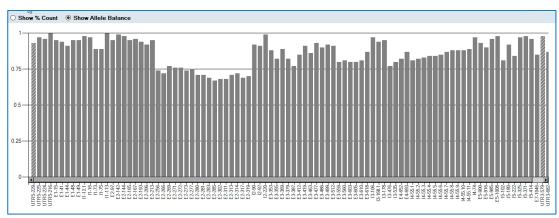
Each of the columns in the Variant Table is can be sorted, including Balance %, giving the user alternate ways to assess and present the analyzed data. Default sort order is by position.

Show Percent Count



Selected by default, this chart shows the relative count of reads for Allele 1 and Allele 2 at each of the variant positions. These values will match the Base Count percentage values on the Variant table. This table will change its sort, and therefore its profile, based on how the Variant Table is sorted.

Show Allele Balance



The Allele Balance graph depicts the relative balance between allele 1 and allele 2 representation within the raw data. At each variant position, a perfectly balanced allele would

have a value of '1' and the bar would display to the top. Allele balance is calculated using the formula in the chart above. Length of the bar will match the corresponding allele balance value in the variant table. As with the Base Count graph, the Allele Balance graph will respond to the sorting options of the Variant Table and change its display accordingly.

Health Stats tab

Health Stats delivers results from Health Metrics configuration.

| | Health Metric | Standard | Value | Pass/Fail | Comments | Include |
|------------|-------------------------|----------|--------|-----------|---|-----------|
| ② | Break in Phase | 0.00 | 1.00 | Fail | Two or more variants cannot be phased. | \square |
| ② | Mismatch in Intron | 0.00 | 1.00 | Fail | Mismatch(es) in an intron. | \square |
| ② | Key Exon Coverage | 100.00 | 100.00 | Pass | Key exons not adequately covered. | |
| ② | Mismatch in Exon | 0.00 | 0.00 | Pass | Mismatch(es) in an exon. | |
| \bigcirc | Allele Balance | 20.00 | 87.24 | Pass | Alleles are not balanced. | |
| ⊘ | Uniformity | 1.00 | 0.27 | Pass | Read depth is not uniform across the gene. | |
| ⊘ | High Background in Exon | 0.00 | 0.00 | Pass | High Background position(s) present in an exon. | |
| \bigcirc | Homozygous Result | 0.00 | 0.00 | Pass | Locus assignment is homozygous. | |
| ⊘ | Unexpected Linkage | 0.00 | 0.00 | Pass | Unexpected linkage detected between locus. | |
| ⊘ | Null Allele Result | 0.00 | 0.00 | Pass | Locus assignment contains a null allele. | |
| ② | Splice Site Variant | 0.00 | 0.00 | Pass | Possible novel variant in splice site. | |

This list will not display in the same order as on the configuration page. On this tab, the failed metrics display at the top of the grid, with the most severe (highest risk) metric listed first. The table shows the standard for the metrics and the actual value the locus along with Pass/Fail status. The text of the comment for failed metrics will display in system comments only if the 'Include' checkbox was checked in configuration.

Statistics tab

The statistics tab contains two tables – Mapped Read Metrics and Locus Coverage.

Mapped Read Metrics

The statistics for allele 1 and allele 2 are combined in the following table for accuracy. If using FASTPlex workflow, the forward and reversed read counts will be reduced by 20 bases, showing 130 instead of the 150 standard for MiSeq sessions.

| Mapped Read Metrics | | | | | |
|------------------------------|-------|--|--|--|--|
| Mapped Read Metrics | Value | | | | |
| Reads for Typing | 11078 | | | | |
| Forward Read Count | 5537 | | | | |
| Averaged Forward Read Length | 150 | | | | |
| Reverse Read Count | 5541 | | | | |
| Averaged Reverse Read Length | 150 | | | | |
| Total Reads | 13702 | | | | |
| | | | | | |

| Statistic | Description | | |
|------------------|---|--|--|
| Reads for Typing | The total number of reads mapping to the alleles after read filtering | | |
| | has occurred | | |

| Forward Read Count | The total number of forward reads mapping the alleles |
|------------------------------|--|
| Averaged Forward Read Length | The average read length of the forward reads |
| Reverse Read Count | The total number of reverse reads mapping to the alleles |
| Average Reverse Read Count | The average read length of the reverse reads |

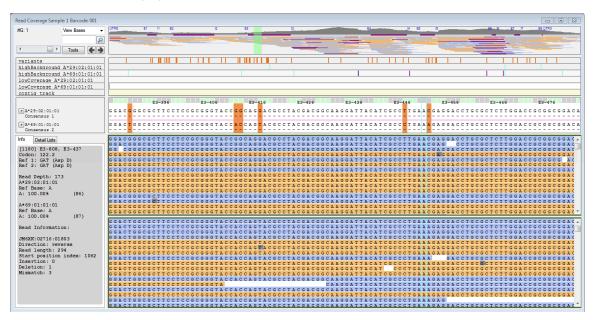
Locus Coverage

The locus-level statistics for the selected locus broken down by gene region.

| | Region | Base Covered (%) | Min Depth | Max Depth | Avg Depth |
|---|---------|------------------|-----------|-----------|-----------|
| | 5'UTR | 100% | 145 | 458 | 311 |
| | Exon1 | 100% | 428 | 463 | 445 |
| Ī | Intron1 | 100% | 302 | 453 | 363 |
| | Exon2 | 100% | 291 | 489 | 388 |
| | Intron2 | 100% | 214 | 369 | 310 |
| | Exon3 | 100% | 217 | 432 | 355 |
| Ī | Intron3 | 100% | 366 | 562 | 461 |
| Ī | Exon4 | 100% | 408 | 583 | 511 |
| | Intron4 | 100% | 337 | 460 | 381 |
| Ī | Exon5 | 100% | 451 | 555 | 514 |
| | Intron5 | 100% | 365 | 521 | 451 |
| Ī | Exon6 | 100% | 399 | 468 | 429 |
| | Intron6 | 100% | 377 | 467 | 430 |
| | Exon7 | 100% | 346 | 372 | 357 |
| | 3'UTR | 100% | 43 | 779 | 416 |
| Ī | All | 100% | 0 | 779 | 413 |

Reads viewer

To access the Reads Viewer, click on the locus name link for any locus. The Sample Detail Interface displays in three main sections to the window.



| | Window | Description |
|---|--------------------------|--|
| 1 | Sequence Coverage Viewer | The Sequence Coverage viewer allows the user to navigate around the regions of the gene that were sequenced. Included are the whole gene view histogram, annotation tracks and nucleotide sequence view. |
| 2 | Data panel | The data panel displays info about a base position and/or a specific read, and recaps some of the data tables from the analysis page. |
| 3 | Reads Tool | The reads tool allows the user to visualize individual sequence reads that cross user-specified positions. |

Sequence Coverage Viewer

Sequence Coverage Viewer is further broken down into different sections: The whole gene viewer, the annotation tracks, and the nucleotide sequence viewer.

Whole Gene Viewer

This histogram across the top of the screen echoes the locus histograms from the session and analysis screens. It provides a view of the entire gene being sequenced and allows for basic navigation through the sequence.

The location of exons are denoted by horizontal dark purple bars, while introns are denoted by light purple bars.

Below the exon/intron indicators, stacked horizontal lines signify reads spanning the region.



Annotation Tracks

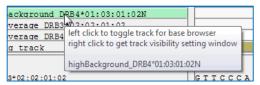
Annotation tracks display under the whole gene view and above the nucleotide viewer. The tracks displayed will vary as needed depending on the locus and genotype. Selected tracks can be browsed using the browser mechanism or the right and left arrow keys on the keyboard.



Tracks will only display as they pertain to the locus selected. Below is a table of possible annotation tracks that may display.

| Track Name | Description | Flag Color |
|--|--|---|
| Variants | Heterozygous positions | Orange/brown |
| MismatchPos_[Allele 1] | Mismatch positions for allele 1 | Red |
| MismatchPos_[Allele 2] | Mismatch positions for allele 2 | Red |
| HighBackGround_[Allele 1] | High background positions and high background in homopolymer for allele 1 | Purple or Light Blue if in homopolymer region |
| HighBackGround_[Allele 2] | High background positions and high background in homopolymer for allele 2 | Purple or Light Blue if in homopolymer region |
| LowCoverage_[Allele 1] | Coverage has dropped below a preset minimum | Green |
| LowCoverage_[Allele 2] | Coverage has dropped below a preset minimum | Green |
| Hetero Positions_[allele name+allele name] | Will display when a comparison sequence is added to the sequence display. Both alleles for comparison are named. | Green |
| Excluded Regions | Displays the regions that have been excluded from analysis. | Pale Yellow |

Hovering over the track names displays a tooltip describing actions that may be taken by right-or left-clicking.

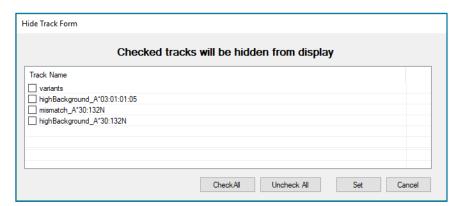


Left-clicking a track name will highlight the track name and make the flags on the track available for browsing via the browser arrows. If no tracks are selected, browser arrows will browse all flagged positions.

If more than one flag applies to a position, the software will split the position. Below, allele 1 displays the flag for mismatch while allele 2 displays the flag for high background in a homopolymer region.



Right-clicking on annotation track name will display the 'Hide Track Form.' User should check the tracks to be HIDDEN, then click 'Set.' Because there must be at least one track displaying, if all tracks are checked, the topmost track on the list will still display.



Nucleotide Sequence Viewer

The consensus Sequence is displayed for each allele next to the sequence for the reference allele. Every matched position displays as a dash in the consensus sequence. Mismatched positions display the consensus base at the mismatch position. Codon position is displayed above the bases.

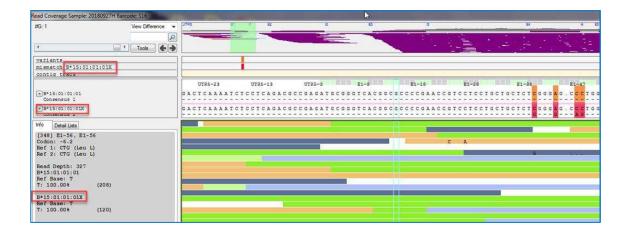
Nucleotides may be shaded in any of the colors orange, purple, light blue, red, or green to correspond to the annotation track flags (see previous entry). The shaded bases in the following illustration are variant positions.



Deletions are represented by single dots in place of the base. If the consensus has a deletion at the same base position, '-' will display to show agreement, just as if it were an actual base. In the illustration below, both reference alleles have deletion locations where the deletions are represented by dots '.'. The corresponding consensus sequences have deletions at the same locations, represented by dashes '-'.

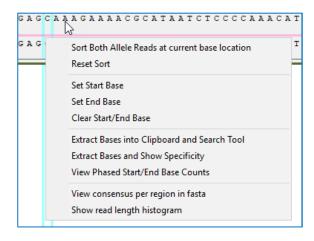


At time the software may make a heterozygous call where the only variant identified is novel, and the typing call results in the same closest matching allele for both the Allele 1 and Allele 2 consensus. In this case, the software will report a heterozygous allele call and the read viewer will display the closest allele sequence with an 'X' appended to the allele name.



Nucleotide Viewer Options

Right-click on the nucleotide viewer and the software displays a number of useful options for deeper sequence analysis.



Sort Both Allele Reads at current base location

Application will show sorted reads by base count at the marked position. This sort can then be reset to original configuration or logged. Selecting 'Log sorted reads' will open a window in Notepad with read name and sequence.

Reset Sort

After viewing reads sorted by base position, "Reset Sort" will re-align to the original alignment. It is necessary to reset the sort prior to sorting alleles at another base location.

Set Start Base

TypeStream Visual allows the user to select multiple base positions by doing the following:

- Right-click in the sequence viewer on the first base you want to include.
- Select Set Start Base.
- Right-click on the last base you want to include.
- Select Set End Base.

When a start base is set, it will appear as a solid line through the nucleotide and reads, whereas the dynamic position indicator appears as an outline.



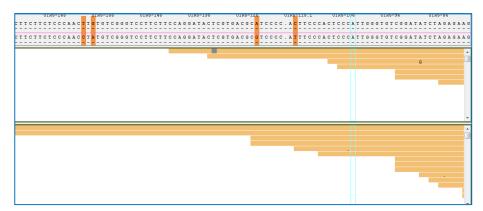
Other reasons to set a start base include:

- Extracting bases to clipboard
- Extracting bases to show specificity
- Getting phased based counts.

Set End Base

Most of the features using "Set Start Base" do not require the user to set an end base. The main reason to do so is to study reads that cross two specific positions of interest.

After setting an end base, the application filters out reads that do not cross both positions. This functionality is helpful when manually reviewing a break in phase or exploring mismatch positions. The reads are sorted by start position as illustrated below.



Clear Start/End Base

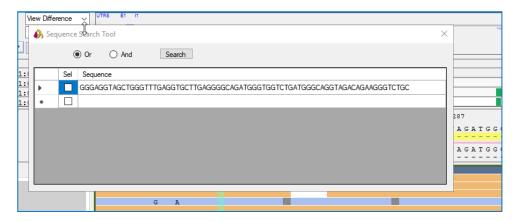
After viewing sorted reads as seen above, using "Clear Start/End Base" will clear the marked positions and return all reads to the original alignment.

Extract Bases onto Clipboard and Search Tool

To extract bases to system clipboard, right-click on the start position and select 'Set Start Base.' Right-click on the desired end position (no need to set an end base) and select 'Extract Bases to Clipboard and Search Tool.' Software copies the base sequence from the set start position to the right-clicked final position and places it on your clipboard.

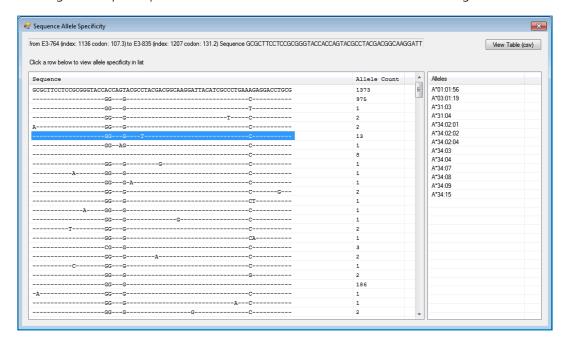
In addition, the application automatically opens the Search Tool and places the sequence on the tool for you. The user may then perform a search or manually add more sequences for a more complex search.

Please be aware that the extracted sequence is from the mapped read, not the original read.



Extract Bases and Show Specificity

Extract bases as described above and select "Extract Bases and Show Specificity." Table displays showing the unique sequences and the alleles that match it in the extracted region.



Data displays in three columns:

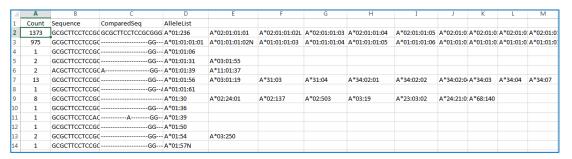
- 1. Sequence the top entry is the extracted sequence. Subsequent entries show all the variant sequences related to the extracted sequence that can be found in the current library
- 2. Allele Count displays the number of alleles in the current library that contain that exact sequence
- 3. Alleles displays the specific alleles that contain the selected sequence.

In the example above, the selected sequence contains five mismatches from the original

extracted sequence. We can see in column two that there are 13 alleles in the library that have that specific sequence. Column three lists each of the 13 alleles.

View Table (.csv)

Clicking the View Table button exports all the data in the Sequence Allele Specificity window to a .csv file which opens automatically in Microsoft Excel.



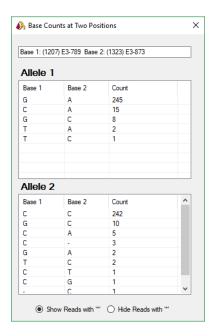
Again, be aware that the extracted sequence is from the mapped read, not the original read.

View Phased Start/End Base Counts

The 'View Phased Start/End Base Counts' tool can be used to confirm the phasing of variants. Some examples:

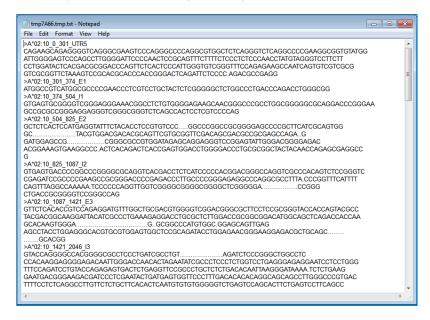
- 1. When System Comments reports that a cis-trans pair has been removed, user can add the removed pair and check the phase of the "flip" positions.
- 2. When a cis-trans is reported, user can check the phase counts to confirm removing one or the other allele.
- 3. For a novel position, user may want to check the phase with surrounding variants to confirm which allele it belongs with.

The tool displays both base positions, the base(s) present at the position for both alleles, and the count of reads that are in phase. Multiple phase count window can be opened simultaneously for comparison.



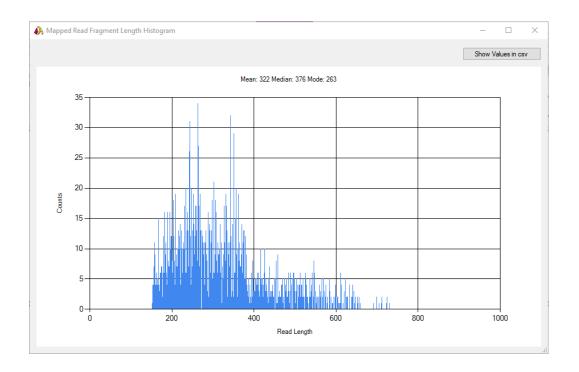
View consensus per region in fasta

Right-click on the sequence few and select "View consensus per region in fasta." Notepad window opens displaying mapped sequence broken out into regions. Allele name and region are clearly marked for each regional sequence.



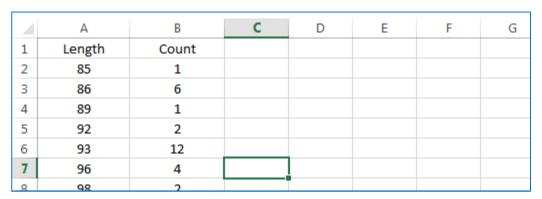
Show Read Fragment Length Histogram

Right-click on the sequence viewer and select "Show read length histogram." A histogram representation of the lengths and their counts for all reads in the locus appears in a separate window displaying a histogram of mapped read fragments. Mean, median, and mode values are also displayed.



Show Values in csv

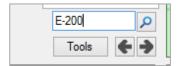
Clicking the button "Show Values in csv" opens a .csv file in Microsoft excel containing the read count values for each read length.



Other Functions in Read Viewer UI

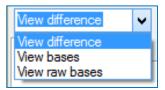
Position Search Tool

Enter position designation to go directly to a position. Can be done cDNA or gDNA format.



View Options

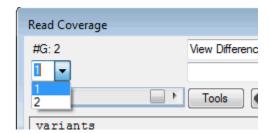
User may select how the reads appear on the reads viewers – view only the variant bases, view all bases, or view raw reads.



If you choose to view raw bases, the reads will not be mapped to the reference sequence, meaning that insertions or deletions have not been added into the sequence in order to force a concordance to a given reference allele. Therefore, a particular base in a particular read may not coincide with the base in the nucleotide viewer.

Genotype Selector

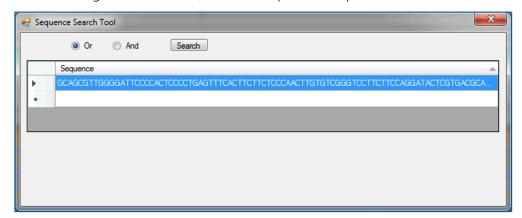
In the case of cis-trans ambiguities, a dropdown selector allows the user to select the particular genotype to display. The number in the corner (#G: 2) indicates how many total genotypes are in the locus.



Sequence Segment Search Tool

Clicking "Tool" button on Reads Coverage window displays tool for searching for specific segments of a sequence. User may input the sequence in one of two ways:

- Type in a sequence manually
- Right-click on a read, obtain its sequence, and paste it into the window.



Click on the second row in the grid to add another sequence to search. Add as many

sequences as needed. Search can be in either of two modes:

- OR application will locate reads and alleles containing any of the sequences
- AND application will locate reads and alleles containing all of the sequences

Results for each search are delivered in a new Notepad window and lists the following:

- Sequence(s)
- Unmapped reads containing the sequence(s)
- Alleles containing the sequence(s)
- Total search time

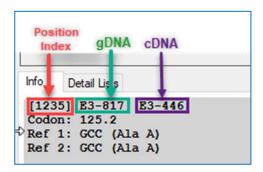
Details panes for base position and/or read information

This panel displays read details or position details for the location over which the mouse is hovering.

Info Tab

The Info tab displays data for reads or for base positions, depending where the mouse is hovering.

The three numbers at the top of the panel represent the position index, gDNA base number, and cDNA base number.



- Position Index The overall reference for base positions from the first upstream position in 5' UTR to the last downstream position in 3' UTR.
- gDNA "Genomic DNA" The position count is continuous, starting with exon 1 (E1) through the remainder of the gene, including 3' UTR; the 5' UTR begins with "-1", at the junction of 5' UTR and E1, and continues upstream with negative numbering.
- cDNA "Complementary DNA" This notation mirrors IMGT in which all introns begin with position "1" and each exon continues numbering from the previous exon.

```
Info
     Detail Lists
[11856] I2-8700, I2-649
Read Depth: 787
DRB3*03:01:03
Ref Base: a
A: 97.41%
                    (414)
G: 2.59%
                   (11)
DRB4*01:03:01:01
Ref Base: A
                    (361)
A: 98.37%
I: 1.36%
                    (5)
G: 0.27%
                   (1)
Read Information:
SY34U:01127:01413
Direction: reverse
Read length: 100
Start position index: 11827
Insertion: 0
Deletion: 1
Mismatch: 0
```

The Info Tab also displays the **read depth** for the combined allele 1 and allele 2 reads. Per allele read count is also broken down by read count per base. Because many reads are assigned to both allele 1 and allele 2, the count per allele may not add up to the total read depth.

The reference, or expected base, is displayed along with all other base represented at that position, with percentages representation.

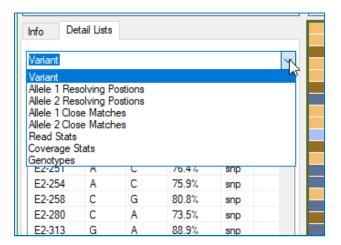
If the mouse cursor is hovering over the reads view panel, Read Information will also display. This includes system-assigned read name, direction, length, start position, and number of insertions, deletions and mismatches positions for the read.

Hover Info

While Positions tab is selected, info data is still visible as a pop-up when hovering over a read. Hover over a base in the sequence viewer displays base data.

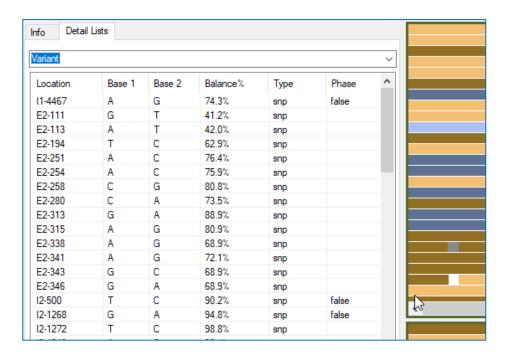
Detail Lists Tab

The details tab displays variant, close matches, resolving positions, and statistics and reflects the data displayed on the Analysis page.



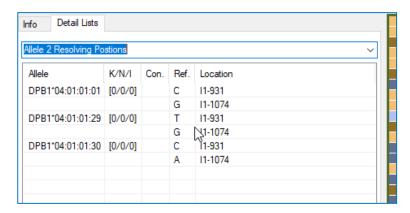
Variant

A subset of the information available on the Variant tab of the Analysis Panel, the Variant list displays position location, base 1, base 2, balance %, and also displays the Type of variant. In most cases the variant will be a single nucleotide polymorphism (snp) but may also indicate if the variant is a deletion (del).



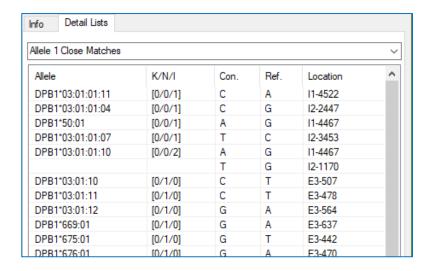
Allele 1 (and 2) Resolving Positions

This information will match the resolving position information from Analysis Panel and reflects the differences in consensus and reference base.



Allele 1 (and 2) Close Matches

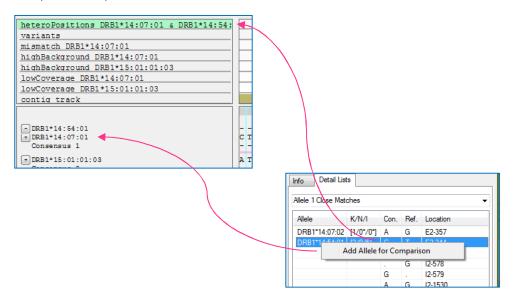
Lists the Closely Matches alleles, their mismatch counts, consensus and reference bases, and location of the resolving position.



Clicking on any of the base positions on the Resolving Positions or Close Matches tab will scroll the reads view, whole gene view and nucleotide view to the selected position.

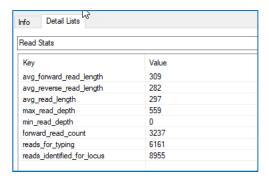
Add directly to allele comparator

In either of the close match or resolving positions list, right-clicking on the ambiguous allele names allows the user to add that allele directly to the comparator. See section below, "Setting Comparison Sequences" for more detail.



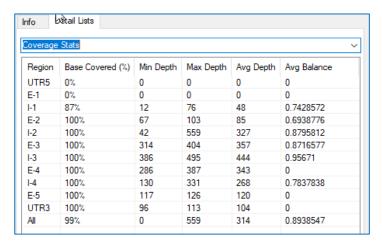
Read Stats

This chart expands on Mapped Read Metrics from Analysis Panel to display additional metrics on read depth and reads identified for locus.



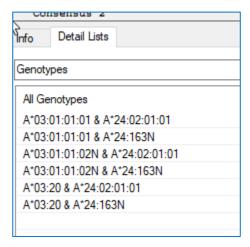
Coverage Stats

Coverage Stats echoes those from the Statistic tab of the Analysis Panel.



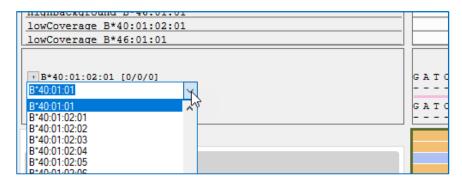
Genotypes List

On reads view, Details Lists, one option is Genotypes. All permutations of allele pairings based on top types plus ambiguities display on this list.

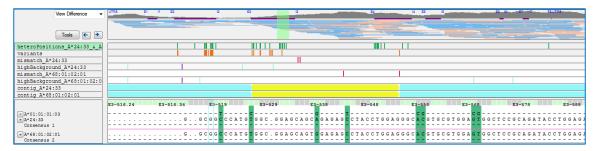


Setting Comparison Sequences.

This functionality allows the addition of one or more sequences for comparison study. To select an allele, click the next to the allele for which you want to do a comparison and select the allele from the dropdown list.



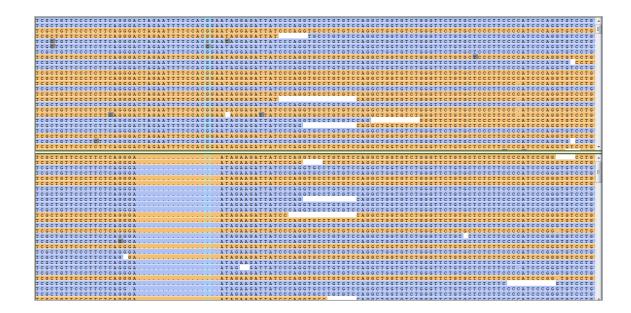
Selected allele name displays above for allele 1 or below for allele 2. Annotation track is added for the comparison sequence. Annotation track flags are shaded green, as are the heterozygous positions on the nucleotide viewer.



User may add multiple comparison alleles for each of Allele 1 and Allele 2.

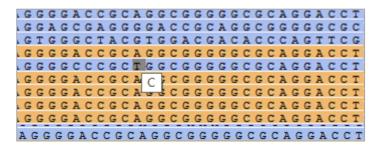
Reads viewer in detail

The reads subview allows users to visualize individual sequence reads. Reads display only for the selected position and are separated by allele. Each of the allele panels scrolls separately.



Insertion Base

The location of insertion bases is displayed with a light gray shading over the previous base. Hovering over the gray shading displays the insertion.



Reads Viewer Options

Right-clicking on the reads viewer offers the user additional functionality from that in the Nucleotide Viewer.



New in v2.0

Modify read colors

Read colors have been set for both Ion S5 and Illumina samples. Beginning in TypeStream Visual 2.0, the user is able to set reads, insertions and deletion to a shade of their own choosing.

Default Read Colors for Ion S5 files

Reads from Ion S5 sequencers display with the following default coloring for reads.

- Dark brown = cross allele 1 & 2 forward reads
- Light brown = single forward reads
- Light blue = single reverse reads
- Dark blue = cross allele 1 & 2 reverse reads

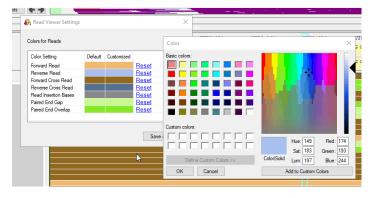
Default Read Colors for MiSeq files

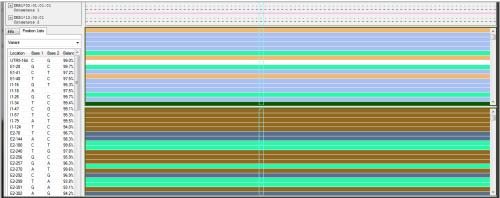
MiSeg paired-end reads display with additional default coloring for reads.

- Dark green = overlapping region in paired-end reads
- Light green = gap between paired-end reads
- Dark brown = cross allele 1 & 2 forward reads
- Light brown = single forward reads
- Light blue = single reverse reads
- Dark blue = cross allele 1 & 2 reverse reads

New Read Colors Available

Right-click within the reads view and select 'Modify Read Colors.' Click on the color bar under 'Customized' for the read type you want to change. Select standard colors or customize your own.





Reset all read colors

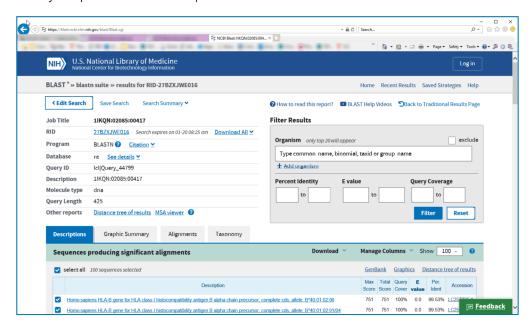
If you then feel you've made a terrible mistake, right-click on reads and select 'Reset all read colors." They will return to defaults.

Extract base into clipboard and Search Tool

Like the functionality of the same name in the Nucleotide Sequence Viewer, a specified sequence will be put on the clipboard and into the search tool. You must use the nucleotide viewer to set the start base and to reset the start/end bases. After the start base has been chosen, you may click the last position from within the reads viewer.

Extract bases into clipboard and blast it online

After setting start base, find last base and select this option. The application with open a browser window that takes the user to NCBI (National Center for Biotechnology Information) website and opens a job request. Web page displays the job request number and is available for any deeper dive into the sequence data.



Blast this read online

This is similar to the previous functional option, but all the user need do is to point the cursor at a particular read he wants to view, then right-click and select this option. The application will take you to the NCBI web page as before.

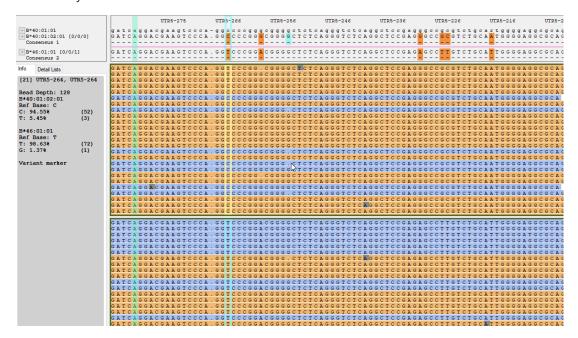
Show Read Details

This options opens a window in notepad with details, including software-generated read name, start and stop positions, sequence, mismatch, insertion and deletion counts.

The read sequence shows the complete sequence as it emerged from the sequencer. The mapped read sequence has had insertions and deletions added in order to match the selected reference allele.

Show sorted reads by base count at current base position

To use this option, set the view option to 'bases' so that all bases can be seen. At the position of interest, right-click and select this option. The example below was sorted at position index 21 and is highlighted. In allele 1 it can be seen that the reads containing the 'T' base are listed first, followed by read with 'C' base. Allele 2 will have the reads sorted in the same order.



Reset sorted read display

When user is finished, this option will set the reads into the original alignment.

Log sorted reads

If the user would like a log of the reads sorted by base count at the position of interest, select this option prior to resetting. The application will open a text file in Notepad with a complete

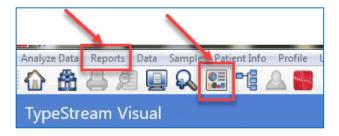
log of the reads sorted at that position.

The last format View Help
[55] C. 10.L TSV/data Jauniel VMS/Daniel VMS/ 3668801 - aa16 - 4aab - 825 - 538750e 884 \ mappedReads . bam
[167] C. 10.L TSV/data Jauniel VMS/Daniel VMS/ 3668801 - aa16 - 4aab - 825 - 538750e 884 \ mappedReads . bam
[167] C. 10.L TSV/data Jauniel VMS/Daniel VMS/ 3668801 - aa16 - 4aab - 825 - 538750e 884 \ mappedReads . bam
[167] C. 10.L TSV/data Jauniel VMS/Daniel VMS/ 3668801 - aa16 - 4aab - 825 - 538750e 884 \ mappedReads . bam
[167] C. 10.L TSV/data Jauniel VMS/Daniel VMS/ 3668801 - aa16 - 4aab - 825 - 538750e 884 \ mappedReads . bam
[167] C. 10.L TSV/data Jauniel VMS/Daniel VMS/ 3668801 - aa16 - 4aab - 825 - 538750e 884 \ mappedReads . bam
[167] C. 10.L TSV/data Jauniel VMS/Daniel VMS/ 3668801 - aa16 - 4aab - 825 - 538750e 884 \ mappedReads . bam
[167] C. 10.L TSV/data Jauniel VMS/Daniel VMS/ 3668801 - aa16 - 4aab - 825 - 538750e 884 \ mappedReads . bam
[167] C. 10.L TSV/data Jauniel VMS/Daniel VMS/Dan

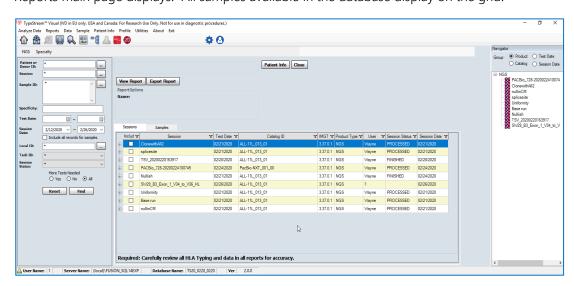


Reports

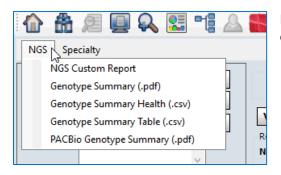
From any page, click 'Reports' on the menu bar or click the Reports icon on the toolbar.



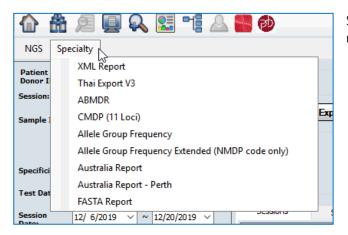
Reports main page displays. All samples available in the database display on the grid.



There are two categories of reports.



Basic reports for all Ion S5, MiSeq, or PACBio data.

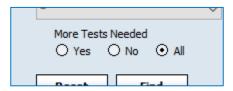


Specialty reports for specific data retrieval.



New in v2.0

For any report, the user has the option of flagging samples for which More Tests are needed. There are three options for inclusion.



They will impact the grid in the following way:

- "Yes" all samples from selected sessions that were marked "More Test" during analysis will be displayed in the grid.
- "No" all samples from selected sessions that were marked "More Test" during analysis will NOT be displayed in the grid.
- "All" all samples from selected session will be displayed in the grid irrespective of being marked for more testing.

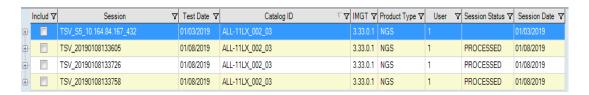
User then selects sessions/samples for inclusion in the reports in the usual way.

Basic Reports

Genotype Summary .pdf

To create a PDF report, click NGS and select Genotype Summary (.pdf).

1. Select the sessions you want to include in the report.



2. Click View Report

The pdf is created. The report displays the following:

- Sample ID, barcode, session name
- TypeStream Visual version, IMGT library version, catalog used
- Analysis and confirmation date and user
- Path to raw file
- Final assignment as saved by user
- Genotyping (including ambiguities)
- Statistics per barcode and locus
- Analysis parameters
- System and user comments

Clicking "Export Report" from the reports page will bypass the preview stage and directly open a navigation page where you may name and save your report, either in the file path set in General Settings or in a separate location of your choosing.

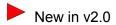
Genotype Summary Table .csv

To create a Genotype Summary .csv report, click NGS and select Genotype Summary Table (.csv).

- Select sessions from session grid.
- Click Export Report

CSV Report is created. You will be asked to enter a report name and then save. You have the option to browse to a different folder to save the report.

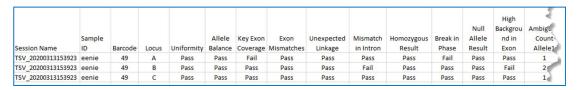
- Final assignment displays with the number of fields selected, as well as in full nomenclature.
- Session name, Sample ID barcode, Locus
- K/N/I values per allele
- Name and date for analysis and confirmation
- Number of ambiguities
- Possible allele assignment and g/l string
- Final assignment definition



User comments display for every locus

Genotype Summary Health .csv

The Genotype Summary Health report (.csv) is a compilation of the health statistics from the Coverage Stats and Health Stats tabs on the analysis page.



| High ckgrou ad in Exon | Ambiguity Count Allele1 | High Background Count Allele1 | High BackGround Non Homopolymer Count Allele1 | Ambiguity Count Allele2 | High Background Count Allele2 | High BackGround Non Homopolymer Count Allele2 | Exon 2 Min Depth | Exon 2 Max Depth | Exon 3 Min Depth | Exon 3 Max Depth | Exon 4 Min Depth | Exon 4 Min Depth |
|---------------------------------|-------------------------------|--|---|-------------------------------|--|---|------------------------|------------------------|------------------------|------------------------|------------------------|------------------------|
| Pass | 1 | 4 | 4 | 1 | 6 | 4 | 44 | 133 | 81 | 172 | 193 | 330 |
| Fail | 2 | 7 | 7 | 1 | 8 | 6 | 60 | 124 | 89 | 207 | 226 | 325 |
| Pass | 1 | 8 | 6 | 1 | 8 | 7 | 80 | 163 | 90 | 211 | 310 | 418 |

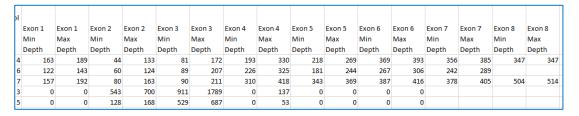


New in v2.0

User may include Non-Key Exons by checking the checkbox prior to exporting the report.



When this is selected, report will include Min and Max Depth columns for all exons.



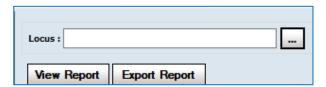
NGS Custom Report

User may create a customized report to suit the needs of the lab. TypeStream Visual can keep numerous uniquely-named report templates ready for use at any time. Data for inclusion may be selected individually or by groups Genotyping, Session Information, and Patient Information.



New in v2.0

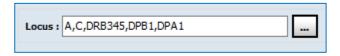
For NGS Custom reports only, the user has the ability to select which loci to include in the report. After selecting NGS Custom report from the file menu, the screen has an addition text box and search button just above the 'View Report' button.



Clicking the search button brings up the Locus selection screen.



Select the loci you would like to include and click OK. The selected loci will appear in the Locus: panel.



If this field is left blank, the software defaults to including all loci in the report.



Final typing information will display in a grid format similar to that of the Genotype Summary Report (.pdf).

| Final Ass | Final Assignment: | | | | | | | |
|-----------|---|---|-----------|-----------------------|----------------|---|--|--|
| Locus | Allele Assignment | Final Assignment | Sero | Saved By | Confirmed By | User Comments | | |
| A | A*02:10 A*11:02:01 | A*02:10 A*11:02:01 | A210 A11 | Daniel, 03/17/2020 | TJ,03/17/2020 | | | |
| В | B*40:01:02:01 B*46:01:01/B*40:01:02:04 B*46:01:01 | B*40:01:02:01/40:01:02:04 B*46:01:01 | B60 B46 | Daniel, 03/17/2020 | TJ, 03/17/2020 | | | |
| С | C*07:02:01:15 C*08:01:01:01 | C*07:02:01:15 C*08:01:01:01 | Cw7 Cw8 | Daniel, 03/17/2020 | TJ, 03/17/2020 | | | |
| DRB1 | DRB1*08:03:02:01 DRB1*09:01:02:01/DRB1*08:03:02:02 DRB1*09:01:02:01 | DRB1*08:03:02 DRB1*09:01:02 | DRS DR9 | Daniel, 03/17/2020 | TJ,03/17/2020 | | | |
| DRB345 | DRB4*01:03:02 DRB4*01:03:02 | DRB4*01:03:02 DRB4*01:03:02 | DR53 DR53 | Daniel, 03/17/2020 | TJ, 03/17/2020 | | | |
| DQB1 | DQB1*03:03:02:02 DQB1*06:01:01:01/DQB1*03:398 DOB1*06:01:01:01 | DQB1*03:03:02/03:398 DQB1*06:01:01 | DQ9 DQ6 | Daniel, 03/17/2020 | TJ,03/17/2020 | | | |
| DPB1 | DPB1+135:01 DPB1+834:01 | DPB1*135:01 DPB1*834:01 | DPw- DPw- | Daniel, 03/17/2020 | | Two or more variants cannot be phased Mismatch(es) in an intron. Two or more variants cannot be phased Mismatch(es) in an intron. | | |

PACBio Genotype Summary .pdf

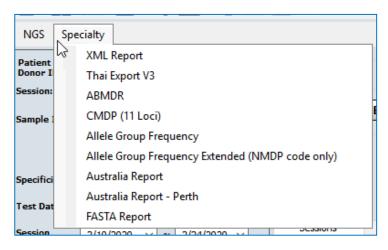
When this option is selected from the dropdown, only PACBio sessions will display on the screen for selection.

See section 'Genotype Summary.pdf' above for the description of the complete functionality for this report.

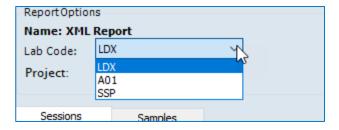
Specialty Reports

Genotype Summary XML Report

To create an XML report, click Specialty and select XML Report.



Select the desired Lab Code from the dropdown.



Select sessions to include as explained above.

Click Export Report

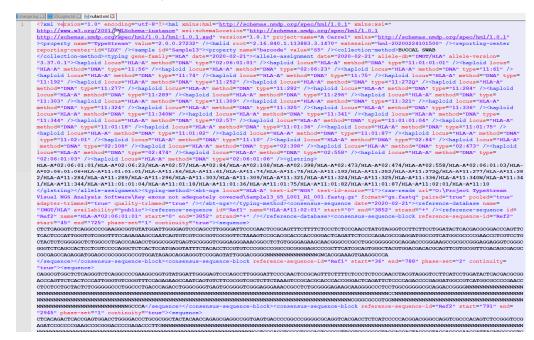
The XML report is created. You will be asked to enter a report name and then save. You have the option to browse to a different folder to save the report.

Please note that session must be **saved** with a final assigned type before the XML Report (.xml) can be run.

The illustration below shows the first part of the .xml file displayed in Notepad ++. Schemas are clearly displayed along with Project Name, sample name and barcode, name and version number of TypeStream Visual application, IMGT library version used, and additional data as needed.

Please note the following:

- 1. Reporting center ID will display as three digits. If actual lab code is longer, it will be truncated. If the actual lab code is short, the remainder will be filled in by trailing '0's.
- 2. If collected method is not included in the original session information, 'BUCCAL SWAB' will be inserted by default.



CMDP (11 Loci) Specialty Report

To create a CMDP (Chinese Marrow Donor Program) specialty report, from the reports page

select Specialty and select "CMDP (11 loci)." Select session(s) to include as explained above.

Click Export Report. Report is created in Microsoft Excel format. You will be asked to enter a report name and then save. You have the option to browse to a different folder to save the report.

CMDP Specialty report contains the following per locus/sample:

- Sample name
- Assigned allele code
- Possible allele pairs
- Code definition
- Assigned serology
- Assigned allele pairs
- User who approved and confirmed the locus and date
- Resolution
- Locus and sample user comments

Note that "Resolution" column is blank by default. User may manually fill in the resolution value and save.

Australia Specialty Report

To create Australia Specialty Report, select Specialty and Select Australia Report. Select session(s) to include as explained above. Click Export Report.

- A separate .csv report will be generated for each session, irrespective of the number selected.
- Each report title will follow the naming convention "TSVExport_[session name]_[date].csv"
- Final genotype and final allele code will be displayed without locus designation or "*" and will display the selected fields only. For DRB345, display shall be "3*xx.xx," "4*xx.xx," and "5*xx.xx" respectively.
- It is recommended to open this report in a text reader, such as Notepad or Notepad++.
- If you want to make adjustments and rerun the report, be aware that the it will overwrite the first copy, if rerun on the same date. To keep both copies, rename the first before running the second.
- Australia Specialty report contains the following per locus/sample:

Session Name Sample ID Patient ID Barcode

Locus Analysis date and user

Locus User comments Allele Code Assignment for each allele

Final assignment for Confirmation date and user

each allele Overall user comments

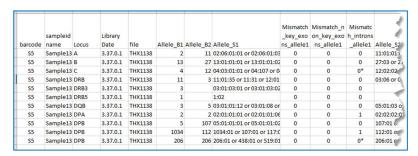


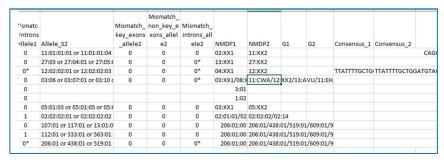
Australia Report - Perth

To create Australia Report-Perth, select Specialty and Select Australia Report-Perth. Select session(s) to include as explained above. Click Export Report.

- A separate .csv report will be generated for each session, irrespective of the number selected.
- Each report title will follow the naming convention "AustraliReportPerth_TSVExport_[session name]_[date].csv"
- Display Allele 1 first digit for Allele_B1 column and Allele 2 first digit for Allele_B2 column.
- Display Allele 1 possible allele pairs for Allele_S1 and Allele 2 possible allele pairs for Allele_S2.

Related to the Australia Report, in the Perth report each row represents a genotype for a sample. If the sample has two genotypes, each row has a genotype row. If either Consensus_1 or Consensus_2 contains "N" value for a base that is not covered, the "N" is replaced with a space.

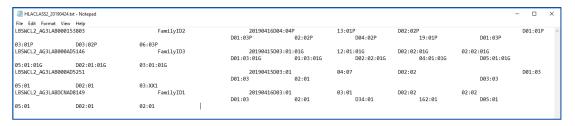




Thai Export V3 Specialty Report

Thai specialty report exports data for a single sample or multiple samples into a text file. Each sample occupies a single row in the file. The first 'field' indicates a standard descriptor with merged metadata following.





In the example above, find the following:

```
"LBSWCL1-AG3" for class I and "LBSWCL2-AG3" for class II
```

First three letters of lab code or displays '000' if none

First three letters of DCN as displayed in sample management window or displays '000' if none

Sample ID

Family ID

Analysis date – "20190416" in example.

Allele code for all Class I or Class II alleles with constant "D" as separator for each locus.

NOTE: File name is auto-generated by the software. Care must be taken not to over-write a file saved on the same day.

ABMDR Specialty Report

To create an ABMDR specialty report, from the reports page select Specialty and select "ABMDR." Select session(s) to include as explained above.

Click Export Report. Report is created in .xml format. You will be asked to enter a report name and then save. You have the option to browse to a different folder to save the report.

To be included in this report, samples must be saved with final allele code.

```
U<hml version="0.2">project name="LAB"> <reporting-center code="labcode"/>
     Sample center-code="090" id="sampleid";
     -Cinterpretation date="20190109">
      <haploid locus="A" method="D" type="03:01:01:01"/>
      <haploid locus="A" method="D" type="03:01:01:01"/>
      <haploid locus="BPR" method="D" type="53:01P"/>
      <haploid locus="BPR" method="D" type="53:01P"/>
      <haploid locus="C" method="D" type="04:01:01:11/04:01:01:14"/>
      <haploid locus="C" method="D" type="04:01:01:11/04:01:01:14"/>
      <haploid locus="DPA1" method="D" type="01:03:01G"/>
      <haploid locus="DPA1" method="D" type="02:01:01G"/>
      <haploid locus="DPB1" method="D" type="01:01:01:01/01:01:01:02/01:01:01:03"/>
      <haploid locus="DPB1" method="D" type="02:01:02:08"/>
      chaploid locus="DQA1" method="D" type="01:02:01:03"/>
chaploid locus="DQA1" method="D" type="01:03:01:02"/>
16
      <haploid locus="DQB1" method="D" type="03:BGCWT"/>
      <haploid locus="DQB1" method="D" type="12:XX"/>
      <haploid locus="DRB1" method="D" type="11:01:02"/>
19
20
      <haploid locus="DRB1" method="D" type="13:01:01:01"/>
      <haploid locus="DRB3" method="D" type="01:01:02:02"/>
      <haploid locus="DRB3" method="D" type="02:02:01:02"/>
      </interpretation>
      </hla-typing></sample>
     L</project> </hml>
```

The example above contains the following:

"LAB" – hard-coded project name

Sample Center-code – hard-coded to "090"

Sample ID as existed or entered when session was created.

The date the sample was analyzed ("interpretation").

Locus order - A, B, C, DPA1, DPB1, DQA1, DQB1, DRB1, DRB345

Allele code assignments.

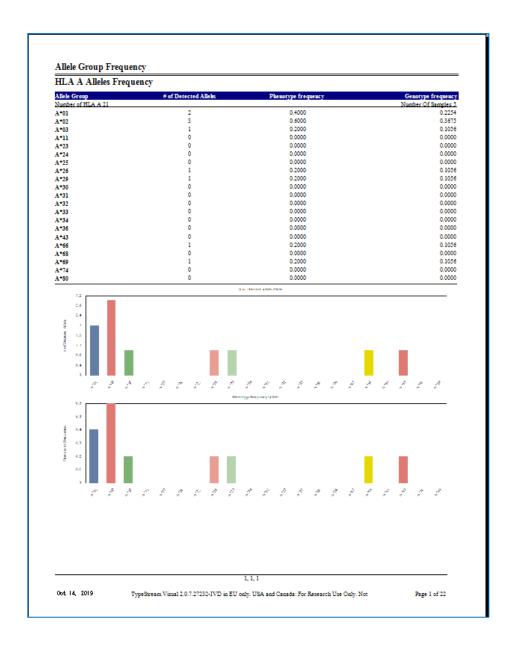
For alleles whose code is represented by "XX1" (e.g.), software shall include only "XX" in this report and leave off the numeral.

B locus display as "BPR"



Allele Group Frequency Report

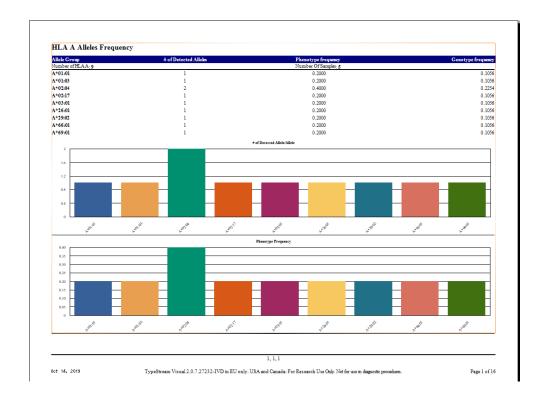
This option generates a .pdf report representing the frequency of each of the loci at the two-field level. Graphical display represents the number of detected alleles, Phenotype Frequency, and Genotype Frequency.





Allele Group Frequency Extended (NMDP code only)

This option generates a .pdf report which extends the functionality of the Allele Group Frequency Report to NMDP code distribution only. Graphical display represents the number of detected alleles, Phenotype Frequency, and Genotype Frequency.





New in v2.0

FASTA Report

FASTA report will generate sequences for all samples from a session in .fasta format.



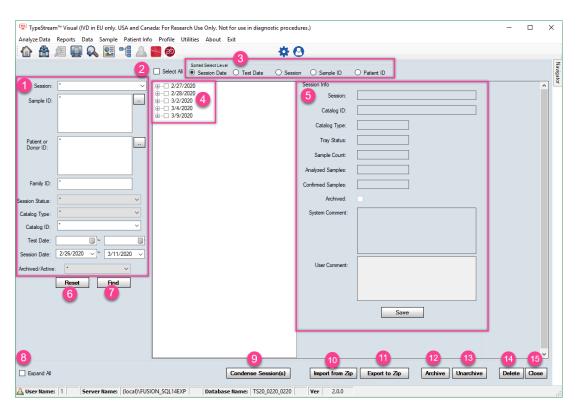
Data Management

To manage your data at the session level, use the Data option from the TypeStream Visual main menu. When you select the Data main menu, the Manage Data window is displayed. From this window the user may manage session files, delete or archive sessions.

Manage Data Window

It is possible to search for specific sessions based on multiple criteria:

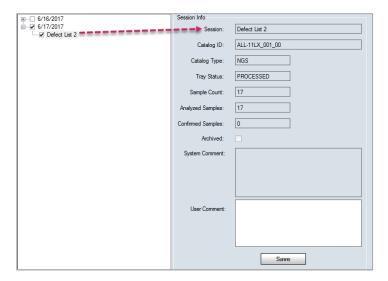
- Session name
- Sample ID
- Patient/Donor ID
- Family ID
- Session Status
- Catalog Type
- Catalog ID
- Test Date
- Session Date
- Archival status



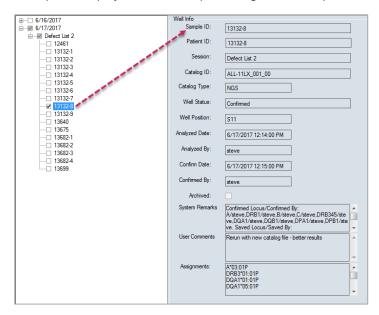
These criteria may be used alone or in combination with others.

| | Item | Description |
|----|-----------------------|---|
| 1 | Search criteria panel | From this panel user may select a single criterion or a combination of criteria upon which to perform a search. |
| 2 | Select All | Will select all sessions in directory tree |
| 3 | Sorted Select Level | Sessions will be sorted per the selected radio button option. Session date (shown above) is the default. |
| 4 | Sessions panel | Search results are returned here in a tree-structured hierarchy. |
| 5 | Session Info | When a specific session is selected in the tree, details of that session display here. |
| 6 | Reset | This button resets all search criteria |
| 7 | Find | This button executes the search based on the selected criteria |
| 8 | Expand All | Expands all the nodes in the hierarchical tree |
| 9 | Condense Session(s) | Allows the user to condense the size of files to save drive space |
| 10 | Import from Zip | Will import a zipped session file to the database |
| 11 | Export to Zip | Will export selected file(s) into a zip file which can be saved to any location. |
| 12 | Archive | This will archive any session selected |
| 13 | Unarchive | This will make active any archived session. |
| 14 | Delete | Will delete the selected session or sample |
| 15 | Close | Closes the data management window |

Select a date and expand the tree structure to display sessions for that date. Select a session and the right-hand panel displays information pertaining to the session.



Expand the tree structure to display samples for that session. Select a session and the right-hand panel displays information pertaining to the sample.



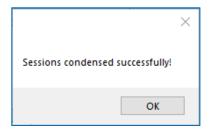


Condense Session(s)

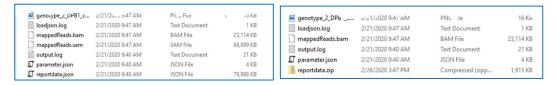
A new feature to help conserve space on your drives, Condense Session allows the user to condense a single or multiple selected sessions.



To use, select a session from the Data Management window and click the Condense Session(s) button. After a moment, a message will display that the session condensed successfully.



During the condensing process, the software takes the two most data-heavy files for each barcode (mappedReads.sam and reportdata.json) and creates a .zip file. In a current example, TypeStream Visual condensed a total 148,887 KB down to a 1,915 KB zip file.

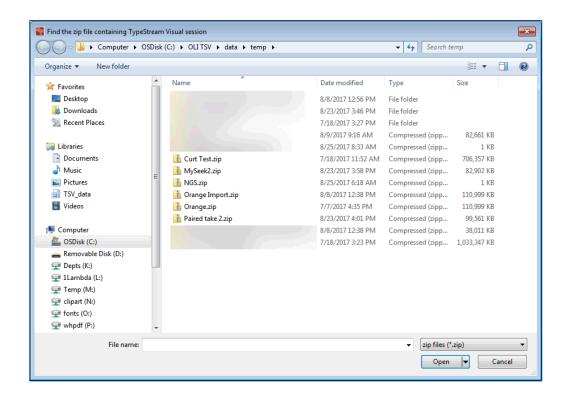


If the user navigates to the read viewer of a condensed session, the software unzips and restores the reportdata.json and mappedReads.sam files and the .zip file is deleted.

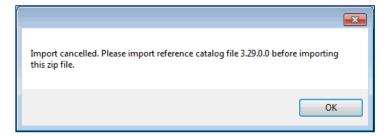
Note – User must have WinZip installed on their computer for this feature to work.

Import Session

On clicking 'Import from Zip' button, software will open a navigation window to the default folder C:\OLI TSV\data\temp. (If exported files have been saved to a different location, user may navigate to that location. This path can be set by navigating to Utilities \rightarrow General Settings \rightarrow Paths and changing the path for 'Temp'.) Select a session (only one session at a time may be imported) and click Open.

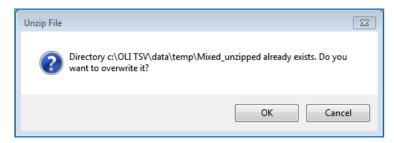


Database must contain the library used for the original analysis. If it is not in the database, the software will display a message like the following:



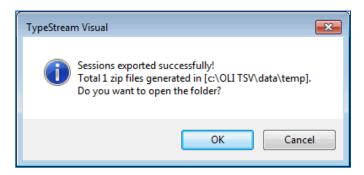
If this happens, simply import the correct library file and perform the import again.

On occasion, you may need to import a session that has the same session name as one previously imported, though it may not be in your active database. In this case you will get a message saying that the unzipped file already exists. What really exists, however is a placeholder in the temp folder and not an actual file. Therefore, you may click 'OK' on the message below without overwriting an analyzed file.



Export Session

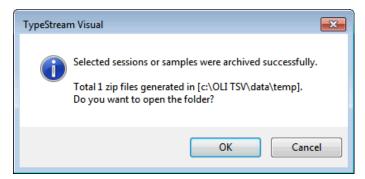
To export a session, select desired session(s) by clicking 'Export to Zip' button. The zipped file is stored by default to C:\OLI TSV\data\temp. When completed, the software will offer to open the folder location.



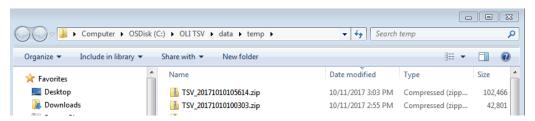
Archive and Unarchive Sessions

The user has the option of archiving an entire session or a subset of samples within the session. Select a session by check the checkbox next to the session name. Click 'Archive' and the software will create a zipped file of the session.

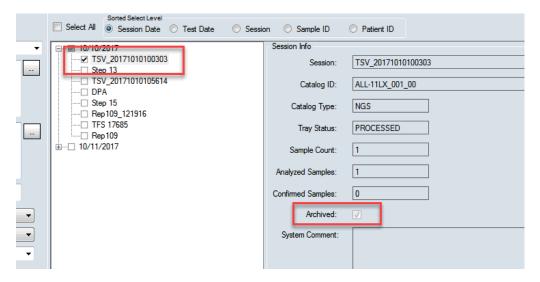
When finished, you will receive a confirmation that the archive was successful and an offer to open the folder to view the file.



On clicking OK, folder opens to display zipped file.

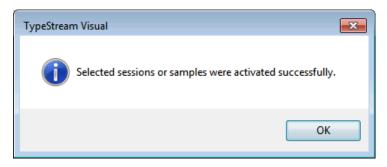


Although zipped files will no longer display in the Navigator and cannot be viewed, they will still display in the Data Management window. When an archived session is selected, it displays as any other session, but the 'Archived' check box will be checked and grayed out.



If at a future point the user wants to view or reanalyze an archived session, the unarchive process is the just the reverse of the archive process.

Check the archived session and click 'Unarchive.' When process is complete a message of successful activation will be displayed.



Delete Session

Any session in the active database may be deleted using the Delete function in Data Management. Select session(s) and click Delete. A confirmation message will confirm that these sessions are to be deleted.

When naming sessions, please be aware of the following: Although local databases do not cross-reference session names, all session folders are stored in the same location − C:\OLI TSV\data\session\NGS by default, though this can be modified by navigating to Utilities → General Settings → Paths. If there are duplicate session names coming from different databases, samples from both sessions will be stored in the same folder.

Therefore, when a 'Delete Session' is about to be executed, the software looks first into the session folder and only deletes the samples associated with session in the active database, leaving the rest and also leaving the session folder.

Example: DB-Alpha and DB-Beta both have a session named 'Test4'.

- On DB-Alpha, 'Test4' contains samples 'RakB', 'Toks', 'Ahm', and 'Est'.
- On DB-Beta, 'Test4' contains samples 'AnLiu', 'Zelm', 'Est', and 'RobS'.
- User is working on DB-Beta and requests to delete 'Test4.'

- Software will look at the samples in the folder and delete 'AnLiu', 'Zelm', 'Est', and 'RobS'.
- Note that because there was also a duplicate sample name, 'Est', it was deleted and will not be available for use by DB-Alpha.
- Similarly, if all sample names were the same for both databases, the software would delete all samples and the session folder.

Sample Management

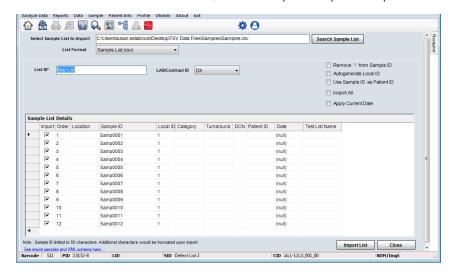
In TypeStream Visual, sample lists are an easy way to input a large list of sample IDs and other sample information into the database for use in analysis sessions. Sample lists may be in .xlm, .csv or .txt file format. From the Sample List Import menu, you can import sample lists or edit sample lists prior to importation.

NOTE: Please verify all data you import as HLA TypeStream performs minimal data validation upon import.

Importing Sample Lists

Sample lists are an easy way to input an extended list of sample ID's and other sample information into the database for use in analysis sessions.

1. From the Main Menu, select Sample > Import Sample List.



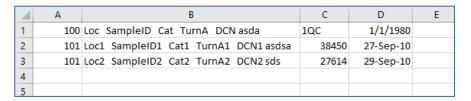
- 2. Click the Search Sample List button; browse for the sample list to be imported; and click Open.
- 3. Type a name in the List ID field, and, if necessary, select a Lab code or Contact ID from the drop-down list.
- 4. Confirm sample information and edit if needed.
- 5. Click to clear the check boxes of any samples you do not want to import.
- 6. Click Import List to import the selected sample lists.
- 7. Click Close to return to the Main Menu.

Three list formats are accepted in TypeStream Visual:

1. Sample List (.csv)

| \square | Α | В | С | D | Е |
|-----------|---------|---------|---------|------|---|
| 1 | local | sample | patient | Date | |
| 2 | B201651 | B201651 | 20743 | | |
| 3 | | | | | |
| 4 | | | | | |

2. Sample List with Packlist (.csv)



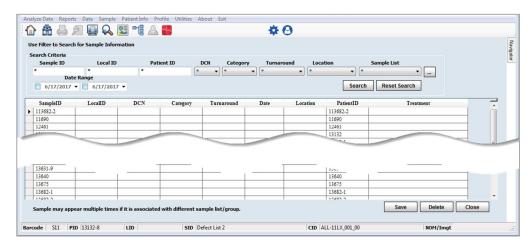
3. Sample List: XML Format

```
SampleList xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance">
       <Patient ID="100"
         <Samples>
           <Sample ID="100001">
            <Date>2009-01-01
            <LocalID xsi:nil="true" />
           </sample>
           <Sample ID="100002">
 8
            <Date>2009-02-01
            <LocalID xsi:nil="true" />
           </Sample>
           <Sample ID="100003">
            <Date>2009-03-01
13
            <LocalID xsi:nil="true" />
14
           </Sample>
           <Sample ID="100004">
16
            <Date>2009-04-01</Date>
18
            <LocalID xsi:nil="true" />
           </sample>
19
           <Sample ID="100005">
20
21
22
            <Date>2009-05-01</Date>
             <LocalID xsi:nil="true" />
23
           </sample>
           <Sample ID="100006">
24
             <Date>2009-06-01
25
26
             <LocalID xsi:nil="true" />
27
           </Sample>
28
           <Sample ID="100007">
             <Date>2009-07-01
29
30
             <LocalID>24</LocalID>
           </Sample>
32
           <Sample ID="100008">
             <Date>2009-08-01
34
             <LocalID>25</LocalID>
           </Sample>
36
         </Samples>
       </Patient>
38
       <Patient ID="10092">
39
         <Samples xsi:nil="true" />
40
       </Patient>
      </SampleList>
```

Viewing and Editing Sample Information

Sample information can be edited but associated patient IDs cannot—only new patient IDs can be added.

1. From the Main Menu, select Sample > Manage Sample Info.



- 2. Use the filters to find samples and click View Sample.
 - a. Wildcards can be used in the Sample ID field to widen the results.
- 3. Edit sample information.
 - a. You can rename a sample by modifying the name in the Sample ID field. Sample IDs are listed alphanumerically, with all IDs beginning with numbers listed first.
- 4. Click Save to save. Or, click Delete to delete the sample.
- 5. Click Close to return to the Main Menu.
 - a. You are not allowed to delete a sample that is part of a session that has already been analyzed.



Patient Management

Patient Information

TypeStream Visual can store patient information and associate sample IDs with patients and donors. You can store all typing and screening information in one location for each patient.

NOTE: Please verify all data you import. TypeStream Visual performs minimal data validation during import operations.

Importing Patient/Donor Lists

After creating a Patient/Donor List, you can import the information into TypeStream Visual.

1. From the Main Menu, select Patient Info > Import Patient List. The Patient Import window displays.



- 2. Select the check box in the Import column for each patient you want to import.
- 3. Click the Import button to import checked patients.
- 4. Click Close to return to the main menu.

The complete list of column headings for the Patient/Donor template is as follows:

| Patient ID | Category Grp | Family ID | First Name | Middle Name | Last Name | SSN |
|------------|-------------------------|----------------------|----------------------|--------------------------|--------------------------|-------------------------|
| DOB | Gender | Ethnicity | Address | City | State | Region |
| Country | ZipCode | Email | Phone | Work Phone | Cellular | FAX |
| Employer | Spouse Name | Spouse Blood Type | Emergency Contact | Emergency Tel | DCN | Hospital Name |
| Division | Blood Type | Disease | Rh Blood Type | Patient/Donor Flag | Associated Sample IDs | Associated Donor IDs |
| HLA1_A | HLA2_A | HLA1_B | HLA2_B | SHLA1_Bw | SHLA2_Bw | HLA1_C |
| HLA2_C | HLA1_DRB1 | HLA2_DRB1 | HLA1_DRB3 | HLA2_DRB3 | HLA1_DRB4 | HLA2_DRB4 |
| HLA1_DRB5 | HLA2_DRB5 | HLA1_DQB1 | HLA2_DQB1 | HLA1_DQA1 | HLA1_DQA1 | HLA1_DPB1 |
| HLA2_DPB1 | HLA1_DPA1 | HLA2_DPA1 | HLA1_MICA | HLA2_MICA | HLA1_MICB | HLA2_MICB |
| HLA_KIR | ClassI_AbSpec | ClassII_AbSpec | MIC_AbSpec | Unacceptable Antigens | Acceptable Antigens | Notes |
| SHLA1_A | SHLA2_A | SHLA1_B | SHLA2_B | SHLA1_Cw | SHLA2_Cw | SHLA1_DR |
| SHLA2_DR | SHLA1_DR345 | SHLA2_DR345 | Shla1_dQ | SHLA2_DQ | SHLA1_DP | SHLA2_DP |
| Donor Type | Include in Donor PRA | Status | Transplant Type | From Other Facility | Donor Groups | PRA Donor Groups |

NOTE: The TypeStream Visual system checks the patient/donor lists you attempt to import to verify that all characters contained in the data are supported by TypeStream. If your list contains unsupported characters, a warning message is displayed and the list is not imported.

Newly imported patient records display alleles in the new nomenclature format. Existing patient records display alleles with the existing allele format

Patient/Donor Management

The Patient/Donor Management function allows you to manage one record at a time via the Patient/Donor Information screen. From here you can do these operations and more:

- Add new patient/donor records
- Search existing patient/donor records
- Edit patient/donor records, including Serological and Molecular test results
- Associate patient/donor IDs with sample IDs
- Associate patient and donor records
- Assign a donor to the Donor PRA
- Print, export and archive patient records

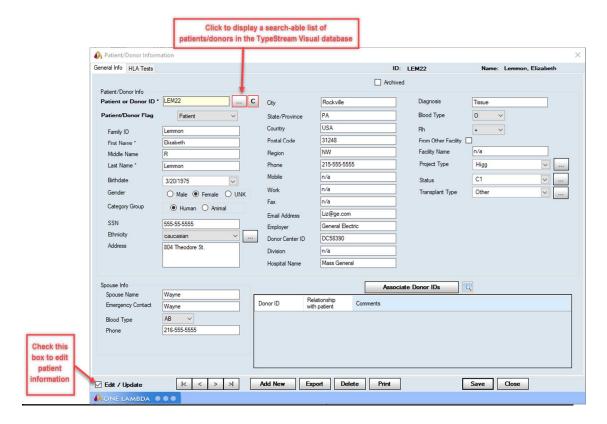
Adding New Patient/Donor Records

You can add patient information using the Patient/Donor Information menu. This is the best

option for adding a small number of patient records.

Steps to Add New Patient/Donor Records:

1. From the Main Menu, select Patient Info > Manage Patient.

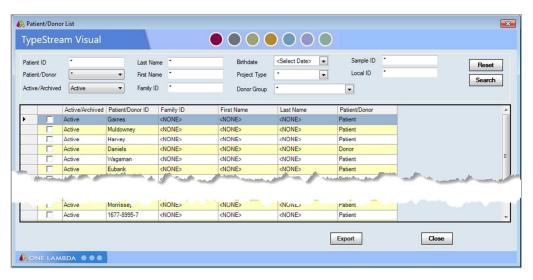


- 2. Enter an ID in the Patient or Donor ID field. The ID can be alphanumeric (contain letters and/or number) or click Search and select a patient/donor from the list.
- 3. Enter patient/donor information to complete the form. Fields with an asterisk (*) are required.
- 4. Click Add New to save the data and add the patient/donor information to the TypeStream database.
- 5. Click Close to close the data entry form and return to the main menu.

Search and Display Patient/Donor Records

This option allows you to browse through patient or donor records, or search for specific ones.

- 1. From the Main Menu, select Patient Info > Manage Patient.
- 2. Click the Search button to browse patient records in the Patient/Donor List. You may look up Patient/Donor records by name, patient ID, whether it is active or archived, etc.:



- 3. Highlight a patient record in the results table and double-click to display or edit.
- 4. You can also find a record by typing the Patient ID or Donor ID directly into the Patient or Donor ID field next to the Search button, and pressing Enter:



5. If the Patient ID you typed is correct, the General Info tab (and other tabs as well) will be enabled and visible and will be populated with the information for that record.

Editing Patient/Donor Records

You must be a Supervisor in order to edit a patient/donor record. All patient/donor information (except patient/donor ID) can be edited.

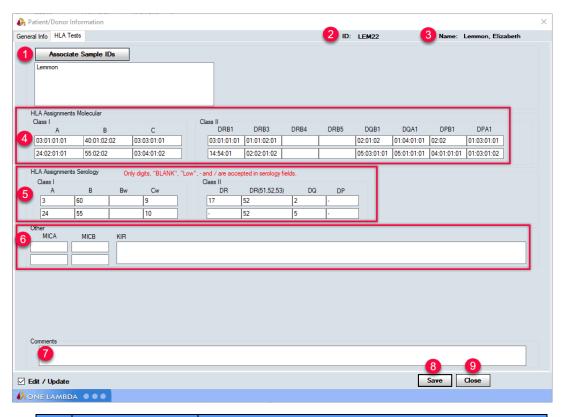
- 1. From the Main Menu, select Patient Info > Manage Patient.
- 2. Search for a Patient/Donor Record (see the search instructions shown immediately above) and select a record to edit.
- 3. Patient/donor information will appear on the General Info tab and any other tabs.
- 4. Before you can change information, you must select the check box next to Edit /Update on the lower left side of the screen.
- 5. Click Save to save your changes.
- 6. Click Close to return to the Main Menu.

Assigning Molecular and Serological Typing Information Manually

Molecular and Serological typing assignments can be entered manually for each patient or donor. To manually assign typing information, do the following:

From the Main Menu, select Patient Info > Manage Patient.

- 1. From the Main Menu, select Patient Info > Manage Patient.
- 2. Open the Patient/Donor List using the search button
- 3. Select a Patient record using the filters and search mechanism, or simply double-click on a Patient record in the table.
- 4. Select the check box next to Edit /Update.
- 5. Click the HLA Tests Tab.
- 6. Enter Molecular and Serological typing values in the spaces provided, then click Save. The system will warn you to only use certain characters in data entry fields (warning appears in red text). You can also enter Comments here (at the bottom of the screen):



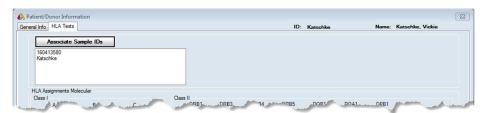
| | Item | Description |
|---|-------------------------|--|
| 1 | Associate Sample IDs | Sample IDs already associated with this patient display in the text field. |
| | | To associate more samples to this patient, click "Associate Sample IDs |
| | | button. (See below.) |
| 2 | ID | Patient ID |
| 3 | Name | Patient Name |
| 4 | Molecular Assignments | May be manually assigned or automatically assigned from the analysis |
| | | page. |
| 5 | Serological Assignments | May be manually assigned or automatically assigned from the analysis |
| | | page |
| 6 | Other Assignments | MICA and MICB assignments, if relevant, must be manually assigned by |
| | | the user. |
| 7 | Comments | User may optionally attach comments to the patient HLA tests |
| 8 | Save | Saves any changes made to the patient, including changes made to |
| | | either of the tabs. |

Associating a Patient/Donor ID with Sample IDs

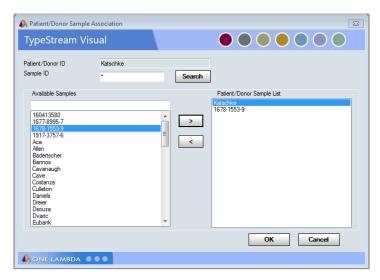
A Sample ID cannot be associated with more than one patient or donor record, but a patient or donor record can have more than one sample ID associated with it.

From the Main Menu, select Patient Info > Manage Patient.

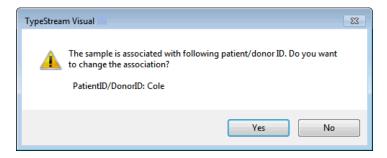
Select the HLA Tests Tab.



- Click the Associate Sample IDs button.
- In the Patient/Donor Sample Association window, highlight a sample ID and click to add it to the Patient/Donor Sample List. Click to remove a highlighted sample ID from the list:



When adding a sample ID to the Patient/Donor Sample List, you may receive this message. If you select Yes, the added sample will become part of the current Sample List for this Patient/Donor even though it is also associated with another Patient/Donor:



5. Click OK to return to the patient record and click Close to return to the main menu.

Associating Patient and Donor Records

A Patient ID can be associated with more than one donor record, and a Donor ID can have more than one patient record associated with it.

- 1. From the Main Menu, select Patient Info > Manage Patient.
- 2. Select a patient/donor record.
- 3. Click Edit/Update
- 4. Click the Test Info tab.
- 5. Click the Associate Donor IDs button.
- In the Patient/Donor Sample Association window, highlight a Donor ID and click >
 to add it to the Patient/Donor Sample List. Click < to remove a highlighted Donor
 ID from the list.
- 7. Click Save to save data.
- 8. Click OK to return to patient record.
- 9. Click Close to return to the Main Menu.

Printing Patient/Donor Records

TypeStream Visual prints both Record Management tabs regardless of which tab is currently being viewed.

- 1. From the Main Menu, select Patient Info > Manage Patient.
- 2. Select a patient/donor record by clicking the Search button to browse patient records and lookup a record by name, patient ID, whether it is active or archived, etc. Select a patient in the results table and double-click to display it.
- 3. The General Info tab will appear with the desired information shown. Click Print to print the displayed record.
- 4. Click Close to return to the Main Menu.

Exporting Patient/Donor Records

Patient/donor records can be exported individually to a CSV file. The file has the same format as a Patient List.

- 1. From the Main Menu, select Patient Info > Manage Patient.
- 2. Select a patient/donor record by clicking the Search button to browse patient records and lookup a record by name, patient ID, whether it is active or archived, etc. Select a patient in the results table and double-click to display.
- 3. The General Info tab will appear with the desired information shown. Click Export to export the displayed record.
- 4. A browse window opens. Select a location to save the CSV file to and enter a file name.
- 5. Click Save then click Close to return to the Main Menu.

Archiving or Reactivating Patient/Donor Records

Archived patient/donor records are not available for reporting or associating. You can still view archived records and reactivate them by clearing the Archived check box, or you can archive records to remove them from system processing. To toggle the Archived status:

- 1. From the Main Menu, select Patient Info > Manage Patient.
- 2. Click the General Info tab.
- 3. Select a patient/donor record to reactivate by clicking the Search button browse patient records and look up a record by name, patient ID, whether they are active or archived, etc. Then set the checkbox next to the record you wish to process and double-click it.
- 4. Click the Edit / Update checkbox.
- 5. Select the Archived checkbox (or unselect it) by single-clicking it.
- 6. Click Save to save, then click Close to return to the Main Menu.

Deleting Patient/Donor Records

Patient/donor records can be deleted through the Manage Patient menu option.

- 1. From the Main Menu, select Patient Info > Manage Patient.
- 2. Click the General Info tab.
- 3. Select a patient/donor record by clicking the Search button ____ to browse patient records and lookup a record by name, patient ID, whether it is active or archived, etc. Select a patient in the results table and double-click it.
- 4. The General Info tab will appear with the desired information shown.
- 5. Click Delete to remove the displayed record from the system.
- 6. If there are associations and references still active, you may receive a message that the record cannot be deleted. Check to make sure that there are no Associated Donors and no Associated Sample IDs (HLA Tests tab).
- 7. Click Delete. If Deletion is successful, you will receive a message confirming this operation.

Creating Patient/Donor Lists

The following is an example of a patient list that can be created and the guidelines for doing so. The patient list must be formatted for import via a program like Excel or Notepad and saved as a Windows compatible CSV file.

The first field/section must contain the names of the patient list fields, each separated by commas.

NOTE: Creating a new patient list can be made easier by first exporting an existing list into CSV format, and using the fields in that to build your new list.

Patient List Field Names and Format CategoryGrp Ethnicity Fax Employer MiddleName PatientID FirstName Region Country ZipCode Email SpouseBloodType EmergencyContact BloodType Disease RhBloodT Gender Address City Dob Cellular WkPhone State SpouseName EmergencyTel PatientDonorFLg DCN HospitalName Associated SampleIDs Disease RhBloodType HLA2_A HLA1_B HLA2_B Division Bloc Associated DonorIDs HLA2_A SHLA2_BW HLA1_DRB4 HLA1_C HI HLA2_DRB4 HLA1_DRB1 HLA1_DRB5 HLA2_DRB1 HLA2_DRB5 SHLA1_BW HLA2_C HLA1_DRB3 HLA2_DRB3 HLA2_DQB1 HLA1_DQB1 HLA1_DQA1 HLA2_DQA1 HLA2_MICA HLA1_DPB1 HLA2_DPB1 HLA1_DPA1 HLA_KIR ClassI_AbSpec Notes SHLA1_A SHLA2_A HI AZ DPA1 HLA1_MICA HLA1_MICB HI A2 MTCB ClassII_Abspec MIC_Abspec SHLA1_B SHLA2_B SHLA1_CW SHLA2_DR345 SHLA1_DQ gens AcceptableAntigens SHLA1_DR SHLA2_DR UnacceptableAntigens SHLA1 DR345 SHI A2 CW SHLA1_DQ SHLA2_DQ SHLA2_DP DonorType SHLA1_DP IncludeInDonorPRA Status TransplantType FromOtherFacility FacilityName DonorGroups PRADonorGroups

Subsequent lines must list the actual patient information, alphanumerically, (can be letters and/or numbers) separated by commas. If there is no information for the patient in a particular field, that field still requires a comma as a placeholder.

For *all* manual serology entries, the locus must precede the value. For example, for an A locus of value 23, you must enter A23.

```
Patient ID, Category Grp. Family ID, First Name, Middle Name, Last Name, Ssp. Dob. Gender, Ethnicity, Address, City, State, Region, Cour
try, ZipCode, Email, Phone, WkPhone, Cellular, Fax, Employer, SpouseName, SpouseBloodType, EmergencyContact, EmergencyTel, DCN, H
ospitalName, Division, BloodType, Disease, RhBloodType, PatientDonorFLg, Associated SampleIDs, Associated DonorIDs, HLA1_A, HLA2_A, HLA1_B, HLA1_B, HLA1_Bw, HLA1_Bw, HLA1_C, HLA2_C, HLA1_DRB1, HLA2_DRB1, HLA1_DRB3, HLA2_DRB3, HLA1_DRB4, HLA2_DRB4, HLA2_DRB5, HLA1_DRB4, HLA2_DRB4, HLA2_DRB5, HLA1_DRB4, HLA2_DRB5, HLA1_DRB4, HLA2_DRB5, HLA1_DRB5, HLA1_DRB4, HLA2_DRB5, HLA1_DRB5, HLA1_
 DRB4, HLA1 DRB5, HLA2 DRB5, HLA1 DQB1, HLA2 DQB1, HLA1 DQA1, HLA2 DQA1, HLA1 DPB1, HLA2 DPB1, HLA1 DPA1, HLA2 DPA1, HLA1 MICA, HLA2 
 _MICB,HLA_KIR,ClassI_AbSpec,ClassII_AbSpec,MIC_AbSpec,UnacceptableAntigens,AcceptableAntigens,Notes,SHLA1_A,SHLA2
  A, SHLA1_B, SHLA2_B, SHLA1_CW, SHLA2_CW, SHLA1_DR, SHLA2_DR, SHLA1_DR345, SHLA2_DR345, SHLA1_DQ, SHLA2_DQ, SHLA1_DP, SHLA2
  DP,DonorType,IncludeInDonorPRA
38450, Human, Neely, Jason, , Neely, 021-09-2987, 2/17/2001, M, caucasoid, 560 Waiting
Street,,CA,NWW,USA,91022,jneely@yahoo.com,(213) 567-0987,(213) 567-0987,(213) 567-0987,(213) 567-0987,MIT
Research, Evvonne, AB, Evvonne, (213) 509-0198, 101, St Judes's Hospital, MARROW Transplant, O, bONE
MARROW+, Patient, DO-, DO-, DP14, DP9,
 27614, Human, Martinez, Daniel, DM, Martinez, 032-11-1934, 9/12/1998, M, hispanic, 40 Driveland Road, East
LA,CA,NWW,USA,90222,mdaniel@aol.net,(324) 489-1430,(324) 489-1430,(324) 489-1430,(324) 489-1430,(324)
Juice, Maria, B, Maria, (324) 489-1430, 103, East LA Hospital, MARROW
Road, Valencia, CA, NWW, USA, 91355, kd@lions.net, (662) 234-1098, (662) 234-1098, (662) 234-1098, (662) 234-1098, Traveller's
Corporation, Juanna, O, Juanna, (323) 345-1098, 103, St Michael Hospital, MARROW Transplant, O, Tissue,
Road, Canyonville, OR, NNW, USA, 97417, sc@msn.com, (541) 839-4467, (541) 839-6509, (541) 299-1098, (541) 760-1986, Juniver
Creek, Elizabeth, O, Elizabeth, (323) 345-1098, 103, St Michael Hospital, MARROW Transplant, O, Tissue,
+,Donor,,,,DR53,-,,,,,42,-,,,,DR53,-,,,,,44717,Human,Dublin,Nikitta,D,Dublin,111-13-1234,11/22/2004,F,asian,345 Ashilly
 Court,Canyonville,OR,NNW,US1,97417,sc@msn.com,(541) 839-4467,(541) 839-6509,(541) 299-1098,(541) 760-1986,Juniper
Creek, Elizabeth, O, Elizabeth, (323) 345-1098, 103, St Michael Hospital, MARROW Transplant, O, Tissue,
Village CA. SNM. USA, 91002, shar 600 yahoo, com. (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), 978-1098, (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714), (714)
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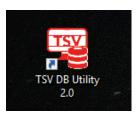


Database Utility

The TypeStream Visual Database Utility allows you to create and connect to SQL Server databases, as well as perform all of the following tasks.

- Create a new database
- Select/connect to an existing database
- Make a backup copy of your database or create a schedule for regular backups
- Restore a database
- Merge database
- Detach from and delete a database
- Attach to a database
- Reconfigure databases
- Optimize Database

It also has a new icon:



Opening the TypeStream Visual Database Utility

The TypeStream Visual Database Utility allows you to connect to any SQL Server on your computer or the network, depending on your permissions and your organization's security policies.

To use any of the TypeStream Visual Database Utilities, you must first connect to a SQL Server. With the exception of connecting to a database, the database tasks can be executed only on the server or on the computer on which the database resides.

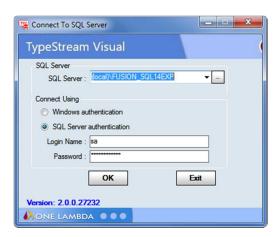
The following are guidelines for using the TypeStream Visual Database Utility:

- You can connect to the SQL Server using either Windows Authentication or SQL Server Authentication. If you use SQL Server Authentication, the Server Dialog Box displays the default database administrator username and password for a local client/server installation.
- It is highly recommended that you do not switch collation and regional settings between databases. The collation of databases and the SQL Server play a major role during database merge and migration. (A *collation* encodes the rules governing the use of characters and numbers for a language or an alphabet).
- Please do not alter the permissions, (i.e., who has the right to make certain changes to the database).
- Double-click the TypeStream Visual DB Utility icon on your computer

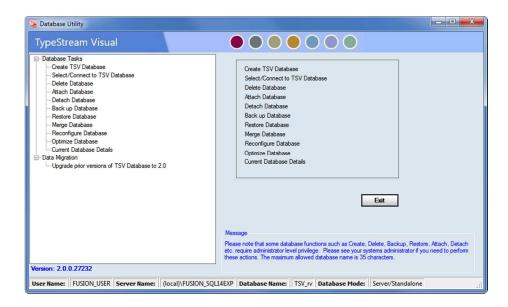


desktop.

The Connect to SQL Server dialog box is displayed.



Make sure your SQL Server information is correct and click the OK button. The Database Utility Main Window is displayed:



The status bar at the bottom of the TypeStream Visual Database Utility main window displays the Active User, Server Name, Database Name, and the Database Mode, (i.e., TypeStream Visual and the database are on the same computer, or the database resides on an external server).

- The Username field will say Not Set if you are using Windows Authentication.
- A Help button is available on every Database Utility window, or by pressing the F1 key.
- Click the +/- signs on the far left to display or hide related database utility menu options.

Database Tasks

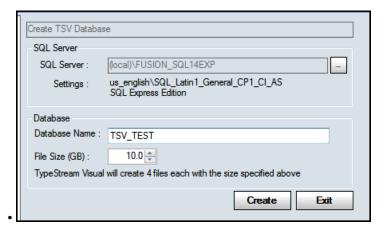
The Database Tasks listed on the left side of the Main Window offer various means to configure, manage and maintain a TypeStream Visual database. These functions are described in the following sections.

Creating a New Database

A new database can be created only on the computer or server on which the SQL Server program resides.

- On the left side of the Database Utility window, click Create Database:
- Using the SQL Server drop-down box, choose a SQL Server version that is correct for the database you want to create.
- Enter a unique Name for the new database.
- Choose the maximum database size and click Create.

•



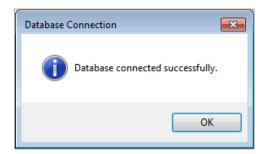
For a purchased, full-version of SQL Server, the maximum database size is one terabyte. Ensure that you have adequate storage space for a database of this size.

Also please note that currently if Microsoft SQL Express 2014 (default choice) is installed, the software will show FUSION_SQL14EXP in drop down lists.

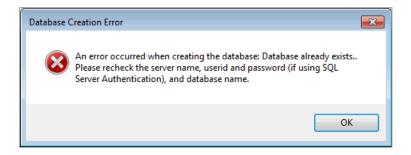
Provided the newly created database name does not already exist, the system creates the new database and displays the following message:



- 1. Click Yes to connect to it. Click No if you do not wish to connect to it at this time.
- 2. If you click Yes, a connection confirmation message is displayed:



- 3. Click the OK button.
- 4. If the newly created database name already exists, the Database Utility displays the following error message.



Click the OK button. Then verify that the database name you entered is unique to the selected SQL Server and retry.

The maximum length of a database name must not exceed 35 characters. Only alphanumeric characters and the underline character '_' are recommended for use when naming databases.

Selecting and Connecting to Database

From the Database Utility Window, you can choose to connect to a database that already exists on the selected server. The subsequent analysis with TypeStream Visual will use the selected database.

- 1. In the Database Utility window, click the Select/Connect to TSV Database option
- 2. Select a database from the Database Name dropdown selector.
- 3. Click Set.
- 4. The following message is displayed:



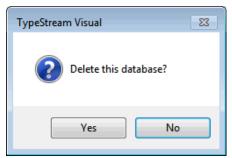
Click the OK button. The database you selected is now listed in the Database Name field in the Status Bar at the bottom of the Database Utility window:

Deleting a Database

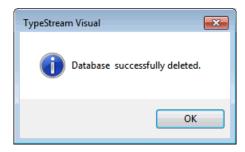
Click the OK button. The database you selected is now listed in the Database Name field in the Status Bar at the bottom of the Database Utility.

- 1. Within the Database Utility window, click Delete Database.
- 2. From the Database Name drop-down list, select a database and click the Delete button.
- 3. Click the Delete button:

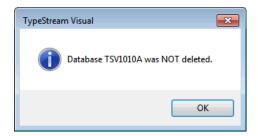
4. A confirmation message is displayed. Click the Yes button to continue with the database deletion.



5. The Database Utility confirms the deletion

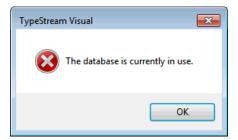


6. If you click No, a message verifying that the database was not deleted is displayed.



NOTE: If you receive a message that the selected database is in use, you must first detach the database from the interface (see Detach a database). You cannot delete an attached database.

7. Click the OK button to exit.



Attaching a Database

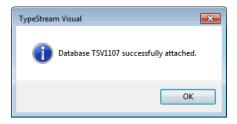
You may use the Attach and Detach Database options together when you want to move a database to another location and then link to that new location. Here is the sequence to follow if you want to do this:

- Detach the database, (see the section: *Detaching a Database* for more information)
- Move the database .mdf file, (which contains the database) to the desired location on another server.
- Attach the database using the steps below, specifying the new location of the moved database.

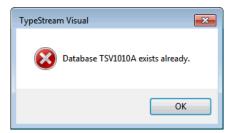
You can use the Attach database function to link to any TypeStream Visual database .mdf file. However, the database .mdf file you are attaching must reside on the selected server.

It is recommended that you back up the database before using the Attach feature.

- 1. Within the Database Utility window, click Attach Database.
- 2. Click the Browse button next to the MDF file to attach field and navigate to the database file you want to attach. Default location of databases is C:\Program Files (x86)\Microsoft SQL Server\MSSQL12.FUSION_SQL14EXP\MSSQL\DATA\.
- 3. Select the database (*.mdf) file and click the Open button. The path to the selected (*.mdf) file displays in the 'MDF file to attach' field.
- 4. Click the Attach button (above), then you will see this message:



If you attempt to attach a database that is already currently attached, you will receive a message like this:



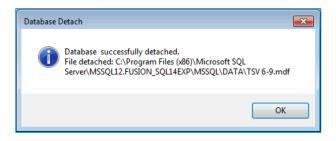
Detaching from a Database

If you wish to move a database file, (.mdf) to another location for disk space considerations or because you no longer want TypeStream Visual to link to it (but do not want to delete it yet),

NOTE: You cannot detach a database which is currently in use.

you must first detach it from TypeStream Visual. You can then relocate it and link to its new location, (see the database menu section entitled: Attaching to a Database).

- 1. Within the Database Utility window, click Detach Database.
- 2. From the Database Name drop-down list (above), select a database and click the Detach button. The following message is displayed.
- 3. Click the OK button.



NOTE: A detached database .mdf file is located in the directory where the TypeStream Visual instance of SQL was installed (e.g., for Microsoft SQL Express 2014, C:\Program Files(x86)\Microsoft SQL Server\MSSQL12.FUSION_SQL14EXP\MSSQL\Data

Creating a Database Backup File

It is recommended that you create regular, frequent backups of your TypeStream Visual database(s). If some event occurs that corrupts a database, or makes it inaccessible, having a backup copy of the database allows you to restore all data up through the date of the most recent backup. Use the Schedule Backup feature to set up automated regular backups of a specified database—any day or time, and as often as desired. For information on restoring a database with a backup copy, see the section, Restoring a Database.

The backed up database must be saved to the local drive of the server or the computer on which you are creating the backup copy. The filename of the backup file is the name of the database with a .bak extension.

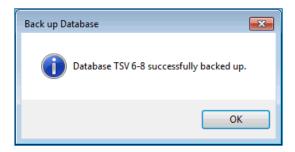
When setting up TypeStream Visual in a networked environment, the Sessions/Batch setting (see General Settings > Paths) must point to a networked, shared location.

You can use a shared or network mapped drive to store backups if the SQL agent is given the appropriate permissions to that directory. For more information, please refer to http://support.microsoft.com.

- 1. Within the Database Utility window, click Backup Database.
- 2. From the Database Name drop-down list (not shown open here, see arrow), select a database.

NOTE: Make sure you select a destination directory that is on the selected SQL Server. If you use your PC as a location for backups, it is recommended that you create a special folder for backups on the C: drive (e.g., C:\DB Backups) and do not store backups on the desktop.

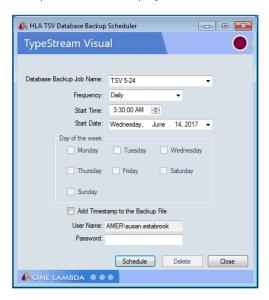
- 3. Click the Browse button in next to the Destination field. A new window displays where you can navigate to a destination folder for the database backup.
- 4. Enter a database backup file name in the Backup File field (by default, it is the database name).
- 5. You may also click the Make New Folder button and create a special folder for your database backups. The backed up files are stored with a (.bak) file extension.
- 6. At this point you have two button options:
 - a. 'Backup' this will perform the backup immediately
 - b. 'Schedule Backup' this will open a window to schedule the backup for another day(s) and time:
- 7. To perform a backup of the database immediately, click the Backup button.
- 8. The following message confirms a successful database backup.
- 9. Click the OK button to exit.



Schedule a Backup

NOTE: The length of time required to back up a database is proportional to its size—the larger the database, the longer it takes to back it up.

To schedule backup(s) for a future date and time, or on an automated schedule, click Schedule Backup. The backup scheduler is displayed.



- 1. Complete the fields in the Database Scheduler to set the backup day and time:
- 2. Database Backup Job Name: Enter a unique name for the backup. Each scheduled backup task requires a unique name.
- 3. Frequency: Use the drop-down arrow to select the backup frequency (Daily, Weekly or Monthly).
- 4. Start Time: Use the up/down arrows to set the time at which to start the scheduled backup. Please note that the length of time required to back up a database is proportional to its size the larger the database, the longer it takes to back up.
- 5. Start Date: Click the drop-down arrow and select the date on which you want the scheduled backup process to begin.
- 6. Days of the week: If you selected a frequency of weekly or monthly, select the check box for the day(s) of the week for which you would like to schedule backups. This option is grayed-out if the specified frequency is Daily.
- 7. Enter your Windows password in the Password field. You must enter this password to ensure you have the correct privileges to back up the database as specified.
- 8. Click the Schedule button.

It is not required to have the application running or to be logged-in to run scheduled backup tasks. However, you must have your computer on during the backup period.

NOTE: The directory you specified for the scheduled backups will contain the database backup file, (.mdf) as well as a log file that documents the backup job status.

If your scheduling is confirmed, a message is displayed.

Deleting a Scheduled Backup

Take the following steps to delete a scheduled backup job.

- 1. Click Schedule Backup. The backup scheduler is displayed.
- 2. Use the drop-down arrow in the Database Backup Job Name field to select a scheduled backup task to delete.

NOTE: The drop-down list may display more TypeStream Visual tasks than just backup jobs. Be careful to select only the TypeStream Visual database backup task you wish to delete. This list only displays the tasks assigned under the current windows username. Other user tasks should be viewed through the task scheduler function in the Windows.

- 3. Click the Delete button. You are asked to confirm the deletion of the task
- 4. Click the Yes button to delete the scheduled backup. If your scheduling has deleted, the following message is displayed.
- 5. Click the OK button to return to the main Database Utility Screen.

To create a new backup task, follow the steps for Scheduling a Backup in the prior section.

Restoring a Database

You can use database backups to restore, (replace) a database. The backup database copy contains all TypeStream Visual data up through the date of the backup creation.

You can restore a database backup to any existing, or new database - except for the current database.

Restoring a database can only be performed on the server or the computer where the backup database file resides.

- 1. Within the Database Utility window, click Restore Database.
- 2. Click on the browse button next to File To Restore text box. This brings up the File Selection window.
- 3. Browse to select the database backup file, (will have a .bak extension) to restore and click the Open button.
- 4. Enter a unique name for the restored database in the Restore as field and click Restore.
- 5. Click the Restore button. The database is restored to the specified filename and the following message is displayed.

NOTE: Microsoft SQL Server does not allow you to restore databases from certain locations, such as from a network drive or from a backup file on your computer desktop.

NOTE: If the user restores a database .bak file from one machine to another, the NGS Session folder must also be copied to the destination machine and the path in General Settings must point to the folder path.

Optimizing a TypeStream Visual Database

Optimizing a TypeStream Visual Database on a regular basis speeds up the analysis process by compacting wasted space, automatically repairing errors and optimizing data storage. To optimize a TypeStream Visual Database, do the following. First, open the TypeStream Visual Database Utility:

- 1. Select Optimize Database from the Database Tasks Menu.
- 2. Select the database you want to optimize from the Database Name drop-down.
- 3. Click the Optimize button.

When the database optimization is completed, you'll see a message indicating that the process was completed successfully.

Note that during optimization, SQL Server will temporarily require additional hard drive space to complete the process. If the additional hard drive space is not available, or your database exceeds the size limitations of SQL Express during optimization, the process may fail.

Here are a few suggestions to solve this problem:

• Reduce the size of the database by moving sessions from the current database to another database.

- If you're using SQL Server 2005 Express, (which has a four gigabyte size limitation) consider upgrading to SQL Server 2014 Express, which allows a larger ten gigabyte database size.
- Purchase the full version of MS SQL Server which offers a nearly unlimited database size.

A database can be optimized automatically in the same way that a database can be backed up on a pre-set schedule.

Scheduling Database Optimization

Setting the TypeStream Visual Database Utility to automatically perform database optimization is accomplished in exactly the same way as scheduling an automatic database backup.

- 1. Select Optimize Database from the list of database tasks in the TypeStream Visual Database Utility.
- 2. Select the database you want to schedule optimization for from the Database Name drop-down list.
- 3. Click the Schedule button.
- 4. The Scheduler window will appear (above). Create a new Database Optimization Job Name or select an existing Database Optimization Job Name from the dropdown list.
- 5. In the next field, Frequency, select the frequency that you want the optimization to run: Daily, Weekly or Monthly.
- 6. In the Start Time field, use the up and down arrows to select a time when the database optimization process will begin.
- 7. In the Start Date field, click the down arrow and choose the first day on which you want the database optimization to run.
- 8. If you selected Weekly in the Schedule Optimize field, select the day, or days, you want the database optimization to run in the Day of the Week section.
- 9. Enter your Username and Password and click the Schedule button.
- 10. The Database Utility will display a message indicating that the Database Optimization job has been successfully scheduled.

Reconfiguring a TypeStream Visual Database

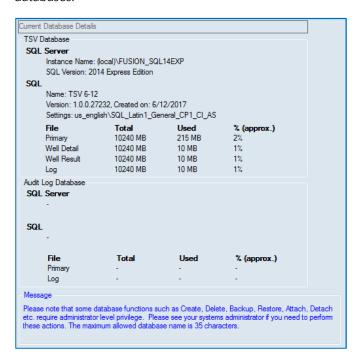
Reconfiguring a Database allows you to increase the size of an existing database. To reconfigure and increase the size of an existing TypeStream Visual Database, please do the following:

- 1. Select Reconfigure Database from the list of Database Tasks in the TypeStream Visual Database Utility.
- 2. Ensure that you're connected to the correct SQL Server.
- 3. If not, click the Browse Button in the SQL Server section to select the correct SQL Server.
- 4. Choose the database that you want to reconfigure by clicking the down arrow at the right side of the Database Name field to select it.
 - a. Increase the size of the database by typing a new size, or by clicking the up and down arrows in the field just below the Database Name,

- b. Or increase the database size to its allowable maximum size by placing an arrow in the Unlimited size checkbox provided for this purpose.
- 5. Click the Set button.
- The Database Utility will display a message that the database reconfiguration was successful.

Current Database Details

Selecting Current Database Details from the menu on the left side of the Database Utility brings up a detailed listing of the most important information concerning your TypeStream Visual databases.



The top part of this screen deals with the main TypeStream Visual database while the bottom section is devoted to the Audit Log database.

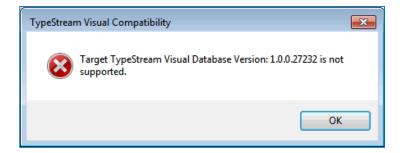
If the percentage of a database file exceeds 90%, it may be time to Optimize and/or Reconfigure the database to free up more space.

Upgrading a TypeStream Visual Database

In the case of an update to TypeStream Visual that requires a change to the database structure, any current database will need to be upgraded before it can be used with the updated system.

Note: For standalone configuration install, users migrating from one computer to another should make sure to move the /data/session folder to the new computer.

Attempting to connect to an older database through the database utility will return the following message:



To upgrade, select a database name from the dropdown list. Version number, size, and settings for the selected database will display below the name. Click Upgrade. A progress bar will display during the upgrade process, after which a message displays verifying a successful upgrade and giving the option to connect to the upgraded database now? If you reply 'No,' you can always connect to it later using the TSV Database Utility.

Create a backup

You may create a backup of your database before upgrading simply by checking the "Backup original database before upgrade" check box. The default location for storage of the backup is c:\OLI TSV\data\temp, but you may set the location to any local folder, with the exception of the desktop, My Documents directory, or a network directory.

View Script

If you would like to know the specific tables affected by the database upgrade, first select a database and click the "View Script" button. A table is displayed containing the available upgrades, e.g., "Upgrading from TSV 1.0 to TSV 1.1 database." Expand the '+' next to the appropriate upgrade. Full text of the database upgrade script displays.

Merging a TypeStream Visual Database

This function allows you to combine two databases into one, regardless of their location. There are certain guidelines to follow when merging databases:

Both databases must be the same version of a TypeStream Visual Database. Both databases should be backed up before performing a database merge. The source database information is copied into the target database.

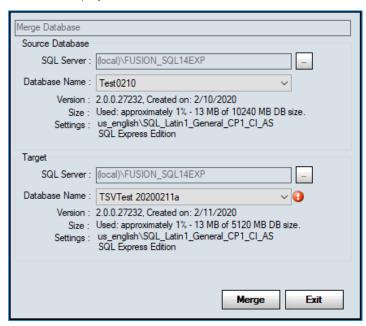
When merging into an *existing* TypeStream Visual Database, ensure that the destination database size is big enough to store the source database. By existing database, we mean that it has lab and user information at minimum. The source database lab data will be copied if it is missing from the target database.

When merging into a new TypeStream Visual Database, first create a new database using the Create Database function and make the size large enough to accommodate the source database.

Note that Donor Group Names, Patient ID's, Test Types, and Test Dates will not be merged if this information already exists in the Target Database.

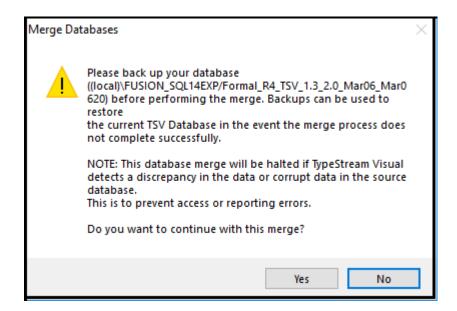
1. Within the Database Utility window, click Merge Database.

2. Select a database from the Database Name drop-down list under Source Database (assumed done; not shown here). The version, size, and settings for that database are then displayed:

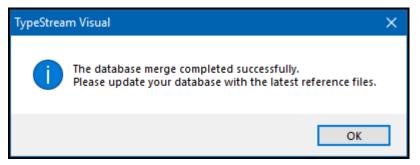


- 1. Select a database from the Database Name drop-down list under Target. The version, size, and settings for that database are displayed once you select (not shown). (The system will prompt you if you do not select a database, as shown by the red exclamation icon above

 1. Select a database from the Database Name drop-down list under Target. The version, size, and settings for that database are displayed once you select (not shown). (The system will prompt you if you do not select a database, as shown by the red exclamation icon above
- 2. You must look at the version, size, and settings of both the source and target database before merging to verify the version and settings match and that the size of the source database is not too large for the target.
- 3. Click the Merge button. You may see this message to please back up your database. If you are ready to continue with the merge operation, click the Yes button:



4. After the Merge, the following message is displayed:



5. Click the OK button to return to the main Database Utility Screen.



Appendix A

Copying BAM Files from Torrent Server

BAM files can be easily exported from the Torrent Server using the FileExporter Plugin.

BAM files can be exported as individual files or as a single compressed file containing all BAM files.

Custom renaming of files is also possible.

Copying Files using FileExporter Plugin:

1. Select Plugin to Run



2. Select FileExporter



- 3. Enter File Exporter information
 - a. Select a desired file type:
 - i. To export individual BAM files, check BAM and leave Archive unchecked
 - ii. To export all BAM files as a single zip file, check both BAM and Archive
 - b. Select File Naming format by drag & drop in desired order
 - c. Select delimiter



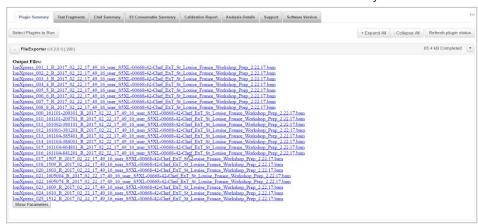
- 4. Click Submit
- 5. Results of FileExporter are displayed:

Archive will export all

bam files in a single

zip file

6. Click each link to download BAM files individually



7. Or Click Compressed Files link to download BAM files in .zip file format (Archive option)



Reference Documents

| Software version | Document Name | Document ID |
|------------------|--|---------------------|
| TSV 2.0 | TypeStream Visual NGS Analysis Software v2.0 Release Notes | TDX-OLI-DMR-PS-3248 |
| TSV 2.0 | TypeStream Visual NGS Analysis Software v2.0 Installation Guide | TDX-OLI-DMR-PS-3226 |

Index

| +Rpt99 | Assignment History | 99 |
|----------------------------------|------------------------------|-----|
| ABMDR Specialty Report137 | Australia Perth Report | 136 |
| Add Fastq/Bam File69 | Australia Specialty Report | 135 |
| Add Fastq/Bam from Folder70 | Auto-analysis | |
| Allele | monitoring | 59 |
| homozygous94 | Auto-Analysis | 55 |
| summary page display83 | folder structure | 61 |
| Allele balance105 | reanalyze after file removal | 62 |
| Allele Balance106 | remove raw data files | 62 |
| Allele Group Frequency Report138 | using planned run name | 60 |
| extended (NMDP code only)139 | view log | 63 |
| ALLType FASTPlex74 | BLAST | |
| Analysis Page96 | Catalog | |
| Analysis Parameters44 | download from website | 37 |
| PACBio46 | importing | 34 |
| Annotation Tracks110 | in creating a session | |
| API Key | manage reference file | |
| Obtain from S556 | update from network drive | |
| Archive | cDNA | |
| catalog40 | cis-trans ambiguity | |
| patient/donor records157 | in reads display | 117 |
| session146 | on session summary | |
| Assign Code | Clone Session | |
| in general options41 | Close Match List | / ∠ |
| Assign, Review, Confirm 84, 98 | | 104 |
| Assigning Typing to Patient98 | on analysis page | |
| | on reads display | 119 |

| CMDP Report135 | .pdf | 130 |
|---|------------------------------|-----|
| Comment | .xml | 134 |
| on session summary82 | Genotype Summary Table | |
| Comparison Sequences 123 | .CSV | 131 |
| Condense a Session143 | Genotypes | |
| Configuration | on reads display | 119 |
| Final Assignment Preference42 | Get Run List | |
| general options43 | Health Level | |
| setting from general options41 | Health Metric | 46 |
| Coverage Stats | on session summary | |
| on reads display119 | Health Stats | |
| Database | on reads display | 119 |
| attaching a database166 | Histogram , , | |
| create backup174 | large scale | 94 |
| create new15, 163 | read fragment length | |
| creating a backup168 | whole gene view | |
| delete a database165 | Home Page | |
| | Homozygous alleles | |
| detaching167 | in session summary | 94 |
| merging174 | Hover | |
| move a database166 | ambiguities | 91 |
| optimizing171 | histogram | |
| reconfiguring172 | read data | |
| restoring170 | | |
| select/connect to164 | IMGT Library | |
| status20 | importing | |
| upgrading173 | Import a Session | 144 |
| Database Utility161 | Insertion base on reads view | 124 |
| connect to162 | | |
| Delete | Installation | |
| catalog41 | Job Manager | |
| files from session import72 | enabling and disabling | |
| in data management142 | session queue | |
| patient/donor records158 | terminating a session | /6 |
| session147 | K/N/I | |
| Disable/Enable | definition | 90 |
| job manager75 | Lab Profile | |
| Exclude Region Tool48 | edit profile | |
| Export a Session | manage lab codes | |
| Extract Base & Show Specificity114 | management | 23 |
| Extract Bases onto Clipboard113 | on initialization | |
| Fasta file116 | License Key Activation | |
| FASTA Report140 | Linkage | |
| FASTPlex74 | table | 93 |
| Fastq<>Sample Name70 | Local Code | |
| Field Chooser83 | creating | 39 |
| Filters88 | updating | 39 |
| Final Assignment97 | Locus | |
| Find28 | filters | 90 |
| gDNA119 | Low Coverage | |
| Genotype List123 | on session summary | 91 |
| Genotype Summary Health Report 131, 133 | Magnifier | 29 |
| Genotype Summary Report | Manually assign type | |

| Manually Assign Typing 155 | on analysis page | 104 |
|--------------------------------------|------------------------------|---------|
| Mapped Read Metrics107 | Resolving Positions | |
| MiSeq data | on reads display | 119 |
| loading from folder70 | Resubmit | 87 |
| on reads view125 | Results Comparison Tool | 49 |
| Navigator 55, 78 | Run with Expected Genotype | 86 |
| show navigator29 | Sample Management | |
| NEW91 | edit sample info | 149 |
| NGS Custom Report132 | import sample lists | 148 |
| NGS Product Configuration41 | Sample Name | |
| NMDP99 | loading via .csv file | 70 |
| NMDP Code | Save locus layout | |
| update from NMDP website39 | Sequence Segment Search Tool | 118 |
| update reference file34 | Serology | |
| Notes91 | flag sero ambiguity | 43 |
| Nucleotide View111 | in general options | 43 |
| Patient/Donor | in patient record | |
| add new records152 | update reference file | |
| assign typing manually154 | Session | |
| associate patient + donor records157 | create session | |
| associating with sample IDs156 | create session - PacBio | |
| create patient/donor list158 | import screen | |
| editing records154 | - | |
| export records157 | management | |
| import patient/donor list151 | save a session | |
| | session builder, NGS | |
| management151 | session builder, PACBio | |
| print records157 | summary display | 79 |
| search and display records153 | Session Name | |
| toolbar icon30 | in creating a session | |
| Phase | Set Start Base | 112 |
| definition95 | Setup | |
| Position Index119 | default URLs | |
| Position Search Tool117 | directory paths | 25 |
| Print | general settings | 24 |
| printer setup25 | printer | 25 |
| Print Screen | Show Specificity | 114 |
| Rare alleles | Side-by-Side Analysis | 102 |
| on session summary91 | Software | |
| Read Colors124 | updates | 8 |
| Read Stats | Sort Reads | 112 |
| on reads display119 | Specificity | |
| Reads View | extracted bases | 114 |
| in detail124 | SQL Server | |
| show read details126 | connecting to | 14 |
| Reanalyze Selected Samples86 | Suffixes in HLA Nomenclature | |
| Reference Files 20, 33 | Switch Database | 52 |
| Remove DQA, DPA88 | Switch User | 52 |
| Replace XX Code88 | System Comments | 92, 101 |
| Reports | System Requirements | |
| quick reports28 | system settings | |
| Resize columns in session summary83 | Technical Support | |
| Resolving positions | Thai Specialty Report | |

| Toolbar | 27 inactivate user | 23 |
|------------------------|-----------------------------------|----|
| Torrent Server | management | 20 |
| copy BAM files from17 | | |
| User Comments10 | on supervisor vs. technician | 20 |
| User login | | |
| forgot password | on reads display 1 | 19 |
| forgot user name | on Reads Viewer 1 | |
| User Profile | View Options | |
| add new users | View Phased Start/End Base Counts | |
| change password | | |
| change user privileges | from reports page 1 | 34 |
| edit profile | , , , | |

Revision History

| Revision | Date | Description of Change |
|----------|------------|--|
| 02 | 07/19/2019 | Updates to manual for new and modified functionality.: 1. Updates made for release of v1.3. 2. Expanded description of linkage and insertion of linkage table. |
| 03 | 10/07/2019 | Addition of EU Authorized Rep symbol and contact information. |
| 04 | Current | Updated contact information and address to reflect change in legal manufacture site. |

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