Automated Cell Line Development: The Data Story

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Introduction

- Cell line development workflow has significant data challenges due to the sheer amount of data generated during high throughput, months-long processes.
- This becomes even more challenging when multiple analytical instruments are used to generate different types of data, often in different formats.
- The hit picking steps require that the data must be tracked with these hits. This involves moving data across different plates and wells.
- The data must be traced throughout the cell line development process to ensure that any cell lines that move into manufacturing have the requisite historical data (e.g. proof of monoclonality) and that all data is easily accessed for reporting needs.
- However, copying and reformatting data in Microsoft Excel is inherently an error-prone process, particularly when trying to correlate data from different analyzers
- Automation can help ensure accurate data tracking throughout a lengthy workflow, such as the months-long multi-step cell line development workflow (**Figure 1**).
- We demonstrate the data handling capabilities of Biomek and DART software, behind the scenes of an automated process.

Figure 1. Cell line development process. The data management for the highlighted steps are described here.

Methods

- The cell line development was carried out in a Biomek i7 hybrid workstation with integrated devices (**Figure 2**).

Figure 2. The Biomek i7 Workstation, along with various integrated devices, was used to automate a cell line development workflow.

- Three weeks after plating cells by limiting dilution and identifying monoclonal wells, data was used in the following steps (**Figure 3**):

1) The barcoded plates are scanned as they move from the integrated incubator to the Biomek and a “Load Data” step in the method retrieves previous data associated with this plate. These include monoclonality data but also any earlier data deemed relevant such as ClonePix (Molecular Devices) colony size and external fluorescence.
2) The plates are scanned for confluence on the CloneSelect™ Imager (Molecular Devices) and a “Create Data Set” step attaches this well-level data to the barcoded plate.
3) Because we only want to assay protein titer from wells with colonies grown from a single cell, we can create a hit picking data set to identify only these wells for sampling. This data set (“MonoGrowth”) can drive the pipetting in a Biomek transfer step. The media from the sampled wells was consolidated and reformatted into 384-well Octet (Pall ForteBio) assay plates.
4) The 384-well plate was assayed on the Octet and the resulting IgG concentrations were attributed to the assay wells through another “Create Data Set” step.
5) Using a “Copy Data Set” step, the Octet (Pall ForteBio) assay results were transferred back into the original 96-well plates containing the colonies. This deconvolution step automatically handles the previously described problem of row vs. column lists.
6) The new data is used to drive another hit picking transfer step such that the monoclonal wells with IgG expression above a set threshold are transferred to 24-well plates for continued expansion and testing. All of the essential data (monoclonality, confluence, IgG levels, etc.) are automatically moved forward to the new wells so there is no need to trace back to the original 96-wells to find the relevant data.

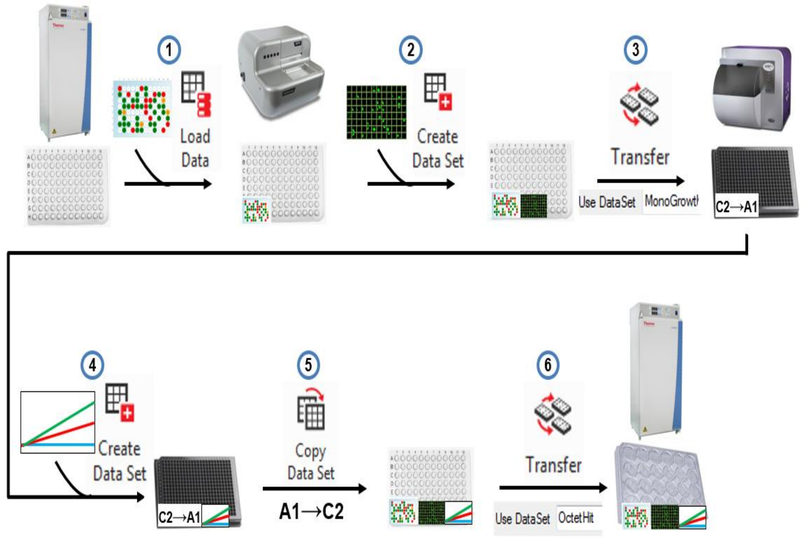

Figure 3. Automated data handling. Biomek and DART software can combine to retrieve previous data, add new assay data to plates, drive reformatting transfer steps, copy assay data back to the source wells, to ensure the proper hits are brought forward.

Results and conclusions

- Biomek and DART **link assay data** to sample wells, correlate data from multiple analyzers, using data to drive transfers for hit picking, and bring all data forward for traceability. These steps are crucial in cell line development.
- DART **stores data** in a database. Storing data for all potential cell lines is essential as it is impossible to know which will ultimately be the lines selected for cell banking.
- DART database can be **accessed** through multiple convenient means. For quick **visualization** in a user-friendly manner, the DART Data Browser (**Figure 4**) can highlight method-, labware-, and well-level data in a standard Google Chrome Browser.
- Data be **viewed remotely**, and can be refreshed to update with live data during runs.
- For **exporting data** in a usable form, the DART Report Builder can be used to generate reports in Microsoft Excel, with a simple interface to choose the data to include in a given report.
- All of this can be done **without any assistance from IT resources** – a common requirement for some larger data management systems.

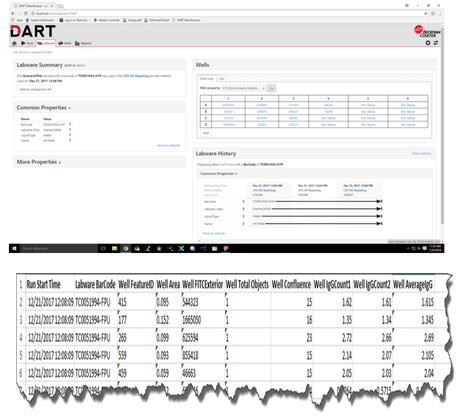

Figure 4. Data viewing and reporting. Data must be easily accessed as needed and DART enables viewing from a standard web browser (A) or selection of data to be included in Microsoft Excel-based reports (B).

- The data generated during any experiment is what makes that experiment worthwhile. For a months-long workflow like cell line development, the risks of data loss or errors are even more significant. By making this data integrity process automatic and easily accessible, Biomek and DART software can provide true value to the cell line development process.

Biomek Automated Workstations are not intended or validated for use in the diagnosis of disease or other conditions. Beckman Coulter Life Sciences genomic reagent kits are for research use only.

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