Investigating phenotypic differences and drug response among glioblastoma stem cell cultures from patients

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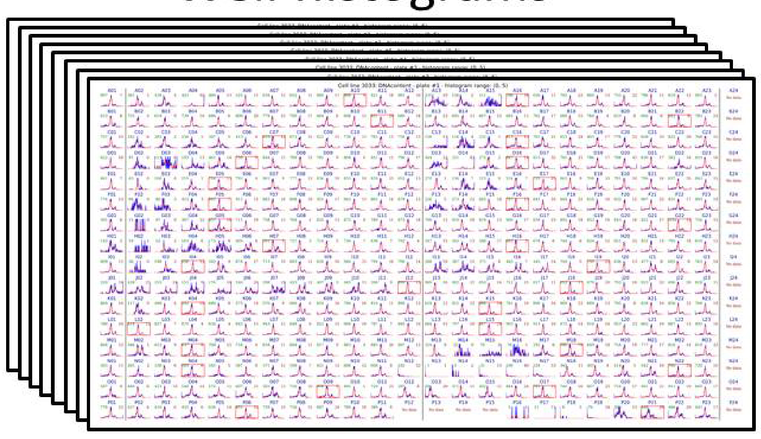
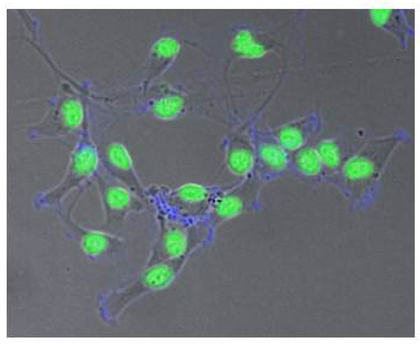
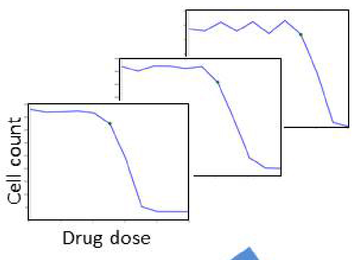
Well histograms





Well selection



Challenges

- Multidimensional (big) data: 100 cell lines, 8 plates per cell line, 16 x 23 wells per plate, 4 distinct images per well, ~100 cells per image, ~250 descriptors per cell,
- Heterogeneity across individual CSCs and cell lines.

Methodology

Cultured cells are imaged by both fluorescence and bright-field microscopy. Meaningful morphological descriptors of individual cells from the images are extracted using CellProfiler and saved to a MySQL database. In order to investigate population dynamics per-cell descriptors are reduced to per-well distributions, each represented by a histogram (a one-dimensional vector). Measurements are extracted directly from the database using Python scripting. Wells of interest, i.e. those with highest drug dose and high cell count, are automatically selected for each treatment across the cell lines. Different treatments and cell lines are compared.

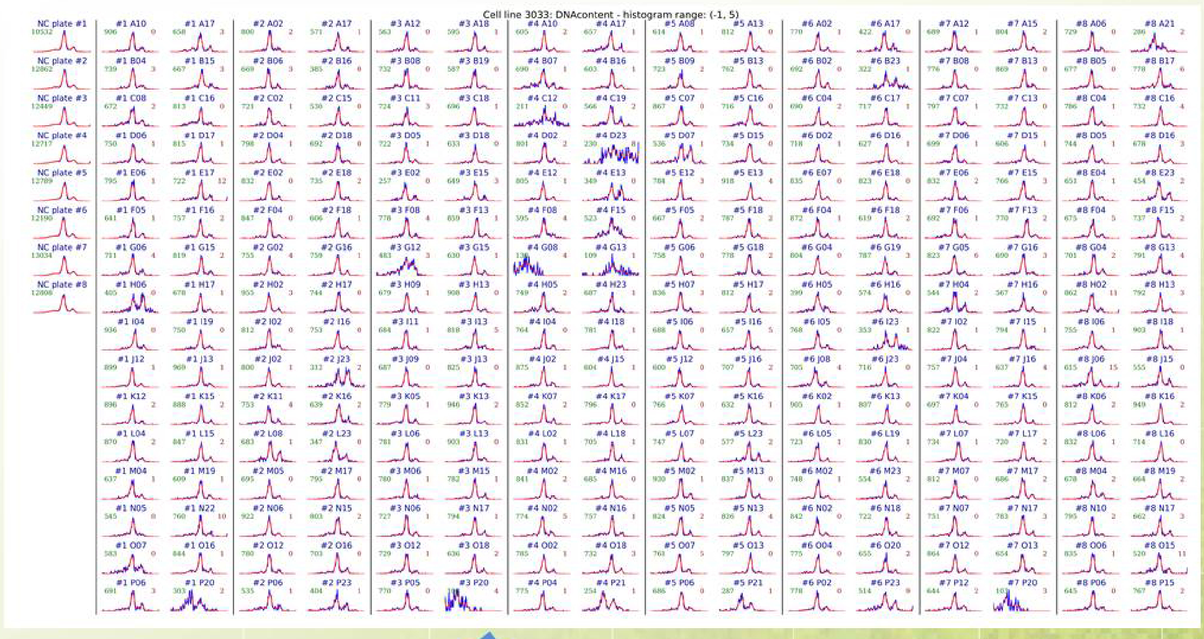
Future Work

- Automatic selection of treatments of interest,
- Combine multiple features,
- Automatic classification of cells and patients clustering according to their treatment responses.

Introduction

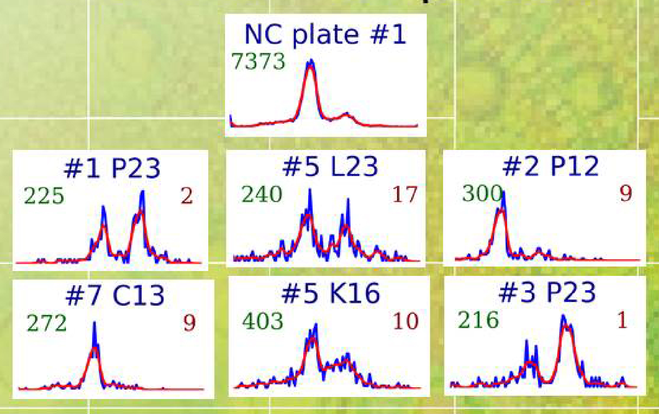
Development of drugs targeting solid tumor cancer stem cells (CSCs) has been limited by the lack of valid model systems and the complex genetic heterogeneity across tumors, factors that make it hard to assess new targets or predict drug responses in the individual patient. We are developing a new highly characterized CSC cultures biobank with continuously collected patient data and established primary cell lines in order to characterize CSCs in glioblastoma patients. The cell lines are exposed to various treatments and doses (more than 2500 different treatments and doses per cell line) and analyzed by image-based high-throughput screening in order to investigate and define the spectrum of therapeutically relevant regulatory differences between cell lines. The aim is to elucidate mechanisms of action and enable accurate targeting of disease subgroups. Here we present a general approach for comparing population statistics, and demonstrate it on DNA-content for cell cycle analysis.

Wells of interest

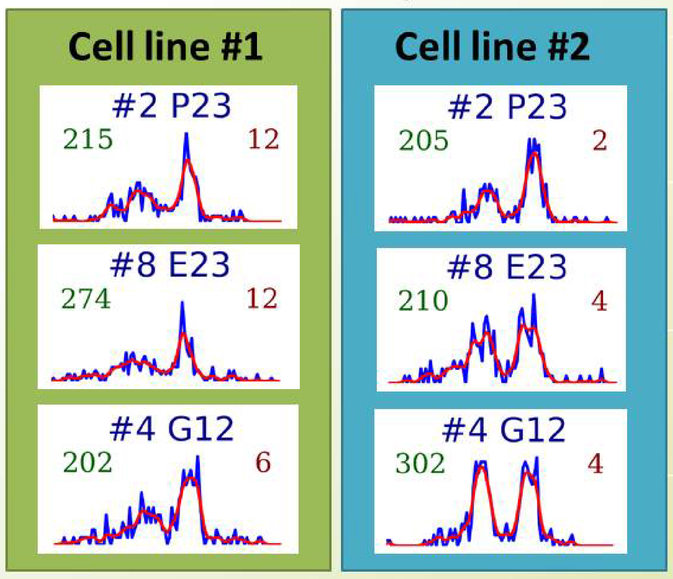


Cell cycle identification

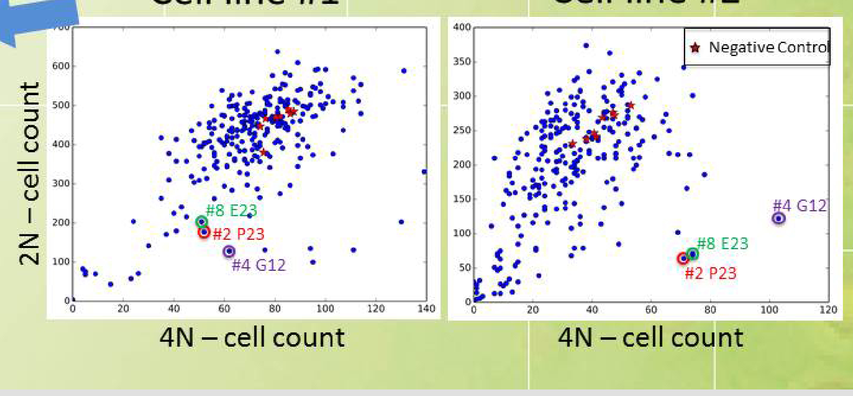
Treatment comparison



Cell line comparison



Treatments of interest



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