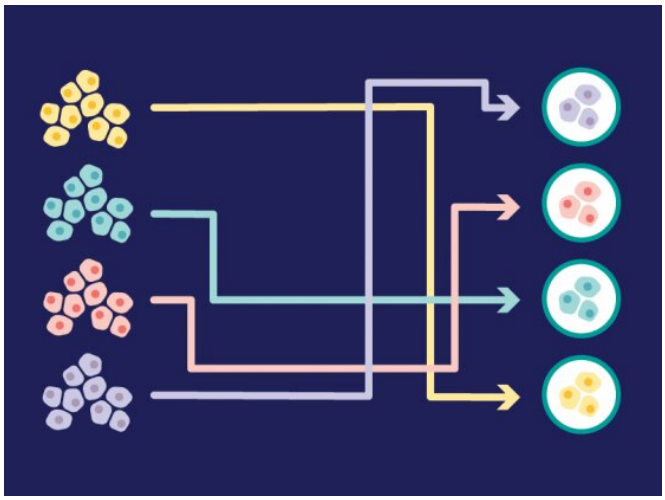
Using gene expression data to compare laboratory cancer models to real tumors

5 January 2021, by Tom Ulrich



Credit: Susanna M. Hamilton, Broad Communications

Cancer cell lines, grown from tumor cells and cultivated under laboratory conditions, are a mainstay of cancer research. They provide valuable insights into cancer genomics and biology, but for several reasons, scientists often struggle to compare data from cell line-based experiments with those from their complementary tumors, or select the best cell lines for modeling particular tumor types.

To help guide those choices, Allison Warren, Aviad Tsherniak, James McFarland, and other members of the Cancer Dependency Map (DepMap) team at Broad have developed Celligner, a computational tool that helps match tumors and cell lines based on gene expression profiling data.

Because cell lines are grown in labs, often for decades, they do not completely reflect the tumors they are supposed to model. For instance, lines can express genes or contain mutations not seen in patients' tumors, which can alter how they respond to anticancer drugs. Tumors, in the meantime, are complex mixtures comprising many cell types, while cell lines generally consist of just one.

Celligner corrects for these differences by comparing and aligning patient tumor and cell line RNA sequencing data (which reveals which genes are active in a cell at a point in time). By using Celligner to compare data from more than 12,000 patient tumors with more than 1,200 cell lines collected by the Cancer Cell Line Encyclopedia, The Cancer Genome Atlas, TARGET, and other projects, the team was able to:

- measure the extent to which particular cell lines mimic the tumors they are meant to represent, highlighting particularly strong—and particularly weak—cell line/tumor matches;
- pinpoint tumor types for which new, more representative cell lines or other models are most needed (such as thyroid and brain cancers); and
- reveal a set of cell lines with a unique expression signature that may represent early steps in the metastasis process.

Their full results are published in *Nature Communications*.

"A goal for the field is to possess a collection of cancer models that reflect all human tumors," said Jesse Boehm, an institute scientist in the Broad's Cancer Program and scientific director of the DepMap team. "Now, with Celligner, we can begin to measure our progress and focus new efforts to close the gaps, and improve our interpretation of molecular predictions to benefit real patients."

More information: Allison Warren et al. Global computational alignment of tumor and cell line transcriptional profiles, *Nature Communications* (2021). DOI: 10.1038/s41467-020-20294-x

Provided by Broad Institute of MIT and Harvard

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