Docket #: S16-087

Personalized cancer therapy with single cell analysis of heterogeneous tumors

Researchers in Prof. Sylvia Plevritis' laboratory have developed an algorithm designed to optimize cancer combination therapy for individual patients by analyzing distinct single-cell responses from heterogeneous tumors. This technology, called “DRUG-NEM”, can incorporate data from Mass Cytometry Time-of-Flight (CyTOF), single-cell RNA-seq, or any single-cell imaging data to identify subpopulations of cells. Then, it creates a nested drug network based on their effects derived from intracellular signaling changes associated with a desired phenotype such as cell death that may be different between these subpopulations. Finally, it systematically scores potential drug combinations to identify or prioritize strategies that will be both economically and clinically sustainable - to maximize the effects with a minimal number of drugs. This algorithm and computational framework can be used to integrate real-time testing of therapeutic agents in cancer clinical trials to provide precise, personalized treatment.

Stage of Research
The inventors used the DRUG-NEM computational framework to individualize drug combinations based on CyTOF data generated from a panel of targeted single drugs applied to single samples. They demonstrated that DRUG-NEM can identify optimal targeted drug combinations for cervical tumor cell lines and primary leukemia samples.

Applications

- **Rationally-designed cancer clinical trials:**
    - integrate real time testing of therapeutic agents to stratify patients based on single cell responses to targeted single drugs

- incorporate data from Mass Cytometry Time-of-Flight (CyTOF), single-cell RNA-seq, or any single-cell imaging data

Advantages

- **Precise, personalized treatment:**
  - integrates single-cell data to account for **intratumoral heterogeneity** to reduce the risk of drug resistance and patient relapse
  - predicts cancer drug combination responses to minimize number of drugs while maximizing response
  - potential to minimize cost and toxicity

Publications

- Benedict Anchang, Kara L. Davis, Harris G. Fienberg, Brian D. Williamson, Sean C. Bendall, Loukia G. Karacosta, Robert Tibshiranie, Garry P. Nolan, and Sylvia K. Plevritis, " DRUG-NEM: Optimizing drug combinations using single-cell perturbation response to account for intratumoral heterogeneity," Proceedings of the National Academy of Sciences May 2018, 115 (18) E4294-E4303; DOI: 10.1073/pnas.1711365115
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- Anchang, B., Do, M.T., Zhao, X., Plevritis S.K. (2014). CCAST: A model-based gating strategy to isolate homogeneous subpopulations in heterogeneous population of single cells. *Plos Computational Biology*, 10(7): e1003664.
- Anchang B, Tom DP Hart, Sean C Bendall, Peng Qiu, Zach Bjornson, Michael Linderman, Gary Nolan, and Sylvia Plevritis. (2016). Visualization and cellular hierarchy inference of single-cell data using SPADE. *NATURE Protocols*, 11, 1264–1279.

Patents

- Published Application: 20170285004

- Published Application: WO2017176946
- Issued: 10,436,771 (USA)

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