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Integration of data in the cancer context: Using CellMiner and the NCI-60 Cancerous Cell Lines for Systems Pharmacology

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Abstract

The study and treatment of cancer are currently in the midst of a fundamental shift as a result of the attempt to understand and utilize the various forms of "omic" data currently becoming available. High-throughput data is increasingly being integrated into the fields of molecular biology and pharmacology. However, a difficult problem has been rapid and fluid access to, and integration of the data. The NCI-60 cancerous cell lines are a premier example of a well-studied system that may act as a test case for gaining understanding of the integration of these types of data. In this context, we present here molecular and pharmacological data, along with a set of web-based tools within our CellMiner web-application. Cell Miner currently contains 16 databases that may be queried using our "Query Genomic Data" tools". Included are multiple forms of molecular data, including transcript expression for 26,065 genes and 360 micro RNAs, as well whole exome (DNA) sequencing. Additionally, CellMiner includes drug activity of 20,602 compounds including 110 Food and Drug Administration (FDA)-approved and 54 in clinical trial drugs, as measured by the Developmental Therapeutics Program. Additional datasets, including gene DNA copy number from array comparative genomic hybridization (aCGH) are in preparation. Integration of these datasets is facilitated by the "NCI-60 Analysis Tools, designed to be rapid and flexible, and to not require expertise in computer science or bioinformatics. Each molecular or drug response parameter creates its own pattern, that can then be compared to others. This approach allows one to search for potential relationships between the parameters in a manner specific to a users area of expertise and interest. Examples of both basic science and translational results will be provided, including the identification of a novel gene of pharmacological importance (SLFN11 for topoisomerase 1 and 2 inhibitors, as well as alkylating agents), and the identification of a novel compound for the treatment of the Core binding factor (CBF) subset of adult acute myeloid (AML) and pediatric acute lymphocytic leukemias (ALL).

Biography

William Reinhold is currently operating as facility head of the Genomics and Bioinformatics Group in the Laboratory of Molecular Pharmacology. He has been a part of this section since April 1998, working with first John N. Weinstein, and then Yves Pommier. He has been central in generating multiple datasets for the NCI-60 cancerous cell lines, available at the CellMiner web-application at http://discover.nci.nih.gov/cellminer/. His activities include running the web site, dissemination and interpretation of this data, encouraging and facilitating collaborations, and providing direction for the development of systems pharmacology within the goup. He received his B.S. in Biochemistry from the University of Maryland in 1978, and currently has 67 peer reviewed publications.

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