Current Awareness Journal Club

M.A. Kayala

Institute for Genomics and Bioinformatics
Donald Bren School of Information and Computer Sciences

January 18, 2010

Disease allele-dependent small-molecule sensitivities in blood cells from monogenic diabetes

PNAS PNAS PNAS **PNAS**

Stanley Y. Shaw, David M. Blodgett, Maggie S. Ma, Elizabeth C. Westly, Paul A. Clemons, Aravind Subramanian, and Stuart L. Schreiber(Harvard, Broad)

High-throughput drug discovery

- Lymphoblast cells derived from a family of patients where 8/17 have a particular allele linked to Maturity onset diabetes of the young 1

- Mut at orphan nuclear acceptor HF4α

- Luminescence-based ATP assay

- HT screen of 3973 small mols (incl. drugs)

- No single mol sig after MT correction, but using GSEA, some *sets* of compounds were.

- Validation in murine pancreatic HF4α KO and in insulin secretion expts.

Disease allele-dependent small-molecule sensitivities in blood cells from monogenic diabetes

Interesting

- HT drug-discovery using genotyped patient derived cells.

- Using microarray techniques in different experiments

Issues

- HF4α KO cells said to be problematic, but then used for validation

- Stat protocol of none significant after MT, then using GSEA, then picking "representative" cmpds seems a little rigged.

jCompoundMapper: An open source Java library and command-line tool for chemical fingerprint
Journal of Cheminformatics

Georg Hinselmann , Lars Rosenbaum , Andreas Jahn , Nikolas Fechner and Andreas Zell (Tubingen)
http://www.jcheminf.com/content/3/1/3

- CDK based Java lib for many different fingerprints
- Configurable, allows different depths, atom-typing, pharmacophore point mapping
- On some benchmarks show comparable results to latest QSAR predictors

Interesting: Do they allow "local" fingerprints around particular defined sites?

Quick Hits

- Comparative Analysis of Threshold and Tessellation Methods for Determining Protein Contacts

    - JCIM -
      `http://pubs.acs.org/doi/abs/10.1021/ci100195t`
    - Compare methods of determining residue contact in proteins. Threshold vs. Laguerre tesselation.

- Large-Scale Learning of Structure-Activity Relationships Using a Linear Support Vector Machine and Problem-Specific Metrics

    - JCIM -
      `http://pubs.acs.org/doi/abs/10.1021/ci100073w`
    - Extend LIBLINEAR with chemoinf specific metrics to run large scale linear SVMs.
    - Not quite as good as state of the art in accuracy, but much faster/scalable.

Quick Hits 2

- Protein-protein interactions: Interactome under construction
  - Nature - Technology review about PPIs (one of several in same issue)
  - `http://bit.ly/fUGhkO`
  - High-level review of PPIs:
  - Construction, validation, challenges, databases, visualization tools, etc.