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Beyond molecular structure: Biomarker discovery and drug repurposing using gene coexpression modules

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Disease diagnosis and therapy are often ineffective if they target individual proteins. Genes and the proteins they code for work together in groups, or modules, and perturbation of these modules can lead to disease. Drugs, in addition to disease, can induce particular patterns of module activation. Identifying these patterns provides important insight into novel diagnoses and therapies. Gene module activation profiles linked to disease can be mined for diagnostic biomarkers. Drugs can be repurposed by finding diseases with gene module activation profiles anti-correlated to that of the drug, or by finding drugs with different indications but similar activation profiles. In the latter case, two drugs with similar module activation profiles can be repurposed to treat each other's disease. When using gene module activation profiles for drug discovery, it is often found that drugs are effective at treating the same disease and share little structural similarity. So the link between module expression profile and disease is strong, the link between said profiles and molecular structure is not. This idea has huge implications for drug discovery, as ligand or structure-based screening and design using molecular shape or protein binding pocket complementarity, will only find a fraction of the total number of molecules effective against a disease. Gene module expression profiles on the other hand, have the potential to identify a much larger universe of compounds potentially active against a disease. In this presentatation, we will illustrate these ideas with a variety of examples and then discuss implications for future research in drug discovery.

Biography

Gregory J Tawa has completed his PhD at New York University and Post-doctoral training at the University of Minnesota. He has moved towards health sciences with emphasis on "drug and biomarker discovery using molecular modeling, bioinformatics and systems biology methods". He has a wide variety of experience, having been a Scientist in academia, small biotech and big pharma. Currently, he is Modeling and Informatics Lead of the National Institutes of Health, National Center for Advancing Translational Sciences, Therapeutics for Rare and Neglected Diseases Program.

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