Translational Informatics Workshop
Drug, Target, Disease, Population: How Informatics can Impact Healthcare

Sponsored by
Illuminating the Druggable Genome Knowledge Management Center
&
Translational Informatics Division, Department of Internal Medicine, UNM

8:30 – 8:45 Introduction – Pope L. Moseley, MD MS, Distinguished Professor and Chair, Department of Internal Medicine, UNM HSC

8:45 – 9:45 Nosology, Drug Therapy, and Personalized Medicine – Stuart J. Nelson, MD, FACP, FACMI, formerly Head, MeSH (NLM)

Nosology has traditionally been used for three main purposes, to provide prognosis, to predict etiology, and to guide therapy. As individualized medicine comes into practice, and as we develop greater and greater understanding of molecular biology, our nosology falls behind, and serves only to guide reimbursement. A model of how to describe patients, and to arrange data describing that patient, may serve to help clarify our learning from that most useful of textbooks, the patient. Finding "patients like mine" will provide a better nosology, with more relevant guides to therapy, prognosis, and etiology.

9:45 – 10:15 Coffee Break

10:15 – 11:15 The emerging network of data linking genes to drugs – Russ B. Altman, MD PhD, Professor of Bioengineering, Genetics, and Medicine, Stanford School of Medicine

Our group is building the Pharmacogenomics Knowledgeable (PharmGKB, http://www.pharmgkb.org/) which is devoted to cataloging all known human genetic variation impacting drug response phenotypes. As part of this work, we curate the literature and build informatics methods for better understanding drug action (efficacy and toxicity) in terms of individual molecular players and pathways. In this talk, I will describe several efforts to link genes and drugs using different information including: molecular information, expression information, textual information. These combine to create a network of data that informs our understanding of drug action, with applications towards repurposing, drug interactions and side effects.

Identifying drug molecular mechanisms is an exciting opportunity for understanding side-effects and for recognizing potential new indications for existing drugs. Current methods for explaining side-effects have focused on known drug targets and their pathways as primary candidates. However, low affinity binding to proteins that are not usually considered drug targets may also drive side-effects. In this work, we have assessed alternative targets by estimating drug’s potential binding to 563 essential human proteins. We have developed an algorithm that combined singular value decomposition and canonical component analysis (SVD-CCA) to predict side-effects based on these novel target profiles. In particular, our analysis produces 2768 triplet associations between essential proteins, drugs and side-effects. We validated a subset of these associations using experimental assay data.

11:45 – 12:15    DrugDB: Integration of chemical and pharmacological knowledge – Oleg Ursu, PhD, Translational Informatics Division, Department of Internal Medicine, UNM

Information on chemical identity for over 4000 pharmaceutical ingredients was collected and stored into a relational database. Information from binding activity, pharmacology, regulatory, classification systems knowledge domains was integrated and linked to active pharmaceutical ingredients. Bridging data across knowledge domains allowed creating domain-focused views centered on pharmaceutical ingredient, biological targets, pharmaceutical formulations and aggregated views where data from different domains can be viewed, queried, and analyzed. Identifiers from multiple sources (INN, ATC, RxNorm, NDC, UNII, PubChem, ChEMBL, etc.) were mapped to pharmaceutical ingredients and allow “translation” between different resources and data linking. Special emphasis was given to expert curation of chemical entities and high quality data sources to ensure creating high confidence links between knowledge domains.

12:15 – 12:45    Lunch Break (pre-registration required)

RSVP to Lydia Montoya, LyMontoya@salud.unm.edu by Tuesday Feb 17 at 10 am if you want lunch.

12:45 – 13:15    Drugs-Targets-Diseases and the Systematization of Knowledge – Tudor I. Oprea, MD PhD, Translational Informatics Division, Department of Internal Medicine, UNM

The IDG KMC is facing the challenge of systematizing knowledge, and organizing content in a manner that is conducive to target prioritization for biomedical research and drug discovery. We have identified a “knowledge deficit” that is best summarized as follows: ~90% of the human proteome lacks small molecule agents or therapeutic drugs; ~70% of the human diseases lack therapeutic agents; and approximately half of the proteome is not well studied, as exemplified by objective metrics that include literature annotation, disease associations, genome-wide association studies, protein expression in tissues, number of (polyclonal) antibodies and gene reference-into-function (RIF) statements.

13:15 – 13:35    Protein biomarker discovery in late onset neonatal sepsis – Subramani Mani, MBBS, PhD, Translational Informatics Division, Department of Internal Medicine, UNM

In this talk we will discuss a focused proteomic biomarker study of late onset neonatal sepsis using a predictive modeling approach based on machine learning (ML) methods. We will introduce the ML framework, the ML algorithms, the clinical domain and the clinical questions we are trying to address based on our biomarker discovery approach. Finally, using the top ranked protein biomarkers of neonatal sepsis we will outline a strategy for druggability profiling which has the potential for discovering new drug targets.
The informatics of (micro)RNA based diagnostics and drugs; unlosing the translation – Christos Argyropoulos MD, MS, PhD, Division of Nephrology, Department of Internal Medicine, UNM

In recent years microRNA based diagnostics and therapeutics have been hailed as significant innovations to fulfill the unmet needs in diverse therapeutic areas. Using examples from our previous work in diabetic nephropathy and experimental studies in acute kidney injury we demonstrate the capabilities of RNA based approaches to deliver novel diagnostics and therapeutics. To fully leverage the potential of microRNAs significant advantages should be made in both the bioinformatics and the clinical informatics fronts in order to carry out effective translation/reverse translation cycles from the bench to the clinic and vice versa.

User design issues with health information and communications technologies – Philip Kroth MD, MS, Section Chief, Clinical Informatics, Translational Informatics Division, Department of Internal Medicine, UNM

The rapid increase in the use of health information and communications technologies (HICT) by physicians has provoked unprecedented changes in the way physicians practice medicine. This has come about despite fairly scant evidence that use of these technologies actually improves the quality of patient care. In addition to the quality of care, the impact of HICT use on physician stress, fatigue, and burnout is virtually unknown. We will describe the preliminary results from the current study in process at UNM and three other institutions designed to determine what specific features of HICT are most associated with physician stress, fatigue, and burnout.

New and Innovative Technology for Whole Genome Sequencing and Assembly – Jeremy Edwards PhD, Chemistry and Chemical Biology, UNM

Recent advances in whole genome sequencing have significantly driven down the associated costs of sequencing and increased the throughput and availability of genetic information to the biomedical research field. However, major roadblocks to discovery and innovation still stand in spite of these breakthroughs. For example, haplotype-resolved whole genome sequencing, a critical element necessary to establish context in disease-association studies, needs to be further developed. We are developing new strategies for ultra-long sequencing based on innovative library construction and direct sequencing of 1MB DNA. These efforts hold the potential for haplotype-resolved whole genome sequencing and a paradigm shift in our understanding of the human genome and complex disease states.

Coffee Break

Leveraging informatics and machine learning for better healthcare – Panel Discussion involving the guests and the audience