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Interactomics: Computational analysis of novel drug opportunities

We have developed a Computational Analysis of Novel Drug Opportunities (CANDO) platform funded by a 2010 NIH Director's Pioneer Award that analyses compound-proteome interaction signatures to determine drug behaviour, in contrast to traditional single target approaches. The platform uses similarity of interaction signatures across all proteins as indicative of similar functional behavior and non-similar signatures (or regions of signatures) as indicative of off- and anti-target (side) effects, in effect inferring homology of compound/drug behaviour at a proteomic level. We have created a matrix of predicted interactions between 3,733 human ingestible compounds (including FDA approved drugs and supplements) × 48,278 proteins using our hierarchical chem and bio-informatic fragment-based docking with dynamics protocol (from over one billion predicted interactions total). We applied our compound-proteome signature comparison and ranking approach to 2030 indications with one approved compound and yielded benchmarking accuracies of 12-25% for 1439 indications with more than approved compound. We are prospectively validating "high value" predictions *in vitro, in vivo,* and by clinical studies for more than forty indications, including dental caries, dengue, tuberculosis, ovarian cancer, cholangiocarinomas, among many others. 58/163 (36%) predictions from twelve studies covering ten indications show comparable or better activity to existing therapies, or micro-molar inhibition at the cellular level, and serve as novel repurposeable therapies. Our approach is applicable to any compound beyond those approved by the FDA, and also include can readily consider mutations in protein structures to enable personalization based on genotype, foreshadowing a new era of faster, safer, better and cheaper drug discovery. Our approach also has other application in areas such as synthetic biology and nano-biotechnology. In this presentation, we will describe the latest developments in the CANDO platform, with a focus on characterization of host-microbiome-drug interactions.

Biography

Ram Samudrala is Professor and Chief of Division of Bioinformatics, State University of New York, Buffalo researching multi-scale modeling of atomic, molecular, cellular and physiological systems with an emphasis on protein and proteome structure, function, interaction, design and evolution. His work has led to more than 115 publications in journals such as *Science, Nature, PLoS Biology*, the *Proceedings of the National Academy of Sciences* and the *Journal of the American Medical Association*. He has joined the University of Washington Faculty in 2001 (where he remains as an Affiliate Professor) after completing his Doctoral research with John Moult at the Center for Advanced Research in Biotechnology in 1997 and his Post-doctoral research with Michael Levitt (2013 Nobel in Chemistry) at Stanford University in 2000, which resulted in him making some of the best predictions at the first three community-wide assessment of protein structure prediction (CASP) experiments.

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