Interactomics: Computational Analysis of Novel Drug Opportunities

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We have developed a Computational Analysis of Novel Drug Opportunities (CANDO) platform funded by a 2010 NIH Director's Pioneer Award (http://protinfo.org/cando) that analyses compound-proteome interaction signatures to determine drug behaviour, in contrast to traditional single (or few) target approaches. The platform uses similarity of interaction signatures across all proteins as indicative of similar functional behaviour and nonsimilar 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 (http://protinfo.org/cando/collaborations), including dental caries, dengue, tuberculosis, ovarian cancer, cholangiocarinomas, among many others. 57/162 prospective predictions across eleven studies covering nine indications have shown comparable or better activity to an existing drug, or micromolar inhibition at the cellular level, and serve as novel repurposeable therapies. We were able to make predictions against the Ebola virus within minutes and are currently working with collaborators to test them in vitro. 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 personalisation based on genotype, foreshadowing a new era of faster, safer, better and cheaper drug discovery.