4.5 Combining proteomics (and other omics) and biological knowledge to extract disease mechanisms

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Proteomics in its various forms provides rich information about cellular processes and their deregulation in disease. This information is complementary to that provided by other omics technologies such as transcriptomics. In this talk I will discuss our work to extract mechanistic information from these data using computational methods that leverage our prior biological knowledge of the underlying mechanisms. I will illustrate them using datasets from various disease contexts.

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4.6 The Cancer Cell Mapping Initiative

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In contrast to the substantial progress in mapping cancer genomes, systematic efforts to map cancer pathways are just beginning. I will describe recent efforts by the Cancer Cell Map Initiative (CCMI) to close this gap, including complete protein-protein interaction landscapes for head-and-neck and breast carcinomas. Integrating the new protein network data with cancer genome sequences, we have produced a comprehensive map of protein complexes and super-complexes under significant mutational pressure in cancer. This map provides a general framework for cancer genome analysis to extract detailed mechanistic insights and therapeutic targets. In particular, we are now using these maps to guide assembly of DrugCell, an interpretable deep learning model of cancer which predicts the response of tumors to therapeutic agents. I will illustrate the predictive performance and mechanistic interpretability of DrugCell in multiple contexts, including cancer cell lines, patient samples and patient-derived xenografts. Finally, I will demonstrate how DrugCell is used to design synergistic drug combinations that we are able to confirm both in vitro and in vivo.

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