Title:

Adding a proteomic component to therapeutic decision making by molecular tumor boards

Abstract:

Most (cancer) drugs act directly on proteins, are proteins themselves or engage cellular pathways controlled by proteins. Hence, adding a proteomic component to the molecular profiling of tumor patients may provide additional information to genomic and transcriptomic data to aid therapeutic decision making by molecular tumor boards (MTBs).

To test if this is indeed the case, we have extended the multi-omics registry trial MASTER (Molecularly Aided Stratification for Tumor Eradication) to the profiling of cancer patient (phospho-)proteomes. Here, we are asking three particular questions:

1. Can the complex logistics be managed such that proteomic data is available in time for MTB meetings where a particular patient is discussed?

2. Does the proteomic information support or contrast the recommendations made on the basis of genomic profiling?

3. Does it make a difference to disease progression and outcome of a patient?

To interpret patient proteome profiles, a number of additional proteomic approaches are aligned to this data. First, for kinase and HDAC inhibitors, we have developed affinity regents that enabled selectivity profiling of >1,000 of these drugs on a proteome-wide scale. Second, integrating phenotypic drug response data with proteome and phosphoproteome profiling data of >500 treatment-naive cancer cell lines to the depth of 10,000 proteins and phosphorylation sites each, can highlight mechanisms of drug sensitivity and resistance. Third, measuring the response of a cancer cell line (phospho-)proteome in response to a drug directly, shows which pathways are actually engaged and what the consequences of this engagement is.

This talk will give examples from the above experiments to illustrate what can be gleaned from such data and how we use this to inform patient proteome data and translate this information into treatment recommendations.