

BIOMARKER DISCOVERY BY ANTIBODY MEDIATED PROTEOMICS

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Discovery and utilization of new, disease specific protein biomarkers will advance clinical diagnostics and treatment as well as accelerate the complex drug discovery and validation process. New biomarkers can also bridge the gap between cellular and animal models as well as human clinical conditions as they are likely to be relevant to drug mechanisms of action as predictors of drug efficacy. The expectation is that disease progression-specific biomarkers will permit the prediction of improvement earlier than such improvement is actually apparent, thus providing a useful tool to measure and predict the efficacy of candidate novel drugs in shorter and less costly clinical trials. Disease specific protein biomarkers can speed up the complex process of drug discovery and assist in optimizing patient stratification for important clinical trials. As of today, these efforts are hampered by the lack of an efficient biomarker discovery platform coupled with an effective validation process. Although frequently used methods of MS profiling and systems biology approaches can generate disease relevant candidates, these markers are usually based on abundant proteins and lack the required specificity, and are thus rarely translated into bedside clinical tests. In this presentation, a novel biomarker discovery strategy will be described that combines high throughput monoclonal antibody-based global disease specific plasma proteome screening technology with multidimensional bio-separation and mass spectrometry-based identification of protein biomarkers. We describe the generation of a highly complex plasma-proteome specific mAb library (>4,000 mAbs) which can be screened multiple times to find the best biomarkers. The approach also makes possible the rapid generation of novel mAb libraries from clinical material to discover biomarkers that are exclusive for a given disease. The availability of mAbs at this scale, with proven diagnostic potential can significantly cut clinical assay (e.g. ELISA) development time.