**CONCEPT CLEARANCE RECORD**
**FY 2016 RESEARCH INITIATIVE – NCATS**

TITLE: Proteome Profiling in the Clinic

OBJECTIVE(S): To establish new clinical tests and protein biomarkers based on quantitative proteomics, phosphoproteomics and validated antibodies; optimize technical and analytical tools and easy-to-use resources and databases for physicians and clinical staff; and perform combined analysis of genetic and proteomic data for decision making in personalized health care. Quantitative read-outs will promote better understanding and longitudinal monitoring of pathophysiology and drug effects. Efficiencies can be achieved through awards made to consortium members working on clinical proteomics.

DESCRIPTION: New sensitive clinical tests, reliable panels of protein biomarkers and quantifiable assays are urgently needed in the clinic. Dynamically regulated proteins are the functional effector molecules in cellular systems and directly define phenotypes in monogenic and complex diseases. Establishing mass spectrometry-based, quantitative proteomics can change the approach to evidence-based personalized medicine and how cellular biopsy material and bodily fluids are analyzed.

IMPORTANCE: The Human Genome Project cannot be used fully for precision medicine without profiling the proteome and its dynamically regulated post-translational modifications (e.g., phosphorylation, ubiquitination). Genomic tools do not allow the analysis of post-translational modifications at all. Indeed, the lack of well-established protein markers might explain some of the failures in clinical trials that are solely based on genetic data. Examples for clinical areas that would benefit tremendously include acute and chronic conditions in oncology (e.g., overactive MAPK and PI3K signaling), brain and muscle diseases (e.g., channelopathies), autoimmune and inflammatory diseases, and endocrine diseases.

HISTORY: Due to relative ease and affordability, genetic analysis and immunoassays are the methods of choice for molecular medicine. However, proteins are more dynamically regulated than genes, and gene expression does not always predict protein expression levels. Mass spectrometry-based, quantitative proteomics has made significant progress over the last 10 years. Hence, new clinical proteomic assays with absolute specificity can replace less-sensitive immunoassays and help to better interpret genetic data.

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