

Targeted Mass Spectrometry Approaches To Detect Kinase Pathways For Personalized Medicine

Tech ID: 27278 / UC Case 2016-746-0

SUMMARY

Researchers at UCLA and their collaborators are developing a platform that will allow clinicians to diagnose a prostate cancer patient by evaluating the phosphoproteome from tissue obtained by biopsy. In addition to diagnosis, this method provides information about kinase activation that a clinician can use for treatment decisions.

BACKGROUND

Early stage prostate cancer is dependent on androgens for survival. Men diagnosed with aggressive prostate cancer initially respond well to anti-androgen therapies but eventually develop a more drug resistant form of the disease. In addition, all prostate cancer patients are essentially treated with the same regimen and there are currently no subtypes to stratify patients for therapeutic purposes. Therefore, the development of new diagnostic biomarkers that predict disease progression or new companion biomarkers that stratify patients for effective personalized therapy are urgently needed.

INNOVATION

Researchers at UCLA along with their collaborators are developing a method that will allow clinicians to diagnose prostate cancer by evaluating the phosphoproteome, or phosphorylated proteome, from patient tissues obtained by biopsy. In order to rapidly transition this method into the clinic, the inventors have optimized the selected ion monitoring (SIM) mass spectrometry technique to screen a patient's phosphoproteome accurately and sensitively. In addition to diagnostics, the proposed prostate cancer phosphoproteome biomarkers can also guide clinicians through treatment decisions by identifying activated kinases. Thus far, the inventors have shown that specific kinases are activated in metastatic castration resistant prostate cancer (CRPC) but not normal tissue or less advanced stages of disease. The advantage of using the phosphopeptides they have selected is that the biomarkers are targets of FDA approved drugs or late-stage clinical trials, allowing the results of their approach to be moved to the clinic very quickly.

APPLICATIONS

- ▶ Diagnose prostate cancer patients based on phosphoproteome profile
- ▶ Determine best available treatment for prostate cancer patients based on kinases that are activated

ADVANTAGES

- ▶ SIM mass spectrometry can provide accurate, precise, and reproducible detection of phosphopeptides from multiple samples with high sensitivity when compared to data-dependent acquisition or shotgun phosphoproteomics.
- ▶ The capability of SIM mass spectrometry to multiplex significantly increases the value and utility of this approach as 50-100 different analytes can be monitored from a single sample source.
- ▶ The dynamic range of SIM can reach over 4 orders of magnitude, which eliminates the need for bulk tissue and paves the way for biopsy-driven analysis of the phosphoproteome in cancer patients.

STATE OF DEVELOPMENT

- ▶ The researchers have established that kinase activity and tyrosine phosphorylation is dramatically increased in CRPC patient tissues by performing immunohistochemical (IHC) staining of prostate cancer tissue microarrays with the tyrosine phosphorylation specific antibody to evaluate phosphotyrosine expression during disease progression.

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INVENTORS

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OTHER INFORMATION

KEYWORDS

Prostate cancer, castration resistant prostate cancer, CRPC, druggable kinase targets, phosphoproteome

CATEGORIZED AS

- ▶ **Medical**
- ▶ Diagnostics
- ▶ Disease: Cancer

RELATED CASES

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▶ They also found that phosphoproteomic profiling identified patient-specific patterns of druggable kinase targets and pathways in metastatic CRPC lesions. 16 metastatic CRPC samples from 13 different patients were analyzed by phosphoproteomic enrichment coupled to quantitative label-free mass spectrometry (MS).

▶ From their phosphotyrosine enrichment and subsequent phosphoserine/phosphothreonine (pSer/pThr) enrichment preparations and mass spectrometry analyses, they identified over 8,000 unique phosphopeptides in CRPC patient tissues.

RELATED MATERIALS

▶ Drake JM, Paull EO, Graham NA, et al. Phosphoproteome Integration Reveals Patient-Specific Networks in Prostate Cancer. *Cell*. 2016;166(4):1041-54.

ADDITIONAL TECHNOLOGIES BY THESE INVENTORS

- ▶ [Nucleic Acid Tetramers For High Efficiency Multiplexed Cell Sorting](#)
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