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J Proteomics Bioinform 2016, 9:11(Suppl)
http://dx.doi.org/10.4172/0974-276X.C1.092

Quantitative proteomic analysis of prostate cancer for biomarker discovery and drug target identification

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Clinical management of prostate cancer (PCa) is marred by excessive diagnose and treatment of indolent tumors and also by paucity of effective therapies for patients harboring metastatic, castration resistant tumors. Proteins are the essential effectors of cellular functions and the targets of most of the currently used or newly developed drugs. Genetic analysis alone cannot be used to predict protein function and concentration changes because protein function is regulated at the translation and postranslational levels (e.g., by ubiquitination, phosphorylation, proteolysis, etc.). Therefore, system level quantitative proteomic analysis can reveal novel information that could be used in the identification of biomarkers or viable drug targets to address important clinical needs. Our investigations have been motivated by our limited understanding of the proteome changes associated with PCa initiation and progression. We will present the results of the most extensive investigations of the prostate cancer proteome to date. We have implemented a stable isotope based methodology to identify and quantify 6000 proteins in minute amounts of formalin fixed paraffin embedded tissue samples and apply it to the analysis of malignant (n=28) and non-malignant (n=8) tissue from prostatectomy samples and bone metastases (n=25). We will describe protein, pathways and processes that are de-regulated at different stages of disease progression. To demonstrate the translational value of this type of analysis, we identified a novel prognostic biomarker, proNPY that can select patients who are at increased risk death among those harboring low Gleason score tumors. The prognostic value of this biomarker was assessed in two independent large cohorts of patients managed by watchful waiting.

Biography

Amilcar Flores Morales completed his PhD in Chemistry from National University of Colombia and Post-doctoral studies from the Karolinska Institute where he became an Associate Professor in 2006. In 2009, he became a Professor of Molecular Endocrinology at the University of Copenhagen. He has a long standing interest in "The application of system-wide molecular profiling (omics) to the characterization of endocrine tumors with a focus on prostate cancer".

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