

INVITED LECTURE H2

Pharmacoproteomics: Strategies for identifying new diagnostic and prognostic markers for colorectal cancer

Richard J. Simpson, Hong Ji, David Greening, Justin Lim, Robert J.A. Goode, Eugene Kapp, Oliver K. Bernhard, Sung-Min Ahn & Robert L. Moritz

Joint Proteomics Laboratory (JPSL), Ludwig Institute for Cancer Research & The Walter and Eliza Hall Institute of Medical Research, Parkville, Victoria 3050, Australia

Colorectal cancer (CRC) is a leading cause of cancer death in the Western World. Early detection is the single most important factor influencing outcome of CRC patients. If identified while the disease is still localized CRC is treatable. To improve outcomes for CRC patients there is a pressing need to identify biomarkers for the early detection (diagnostic markers), prognosis (prognostic indicators), tumor responses (predictive markers) and disease recurrence (monitoring markers). Despite recent advances in the use of genomic analysis for risk assessment, in the area of biomarker identification genomic methods have yet to produce reliable candidate markers for CRC. For this reason, attention is now being directed towards protein chemistry or proteomics as an analytical tool for biomarker identification. Here, we discuss various proteomics technologies with reference to how they may contribute to CRC biomarker discovery. One such strategy uses a combination of continuous free flow electrophoresis (FFE) in the first dimension, a liquid-based IEF technique, followed by rapid RP-HPLC (1-6 min/analysis) in the second dimension. Imaging software has been developed to present the FFE/RP-HPLC data in a virtual 2D format. Demonstration of the method is presented using proteome analysis of human plasma and urine specimens. Additionally, we describe strategies for analyzing the 'secretome' of human CRC cell lines, the human platelet membrane proteome, tissue interstitial fluid from tumor-derived human colon carcinoma cell line xenografts, and a proteomics approach for analyzing the effect of non-steroid anti-inflammatory drugs on human colorectal carcinoma cell lines.