PROGNOSTIC BIOMARKER DISCOVERY IN COLORECTAL CANCER USING PROTEOMICS

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The rising health burden associated with colorectal cancer in Australia and the western world demands more efficient and reliable approaches to treating these patients. Prognostic biomarkers that inform on patient outcome, tumour response, and toxicity to chemotherapies would greatly assist in determining appropriate personalised patient care. We are applying proteomic techniques in two studies to identify candidate prognostic biomarkers. In one study we have used iTRAQ mass spectrometry to compare protein expression levels between tumours and matched adjacent normal mucosa from 16 CRC patients, covering A-D stage disease (ACPS). On average, approximately 800 proteins were quantitated per sample, and statistical tests have identified 118 proteins as differentially expressed (45 over-expressed). There appeared to be little correlation between tumour stage and protein expression in the limited number of samples analysed. We chose 11 proteins (anterior gradient protein 2, CEA, maspin, beta-catenin, caldesmon, galactin-3, S100A8/A9, Stat-1, transglutaminase, HLA-DR, CK20) to validate using immunohistochemistry; and these showed reliable concordance with iTRAQ data. We are undertaking more extensive validation using a tissue microarray of 300 Stage C tumours with known clinical outcomes. We expect that this approach will propose prognostic biomarkers that differentiate patient outcomes.

A second study is examining patient plasma for prognostic biomarkers of early chemotoxicity, response and outcome. We have designed multiple reaction monitoring (MRM) mass spectrometry assays to quantitate the level of circulating plasma proteins in patients prior to and during chemotherapy. We will correlate the changes of protein levels with standard toxicity assessments. In advanced CRC patients we will also correlate changes in protein levels with response and outcome to evaluate the utility of these as prognostic biomarkers.