Associate Professor Mark P Molloy  
mark.molloy@mq.edu.au

Room E8C 311  T: (02) 9850 6218

CANCER and BIOMEDICAL PROTEOMICS

Proteomics is the large-scale analysis of proteins present in biological matrices including cells, tissues and fluids. My research uses proteomic technologies (mostly mass spectrometry) to investigate dysregulated proteins functions that often underlie human disease. As the proteome is highly dynamic our research involves comparisons of samples to measure temporal changes in protein levels and interactions. A main area of interest is in translational cancer biology which involves collaboration with clinicians to analyse patient specimens to better understand and treat disease. For example, we are interested in discovering protein biomarkers relevant to cancer progression, patient response to treatment and in understanding how cell signaling networks are altered in cancers. To facilitate these studies we need to optimize sample handling procedures and analysis methods using quantitative mass spectrometry. Examples of studies we perform include: regulation of protein post-translational modifications, protein-protein interactions, quantitation of protein biomarkers in cells and fluids, examining protein expression responses to drugs and gene knock-downs. My research utilises the state-of-the-art equipment located within the Australian Proteome Analysis Facility (APAF). The projects below are examples and can be tailored for PhD or MRes students.

PHOSPHOPROTEOMICS REVEALS HIDDEN SIGNALING ACTIVITIES IN CANCERS

Cells use protein phosphorylation as rapid switches to control intracellular signaling and gene expression. In cancer, the mutation of various kinases causes signaling dysregulation leading to aberrant cellular proliferation. This project seeks to investigate the phosphoproteome of various cancers (colon, melanoma, etc) to delineate hidden signaling networks. This knowledge may lead to improved targeting of drug inhibitors to control signaling pathways. We modulate signaling pathways by use of inhibitors or genetic disruption, then profile the phosphoproteome using advanced mass spectrometry.

Two current projects are examining the role of oncogenic BRAF and Protein kinase CK2 in various cancers.
Students will learn techniques including mammalian cell culture, protein/peptide biochemistry, chromatography, quantitative protein mass spectrometry and bioinformatic data analysis.

![Diagram of proteomics workflow](image)

![Phosphoproteomics data analysis](image)
INVESTIGATING STROMAL CYTOKINE SECRETION TO IMPROVE IMMUNOTHERAPY

The contribution of stromal cells (immune cells, fibroblasts) in the tumour microenvironment to tumour expansion is becoming increasingly realized. These cells produce numerous cytokines that can be exploited by tumours to increase their growth. Immunotherapy is a hot new approach in cancer treatment with some remarkable results observed in some cancers, but responses are variable. This project seeks to investigate whether controlling signaling from stromal cells would improve responses to immunotherapy. The project uses proteomics to study how colon cancer cells respond to these cytokines to identify strategies to improve immunotherapy outcomes.

CANCER DRUG MONITORING BY MASS SPECTROMETRY

Mass spectrometry (MS) is used to quantitate the levels of small molecule drugs from patient blood. My group is working with oncologists to monitor the levels of kinase inhibitors from patient blood and correlate this with clinical outcomes such as response and toxicity. This requires the development of validated MS bioassays developed on high resolution Orbitrap MS platforms. As this approach is very sensitive we are investigating novel approaches to introduce microliter volumes to the MS, for example via paper spray ionization. The detection of drug levels from dried blood spots is likely to become a common approach to monitoring patient response to drugs. The project suits students with interests in bioanalytical chemistry and instrumentation.

Selected Publications


https://directory.science.mq.edu.au/users/mmolloy