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 changes in protein levels over timecourses. One of my main interests 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 knockdowns. My research utilises the state-of-the-art equipment located within the Australian Proteome Analysis Facility (APAF) and the Biomolecular Frontiers Research Centre. 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.
THERMAL SHIFT PROTEOMICS IDENTIFIES DRUG/NATURAL PRODUCT PROTEIN TARGETS

It is well known that ligand bound protein complexes have greater resistant to melting than unbound proteins. This characteristic can be exploited to identify soluble protein binders to new drugs and natural products and to determine off-target effects. By using mass spectrometry as the detection method analyses can be carried out in vivo, in a large-scale unbiased manner to detect such proteins. Through collaborations we have a number of drug molecules where the thermal shift profiling can be applied. This is a “hot” new technique in proteomics and drug discovery and would be of interest to students with interest in medicinal chemistry and medical science.

MICROSAMPLING AND THERAPEUTIC DRUG MONITORING

Only a small volume of blood or plasma is required for mass spectrometry detection of chemotherapeutic drugs. We are investigating novel approaches to introduce microliter volumes to the mass spectrometer to detect drug levels in patients, enabling therapeutic drug monitoring to ensure appropriate patient dosing. The project suits students with interests in bioanalytical chemistry.


Selected publications


3. Lin, C-H., Chik, J., Packer, NH., Molloy, MP. Multi-dimensional fractionation is a requirement for quantitation of Golgi-resident glycosylation enzymes from cultured human cells. *J. Proteome Res.* 2015, 14, 747-55.

