NSW Clinical Mass Spec Forum presents…

The role of mass spectrometry in the diagnosis of primary aldosteronism

Date: Wednesday 8th November 2023

Location: University of Technology, Sydney, CB04.05.430

Online link:
https://zoom.uts.edu.au/j/86292321488

Meeting Chair:
Prof. Andrea Rita Horvath, MD, PhD, FRCPath (UK), FRCPA
Director of Chemical Pathology | NSW Health Pathology

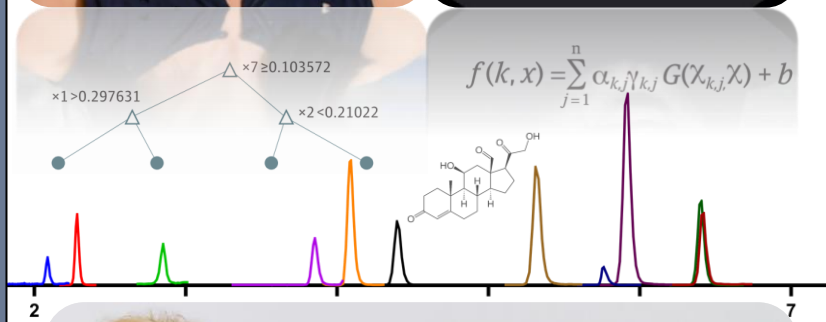
5:30 – 6:00pm
Arrival and refreshments

6:00 – 6:25pm
A/Prof. Jun Yang, MBBS FRACP PhD
Head of Endocrine Hypertension Service, Hudson Institute of Medical Research

6:30 – 6:55pm
Kevin Mantik
Senior Hospital Scientist CMS Section NSW Health Pathology, Randwick

7:00 – 7:30pm
Prof. Graeme Eisenhofer PhD & Dr. Christina Pamporaki, MD PhD
Technische Universität Dresden, Germany

7:30 – 8:30
Refreshments and Networking



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6:00 - 6:25pm | *What's the fuss about aldosterone assays for the diagnosis of primary aldosteronism?*

Associate Professor Jun Yang is the Head of the Endocrine Hypertension Group at Hudson Institute of Medical Research, Consultant Endocrinologist at Monash Health and Senior Researcher in the Department of Medicine at Monash University, Victoria, Australia. Jun graduated from Monash University with a MBBS (Hon) in 2001, obtained the FRACP in 2010 and completed her PhD on tissue-selective coregulators of the mineralocorticoid receptor (MR) in 2013. She has continued basic and clinical research in the field of MR-MR-driven cardiovascular disease, in particular, primary aldosteronism. She established the Endocrine Hypertension Service in 2016 and co-leads the NHMRC Centre of Research Excellence in Primary Aldosteronism. Together with national and international collaborators, her research program seeks to improve the detection and understanding of primary aldosteronism so as to achieve improved patient outcomes.

Abstract

Primary aldosteronism is a common but under-diagnosed cause of hypertension which confers higher risk of cardiovascular and renal disease than essential hypertension. Timely diagnosis is crucial as targeted medical treatment with mineralocorticoid receptor antagonists or surgical treatment with adrenalectomy can ameliorate the risks associated with aldosterone excess. The aldosterone to renin ratio is the current screening test for primary aldosteronism while a seated saline suppression test is performed to confirm the diagnosis. The failure of aldosterone to decrease below a set threshold following saline infusion is considered diagnostic of primary aldosteronism. Whilst the exact diagnostic threshold is debated, the assay used to measure aldosterone concentration can also impact the final diagnosis.

6:30 - 6:55pm | *Development and validation of an LC-MS/MS steroid panel for diagnosis of primary aldosteronism*

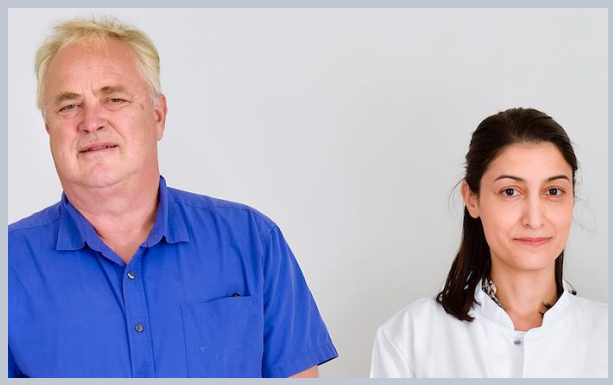
Kevin Mantik is a scientist with over 20 years of experience in Clinical Mass Spectrometry, starting his pathology career in the Biochemical Genetics laboratory at the Alberta Health Service in Canada. Since moving to Australia in 2014, Kevin has worked in both private and public pathology developing and maintaining LC-MS/MS assays across multiple analyte classes. Kevin's current position includes the management of a team at the Chromatography and Mass Spectrometry section, Chemical Pathology, Prince of Wales Hospital. This role involves the development and validation of clinical assays and giving oversight to the technical, operational, quality and regulatory integrity of the department. Analyses performed in the CMS lab include biogenic amines, steroid hormones, vitamins, mercaptopurines, immunosuppressants, and IGF-1. Areas of research and collaboration span from: steroid profiling and primary aldosteronism, oncometabolites and TCA cycle intermediates, markers for CKD and cardiovascular health, paracetamol metabolites, protein and peptide applications.

Abstract

Steroid profiling by liquid chromatography-tandem mass spectrometry (LC-MS/MS) combined with machine learning (ML) can aid in diagnosis of PA while avoiding the known limitations of immunoassay. As part of an international study, an expanded LC-MS/MS steroid profiling method has been developed locally, adapted from published methods and utilising the CMS laboratory's decade of experience in steroid analysis by LC-MS/MS. This talk will explore some of the challenges of steroid analysis and highlight novel aspects of the new method.

In addition to the new method, a standard operating procedure for validation of clinical LC-MS/MS assays has been developed and applied in the validation of the new steroid panel. Highlights from the SOP and its accompanying template will be presented.

7:10 - 7:30pm | *Steroid profiling with machine learning for diagnosis of primary aldosteronism: challenges for translation into routine clinical practice*



Graeme Eisenhofer PhD and **Christina Pamporaki MD, PhD** have been working together at Dresden for the past 12 years. While Graeme is a bench level scientist broadly engaged in applications of laboratory analytics in clinical studies, Christina is an endocrinologist with research interests in disorders of the adrenal. These complimentary activities have recently evolved into applications of machine learning and mass spectrometry-based analytics for improved diagnosis of patients with endocrine hypertension, particularly catecholamine-producing tumours and primary aldosteronism.

Abstract

The explosive growth in use of artificial intelligence (AI) in medicine is now beginning to bear fruit for diagnostic interpretation of mass spectrometry-derived data. Use of steroid profiling for diagnosis of primary aldosteronism and stratification of patients for therapeutic intervention is one approach that offers promise to streamline what is currently a burdensome diagnostic process. Many challenges, however, lie ahead before such approaches can gain a foothold in the routine laboratory. Use of AI in diagnostics relies on supervised machine learning (ML) to train the system in a series of workflow steps based on disease classifications. For models to be useful, those classifications must be correct and there must be a sufficiently large and comprehensive dataset for both training and internal validation. The process is finalized by external validation with a new dataset previously unknown by models. ML models can then be integrated within clinical decision support systems that include automated ML-derived disease probability scores and patient-specific interpretations to assist clinicians towards diagnostic decision-making. There are evolving nation-specific regulatory requirements to address before models can be deployed. In some countries, ML models are considered medical devices that must be validated according to associated regulatory hurdles. For models based on laboratory measurements in biological fluids, they should show robustness in terms of reproducibility of output probability scores within and between laboratories. To meet regulatory hurdles and be accepted by the medical community, it must be clear that the technology offers advantages over currently available approaches. For primary aldosteronism, it is particularly important to break through a deeply embedded clinical mind set and overcome lack of vision for new technologies. Carefully designed randomized trials will therefore be necessary, and for this there is need for funding and academic-industry partnerships to both support those trials and assist with translation into the clinical routine.

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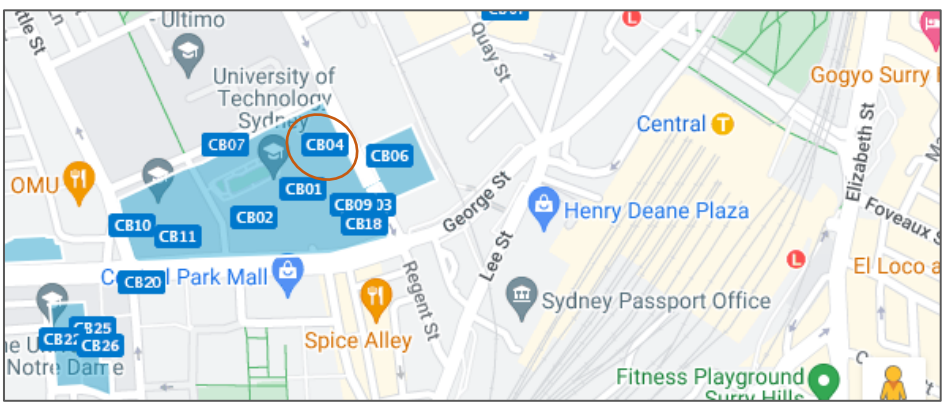

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