COMPARISON OF LC-MS, GC-MS AND CE-MS FOR THE DETERMINATION OF EARLY STAGE MARKERS OF KIDNEY DISEASE

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Chronic kidney disease affects over 10% of the Australian population and is associated with chronic morbidity and premature mortality including premature death due to cardiovascular disease. Within the European Union the costs of these diseases are in the range of 500 billion Euros per year, increasing at a rate of ca. 10 % per year. Despite significant improvements in the treatment of chronic kidney disease through dialysis, over 50% of patients still die within 3 years whilst treated with modern dialysis. People with kidney function less than 30% are also 10-times more likely to die of cardiovascular disease than reach end-stage kidney failure.
To date, measurement of kidney function and adequacy of dialysis have concentrated on the concentration of small molecules in the serum such as urea and creatinine. With dialysis, achieving urea clearances above 65% with each dialysis has been determined to be the minimum standard, although urea itself does not cause the toxic effects of uraemia, thus removal of it is used as a surrogate for other, more relevant, toxic molecules that are accumulated in kidney disease. As it is currently impossible to cure these diseases at advanced stages, identification of these uraemic toxins offers the best opportunity for early stage diagnosis so that treatment can be used to reduce or even stop disease progression.
This presentation will demonstrate and compare the application of three complementary separation methods - liquid chromatography, gas chromatography and capillary electrophoresis coupled to mass spectrometric detection (LC-MS, GC-MS and CE-MS) for non-biased profiling of small molecule markers (< 1000 Da) associated with chronic kidney disease. Pre- and post-dialysis blood serum samples from patients at various stages of chronic kidney disease will be compared as well as those from individuals with no signs of kidney disease. We will also demonstrate how this general approach can be used for identification of molecules that signal early kidney disease as well as identification of toxic molecules that contribute to symptomatic kidney disease and those that contribute to premature cardiovascular death. The relative strengths and weaknesses of each of these techniques for identification of small molecule biomarkers will also be discussed.