

10th European Nephrology Conference

October 24-26, 2016 Rome, Italy

Precise quantitation of urinary proteins for biomarker assessment

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Quantitative MS is increasingly being performed in the proteomics field to address biological- and medical-related queries. While this can be achieved with a relative or absolute technique, it is the latter that is more informative and better suited for protein biomarker evaluation of pre-clinical and clinical samples. Such absolute quantitative techniques determine endogenous protein concentrations and require the use of stable isotope-labeled standards (SIS), along with a targeted form of MS detection (typically MRM), to be employed within a bottom-up analytical workflow. Using that approach on non-invasively collected urine samples, we have systematically advanced the methodology of extended breadth and depth of protein quantitation. The final method enabled the reproducible quantitation of 136 proteins spanning >5 orders of magnitude in concentration (from 8.6 µg/mL to 25 pg/mL). The lower complexity of the urine matrix enabled lower-abundance plasma proteins (e.g., osteopontin) to be detected without pre-fractionation, which is a significant advantage of using urine for protein biomarker screening. This quantitative method was then applied to the analysis of 53 time-course urine samples to estimate excretion rates of proteins from the kidneys. This presentation will discuss the method development, provide an overview of its application and its extension to kits for the research community.

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Early pre-operative and prolonged post-operative nephrological consultation might prevent the worsening of renal impairment in renal cancer patient candidates to nephrectomy

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Background: Partial nephrectomy (PN) is recommended as the preferred surgical option in organ confined renal tumors measuring up to 7 cm, whilst radical nephrectomy (RN) is the preferred option for tumors of more than 7 cm; RN is also recommended if PN is not technically feasible. RN in particular may affect renal function, especially in patients (pts.) with pre-existing chronic kidney disease (CKD).

Patients & Methods: From December 2012 to January 2015, 97 pts. candidates to RN were referred to our Ambulatory of Onco-Nephrology; of these pts., 21 had a pre-existing stage III to V CKD. Nephrological consultation was performed before surgery, immediately post-surgery, and then every 3 months for the first 3 years post-RN. Primary endpoint of this single-arm, prospective, pilot study was the percentage of pts. who developed some worsening of kidney function over the 3-years follow-up. Interventions during Nephrological consultations included management of co-morbidities and risk factors (e.g. hypertension, diabetes, etc.), prevention of further renal damage from potentially nephrotoxic drugs (e.g. NSAIDs) and protocols of hydration before contrast medium administration for routine oncological follow-up.

Results: Immediately post-RN, 46 pts. presented a reduction in eGFR (9 within the group with pre-existing CKD, and 37 in the group without known renal impairment). Of these 46 pts., at 3-months post-RN, 30 recovered to their pre-nephrectomy renal function, while the remaining 16 did not show any further decrease in eGFR. Only 5 pts. (out of 97) were lost at follow-up during the 3 years subsequent to RN. Of the 92 pts., who reached the 3 year post-RN mark, just 2 showed a decline in eGFR.

Conclusions: An early and prolonged nephrological consultation in cancer pts. Candidates to RN might prevent kidney impairment.

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