PROJECT 1

DoS: Marco Simonini

Title: New bio-humoral compound for renal early diagnosis and prognosis.

Curriculum: Experimental and Clinical Medicine

Residency Program: Nephrology/Genomics of Renal Diseases and Hypertension

Link to OSR/UniSR personal page:

Project description (*Number of characters*, *including spaces*: 2.000 - 3.000):

Acute kidney injury (AKI) and, as consequence, chronic kidney disease (CKD), are both important health problem associated with increased mortality rate, hospitalization time, and health-related costs. In this way, the possibility to find new biomarkers and predictive models, allowing early identification of patients with an increased risk of AKI or CKD, remains a main challenge. Recently, it was shown that Endogenous Ouabain (EO), a stress hormone secreted by the adrenal gland with hemodynamic effect, contributes to the development and maintenance of AKI (in critically ill patients) and CKD (in hypertension related disorders) [1-2].
One hypothesis is that high plasmatic or intrarenal EO levels, alone or in combination with specific genetic background (represented by SNPs encoding for synthesis, vascular or kidney activity of EO), may induce glomerular podocyte and/or tubular changes that could promote kidney [1].
Starting from these evidences, the goals we propose is to:
1) confirm the role of EO in AKI/CKD prediction in large cohorts of patients;
2) investigate in humans the importance of specific genetic background, associated with EO metabolism, on both EO levels and on the predisposition/development of kidney damage;
3) create a transgenic animal model to better understand the molecular association between genetic background, plasmatic/tissue EO levels and AKI/CKD;
4) use of new and update technologies (as Flow Cytometry Resource, Advanced Cytometry Technical Applications Laboratory (FRACTAL)) to characterize the presence, in both plasma and urine, of specific elements that could lead to early identification of specific pathological condition (i.e. hypertension, lupus nephrites, membranous glomerulonephritis…).

This study will be conducted in collaboration with different unit of San Raffaele Hospital and with external collaborator. This will allow to collect and study samples of large cohorts of patients with different pathological conditions. The final aim of this work will be the creation of few personalized risks score for specific condition (i.e. post-operative AKI, CKD-related hypertension, lupus nephrites…) based on clinical variables, EO, individual genetic background and specific biomarkers. This might help physicians in decisions making for everyday clinical practice [3].

Skills to be acquired by the student:

- Liquid Kidney Biopsy
- Flow Cytometry Resource, Advanced Cytometry Technical Applications Laboratory
- DNA extraction, Genotyping
- RIA-Spa endogenous ouabain determination.
- Statistical analysis SPSS data set

References (max. 3)

1. **Lanosterol Synthase Genetic Variants, Endogenous Ouabain, and Both Acute and Chronic Kidney Injury**. Iatrino R, Lanzani C, Bignami E, Casamassima N, Citterio L, Meroni R, Zagato L, Zangrillo A, Alfieri O, Fontana S, Macrina L, Delli Carpini S, Messaggio E, Brioni E, Dell'Antonio G, Manunta P, Hamlyn JM, Simonini M. *Am J Kidney Dis. 2019 Jan 16*

2. **Endogenous Ouabain: An Old Cardiotonic Steroid as a New Biomarker of Heart Failure and a Predictor of Mortality after Cardiac Surgery**. Simonini M, Pozzoli S, Bignami E, Casamassima N, Messaggio E, Lanzani C, Frati E, Botticelli IM, Rotatori F, Alfieri O, Zangrillo A, Manunta P. *Biomed Res Int. 2015*

3. **A new clinical multivariable model that predicts postoperative acute kidney injury: impact of endogenous ouabain**. Simonini M, Lanzani C, Bignami E, Casamassima N, Frati E, Meroni R, Messaggio E, Alfieri O, Hamlyn J, Body SC, Collard CD, Zangrillo A, Manunta P; CABG Genomics Investigators. *Nephrol Dial Transplant. 2014 Sep.*