

PROJECT 1**DoS:** GIUSEPPE VEZZOLITitle: Irisin as a bridge among bone, muscle and cardiovascular alterations in CKD patients

Curriculum: _____

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):

Myokines are compounds delivered by muscle cells during physical exercise. Among them, irisin is able to influence bone remodeling with a mechanism involving sclerostin production by osteocytes; it may have a role in osteoporosis, sarcopenia and atherosclerosis and its low serum levels may be independent predictor of these disorders in patients with normal and decreased renal function. Irisin production progressively decreases in patients with chronic kidney disease (CKD) who have an increased fracture and cardiovascular risk and are often sarcopenic. Therefore, the interplay of irisin with calcium metabolism factors, like FGF23, PTH, vitamin D, Dkk1 and sclerostin, may be crucial for bone and cardiovascular involvement in CKD.

In keeping with these findings, the present project is aimed at defining the potential role of irisin as a predictor/determinant of cardiovascular, muscle and bone alterations in CKD patients.

Methods

Patients. One hundred hemodialysis patients and eighty patients with CKD stage 3-5 (before dialysis) will be enrolled. These patients will sign an informed consent and will undergo a blood collection every six months to measure serum calcium, phosphate, PTH, 25(OH)D, 1,25(OH)D, FGF23, sclerostin, Dkk1, bone alkaline phosphatase, CTX, Klotho and irisin. Every year they will undergo the following exams:

- Food-frequency questionnaire to test nutrient intake.
- Bioimpedance analysis (BIA) and physical tests such as gait speed test and 6-min walk test to test sarcopenia.
- Dual energy x-ray absorptiometry (DXA) and dedicated echography (Bindex) to estimate bone mineral density.
- Radiography of lumbar aorta in lateral projection to measure vascular calcification using Kauppila method.
- Dorsal and lumbar spine radiography in lateral projection to explore vertebral fracture by morphometric analysis.
- Echocardiogram to evaluate morphology and function of heart.
- Echocolor Doppler of carotid arteries.
- The variation of serum irisin after a standard physical exercise.

All these data will be recorded in the clinical documents of the patients and database of the study.

Characteristics of patients stratified according to irisin levels will be explored at baseline and at the end of follow-up. Specific attention will be given to variations of BMD, muscle mass, myocardial wall and vascular calcification and to patient mortality.

In vitro experiments: The in vitro effect of irisin on human cells will be tested in osteoblasts and osteoclasts isolated from femoral neck of patients undergoing hip replacement and cultured in specific medium assay added with recombinant irisin at growing concentrations. Hip from dialysis patients will be possibly used to isolate bony cells.

Skills to be acquired by the student:

Educational aims are the following:

1. To improve the student capability to interact with and manage patients in a clinical study
2. To teach statistical analysis for population screening
3. To provide criteria and strategy to conduct a genetic epidemiology study
4. To acquire criteria to study mineral metabolism
5. To teach method to measure muscle and bone condition.
6. To learn the interaction with basic science researchers

References (max. 3)

Lee MJ, Lee SA, Nam BY et al. Irisin, a novel myokine is an independent predictor for sarcopenia and carotid atherosclerosis in dialysis patients. *Atherosclerosis* 2015; 242: 476–482.

Colaizzi G, Cuscito C, Mongelli T et al. The myokine irisin increases cortical bone mass. *Proc Natl Acad Sci USA* 2015; 112: 12157–62

He L, He WY et al. Lower serum irisin levels are associated with increased vascular calcification in hemodialysis patients. *Kidney Blood Press Res* 2018; 43: 287-295