PROJECT

Supervisor:	Prof.ssa Chiara Livia Saveria Lanzani
Title:	**Multidisciplinary dissection of renal effects of glyfozines on elderly patients: from molecular aspects to clinical indications.**
Curriculum:	Clinical and Experimental Medicine
Link to the personal page of the University or relevant hospital site website:	https://www.unisr.it/docenti/l/lanzani-chiara-livia-maria

Description of the Project (max 3,000 characters including spaces)

Background/gap of knowledge

Human aging leads to molecular, structural, and functional changes in organ systems, increasing the prevalence of complex diseases such as Type 2 Diabetes (T2DM), Chronic Kidney Diseases (CKD), Cardiovascular Diseases (CVD), obesity, and sarcopenia.

This clinical complexity translates into polytherapy, itself associated with frailty. Individual aging and disease trajectories are under genetic and environmental control [1].

Sodium-glucose cotransporter inhibitors (SGLT2i) are a new class of anti-diabetic drugs that decrease proximal tubular glucose reabsorption. In addition to their glucose-lowering effects, SGLT2i prevent both renal damage and cardiovascular events [2,3]. The molecular bases underlying these unexpected benefits are not fully understood [4].

Given the high prevalence of T2DM, CKD, and CVD in the elderly, a significant number of geriatric patients are expected to receive SGLT2i according to recent recommendations. However, the biological effects and clinical benefit of SGLT2i in elderly patients remain to be clarified [5].

Rationale and hypothesis

The increasing use of SGLT2i, prompted their pleiotropic beneficial effects documented in young adults, encourages their use in old, comorbid patients. However, comprehensive data on their effects in elderly patients are lacking, and initial evidence raises concerns on potential detrimental effects, cautioning against a liberal use of SGLT2i in geriatric patients.

Objectives and specific aims

The primary objective of our research project is to investigate the renal and metabolic effects of SGLT2i on elderly patients through a real-life observational prospective study entailing the collection of clinical and biological data from 300 elderly patients undergoing SGLT2i therapy [6] before and after the 6-month treatment period. To achieve this goal, we designed three dedicated specific aims :

-Generate a multidimensional clinical dataset, integrating data from geriatric patients before and after 6 months of SGLT2i treatment to assess the short-term impact and interdependence among risk factors at the clinical and biological levels.
-characterize phenotypical and functional aspects of renal pathways in urine and blood, to explore the specific biological systems influenced by SGLT2i in the elderly population.
- identify genetic and epigenetic signatures capable of predicting treatment outcomes, by genome-wide genotyping.
Molecular information, clinical data and the existing literature will be integrated to identify specific signatures associated with different clinical and biological effects of SGLT2i.

Expected outcomes
Our research plan aims to achieve novel clinical and biological insight effects of SGLT2i in geriatric patients, with the general scope to devise evidence-based personalized approaches to complex diseases in this vulnerable population.

Skills that the student should acquire (max. 600 characters including spaces):

The PhD student will develop concrete scientific knowledge and in the field of clinical and experimental nephrology.
More specifically he/she will acquire proficient knowledge in pathophysiology of renal ageing in particular clinical settings and therapies.
He/she will develop adequate skills in order to design of primary and alternative experimental strategies, to collect patient's data, to create database. He/she will also learn how to carefully analyze the results of the investigation, how to perform specific statistical analysis and how to appropriately discuss the strengths and the limits of his/her work. He/she will develops predisposition for critical presentation of data in internal seminars and at national and international meetings.
Eventually the PhD student will acquire adequate skills in order to conceive and design an independent investigation and to apply to a grant.

References (max. 15)

1. Bin-Jumah MN, et al. PMID: 35163422
2. The EMPA-KIDNEY Collaborative Group, et al. PMID: 36331190
3. Salvatore T, et al. PMID: 35409011
4. Ma C, et al. PMID: 37046125
5. Richardson TL Jr, et al. PMID: 37155984
6. Note AIFA 100, N° Det. 19/2022; 21/1/2022 (https://www.aifa.gov.it/web/guest/elenco-note-aifa)