The undersigned

SURNAME LANZANI

FIRST NAME CHIARA LIVIA SAVERIA

born in *MILAN* Prov. MI on 23/09/1969

Unit: *NEPHROLOGY AND DIALYSIS*

Residency/Postgraduate School[1]:

Email address: *lanzani.chiara@hsr.it*

Role:

☒ Vita-Salute San Raffaele University Professor/Lecturer

☐ Vita-Salute San Raffaele University Researcher/Lecturer

☐ Group Leader of the hospital site _____

☐ Project Leader of the hospital site _____

☐ Other _____

I hereby declare that, within the framework of the PhD Course for which I wish to submit the project described below:

☐ I am already a Supervisor;

☐ I am applying for the first time as a Supervisor (CV attached);

☒ I am applying as a Supervisor as three years have elapsed since my last Application as Supervisor and the submission of a research project (CV attached).

I further declare that (select the applicable option(s)):

☐ although I am less than four years away from retirement as a university professor/researcher, I will hold a documented institutional role at the hospital _____, for at least one year beyond the official duration of the course.

☐ I serve as Supervisor for no. __ PhD candidates enrolled at other universities and I comply with the University requirement regarding the maximum number of five PhD candidates that may be supervised.

I would like to present a project:

[1] To be indicated only for research projects associated with the Physician Scientist programme

☐ **With a duration of three years**

☒ **With a duration of two years within the Physician Scientist (PhS) programme**

as part of the PhD course in:

☒ Molecular Medicine

PhD Curriculum:

☐ Basic and Applied Immunology and Oncology

☐ Cell and Molecular Biology

☒ Clinical and Experimental Medicine

☐ Neurosciences and Experimental Neurology

☐ Gene and Cell Therapy

☐ Cognitive and Behavioural Sciences

The project consists in:

1.	Basic Research	☐
2.	Translational Research	☐
3.	Basic/ Translational research using animal models	☐
4.	Clinical research	☐
5.	Clinical research involving interaction with patients	☒

If items 2 and/or 3 is/are selected, I declare that

☐ I HAVE OBTAINED the approval of the responsible Institutional Animal Care and Use Committee-IACUC number _____

☐ I HAVE NOT YET OBTAINED the approval of the responsible Institutional Animal Care and Use Committee-IACUC

If items 4 and/or 5 is/are selected, I declare that the project:

☐ **HAS NOT YET OBTAINED** approval from the Ethics Committee (EC)

☐ **HAS OBTAINED**, or is part of a broader study that has obtained, approval from the Ethics Committee (EC); study code and date: **GEN/NEFRO/01 - OSR EC (04.05.2006); RETURN – Amendment no. 3 (31.08.2021)**

If items 4 and/or 5 is/are selected, I declare that the project:

☐ **HAS NOT OBTAINED** the resolution of the Institution

☐ **HAS OBTAINED** the resolution of the Institution on _____

I further declare (select the applicable option(s)):

☐ that I have the availability of the funds necessary to finance a scholarship for the proposed project and I confirm that I have contacted the Doctoral Office regarding the management of the administrative procedures related to the funding;

☒ that I have the availability of funds to support the research (i.e. funds for materials, reagents, and instruments required for research activities);

☐ that, in the case of a clinical research project, it will include a basic or translational research component to be carried out in a laboratory to be specified in the research plan, whose head will act as co-supervisor.

☒ that I have adequate workspace and a permanent workstation available for the PhD candidate who will be selected to carry out the project;

☒ that the proposed project can be reasonably completed within the three-year legal duration of the programme;

☒ that the PhD student, within the activities of the relevant PhD program, will carry out only their specific doctoral project;

☒ that the PhD student will be the first author/author of the main publication resulting from his/her project and of all publications (also after graduation) that are mainly based on his/her experimental work;

☐ that, in the event that the PhD student is not the recipient of a UniSR grant (i.e. has won a position without a grant), I am willing to cover the cost of their scholarship with funds at my disposal. I am aware that the grant must not amount to less than the minimum required by the Ministerial Decree of 23 February 2022, amounting to € 16,243 gross per year, for three years;

☐ that the study is co-funded by an industrial partner or that a commercial exploitation of the findings resulting from the project's research activity is conceivable, with a potential delay in the publication of the results. I therefore commit to promptly inform potential candidates of such circumstances.

Chiara Lanzani

Prof. Chiara Livia Saveria Lanzani

Date 12/03/2026

When applicable:

Group Leader Prof. Paolo Manunta

Signature _____

Date 12/03/2026

Please note that the information provided on the following pages (unless otherwise indicated) will be made public on the University website. Therefore, it is important not to include confidential information, in compliance with any confidentiality obligations towards third parties and to protect the potential patenting of such information. For any questions, please consult the PhD Office.

PROJECT

Supervisor:	Prof.ssa Chiara Livia Saveria Lanzani
Title:	**Evaluation of metabolic, biohumoral, body composition and quality of life effects of low-protein diet (LPD) in chronic kidney disease (CKD).**
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

In Italy, the prevalence of Chronic Kidney Disease (CKD) in the adult population is 6.3%. CKD imposes substantial individual and societal costs, necessitating early intervention to prevent progression to dialysis and reduce associated morbidity and mortality. Therefore, it is crucial to adopt conservative management strategies for CKD patients. In this way, a low protein diet (LPD) represents a cornerstone of conservative management in most patients. The objective of LPD is to ensure optimal nutritional status, prevent or correct complications related to CKD, and delay dialysis initiation. Recently, a consensus document has been published, emphasizing the importance of LPD in improving and maintaining the clinical condition of CKD patients, and establishing clear guidelines for proper dietary management. However, some concerns remain about the safety of this therapeutical approach in specific cohorts of CKD patients such as diabetes mellitus (DM), autosomal dominant polycystic kidney disease (ADPKD), and protein-energy wasting patients (PEW).

Rationale and hypothesis

The rationale for the LPD is based on reducing the nitrogen load and consequent glomerular hyperfiltration while maintaining adequate caloric intake by increasing the proportion of carbohydrates and lipids. However, it is not known whether this approach is risk-free in patients with impaired glucose metabolism as some authors have pointed out that the metabolic benefits in terms of reduced azotemia values, improved acidosis status, and reduced oxidative stress outweigh any potential risks.

Objectives and specific aims

The main objective is to evaluate the metabolomic substrate determined by a LPD (0.6 g/kg/day) and its efficacy on the progression of CKD as a function of the metabolomic substrate. The secondary objective is to estimate glycemic tolerability, and potential side effects of the LPD in these cohorts of patients. The study will be conducted as a prospective observational case-control study, involving CKD. Participants will undergo baseline assessments and be followed for 24 months, during which clinical (Cardiovascular events, serum urea, phosphate and bicarbonate), anthropometric variables (BMI, body weight), renal variables (GFR, protein and urea excretion), and body composition parameters (skeletal muscle mass, free fat mass) and the urinary metabolomic pattern will be monitored to evaluate the variation of these variables induced by the LPD. The collected data will be analyzed by appropriate statistical methods to assess any differences in the changes in the assessed parameters within the three individual groups and between these patient cohorts and the other CKD patients already treated with a hypoproteic diet.

Expected outcomes

We expect that this study will confirm how dietary nutritional therapy and the development of a personalized protein-controlled diet constitute an essential element of conservative nephrology therapy in all CKD patients.

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

The PhD student will develop scientific knowledge in dietary nutritional therapy with a particular focus on the nephrology field. More specifically, the acquisition of proficient knowledge in the assessment of the nutritional status and the body state composition, drafting personalized diets with adequate protein-caloric content, and interpretation of laboratory tests referring to nutritional status in the context of CKD.

Moreover, the acquisition of adequate skills to 1) figure out and design their investigation; 2) submit a grant application; and 3) lead an independent research group.

References (max. 15)

(1) De Nicola L, Dal Canton A; Gruppo di Ricerca CARHES. Epidemiology of chronic kidney disease in Italy: the CARHES study. G Ital Cardiol (Rome). 2010;11(5 Suppl 3):106S–108S.

(2) Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2024 Clinical Practice Guideline for the Evaluation and Management of Chronic Kidney Disease. Kidney Int. 2024;105(4S):S117–S314. doi: 10.1016/j.kint.2023.10.018

(3) Ikizler TA, Burrowes JD, Byham-Gray LD, et al. KDOQI Clinical Practice Guideline for Nutrition in CKD: 2020 Update. Am J Kidney Dis. 2020;76:S1–S107. doi: 10.1053/j.ajkd.2020.05.006

(4) Cupisti A, Brunori G, Di Iorio BR, et al. Nutritional treatment of advanced CKD: twenty consensus statements. J Nephrol. 2018;31(4):457–473. doi: 10.1007/s40620-018-0497-z

(5) Bellizzi V, Cupisti A, Locatelli F, et al. Low-protein diets for chronic kidney disease patients: the Italian experience. BMC Nephrol. 2016;17(1):77. doi: 10.1186/s12882-016-0280-0

(6) Piccoli GB, Cederholm T, Avesani CM, et al. Nutritional status and the risk of malnutrition in older adults with chronic kidney disease: a critical review endorsed by ERN-ERA and ESPEN. Clin Nutr. 2023;42(4):443–457. doi: 10.1016/j.clnu.2023.01.018

(7) Hahn D, Hodson EM, Fouque D. Protein restriction for diabetic kidney disease. Cochrane Database Syst Rev. 2023;1:CD014906. doi: 10.1002/14651858.CD014906.pub2

(8) Mihalache A, Garneata L, Mocanu CA, et al. Low protein diet reduces proteinuria and decline in glomerular filtration rate in advanced, heavy proteinuric diabetic kidney disease. Nutrients. 2024;16(11):1687. doi: 10.3390/nu16111687

(9) Narasaki Y, Rhee CM, Kramer H, Kalantar-Zadeh K. Protein intake and renal function in older patients. Curr Opin Clin Nutr Metab Care. 2021;24(1):10–17. doi: 10.1097/MCO.0000000000000712

(10) Klahr S, Breyer JA, Beck GJ, et al. Dietary protein restriction, blood pressure control, and the progression of polycystic kidney disease. Modification of Diet in Renal Disease Study Group. J Am Soc Nephrol. 1995;5(12):2037–47. doi: 10.1681/ASN.V5122037

(11) Fazel Sahranavard A, Pahlavani N. The effect of dietary protein on the progression of polycystic kidney disease: a review on current evidences. Clin Nutr Open Sci. 2023;50:109–117. doi: 10.1016/j.nutos.2023.09.004

(12) Chebib FT, Nowak KL, Chonchol MB, et al. Polycystic kidney disease diet: what is known and what is safe. Clin J Am Soc Nephrol. 2024;19(5):664–682. doi: 10.2215/CJN.0000000000000326

(13) Geertsema P, Koorevaar IW, Ipema KJR, et al. Effects of salt and protein intake on polyuria in V2RA-treated ADPKD patients. Nephrol Dial Transplant. 2024;39(4):707–716. doi: 10.1093/ndt/gfad218

(14) (Simonini M, Vezzoli G. New landmarks to slow the progression of chronic kidney disease. J Clin Med. 2023;12(1):2. doi: 10.3390/jcm12010002

(15) Bologna A, Brambilla Pisoni M, Avino M, Giambo F, Arcidiacono T, Vezzoli G. Evaluation of protein malnutrition in CKD patients on low-protein diet. Nephrol Dial Transplant. 2023;38(Suppl 1):gfad063c_5541. doi: 10.1093/ndt/gfad063c_5541

The information below will not be displayed on the University website in the description of the projects offered for the academic year, and will be used for internal project assessment only.

Experimental plan (Between 2,000 and 3,000 characters including spaces):

To be completed for all types of projects; however, for CLINICAL PROJECTS, please specify:

1. *If Observational prospective, cross-sectional, or retrospective) or retro/prospective, quality of life, pharmacological, pathophysiology, genetics, epidemiological, registry/data collection, biobank, diagnostic accuracy, in vitro diagnostic device (IVD), nutraceutical/supplement, appropriateness; OR interventional (pharmacological, surgical, procedure, or medical device, and if a drug will be used, indicate the phase – I, II, III, or IV);*
2. *If a drug will be used, specify whether it has a marketing authorisation (MA), whether it will be used according to the MA or whether it does not have a MA;*
3. *If the study does not regard a drug, specify what will be studied (e.g. medical device, surgical procedure, diagnostic procedure, food supplement, etc.). If the study will use a medical device, please specify: whether it is CE marked. If CE marked, please indicate whether it will be used according to the approved use or for a new use.*
4. *Indicate the laboratory on which you intend to rely for the basic or translational part.*

The proposed study is a prospective observational case-control study with four parallel groups, non-randomized, focusing on a total of 120 patients with chronic kidney disease (CKD). The distribution of patients will be as follows:

1. 40 patients with CKD and DM
2. 20 patients with CKD secondary ADPKD
3. 20 patients with CKD and PEW
4. 40 patients with non-diabetic CKD (control group)

Inclusion criteria: patients of both sexes aged over 18 years, CKD stage 3b or higher (estimated glomerular filtration rate < 45 ml/min/1.73m2), and actively followed up for CKD at outpatient clinics. Patients with acute kidney injury (AKI), psychiatric eating disorders, decompensated diabetes mellitus, and those on corticosteroid therapy will be excluded.

All patients will be treated with dietary nutrition therapy (DNT) based on a low-protein diet (0.6 g/kg/day), as recommended by guidelines in CKD patients, to evaluate the tolerability, efficacy on the progression of CKD, glycemic tolerability, improvement of life quality and potential side effects in these specific cohorts.

The total duration of the study will be 36 months, with 12 months for recruitment, 24 months for follow-up, and 3 months for statistical analysis and study conclusion.

Patients will be recruited from the MA.RE.A outpatient clinic at San Raffaele Hospital and undergoes initial screening including anthropometric, renal, laboratory, and body composition measurements. At the baseline visit, the patient's diet will be assessed by a nutritionist, and a dietary therapy characterized by specific nutritional parameters will be prescribed for 24 months. During the follow-up, these variables will be monitored periodically at 4-month intervals.

Variables evaluated will include anthropometric, dietary, renal, blood, and urinary laboratory analyses (both rutin and experimental, such as FGF-23 and Klotho levels) and clinical parameters, as well as quality of life through specific questionnaires. Changes in body composition will be studied with both bioimpedance and specific assays (including irisin and myostatin). Urinary metabolic pattern and specific plasma markers of inflammation will be monitored to assess LPD-induced change in these parameters.

Primary aim is to demonstrate a similar evolution of clinical conditions among patients with CKD associated with DM, ADPKD, PEW, and CKD without these comorbidities. Morover, other endpoints include changes in diabetes-related clinical parameters, reduction in glomerular filtration rate, changes in body composition, incidence of cardiovascular events and diabetic complications, improvements in blood levels of urea, and phosphate, as well as improvement in quality of life.

A dietary questionnaire and bioimpedance analysis will be used to assess the nutritional intake and body composition of patients. Optimal conservative therapy for CKD will be maintained during the study.

Available methods and experimental models (max. 600 characters including spaces):

To be completed for all types of projects; however, for CLINICAL PROJECTS, please specify:

1. *whether participants (patients and/or healthy volunteers) will be recruited;*
2. *whether biological samples will be taken from participants (patients and/or healthy volunteers);*
3. *whether the biological samples will be stored in a Biobank (specify which Biobank);*
4. *whether biological samples are already stored and available in a Biobank (specify which Biobank);*
5. *whether biological samples or data will be collected in addition to those already included in the routine standard of care from routine practice (specify type of samples/data, quantity and timing);*
6. *whether procedures will be required in addition to those already included in the routine standard of care from routine practice (e.g. Consultations, laboratory tests, clinical/instrumental examinations). Specify the additional procedures, quantity and timing).*

Patients will be recruited from the MA.RE.A outpatient clinic at our hospital. Nutritional control visits, bioimpedance analysis, will be performed at every follow-up visit (every 4 months). Additional blood (20 ml) and urine (50 ml) samples will be collected and stored in the institutional biobank.

Most of the diagnostic and monitoring tools used are stackable to routine clinical practice and they are covered by the NHS.

Urinary and plasma samples collected at each follow-up visit will undergo metabolomic profiling.

Role of the PhD student (max. 600 characters including spaces):

Assessment of the patient in terms of nutrition. Perform a BIA study and correctly interpret the subject's body composition. Evaluate adherence to the diet and support in the medium to long term the patient with any corrections and counseling also in order to reshape the dietary therapy if necessary. Assessment of the patient's nutritional and inflammatory status. The PhD student will also develop core research competencies, including design and management of clinical observational studies, construction and maintenance of clinical databases, application of statistical methods for data analysis

Impact of the expected results in the field of research (max. 600 characters including spaces):

This study will provide original evidence on the safety and efficacy of LPD in three high-risk CKD subgroups currently underrepresented in the literature. By characterizing subgroup-specific metabolic and urinary metabolomic responses to protein restriction, it will support the development of personalized dietary protocols beyond a one-size-fits-all approach. The expected results will directly inform clinical decision-making in conservative nephrology, contributing to a reduction in GFR decline, delayed dialysis initiation, and improved quality of life in complex CKD patients.

In the case of clinical research, include the timeline for the project approval process up to the authorizing resolution of the Institution.

Project already approved by the Ethics Committee.

Period of attendance at a foreign institution
Mandatory for the PhD course in Cognitive and Behavioral Sciences

The PhD course in Cognitive and Behavioral Sciences encourages attendance at foreign universities and research institutes, promoting the acquisition of advanced skills and methodologies in international contexts.
Please indicate whether a period of activity at a foreign institution is planned. If so, specify:

- *Host institution (name of the University/Institute and country)*

- *Duration of stay (not less than 3 months)*
- *Integration with the research project (describe how this experience will contribute to the objectives of the proposed project)*

The information provided is not binding and may be subject to modifications based on the project's development and available opportunities.

For the use by the PhD Office

FOR OPINION - *(ONLY for Programs divided into Curricula)*

Signature of the Curriculum Supervisor _____ *Date* _____

FOR APPROVAL

Signature of the PhD Course Coordinator _____