EVALUATION OF INSULIN RESISTANCE, MARKERS OF HEPATIC INSULIN RESISTANCE, ENDOTHELIAL FUNCTION IN VITRO AND IN VIVO STUDIES. DR. LUCILLA MONTI, DR. ELENA GALLUCCIO, DR. SERENA SPADONI, DR. BARBARA FONTANA

State-of-art and future development/perspectives of the research area at international level (max 2000 characters):

Type 2 diabetes (T2D) is associated with a very high cardiovascular risk.

This is due to the sharing of several factors: dysglycemia per se (and its immediate consequences in the heart and liver) insulin resistance (a phenomenon shared by T2D and essential hypertension) and the appearance of microvascular complications (a clear sign of systemic endothelial dysfunction).

Our group has worked very hard in the field of both insulin resistance and endothelial dysfunction with a view to finding new markers of cardiovascular disease.

A number of publications have been accepted internationally in peer reviewed journals (the last in 2021: N Engl J Med. 2021 Sep 2;385(10):896-907. doi: 10.1056/NEJMoa2108269. Clin Nutr. 2021 Apr;40(4):1519-1529. doi: 10.1016/j.clnu.2021.02.040.; in 2022:Endocrine. 2021 Sep 21. doi: 10.1007/s12020-021-02868-x.

In order to maintain and improve our level of international visibility, we are more committed in evaluation in deep of insulin resistance in hepatic cells line and endothelial dysfunction in a human endothelial cell line.

Actual lines of research (as is) of the Diabetes Research Institute (max 2000 characters):

Evaluation of L-arginine administration in the prevention of endothelial dysfunction in human endothelial cell line (EA.hy926) and evaluate whether there is a metabolic memory

Study of hepatic insulin resistance in human hepatic cell line (HEPG2)

Define the pathogenetic mechanisms of systemic and hepatic insulin resistance

Validate, with clinical trials, drugs for the prevention and treatment of T2D and cardiovascular disease

Assess the effects of nutraceuticals on insulin resistance, oxidative stress and endothelial dysfunction in vivo (new study project)

Strengths of the research area (as is) of the Diabetes Research Institute (max 2000 characters):

Continue to partecipate in Cardio Diabetes Prevention Program (in collaboration with Dr. Piatti Group): which involves:
oral glucose tolerance test,
measurements of blood glucose, insulin, lipid profile and surrogated measurements of hepatic insulin resistance performed by our laboratory, medical examination report delivery in the same day of the test.

Maintain collaboration with Transplant Medicine Unit (Antonio Secchi, Paola Maffi) for the analysis of glycaemia, insulin and c-peptide of type 1 diabetic patients; sample handling; serum collection and storage of type 1 diabetic-transplanted patients.

Keep Clinical Trial expertise: from the sample handling to the shipment delivery and storage

Support Dr. Piatti Group in relationship with study design, ethical committee; patient recruitmen and drug administration.

Weaknesses of the research area (as is) of the Diabetes Research Institute (max 2000 characters):

Need to increment the visibility of the Cardio-Diabetes and Core Lab Unit

Support with funding from DRI to maintain the research of the Laboratory.

At the present, no availability of PHD students from UniHSR to learn new techniques and to help with the daily work of the Laboratory.
Need of more spaces for the laboratory

Short-medium term OSR/UniSR goals (0-18 months): milestones and deliverables (max 1000 characters):

Evaluation of L-arginine pre-treatment effects in human endothelial cell line to prevent or reduce oxidative stress markers' accumulation caused by over nutrition (high glucose, insulin and lipid levels, typical of insulin resistance syndrome). Understanding of long-term L-arginine effects even after treatment discontinuation.
-gene and protein expression profile of endothelial cell (samples already collected)
-analysis of results
In collaboration with Dr. Piatti Group, design the different impact of different diets (Mediterranean, vegetarian, vegan, high L-arginine supplemented diet) on insulin resistance and endothelial dysfunction in healthy subjects, subjects at high risk for T2D and diabetic patients, submission to Ethical Committee, validation of physical activity and food diary questionnaires.
Evaluation of impact of high saturated fat diet on hepatic insulin resistance, and endothelial function in subjects at high risk for T2D (Post-hoc of L-arginine study)

Medium term OSR/UniSR goals (18-36 months): milestones and deliverables (max 1000 characters):

Evaluation of high lipid treatment effects in human hepatic cell line to study the molecular mechanisms of hepatic insulin resistance
-cell culture of HEPG2 in different conditions, sample collection
-gene and protein expression profile of hepatic cell samples
-intracellular assays
-analysis of results
For the new in vivo protocol
- start patient recruitment
-assign different type of diet for 18-36 months
-medical examination, physical activity and food diary questionnaires and blood analysis every 6 months
-Collect Adverse Events or Serious Adverse Events, if any
Analysis of data, write an intermediate report

Long term OSR/UniSR goals (36-60 months): milestones and deliverables (max 1000 characters):

In order to conclude the Protocol "Evaluation of different diets (Mediterranean, vegetarian, vegan, high L-arginine supplemented diet) on insulin resistance and endothelial dysfunction in healthy subjects, subjects at high risk to develop type 2 diabetes and diabetic patients.
-Collection of data
-Complete CRF of the study
-Results analysis
-Write the report
All in all, our research will help to validate, with in vitro and in vivo studies, to validate new drugs for the prevention and treatment of T2D and cardiovascular disease

Investments of the Diabetes Research Institute (e.g. personnel, space, technology) to achieve the short-medium-long term goals (max 2000 characters):

Maintenance of current human resources: laboratory technicians, researcher

Increase of laboratory spaces

Implementation and improvement of cell culture room, increase and better distribution of sterile cabinets, or all cabinets available for every group
Inverted optical microscope, automatic cell counter.