



PROJECT

Supervisor: Prof.ssa PATRIZIA ROVERE QUERINI

Title: Identification and validation of early biomarkers of Metabolic Dysfunction -Associated Steatotic Liver Disease development and severity in overweight and obesity.

Curriculum: Clinical and Experimental Medicine

Link to the personal page of the University or relevant hospital site website: <https://www.hsr.it/dottori/patrizia-rovere-querini>

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

Background/gap of knowledge

Overweight and obesity are rising pandemics and serve as key contributors to the increasing prevalence of severe chronic diseases such as Metabolic Dysfunction -Associated Steatotic Liver Disease (MASLD). This condition represents a growing public health challenge linked to increased risks of cardiovascular disease, liver cirrhosis, and hepatocellular carcinoma, with significant implications for healthcare costs.¹

There are still no valuable diagnostic and prognostic tools that specifically predict the risk of developing MASLD in patients with overweight or obesity.

Identifying patients with higher risk of developing MASLD is crucial to anticipate patient risk stratification and thus optimizing preventive treatments.

This study aims to identify reliable biomarkers of MASLD in human patients by integrating and validating results obtained in a murine model of obesity. The translational approach will enable the confirmation of experimental findings in a well-characterized human cohort, addressing a critical unmet clinical need.

Rationale and hypothesis

The identification of specific biomarkers for MASLD represents a significant unmet clinical need. Current methods lack precision in predicting which patients with excess adiposity will develop liver disease, limiting timely patient management.

In obesity, maladaptive adipose tissue expansion leads to ectopic fat deposition in non-adipose tissues such as the liver. This process induces progressive liver dysfunction, which, at least at early stages, might be underdiagnosed. We hypothesize that liver-derived proteins start to be released in the circulation when MASLD has not yet become clinically evident and could serve as early predictive biomarkers. By analyzing the temporal evolution of the liver secretome in a murine model of obesity already shown to develop MASLD and validating findings in human samples, we expect to identify a signature panel of circulating proteins that accurately predicts MASLD onset and progression, enabling targeted preventive interventions in high-risk individuals.

Objectives and specific aims

This study aims to identify early biomarkers of MASLD development and severity in a preclinical model of diet-induced obesity and to validate findings in humans.

Specifically, this project aims to:



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-Identify biomarkers of MASLD using liver-specific RNA-seq of secreted proteins in a preclinical model of diet-induced obesity.

-Validate the identified biomarkers in human blood samples from a well-characterized cohort of patients with overweight or obesity.

Expected outcomes

The Identification and validation of secreted proteins involved in the development and severity of MASLD, will support risk stratification and management of patients with overweight or obesity.

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

- Expertise in clinical and experimental research, focusing on liver disease pathophysiology in overweight and obesity.
- Skills on collecting human biological specimens (i.e. blood samples) linked to relevant clinical data (biobanking).
- Technical skills required for the pre-clinical analyses needed for development of the project.
- Skills linked to the acquisition, extraction, cleaning and manipulation of large datasets ("data scraping").
- Conduction of statistical analysis.
- Ability to critically discuss project results at seminars or meetings.

References (max. 15)

- 1.** Reframing obesity and MASLD. Nat Rev Gastroenterol Hepatol. 2025 Mar;22(3):147. doi: 10.1038/s41575-025-01046-y. PMID: 40021741.
- 2.** Njei B, et al. Cureus. 2024 Oct 13;16(10):e71366. doi: 10.7759/cureus.71366. PMID: 39534801; PMCID: PMC11556413.
- 3.** Xie Y, Choi T, Al-Aly Z. Mapping the effectiveness and risks of GLP-1 receptor agonists. Nat Med. 2025 Mar;31(3):951-962. doi: 10.1038/s41591-024-03412-w. Epub 2025 Jan 20. Erratum in: Nat Med. 2025 Mar;31(3):1038. doi: 10.1038/s41591-025-03542-9. PMID: 39833406.