



PROJECT

Supervisor: Riccardo Vago
Title: Analysis of extracellular vesicle-carried factors leading to bladder cancer progression
Curriculum: Cell and Molecular Biology

Link to the personal page of the University or relevant hospital site website: <https://research.hsr.it/en/institutes/urological-research-institute/extracellular-vesicles-and-toxins.html>

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

Background/gap of knowledge

Tumors depend on a crosstalk with the surroundings to guarantee their survival (angiogenesis, immune escape), to support phenotypic changes (epithelial-to-mesenchymal transition) required to leave the primary tumor mass and to prepare the bone marrow and pre-metastatic organs allowing migrating tumor cells to settle and grow. Extracellular vesicles (EVs) are emerging as important vehicles for tumor-derived factors to sustain tumor development, prepare pre-metastatic sites and reduce immune surveillance.

Rationale and hypothesis

EVs produced by cancer cells carry a plethora of factors that transform surrounding cells, modelling the tumor microenvironment and preparing the way for the tumor cell diffusion. Among multiple factors, regulatory RNAs orchestrate these processes once transferred to recipient cells. Preliminary data indicate that a group of EV lncRNA found in urine derived from bladder cancer patients are over-represented by increasing the tumor grade and stage. We hypothesize that such lncRNAs are important molecules for tumor development and can be used as biomarkers as well as therapeutic targets.

Objectives and specific aims

1. Investigate the effect of regulatory RNAs of interest in bladder cancer cellular models to confirm their pro-tumoral effects.
2. Define a network among regulatory RNAs (lncRNAs and miRNAs) as part of the mechanism of action to translate in patients' urine.
3. Interfere with lncRNA-mediated cellular pathways in order to develop a therapeutic strategy.

Expected outcomes

We expect to shed light on the complex regulatory network promoting the bladder cancer development, identify a panel of biomarkers suitable to monitor the disease progression and of targets to consider in a therapeutic approach.

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

The student will use the most common molecular, cell biology and biochemistry techniques. He/she will acquire skills in isolating extracellular vesicles; in analyzing vesicular content; in defining the effect of the delivery of specific cargoes to recipient cells.

References (max. 15)



UniSR

Università Vita-Salute
San Raffaele

**APPLICATION TO ACT AS SUPERVISOR
AND RESEARCH PROJECT PROPOSAL**

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- (1) Peinado et al. (2012) Nature Med. 18, 883–891
- (2) Hoshino et al. (2015) Nature 19;527(7578):329-3
- (3) Vago et al. (2022) Sci. Rep. 21;12(1):17663