Speaker: **Prof. Valentina Cauda,** Politecnico di Torino, Italy
Title: **Rational Design of nanoparticles mimicking extracellular vesicles**

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Extracellular Vesicles (EVs) are nowadays of utmost interest in the nanomedicine field, being responsible for the delivery of key biomolecules and signaling moieties throughout the body with incredibly high efficiency and *in vivo* site-selectivity. For this reason, pristine, engineered EVs or other EV by-products are employed as nano-sized particles to build drug delivery and even theranostic tools. However, the large-scale production of EVs at standardized and suitable clinical grade levels is very expensive and time-consuming and this hinder the EV translation to clinics. Here we propose an innovative approach to design fully artificial EV-mimicking nanopoarticles (EV-mimics) for theranostics scopes; in particular, we decided to mimic EVs produced by metastatic cancer cell line (in particular prostate and colon rectum), which have been demonstrated to have a strong tropism towards other tissues, like bone, liver and lung. Different lipidic compositions were conceived with increasing complexity, starting from a consolidated liposomal formulation and getting gradually closer to the natural reference composition. This was achieved through a bottom-up approach, employing commercial lipids as building blocks, to obtain artificial lipid bilayers with controllable size, which can be further decorated with key molecules such as peptides to resemble their natural counterparts in terms of cargo delivery efficacy. EV-mimics were produced, experimentally characterized in vitro and in vivo, and, in parallel, analyzed through coarse-grained molecular simulation methods, which provided fascinating insights into lipid organization and dynamics.

The proposed approach holds great promise in research and industrial fields. Indeed, EV-mimics can become a cost-effective, very powerful off-the-shelf theranostic product, with high reproducibility of morphological and *in vivo* functional properties, in compliance with regulatory standards.

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