

Report of the SIBBM Lecture

On March 20th 2019, a SIBBM Lecture was held in Padua on the role of metabolism in physiological and pathological contexts. The attendance was extremely good, with ~200 participants including younger and senior scientists, sparking multiple questions to all speakers and a lively discussion.

After a brief introduction to our Society and the activities organized by SIBBM by Valeria Poli, Professor of Molecular Biology at University of Turin and President of SIBBM, the mini-symposium included two short-talks from local Junior scientists, followed by the Lecture from **Prof. Matthew Vander Heiden**, Director of the Koch Institute for Integrative Cancer Research at MIT, Boston. Patrizia Romani, a Postdoctoral fellow in the laboratory of Professor Sirio Dupont (Dept. of Molecular Medicine – UniPD), presented her work on the interplay between mechanical cues and lipid metabolism. Patrizia showed how a vast range of mammalian cells respond to mechanical cues, such as the interaction with soft substrates, by increasing their lipid content. Chemical inhibition of cytoskeleton components used to sense the environment stiffness also resulted in increased lipid production. Such effects are mediated by SREBP, a master regulator of lipid biosynthesis, whose activity is under the control of the mechanical properties of the Golgi apparatus. In other words, the stiffens of the extracellular environment reverberates on the mechanical properties of specific organelles, ultimately affecting lipid metabolism. Such results were recently published in Nature Cell Biology (Romani et al., 2019).

Giovanna Pontarin, Assistant Professor and member of the laboratory of Prof. Massimo Santoro (Dept. of Biology – UniPD), The focus of the talk, entitled “Decoding the role of glutaminolysis in developmental and tumor angiogenesis” was to decipher the role of glutamine metabolism in endothelial cells. Taking advantage of mice strain carrying endothelial-specific deletion of glutaminase enzyme GLS1, Giovanna and coworkers revealed a role for this aminoacid metabolic pathway in retina and tumor angiogenesis. Giovanna and coworkers showed novel data about how this metabolic pathway can regulate endothelial specific signaling such as VEGF and Notch. Finally, **Prof. Matthew Vander Heiden** delivered his lecture “Understanding metabolic limitations in cancer”. The metabolism of cancer cells is highly dependent on nutrient availability, which is determined by both the diet and the tissue microenvironment in which a cancer develops. This idea was exemplified by the findings that physiological serine availability in bodily fluids restrains growth of certain tumors, such that tumors arising in serine-limited environments acquire a fitness advantage by upregulating serine synthesis pathway enzymes including PHGDH. Further on this idea, the the team of Prof. Vander Heiden measured the abundance of metabolites in the plasma and in the fluids perfusing tumors, and observed that they were significantly different. Moreover, different tumor types showed different composition of their interstitial fluids and, remarkably, when the same cancer cells were transplanted at a different anatomical location, their nutrient content changed accordingly. This highlighted how tumor type, anatomical location and animal diet affect local nutrient availability, and that it is critical to use orthotopic mouse models of cancer to recreate a more physiological metabolic environment.

The SIBBM Lecture was organised by two SIBBM members, Prof. Sirio Dupont and Graziano Martello, with the support of the PhD School of Molecular Medicine of the University of Padua and of the Venetian Institute of Molecular Medicine.