MPI-NAT SEMINAR SERIES


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Metabolic rewiring driving metastasis formation

Metabolism is a network of biochemical reactions that converts nutrients into metabolites needed to fuel the biosynthetic and bioenergetic requirements of a cell. Since the research of Otto Warburg almost 100 years ago it is known that cancer cells have increased metabolic needs to sustain uncontrolled proliferation. This dependency allowed Sidney Farber to develop the first chemotherapeutic agents against non-solid tumors in the 1940s. However, cancer cells not only proliferate but they also spread to distant organs in a process called metastasis formation. Unfortunately, metastasis formation is nowadays the leading cause of death in cancer patients.

We discovered that metabolic rewiring is particularly important for metastasis formation beyond the mere conversion of nutrients into biomass and energy. Therefore, we investigate metabolic signaling in the context of metastasis formation using single cell and spatial multi-omics techniques in mouse models and patient samples. We discovered that extracellular remodeling of the metastatic niche, a process essential to metastasis formation, requires a transcriptional-independent regulation via the metabolites. Moreover, we provide unprecedented knowledge on intratumor heterogeneity of metabolism and its role in metastasis formation. Specifically, we discovered that heterogeneity in the metabolic enzyme phosphoglycerate dehydrogenase (PHGDH) predicts in cancer patients the risk for metastasis formation. Strikingly, loss of PHGDH protein expression drives early dissemination of cancer cells due to a novel mechanism leading to the posttranslational modification of cell surface integrins.

Thus, we study metabolism beyond the classical textbook knowledge with the ultimate goal to define novel therapeutic strategies against metastatic cancers.

Monday, 27.06.2022, 13:00 (online)

Host: Ursula Fünfschilling

online

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