Universität Basel

Research Project

Discovery of fundamental mechanisms underlying the development of cancer metastasis

Third-party funded project

Project title Discovery of fundamental mechanisms underlying the development of cancer metastasis
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Each year, breast cancer is diagnosed in more than one million women, and as many as 500'000 lives are lost to this disease worldwide. Patients with breast cancer die unequivocally because of the development of incurable distant metastases and not because of symptoms related to the primary site. Understanding the complex, yet fundamental mechanisms driving breast cancer metastasis is hence critical to develop therapies tailored for this disease. Cancer cells that leave the primary tumor site and are transported through the circulation to distant organs are referred to as circulating tumor cells (CTCs), and they hold the key to understanding the biology of blood-borne metastasis. CTCs are extraordinarily rare in patients with cancer (approximately one CTC per billion normal blood cells), and their isolation is greatly dependent upon technological constraints. However, recent breakthrough advances in microfluidics technology have made it possible for the first time to analyze human CTCs with great precision, revealing unexpected features. For instance, our recent findings showed that CTC-clusters, held together by interepithelial cell-cell junctions, are precursors of breast cancer metastasis (Aceto et al., Cell, 2014). This represents a previously unappreciated and potentially targetable mechanism of cancer dissemination. Further, our preliminary data obtained with single cell resolution RNA sequencing of CTCs from breast cancer patients with bone metastasis, highlighted the expression of specific candidate genes that could explain breast cancer tropism to the bone as a primary metastatic site. Altogether, our observations lead to two major goals. First, we aim to identify and target those cell-cell junction components required for CTC-clustering and metastasis. Second, we aim to apply single cell resolution analysis of human CTCs to dissect major signals driving breast cancer to specific metastatic sites (i.e. bone, lung and brain). Our research has the long-term ambition to identify major drivers of breast cancer metastasis and enable the development of metastasis-tailored therapies for patients with cancer.

Keywords Breast Cancer, Cell-cell junctions, Circulating tutor cell clusters, Single cell analysis, Metastasis-tailored therapy, Breast Cancer Tropism, Metastasis, RNA-sequencing, Circulating tumor cells, Microfluidics
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