Seminar series FOR2127 – Selection and adaptation during metastatic cancer progression

Thursday, 03 May 2018
Hörsaal, Biopark I
14.00 h

Dr. Ilaria Malanchi
The Francis Crick Institute,
Tumour-Host Interaction Laboratory, London, UK

"Cancer: The Evil Companion Corrupting Good Behaviour"

The tumour microenvironment or niche is the vital non-cancerous compartment of the tumour structure. Tumour cells and their microenvironment establish a synergistic cooperation that characterizes all aspects of tumour growth, from onset to metastasis. Importantly, this ever-changing interaction is a key source of cancer cells' plasticity and plays an important role in every aspect of tumour progression. Indeed, cancer cells with higher ability to establish favourable crosstalk with their surrounding are more tumorigenic (1). Thus, targeting non-tumour-derived cellular components represents a promising avenue to better therapeutic interventions. For instance, we identify neutrophils as the main component and driver of metastatic establishment within the pre-metastatic lung microenvironment in mouse breast cancer models. Importantly, we find that neutrophil-derived leukotrienes aid the colonization of distant tissue by selectively expanding the sub-pool of cancer cells that retain high tumorigenic potential. Pharmacologic inhibition of the leukotriene-generating enzyme arachidonate 5-lipoxygenase (Alox5) reduces metastasis, revealing the efficacy of using targeted therapy against a specific tumour microenvironment component (2).
References

Selected reading:

Del Pozo Martin Y, Park D, Ramachandran A, Ombrato L, Calvo F, Chakravarty P, Spencer-Dene B, Derzsi S, Hill CS, Sahai E, Malanchi I. (2015) Mesenchymal Cancer Cell-Stroma Crosstalk Promotes Niche Activation, Epithelial Reversion, and Metastatic Colonization. Cell Rep. 13(11):2456-69

Wculek SK, Malanchi I. (2015) Neutrophils support lung colonization of metastasis-initiating breast cancer cells. Nature. 528(7582):413-7