

The role of the lymph node vasculature in tumour metastasis and anti-tumour immunity

Research area:

Cancer immunology

Brief description

The lymph nodes have essential roles in adaptive immune responses, including anti-tumour immune responses, and are major sites for tumour metastasis. Our group is interested in the stromal changes that occur in the tumour draining lymph nodes and particularly the changes of the vasculature and how this affect tumour metastasis and anti-tumour immune responses.

Aim

The research is aimed to understand the impact the highly specialized lymph node vasculature has on the structure and function of the lymph node in the regulation of anti-tumour immune responses and tumour metastasis.

Background

The lymph nodes are closely integrated with the lymphatic system, often arranged in chains along the vessels. They consist of a complex network of lymphatic sinuses, blood vessels, specialized fibroblasts and different types of immune cells. Lymph nodes are essential both for induction of effective immune responses and maintenance of tolerance in the body. Data supports that the crosstalk between the developing tumour and the lymph nodes can help the tumour to evade the immune response. Tumour draining lymph nodes may also provide an environment that protects metastatic tumour cells from the host immune response.

Metastatic dissemination to lymph nodes is common and can in some tumor types, e.g. malignant melanoma and breast cancer, be a separate prognostic indicator, associated with increased risk for further metastatic dissemination in the body and disease recurrence after surgical removal of the primary tumour. Consequently, lymph node status is clinically used to justify selection of patients for adjuvant therapy.

We and others have shown that the vessels in the lymph nodes have unique expression of immunomodulatory genes that cannot be found in the vessels of other organs. Further, the vessels contribute to regulation of the lymph node immune responses and immune cell migration through the expression of these genes. Our data supports that growing tumours and metastatic tumour cells; affect the expression of these genes.

Project plan

Our work is focused on understanding more both about the general specialization of the vasculature in the lymph node and how it contributes to immune regulation. Further, by analyzing the changes that are induced in the lymph node vasculature in cancer and in lymph node metastasis we aim to identify new and complementary therapeutic strategies to promote effective anti-tumor immune responses and to find ways to interfere with metastatic disease.

It is possible to work on different subprojects in our lab.

Our lab is specialized in advanced flow cytometry and cell sorting for stromal cell analysis where we combine traditional antibody labelling with novel fluorescent reporters to sort rare subsets of endothelial cells with high specificity. Multicolor cell sorting is followed by expression analysis to expression profile specific subsets of endothelial cells to learn more about the gene expression that define different types of endothelium in the resting state, after different types of immune stimuli and when there is a growing tumour in the body. This is combined with confocal imaging to spatially map different types of vessels, analyze changes in protein expression and to understand the interactions between vessels, immune- and cancer-cells.

We use different transplantable tumour cell lines that can be modified to be imaged by bioluminescence through expression of firefly luciferase. These models are used to evaluate the effects of tumour growth, metastasis and different treatments on the lymph node vasculature and on the activation of different immune cells. Methods for analysis include for example flow cytometry, ELISA and confocal imaging.

We combine our experimental research with analysis of human tumour draining lymph nodes to help us identify genes that can be of clinical relevance for human cancer treatment and therefore are of interest for further studies.

Contact details

If you are a highly motivated student, interested in immune regulation in cancer and/or tumour metastasis you are very welcome to contact me for further information on specific projects available in my group.

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