**OVERVIEW**

Our laboratory is interested in analysing the main mechanisms involved in tumour-microenvironment communication during metastasis. Extracellular vesicles (EVs) and soluble factors are key players during this process. Tumour cells benefit from the secretion of these factors partly by influencing the behaviour of neighbouring cells in the tumour microenvironment. We are exploring the role of secreted factors and vesicles in metastasis using different approaches: 1) decoding the messages packaged in tumour-derived exosomes during melanoma metastasis, 2) defining novel factors involved in the crosstalk between adipose tissue and tumour, and 3) testing new therapies to prevent metastasis in rare diseases such as neurofibromatosis.

"We aim to block tumour-microenvironment communication as a novel way to control metastatic progression."

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**RESEARCH HIGHLIGHTS**

**Decoding tumour-microenvironment communication in metastasis**

Tumour-secreted extracellular vesicles constitute a network of communication secreted by primary tumours favouring metastasis. In melanoma, tumour-adjacent lymph nodes (a.k.a. sentinel lymph nodes) are normally the first sites of metastasis. In this project, we are focused on unravelling the role of tumour-derived exosomes as entities promoting cellular and molecular alterations in the lymph node microenvironment, facilitating metastasis (FIGURE). In particular, we are investigating the effects of tumour exosomes in the lymphatic vasculature. In addition, we are developing nanoparticles (FIGURE, left panel) as sensors of pre-metastatic niches mimicking tumour-derived exosomes (FIGURE, right panel) that will help to identify future areas of metastasis. These studies will lead to the development of novel technologies and therapies to block metastatic disease.

**Fatal triage: adipose tissue, coagulation and metastasis**

Over the past few decades, the incidence of overweight and obesity has been increasing very rapidly in both developed and developing countries, making obesity one of the most serious health problems worldwide. Increasing evidences have revealed a link between obesity and the development of certain types of cancer, still the impact of obesity on metastasis is not well established. Recent data support a role for secreted factors [e.g. soluble factors and EVs] in the communication between tumour cells and adipose tissue during tumour metastasis. In this project, we are investigating the local crosstalk between the adipose tissue and tumour cells, analysing secreted factors and EVs as well as the role of platelets as systemic players in the metastatic process.

**Testing new therapies to prevent metastasis**

Neurofibromatosis type I (NF1) is a genetic disorder which can progress to Malignant Peripheral Nerve Sheath Tumour (MPNST), a highly aggressive sarcoma. In this project, we are analysing the main pathways involved in tumour-microenvironment crosstalk during metastatic progression. In order to find potential biomarkers and candidates to target the progression of the disease, we investigated the molecular signature of exosomes secreted by MPNST cell lines. We have identified several candidates and we are currently performing a multidrug screening in combination with these markers in order to find new therapies for the treatment of this disease.