

MICROENVIRONMENT & METASTASIS JUNIOR GROUP

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OVERVIEW

Cancer treatment is no longer only focused on tumour cell analysis. The Microenvironment and Metastasis Group studies the communication between tumour and stromal cells along tumour progression. Cancer treatment requires the analysis of the tumour microenvironment to define specific therapies targeting both the tumour and surrounding cells. Data support that combination of therapies against the tumour and its microenvironment are the future of cancer treatment. In our laboratory, we have focused on understanding the message of a novel 'language' between tumour cells and the environment; these are small extracellular vesicles called exosomes. Our data support that tumour-secreted exosomes contain specific signatures of molecules (e.g. proteins, DNA). Exosomes secreted from the tumour can reach metastatic organs and prepare pre-metastatic niche formation, aiding metastatic homing and further metastatic progression.

“Tumour-secreted exosomes are “the forefront edge” of tumour metastasis, they reach local and distant microenvironments facilitating metastatic spread.”

Post-Doctoral Fellows
Marta Hergueta, Laura Nogués
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Graduate Students
Ana I. Amor, Teresa González,
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Technicians
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Student in Practice
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RESEARCH HIGHLIGHTS

Novel factors involved in melanoma progression, the future of liquid biopsies

In this project, we study the function of tumour-secreted exosomes in the establishment of pre-metastatic niches within the lymph node (FIGURE). We are analysing the role of the matrix-anchored proteins and neurotrophin receptors in lymph node metastasis and melanoma progression. We are also using novel biofluids (e.g. lymph node exudative seroma obtained post-lymphadenectomy) as a source of biomarkers, analysing protein cargo and BRAF mutations. Our laboratory is also interested in the study of microenvironmental factors influencing melanoma progression such as obesity.

Obesity modulates breast cancer behaviour

Obesity has drastically increased to become one of the most serious health problems worldwide and is now recognised as a risk factor for breast cancer incidence, progression, and prognosis. In this project, we aim to understand cellular and molecular mechanisms that underlie inflammation, obesity, and breast cancer metastasis. Furthermore, we are analysing the interaction of cancer cells with immune cells and platelets in metastasis and evasion of immune supervision. Our goal is to understand how obesity modulates breast metastatic behaviour defining novel factors involved and to define new therapies.

Defining novel targets in rare diseases

Malignant peripheral nerve sheath tumours (MPNSTs) are highly aggressive and metastatic sarcomas with poor prognosis

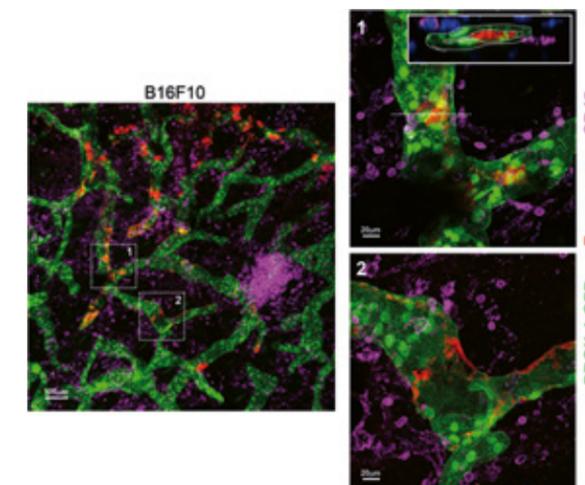


Figure Analysis of the distribution of tumour-derived exosomes from B16-F10 melanoma cells (red) in GFP-PROX mice (lymphatic endothelial cells in green), demonstrating that tumour-derived exosomes

use the lymphatic vasculature to be transported from the injection site to lymph nodes. Image from collaborators Raghu Kataru and Babak Mehrara at the Memorial Sloan Kettering Cancer Centre.

that are commonly related to neurofibromatosis type 1 (NF1) disease. In this project, we aim to find new biomarkers and novel therapeutic targets to prevent MPNST progression. The data obtained from a multidrug screening on MPNSTs cell lines and the mass spectrometry analysis of their exosomes identified several proteins as top candidates. Thus, we are currently testing the combination of MEK inhibitors, which are already used in the clinic, with novel drugs targeting these two proteins in order to define a new therapeutic window for MPNSTs. ■

PUBLICATIONS

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PATENT

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