MICROENVIRONMENT & METASTASIS JUNIOR GROUP

Héctor Peinado
Junior Group Leader

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Post-Doctoral Fellows
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Graduate Students
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OVERVIEW

Our laboratory is focused on understanding metastatic progression. During this process, tumour cells communicate actively with the tumour microenvironment. Among all factors involved in metastasis, our laboratory is specifically interested in defining the role of secreted exosomes during pre-metastatic niche formation. Exosomes are actively involved in cell-cell communication during both physiological and pathological processes. Our data support that tumour-secreted exosomes are involved in: 1) pre-metastatic niche formation and metastatic organotropism depending on the integrin expression profile on their surface; and 2) stromal cell reprogramming by horizontal transfer of molecules (i.e. oncoprotein c-MET) and/or influencing the expression of pro-inflammatory and pro-vasculogenic molecules.

"Exosome secretion by metastatic cells is an adaptive strategy for tumour cells to corrupt the surrounding microenvironment, thereby favouring tumour progression."

Technicians
Marina Mazariegos, Cristina Merino, Sara Sánchez-Redondo (since June)

Visiting Scientist
Olwen Leaman

RESEARCH HIGHLIGHTS

Role of tumour-derived exosomes in lymph node metastasis

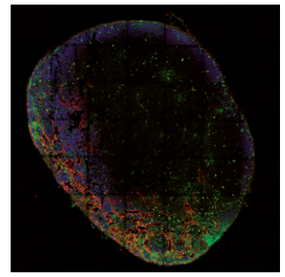
Melanoma-secreted exosomes have been shown to home to specific niches in lymph nodes. We are studying how tumour-secreted exosomes promote cellular and molecular alterations in the lymph node microenvironment, fostering metastasis (FIGURE, A). The goal of the current project is to determine the mechanisms through which tumour-derived exosomes promote lymph node and distal metastasis. Our studies in melanoma patients will be the first ones evaluating the use of circulating vesicles in lymphatic fluid as biomarkers to predict relapse and metastatic potential.

Linking obesity with metastatic risk

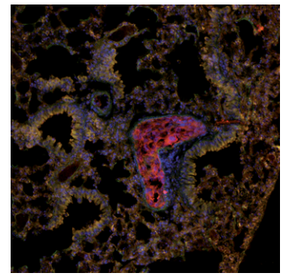
Obesity has been associated with the increased risk of developing metastasis in certain cancers. Although the implication of obesity in cancer is clear, there is, to date, a lack of studies analysing the impact of obesity on metastasis. We are investigating the mechanisms involved in the crosstalk between the adipose tissue, platelets and tumour cells during the metastatic process (FIGURE, B). We are dissecting the systemic effects of tumour-derived exosomes in adipose tissue as well as the involvement of platelets, determining their role in metastasis. Ultimately, we aim to determine specific signatures in circulating exosomes and platelets of cancer patients in order to define new prognostic and therapeutic markers that can be applied in the clinical setting.

Novel pathways involved in neurofibromatosis progression

Although neurofibromatosis is a genetic disorder, in this project we aim to develop a very innovative concept, which focuses on unveiling unknown pathways involved in exosome secretion during neurofibromatosis progression. We are investigating the molecular signature of exosomes secreted from highly metastatic neurofibromatosis models. Our data support that tumour-secreted exosomes carry a specific signature that can be detected in the circulation. This approach will result in the development of new diagnostic tests and therapies to block neurofibromatosis progression. ■



A



B

Figure (A) Analysis of exosome distribution in sentinel lymph nodes. Green-labelled exosomes from B16-F1R2 melanoma cells were injected in the footpad and followed for 16 hours. Analysis of lymph nodes demonstrated that exosomes reach popliteal (sentinel) lymph nodes with a specific distribution found mainly in subcortical areas co-localising with lymphatic endothelial cells (in red). **(B)** Metastasis of breast cancer cell lines in lung metastatic niches. Tumour breast cancer cell lines (in red) were injected by tail vein in mice, in combination with platelets. Analysis of metastasis demonstrates that tumour cells reach metastatic lungs in areas surrounding terminal bronchioles, formerly known as areas where pre-metastatic niches were formed.

PUBLICATIONS

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- Torrano V, Royo F, Peinado H, Loizaga-Iriarte A, Unda M, Falcón-Perez JM, Carracedo A (2016).Vesicle-MaNiA: extracellular vesicles in liquid biopsy and cancer. *Curr Opin Pharmacol* 29, 47-53.
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AWARDS AND RECOGNITION

- *XVII Fundacion Pfizer* Research Award 2016, Spain.
- FERO Grant for Translational Research in Oncology (*XI BECA FERO* 2016), FERO Foundation for Oncology Research, Spain.