Roger Gomis

Tumoral Metastasis Laboratory (MetLab)

Intricate signalling networks control cell division, differentiation, movement, organisation and death. Cancer cells disobey these signals during tumour progression and metastasis, which is the final step in 90% of all fatal solid tumours. Metastasis is therefore a grave public health problem and consequently a field of considerable pharmaceutical interest. A major research focus of our laboratory is to identify and study the genes and functions that allow tumour cells to achieve metastatic colonisation of vital organs.

Growth control and cancer metastasis

Our research focuses on the growth factors, signalling pathways, and gene expression programmes underlying cancer cell metastasis. Focusing on a TGF-beta cytostatic programme involving the transcriptional regulation of cell cycle inhibitors and growth-promoting factors, we are studying the ways in which cancer cells evade tumour suppressor mechanisms and engage in metastatic behaviour. By combining *in vivo* selection of human metastatic cells, transcriptomic profiling and functional testing, we identify genes that selectively mediate breast metastasis to specific organs. Gene transfer techniques and RNAi-mediated gene silencing are used to functionally validate candidate genes. We are encouraged by the recent validation of these findings in clinical samples. Several of these genes encode products that are susceptible to therapeutic targeting.

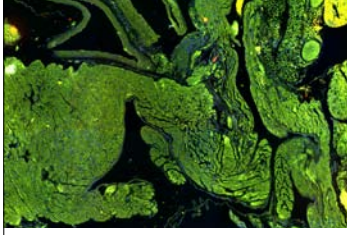
The Tumoral Metastasis Laboratory (Metlab) focuses on the study of the molecular mechanisms involved in metastasis. Our research focuses on aberrant gene responses that enable invasion and metastasis in tumour cells. We seek to elucidate the mechanisms that mediate tissue-specific metastasis, in particular breast cancer metastasis. Metastasis, a complex process caused by elaborate interactions between tumour cells and the surrounding healthy tissues in several vital organs, accounts for 90% of all deaths from cancer in patients with solid tumors. The molecular and cellular mechanisms that lead primary tumours to form metastases must be understood in order to better address this major life-threatening disease. The identification of metastatic genes and mechanisms is essential for understanding the basic biology of this lethal condition and its implications for clinical practice. Previous research has revealed the complexity of the metastatic process. However, it has largely failed to explain how and why metastasis from Estrogen Receptor-positive (ER+) breast cancer subtype occurs. Neither has it identified the mechanisms that make metastasis a tissue-specific process, the events that allow dormant metastases to become active and lethal many years after removal of a primary tumour, or the metastasis-mediating genes with potential as therapeutic targets.

Our contribution to the field builds on an experimental approach based on the use of moderately metastatic cells that are injected into a mouse model for the selection of highly metastatic ER+ breast cancer subpopulations. Live-animal imaging techniques are used to track the spread, homing, and outgrowth of the metastatic cells in different organs. After harvesting metastatic lesions and verifying that highly metastatic cells have been selected, we plan to use genome-wide transcriptomic profiling to identify and clinically validate metastasis-linked genes. Gene transfer techniques are then used to assess the contribution of individual genes to various steps (invasion, homing, outgrowth, angiogenesis, and stroma adaptation) of metastasis. Using this approach, the laboratory has recently identified a preliminary set of genes that cooperatively mediate ER+ breast cancer metastasis to the bone. We also aim to define the role of bone metastasis genes in ER+ breast cancer metastasis, and how ER status influences the choice of metastatic mechanisms. Finally, we will evaluate the potential use of metastatic mediators as targets of therapy.

Two years ago, we initiated a project in the laboratory that focuses on breast cancer metastatic suppressor genes and their functions in metastasis. Our initial efforts are devoted to study the group of metastatic suppressor genes necessary for breast to lung metastasis, first identified at Joan Massagué's laboratory (Minn *et al*, 2005). With this purpose, we are using the MDA-MB-231 breast cancer cell line model and its derivatives #4175 and #1833, which have a strong metastatic capacity to lung and bone. Furthermore, we are also screening new metastatic cell populations from pleural effusions derived from breast and lung cancer patients in order to identify new metastatic gene signatures.

For this purpose, on the basis of collaborations with clinical and basic researchers at the Hospital Clínic and Hospital de Sant Pau, in Barcelona, and the Memorial Sloan-Kettering Cancer Center, in New York, the MetLab team continues to work on the isolation of metastatic cells from pleural effusions derived from lung and breast cancer patients. Once in-

jected into mice, these metastatic cells are labeled with the GFP-Luciferase-TK protein fusion and visualised by bioluminescent techniques. On the basis of these metastatic cell populations, we intend to isolate highly aggressive subpopulations with tropism to specific tissues. These subpopulations will be used to identify and validate metastatic gene signatures by means of gene expression profile analyses and biochemical, cellular and molecular biology techniques.



Research Group Members

MetLab Managing Director:
Roger Gomis

IRB Barcelona Adjunct Director:
Joan Massagué

Research Associate:
Mònica Morales

PhD Students:
Anna Arnal, Milica Pavlovic, Maria Tarragona

Lab Technician:
Esther Fernández

Lab Manager:
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Visiting Scientists:
Xabier Adrian García, Cristina Nadal (members of the Institut d'Investigacions Sanitàries IDIBAPS-Hospital Clínic/IRB Barcelona)

Scientific output

References

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Research networks and grants

Estudio de los mecanismos moleculares de la metástasis del cáncer de mama a pulmón: función y potencial terapéutico de genes supresores de metástasis
Spanish Association Against Cancer (2008-2011)
Principal investigator: Roger Gomis

Papel de C/EBPb en los mecanismos moleculares de regulación de la respuesta citostática al TGFb; implicaciones fisiológicas y sus alteraciones en el cáncer de mama
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Principal investigator: Roger Gomis

Other funding sources

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Collaborations

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Eduard Batlle, IRB Barcelona (Barcelona, Spain)

Awards and honours

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