

EPITHELIAL CELL BIOLOGY JUNIOR GROUP

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OVERVIEW

Tumour cells evolve into a progressively complex interplay between heterogeneous tumour cells and their tissue macroenvironment, which influences their proliferation and malignancy. Identifying the signalling mechanisms and cell types that sustain this complexity is one of the major goals in cancer biology. In adult skin, epithelial progenitor cells have been identified as the cell of origin of skin carcinomas. Several studies have been instrumental for defining regulatory pathways controlling their proliferation and/or differentiation. However, the identification of extrinsic factors modulating stem cell behaviour has not progressed very far to date. Using skin as a model system and employing mouse genetics and human samples, our research aims to understand how the interactions between epithelial progenitor cells, and also the interactions with their surrounding macroenvironment, sustain

“During 2016, we continued our efforts to uncover novel events controlling the behaviour of skin stem cells in order to open up new insights into the mechanisms that control their regenerative characteristics, and how when disrupted they can lead to cancer.”

skin homeostasis, regeneration, and when perturbed lead to cancer. This information may provide insights for the future development of regenerative and anti-cancer therapies.

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**Titulado Superior* (Advanced Degree)

RESEARCH HIGHLIGHTS

Regulation of epidermal progenitor cells self-renewal and differentiation

During 2016, we continued exploring how tissues acquire an adequate control of cell division and differentiation. In particular, using mouse epidermal development as a model system, we investigated the contributions of mitotic and cytoskeletal proteins in the regulation of skin progenitors' self-renewal through oriented cell divisions.

Contributions of stromal cells to the skin stem cell niche in homeostasis

We have recently identified a novel connection between macrophages and skin progenitor cells, which modulates their stem cell properties and regenerative potential. We are expanding these results to decipher how other signals, and cells from the stroma, are connected with the skin stem cell niche and regulate skin regeneration.

Contributions of stromal cues in cancer stem cell maintenance and tumour progression

The formation of tumours and their progression to malignancy undoubtedly involves the contributions of the tumour macroenvironment. Identifying the signalling mechanisms and cell types that contribute to tumour initiation and progression to malignancy is instrumental for detecting potential targets for clinical applications aimed at eradicating tumours.

The macroenvironment of many tumours is rich in cytokines, chemokines, and inflammatory enzymes. During 2016, we continued exploring the role of diverse cell-derived soluble mediators in modulating proliferation, migration and survival of skin cancer stem cells.

In addition, we focused our efforts on dissecting the contributions of immune cells to the cancer stem cell niche in tumour initiation and development. We are employing conditional loss- and gain-of-function studies in genetically modified mice in order to demonstrate the role of specific cell types and their derived soluble mediators in tumorigenesis; this may provide further insights for the potential development of immunotherapeutic approaches. ■

Figure Skin carcinoma showing the presence of a high density of inflammatory cells within the tumour. Inset shows a magnification of immune infiltrates within the tumour. *Arrows point to some immune cells

