

Epithelial Cell Biology *Junior Group*



Mirna Pérez-Moreno

Junior Group Leader

Mirna Peréz-Moreno born in Acapulco (Mexico) obtained her PhD degree in Physiology in 1999 from the *Centro de Investigación y Estudios Avanzados* (CINVESTAV), Mexico City (Mexico). She carried out a short postdoctoral training at the *Instituto de Investigaciones Biomédicas* in Madrid and later at the Memorial Sloan-Kettering Cancer Center, New York (USA).

In 2002 she joined E. Fuchs' Laboratory at the Howard Hughes Medical Institute, Rockefeller University, New York (USA), as a Postdoctoral Fellow. She was a recipient of the Breast Cancer Research Programme Fellowship of the U.S. Department of Defense.

In May 2008 she joined the BBVA Foundation – CNIO Cancer Cell Biology Programme as Junior Group Leader. Her lines of research focus on the fundamental aspects of skin biology, development and cancer. In particular, her group studies the molecular mechanisms regulated by intercellular adhesion molecules and the contributions of signals arising from the tissue microenvironment in skin physiology and disease.

The BBVA Foundation – CNIO, the *Ministerio de Ciencia e Innovación* (MICINN), and the Association for International Cancer Research-UK (AICR-UK) support the research carried out in her lab.

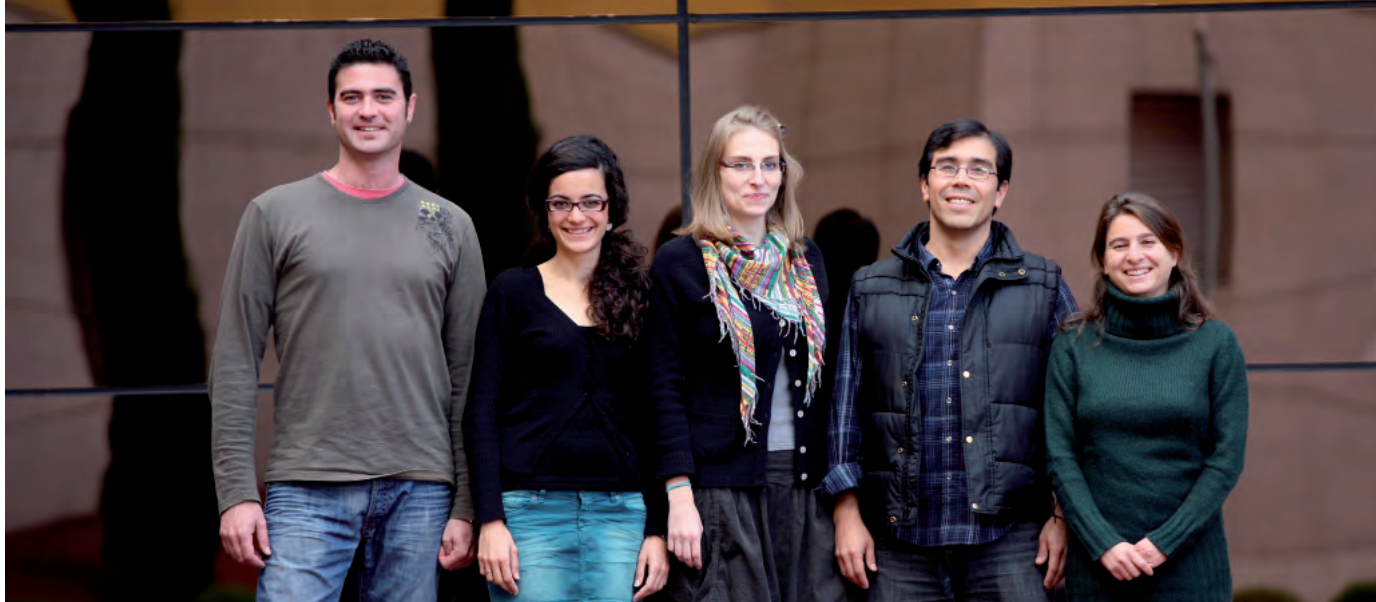
Summary

Our research aims at advancing insight into the events that regulate the physiology of epithelial tissues and how perturbations in this process may result in disease, including cancer. The primary epithelial tissue we study is the skin. We focus on dissecting how interactions between epithelial progenitor cells, including interactions with their surrounding microenvironment, maintain tissue architecture and modulate cell adhesion, proliferation, migration, and gene expression.

In order to investigate how alterations in the interactions between epithelial cells and their neighbouring cells and/or surrounding tissue microenvironment correlate with hair and epidermal diseases, we employ mouse genetics, *in vitro* cell culture systems, and human skin sample analyses.

Strategic Goals

- Analyse the role of the intercellular-adhesion protein p120-catenin in epithelial cell polarity and tissue architecture. Elucidate the role of p120-catenin in tissue repair and the implications of its loss in cell migration, chronic-inflammation and skin cancer
- Identify if cytokines exert mitotic effects on postmitotically-arrested cells, inducing additional genetic imbalance and tumour progression
- Understand if the crosstalk between inflammatory cells and epithelial progenitor cells regulates tissue regeneration



Post-doctoral fellows: Carolina Epifano and Donatello Castellana. **Graduate students:** Ljiljana Dukanovic and Marta N. Shahbazi. **Technician:** Luis G.F. Leiva (until October).

Highlights

Using skin as the primary tissue of study and mice as a genetic model system, we are investigating how epithelial skin progenitor cells preserve their dynamic interactions and communicate with their microenvironment to maintain tissue homeostasis and promote tissue repair upon injury. This is helping us to understand how deregulations in these events lead to alterations in skin regeneration and promote tumourigenesis.

We are currently addressing the following aspects:

- The role of the intercellular adhesion protein p120-catenin and its connection with the cytoskeleton in the maintenance of cell polarity and polarised cell divisions. Using a yeast-two hybrid screen we found that p120 interacts with the microtubule-associated protein CLASP2, which is involved in cell polarity and mitotic spindle organisation. We are currently analysing the physiological relevance of this interaction.
- The role of p120-catenin in promoting proper cell-migration, resolution of inflammatory responses and epidermal remodelling upon tissue injury. It is known that reduction in p120-catenin occurs frequently in skin carcinomas. We therefore aim to understand the underlying molecular events regulated by p120-catenin that are implicated in chronic inflammation and cancer.
- Identify whether chronic inflammatory responses are sufficient to initiate new divisions of postmitotically-arrested cells. Additionally, we would like to determine if these are causal events in promoting additional genetic imbalance and tumour progression.
- Analyse whether the crosstalk between inflammatory cells (e.g. macrophages) and epithelial progenitor cells regulates skin regeneration (Figure). Unveiling these processes will lead to more targeted therapy

options for skin regeneration. It will also help us to understand the contributions of inflammatory cues in the proliferation/differentiation balance of progenitor cells in inflammation-related skin diseases, including cancer.

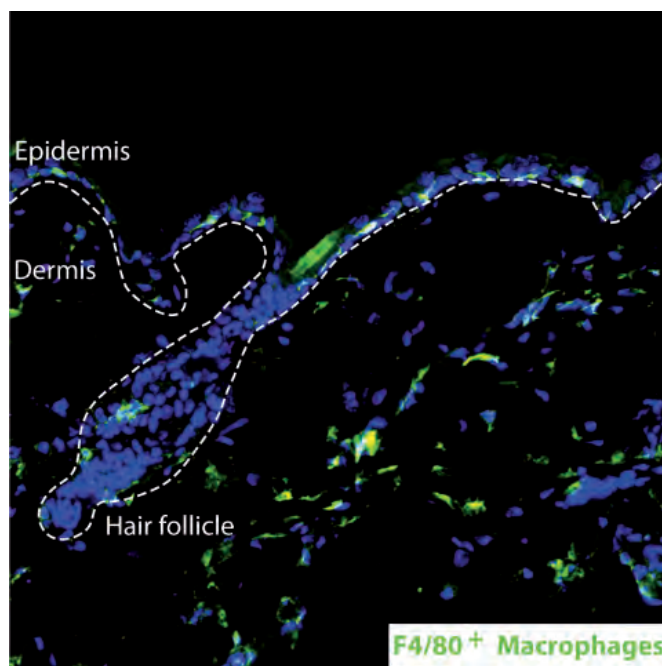


Figure: Skin section showing the presence of macrophages (green) positive for the F4/80 marker. Note the presence of macrophages in the epidermis and hair follicles localised close to keratinocytes. Image by D. Castellana.

Publication

Bartlett JD, Dobeck JM, Tye CE, Perez-Moreno M, Stokes N, Reynolds AB, Fuchs E, Skobe Z (2010). Targeted p120-catenin ablation disrupts dental enamel development. *PLoS One* 5, e12703.