Research Group Details

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Short Introduction to the lab

We are interested in cell biological events in embryonic development of ectodermal organ systems the tooth, hair and salivary gland. We use advanced tissue imaging techniques of fluorescent mouse models to understand development on a single cell level in living tissue. Our recent research characterizes the cellular events in the forming hair placode and the specialized signaling centers regulating the incisor tooth morphogenesis.

Project Outline

Title

Imaging cellular mechanisms of embryonic hair and tooth development

Short introduction to the research problem

Epithelial reorganization involves coordinated changes in cell shapes and movements, proliferation and differential adhesion. It occurs in embryos during placode formation (epithelial thickenings that initiate the morphogenesis) and subsequent invagination of the epithelium that forms the ectodermal organs, such as hair, teeth and different glands. These processes are regulated by reciprocal interactions between the epithelial and mesenchymal tissues and share morphological and molecular similarities among ectodermal organs. Studies in humans and in mouse models have already elucidated the details of genetic regulation of signaling pathways in normal development and in hereditary diseases and they have also been linked to cancer. While studies using reporter mice and mouse have unraveled the genetic networks, the cellular mechanisms remain elusive. Only recently, light microscopy imaging techniques have advanced enough to enable tracking the single cell fate in live tissue, which is crucial in understanding the underlying cell biological processes in epithelial morphogenesis.

Statement of experimental aims and methods

The study focuses on the cellular events between the genetic signaling networks and phenotypes in transgenic mouse models. This multidisciplinary study combines the conventional developmental biology approaches with the forefront of functional cell biology imaging techniques and both the cell biology and developmental tissue engineering toolbox for manipulations. Applying cell biological approaches on whole tissues will help in understanding how changes in cell polarity, migration and proliferation contribute to morphogenesis in whole live organisms. In particular the results will shed light on the role of the Eda/Edar/NF-κB, Hh and Wnt/β-catenin and non-canonical Wnt signaling and planar cell polarity pathways in these processes. The aims of the study are overlapping but also independent as the work explores similar and possibly divergent mechanisms regulating epithelial

reorganization in different organs. This study explores novel ways to utilize live confocal fluorescence imaging to understand dynamic cellular processes that have remained elusive because of the lack of tools to study them.

Specific aims:

- Dissect the role of cell proliferation together with actin induced epithelial layer invagination, cell shape, polarity and adhesion changes in tooth budding morphogenesis in the wt mouse incisor and molar tooth using reporter mouse lines.
- Characterize the identity and regulation of the proliferating cell population in early hair budding morphogenesis.
- Compare wild type to placode/bud mutant mice lines (both crossed with reporters), or phenotypes induced by pharmacological interventions, as a tools to reveal critical events in morphogenesis contributing to dysplasias and neoplasms.

Project time table

The project according to current aims is expected to be completed in four to five years.

Collaborators or external secondments relevant to the project

Collaboration with Dr.G.Martins for use of Light Sheet Microscopy at the IGC-UIC Instituto Gulbenkian de Ciência, Portugal.

Forkhead-box transcription factor Foxi3 conditional KO tooth bud mutant mouse (available via collaboration with Prof. I. Thesleff and Dr M. Jussila, Institute of Biotechnology)
Lifeact-EGFP for fluorescent actin cytoskeleton visualization (available via collaboration with Dr M.Sixt Max Planck Institute of Biochemistry, Martinsried, Germany)

Max 5 references relevant to the project

- Ahtiainen L, Lefebvre S, Lindfors PH, Renvoise E, Shirokova V, Vartiainen MK, Thesleff I, Mikkola ML. Directional cell migration, but not proliferation, drives hair placode morphogenesis. Developmental cell. 2014, 28:588-602.
- Jussila M, Aalto AJ, Sanz Navarro M, Shirokova V, Balic A, Kallonen A, Ohyama T, Groves AK, Mikkola ML, Thesleff. Suppression of epithelial differentiation by Foxi3 is essential for molar crown patterning. Development. 2015, 142:3954-63.
- Sakaue-Sawano A, Kurokawa H, Morimura T, Hanyu A, Hama H, Osawa H, Kashiwagi S, Fukami K, Miyata T, Miyoshi H, Imamura T, Ogawa M, Masai H, Miyawaki A. Visualizing spatiotemporal dynamics of multicellular cell-cycle progression. Cell. 2008, 132:487-98.
- Jernvall J, Thesleff I. Reiterative signaling and patterning during mammalian tooth morphogenesis. Mech Dev. 2000, 92:19-29.
- Biggs LC, Mikkola ML. Early inductive events in ectodermal appendage morphogenesis. Semin Cell Dev Biol. 2014, 25-26:11-21.