Biography

Salvador Aznar Benitah obtained his Honours Degree in Molecular Biology and Biochemistry at McGill University (Montreal, Canada) in 1998. He then obtained his PhD studies (Magna Cum Laude) in 2003 in Molecular Oncology at the Biomedical Research Institute in Madrid (Spain). In 2003 he moved to London as a postdoctoral fellow in the laboratory of Prof. Fiona Watt at the London Research Institute (Cancer Research UK) where he became interested in studying the behavior of adult stem cells. He established is own lab at the Center for Genomic Regulation in 2007. His lab aims at identifying and characterizing the molecular mechanisms underlying the function of adult stem cells, in particular those that are responsible for the maintenance of stratified epithelia. The recent work of his lab has been mainly focused in understanding how adult stem cells are spatiotemporally regulated, how they communicate with their local and systemic environment, and how does stem cell misfunction contribute to tissue aging and tumorigenesis. Salvador is the recipient of an ICREA Research Award.

Project

European Research Council Starting Grant
Project acronym: STEMCLOCK
Project full title: Spatiotemporal regulation of epidermal stem cells by circadian rhythms: impact on homeostasis and aging

Overview
Adult stem cells maintain tissue homeostasis by continuosly replenishing non-functional cells with healthy ones. Most mammalian adult stem cells are compartmentalized in functionally deterministic niches. From there stem cells are instructed by unique combinations of signals and spatial tensile forces which they translate into a specific behavior. However, how stem cells spatiotemporally coordinate their intrinsic stem cell potential with niche- and systemic cues, is still poorly understood. These issues are essential for proper tissue function, since perturbations in the signals that govern stem cell function can cause tissue malfunction, such as tumorigenesis, and aging.

In this project, we aim at performing a systematic analysis to identify the molecular causes that underlie epidermal stem cell aging, and their impact on tissue malfunction. In particular, we will focus on the interplay between circadian rhythms and epidermal stem cell function. The circadian machinery anticipates and synchronizes the daily function of tissues according to the entrainment by natural changes in light and metabolism. We have previously shown that the molecular clock fine-tunes the behavior of epidermal stem cells by imposing transcriptional oscillations in the expression of stem cell regulatory genes. These oscillations provide epidermal stem cells with a spatiotemporal axis for responding to dormancy, activating, and pro-differentiation cues. Notably, the clock of epidermal stem cells is naturally dampened upon aging, and forced circadian arrhythmia in epidermal stem cells causes severe epidermal aging as well as predisposition to tumorigenesis.

We now propose to understand how the circadian clock coordinates the communication between stem cells with local and systemic cues, and how these are perturbed during aging. Specifically we aim: i) To study whether circadian rhythms coordinate the function of niche cells and epidermal stem cells; ii) To identify the molecular causes underlying the age-related dampening of the clock in epidermal stem cells. To do so, we will combine 3 approaches: high throughput genomic and transcriptome data from murine epidermal stem cells in vivo, mouse models of circadian arrhythmia, and bioinformatic analysis. We hope to identify some of the long-term molecular and epigenetic causes underlying the loss of proper communication between epidermal stem cells with their environment, resulting in tissue aging.