Les mardis de L'IAB

IAB
EPIGENETICS • ENVIRONMENT
CELL PLASTICITY • CANCER

MARIA OUZOUNOVA

CRCL, Lyon, France

EPIGENETIC CHARACTERIZATION OF CELLULAR PLIANCY IN BREAST CANCER

2.APRIL 2024 – 11 AM – LECTURE HALL

The intrinsic competence of the cell-of-origin profoundly impacts the road to tumorigenesis and implies a strong interplay between cell differentiation state and malignant transformation. In this context, we introduced the cellular pliancy concept as the intrinsic capacity of a cell to adapt to an oncogenic event and hypothesized that each differentiation state is associated with a unique level of pliancy that is epigenetically determined. Therefore, the defined hierarchy of the mammary tissue is a unique model to study the influence of cell state in an early response to an oncogenic event. Our team demonstrated that mammary stem cells display a unique capacity to withstand aberrant RAS oncogene activation compared to more differentiated cells within the mammary hierarchy, concomitant with aberrant activation of the epithelial-mesenchymal transition (EMT)-inducing transcription factors (EMT-TFs).

Based on these hypotheses, we investigated how the epigenetic landscape at different levels may impact the EMT-induced cancer cell plasticity at the early steps of cancer initiation. We provided the first framework characterizing the interplay between mammary epithelial cell differentiation state and cellular pliancy and enabled to decipher the impact of cellular pliancy on neoplastic transformation. Moreover, we established for the first time a pliancy score which quantifies the early response of mammary cells to RAS oncogenic stress depending on their differentiation state. In addition, a comprehensive analysis of the epigenetic landscape of normal mammary epithelial cells in response to an oncogenic activation allowed us to identify key players involved in the configuration of the epigenome, enabling the onset of gene expression programs that determine pliancy levels. Additionally, multiomic epigenetic and transcriptomic profile analysis of mammary subpopulations during the response to oncogenic activation of RAS have enabled us to propose a new model of the mammary hierarchy by the definition of new clusters that integrate gene expression profile and the chromatin accessibility status and to demonstrate that the trajectory taken by epithelial cells in response to RAS is intrinsically linked to their original phenotype.

Overall, we proposed a new approach to understanding the interplay between epigenetic mechanisms, cellular differentiation, and oncogenic insult making a link between cellular identity via phenotypic and transcriptomic data and the cellular potentiality via epigenomic data for unravelling the complex nature of tumorigenesis and the pathway of normal breast cells from RAS-related oncogenic stress to transformation.

Invited by : Guillermo Orsi

Twitter : IAB_Officiel
Website : https://iab-grenoble.fr/

Allée des Alpes, 38700 La Tronche (tram line B, stop : Grand Sablon)
The seminar is followed by discussions and exchanges with the speaker and a sandwich buffet is offered

UGA Université Grenoble Alpes · Inserm La science pour la santé From science to health · cnrs · CHU Grenoble Alpes · EFS Établissement Français du Sang Du donneur aux patients