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ULB

Département **Service Communication Recherche - com.recherche@ulb.ac.be**

Relations Extérieures **Mathieu Léonard : +32 (0)2 650 98 98 / +32 (0) 473 97 22 56**
Nathalie Gobbe : +32 (0)2 650 92 06 / +32 (0) 474 84 23 02

Press Release

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Cell-cell communication in stem cell fate choice identified

Publication in Nature: researchers at the Université libre de Bruxelles, ULB identify for the first time the mechanisms by which cell-cell communication control the fate of mammary and prostate *stem cells.*

Mammary glands and the prostate are composed of two types of cell lineages: the basal cells and luminal cells. These two cell lineages are maintained by distinct pools of basal and luminal stem cells. Although adult basal stem cells only give rise to basal cells in normal conditions, basal stem cells can give rise to both basal and luminal cells and therefore called multipotent (for multiple cell lineages) in conditions such as transplantation and cancer initiation. The mechanisms that restrict multipotent lineage differentiation of basal stem cells during normal conditions are currently unknown.

In a new study published and that make the cover of the prestigious *Nature* journal on Wednesday August 26, researchers lead by **Pr. Cédric Blanpain - WELBIO investigator, director of the Laboratory of Stem Cells and Cancer, Faculty of Medicine, Université libre de Bruxelles** -, uncovered that communication between basal and luminal cells restricts multipotency in the mammary gland and the prostate and identified the signaling pathways that restrict multipotency in normal conditions and that activate basal stem cell multipotency in regenerative conditions.

To assess whether luminal-basal cell communication controls basal cell multipotency, Alessia Centonze and colleagues developed a novel genetic approach that allows to specifically mark basal cells with a fluorescent tag, kill luminal cells and then assess the fate of basal stem cells overtime. Interestingly, they found that ablation of luminal cells leads to activation of basal stem cell multipotency and the replenishment of the luminal cells by basal stem cells in multiple tissues including mammary gland,

prostate, sweat gland and salivary gland. They show that the activation of multipotent-activated basal cells lead to the formation of a hybrid cell population presenting basal and luminal differentiation program. To identify the molecular mechanism leading to the activation of multipotency, the researchers of ULB in collaboration with Pr Thierry Voet – KULeuven – perform single cell RNA sequencing allowing to monitor the molecular identity of individual cells following luminal cell ablation. They defined the lineage trajectory of basal stem cells and the unique gene signature of activated multipotent basal stem cells and how these cells give rise to new luminal cells. “It was very exciting to identify this new cell state that accompanied regeneration of different tissues and demonstrated that that the switch from basal to luminal differentiation is a dynamic process in which basal cells lose their basal identity while acquiring luminal characteristics, passing through a hybrid state reminiscent of the cell state observed during embryonic development” comments **Alessia Centonze**, the first author of this study.

The researchers then identify the molecules that restrict multipotency in normal condition and the molecules that promote multipotency upon luminal cell ablation. “The identification of the molecules that controls stem cell multipotency will be interesting to inhibit cancer formation as multipotency is associated with breast and prostate cancer formation” comments Pr **Cédric Blanpain**, the senior author of the study.

In conclusion, this new study identifies the key role of cell-cell interaction to restrict multipotency in adult stem cells and uncovers the molecular mechanisms that controls multipotency in different tissues, which have important implications for cancer formation.

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Scientific contact :
Professor Cédric Blanpain, MD, PhD

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Professor of Stem Cell and Developmental Biology
WELBIO investigator
Director of the Laboratory of Stem Cells and Cancer
Université Libre de Bruxelles (ULB)
Office: 32-2-555 4175
Email: Cedric.Blanpain@ulb.ac.be
PA Marylène Poelaert: Marylene.Poelaert@ulb.ac.be
Lab Website: http://blanpainlab.ulb.ac.be/index.htm