MedicalXpress

New mechanism that regulates tumour initiation and invasion in skin basal cell carcinoma

June 24 2015

Researchers at the Université libre de Bruxelles, ULB uncover a new mechanism that regulates tumour initiation and invasion in skin basal cell carcinoma.

Basal cell carcinoma (BCC) is the most common cancer found in human with several million of new patients affected every year around the world. The mechanisms that control BCC initiation and invasion are poorly known.

In a new study published in *Cell Stem Cell*, researchers led by Pr. Cédric Blanpain, MD/PhD, professor and WELBIO investigator at the IRIBHM, Université libre de Bruxelles, Belgium, report that Sox9, directly controls skin cancer formation by regulating the expansion of tumor initiating cells and the invasive properties of cancer cells.

Jean-Christophe Larsimont and colleagues used state of the art genetic mouse models to dissect the functional role and molecular mechanisms by which Sox9 controls skin cancer initiation and invasion. In collaboration with Pr Véronique Del Marmol (Department of Dermatology, Erasme Hospital, ULB) and the group of Pr François Fuks (Laboratory of cancer epigenetics, Faculty of Medicine, ULB), Larsimont and colleagues demonstrated that while Sox9 is not expressed in the normal skin cells, Sox9 begins to be expressed in pre-cancerous lesions and is maintained in invasive tumors. Deletion of Sox9 prevents

skin cancer formation demonstrating the essential role of Sox9 during tumorigenesis and leads to the progressive disappearance of the oncogene expressing cells. "It was really exciting to see that the deletion of only one gene was sufficient to completely prevent tumor formation. It was even more surprising to observe that in absence of Sox9, pre-cancerous cells disappear over time, suggesting that we can eliminate oncogene expressing cells before cancer formation" comments Jean-Christophe Larsimont, the first author of this study.

The authors uncover the cellular and molecular mechanisms, as well as the gene network regulated by Sox9 during the early steps of skin tumor initiation and demonstrates that Sox9 controls the long term maintenance and expansion of oncogene expressing cells by promoting self-renewing division and inhibiting differentiation. In addition, Sox9 acts also as key orchestrator of the extracellular matrix remodeling, cell adhesion and cytoskeleton dynamics required for tumor invasion. These results have important implications for the development of novel strategies to block tumor formation and invasion in the most frequent cancer in humans. "Given that the majority of human cancers express Sox9, it is likely that the results of this study will be relevant for other cancers in humans and will help to define
new strategies to prevent cancer formation and block tumor invasion" comments Cédric Blanpain, the last and corresponding author of this study.

More information: "Sox9 Controls Self-Renewal of Oncogene Targeted Cells and Links Tumor Initiation and Invasion." *Cell Stem Cell* 2015, dx.doi.org/10.1016/j.stem.2015.05.008

Provided by Université libre de Bruxelles