

Researchers define how cancer cell of origin controls invasive and metastatic properties of tumor cells

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Researchers at the Université libre de Bruxelles, ULB define for the first time how the cancer cell of origin controls invasive and metastatic properties of tumor cells.

Tumor heterogeneity describes the differences between tumors in different patients and between the different cells within a given tumor. These differences have major implications for the diagnosis, prognosis, and therapy of cancer patients. Different mechanisms have been proposed to account for tumor heterogeneity such as epithelial to mesenchymal transition (EMT), a process in which epithelial tumor cells loose their adhesion and acquired mesenchymal migratory properties that are associated with metastasis and resistance to therapy. The reason for why some tumors undergo EMT and other not might reflect their cell of [origin](#), although this possibility was not been investigated so far.

In a new study, researchers lead by Cédric Blanpain, MD/PhD, WELBIO investigator and Professor at the Interdisciplinary Research Institute (IRIBHM), Université libre de Bruxelles, Belgium, demonstrated for the first time, that the cancer cell of origin controls EMT in skin squamous cell carcinoma, the second most frequent skin cancer.

Mathilde Latil and colleagues used state of the art genetic mouse allowing lineage tracing of the cancer cell of origin together with

expression of mutated genes that induced cancer formation in different compartments of the skin epidermis including hair follicle cells and the interfollicular epidermis, the cells that formed the skin barrier.

Surprisingly, while the skin cancers arising from the interfollicular epidermis were epithelial well-differentiated cancers, tumors that arise from the hair follicle, were in general very invasive mesenchyme-like cancers that underwent EMT. These data demonstrate that hair follicle stem cells and their progeny are prone to undergo EMT, and give rise to metastasis, demonstrating that the cancer cell of origin is associated with tumor aggressiveness.

To understand the mechanisms by which cell of origin controls this malignant transition, Mathilde Latil and colleagues studied the changes in the transcriptional (all the genes that are expressed by a cell) and the epigenetic landscape (the accessibility of DNA that allows the expression of genes) of the cancer cell of origin and their resulting tumors. They found that the epigenetic and transcriptional landscapes of the cancer cell of origin primed the oncogene-targeted cells to develop into either well-differentiated or more invasive tumors characterized by EMT, underscoring the importance of the cancer cell of origin in controlling this transition. " It was really exciting to observe this remarkable and unexpected similarity in the epigenetic and transcriptional landscape of [hair follicle](#) lineage and the [invasive tumor cells](#) suggesting that the EMT genes are primed in the cancer cell of origin, which facilitate the development of EMT in [cancer cells](#)" said Mathilde Latil, the first author of this study.

In addition, this study allowed identifying the gene network that control tumor initiation and EMT related heterogeneity. "By combining genome wide transcriptional and epigenetic profiling, we can now define for each genes which are the factors and the specific DNA regions they bind that regulate gene expression in [tumor cells](#). The identification of these gene networks that regulate different tumor functions will be

instrumental to design new strategy to block tumorigenesis and EMT, which may improve cancer response to therapy and decrease metastasis " explains Pr Cédric Blanpain, the senior author of this *Cell Stem Cell* paper.

More information: Mathilde Latil et al. Cell-Type-Specific Chromatin States Differentially Prime Squamous Cell Carcinoma Tumor-Initiating Cells for Epithelial to Mesenchymal Transition, *Cell Stem Cell* (2016). [DOI: 10.1016/j.stem.2016.10.018](https://doi.org/10.1016/j.stem.2016.10.018)

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