

Key factor sustaining malignant tumor state identified

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In a study published in *Nature Cancer*, researchers led by Prof. Cedric Blanpain, WELBIO investigator, Director of the Laboratory of Stem Cells and Cancer and Professor at the Université libre de Bruxelles (ULB), Belgium, demonstrated that NR2F2 is an essential regulator of malignant tumor state by controlling cancer stem cell and tumor

maintenance in mouse and human cancers.

Federico Mauri and colleagues used a combination of state-of-the-art genetic models to assess the role of NR2F2 in mouse and human skin [cancer](#). The authors discovered that NR2F2 is expressed in malignant cancers. Inactivation of NR2F2 blocks the progression of benign to [malignant tumors](#) and represses essential [tumor](#) functions, leading to tumor regression. "It was very exciting to observe that genetic or pharmacological inhibition of NR2F2 can cause tumor regression or prevent the progression to invasive malignant tumor states responsible for metastasis" comments Federico Mauri, the first author of this study.

By performing a detailed histological and molecular characterization of the tumor states following NR2F2 genetic gain and loss of functions studies during tumor progression, the authors unravel the [molecular mechanisms](#) by which NR2F2 regulates malignant tumor progression, and tumor growth. NR2F2 promotes tumor cell proliferation, and invasive features, while repressing cell death, tumor differentiation and immune cell infiltration of the tumor.

"One of the most remarkable findings of this study is the demonstration that inactivation of NR2F2 promotes tumor differentiation, leading to tumor regression. Despite the spectacular efficacy of pro-differentiation therapy for the treatment of pro-myelomonocytic leukemia, very few pro-differentiation therapies are currently used to treat solid cancers. The development of NR2F2 inhibitors should keep in check many essential cancer functions and is thus a very promising strategy for the development of novel anticancer therapy," comments Pr Cedric Blanpain, the senior author of this study.

Cédric Blanpain, together with ULB, and private and public investors founded a company called ChromaCure to discover and develop first-in-class small molecule therapeutics targeting NR2F2 for unmet clinical

needs in oncology.

More information: Federico Mauri et al, NR2F2 controls malignant squamous cell carcinoma state by promoting stemness and invasion and repressing differentiation, *Nature Cancer* (2021). [DOI: 10.1038/s43018-021-00287-5](https://doi.org/10.1038/s43018-021-00287-5)

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