

# PHD2 targeting overcomes breast cancer cell death upon glucose starvation

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Micrograph showing a lymph node invaded by ductal breast carcinoma, with extension of the tumour beyond the lymph node. Credit: Nephron/Wikipedia

B55 $\alpha$  is one of the regulatory subunits of the PP2A phosphatase. This phosphatase has been associated to the control of many biological functions but the multiplicity of complexes that can be formed by the combination of different subunits renders this protein hard in its understanding. The Massimiliano Mazzone group (VIB-KU Leuven) has recently demonstrated that PP2A/B55 $\alpha$  promotes the growth of colorectal cancer, by dephosphorylating PHD2 and modifying its enzymatic properties. PHD2 is a member of a family of enzymes crucial for the cellular response to hypoxia.

In this new work Giusy Di Conza and colleagues from the Massimiliano Mazzone lab investigated the molecular interaction between PHD2 and B55 $\alpha$  in response to glucose starvation in the context of [breast cancer cells](#). They showed that in a context of glucose starvation, PHD2 reduces B55 $\alpha$  protein levels, which correlates with breast cancer cell death. In breast cancer cells, PHD2-knockdown prevents B55 $\alpha$  degradation and overcomes cell death in response to glucose starvation. PHD2-silenced MDA-MB231 xenografts show accumulation of B55 $\alpha$  and resistance to the glucose-competitor 2DG. Accordingly, targeting of B55 $\alpha$  sensitizes breast cancer [cells](#) to glucose starvation.

Massimiliano Mazzone (VIB-KU Leuven): "Thanks to this work, we now better understand how some tumors can escape cancer cell death in the context of nutrient starvation. Our data show the importance of blocking PP2A simultaneously to glucose metabolism in order to induce breast [cancer](#) cell death. Overall, these findings can open new possible therapeutic perspectives in [breast cancer](#)."

**More information:** PHD2 targeting overcomes breast cancer cell death upon glucose starvation in a PP2A/B55 $\alpha$ -mediated manner, Di Conza et al., *Cell Reports* 2017

Provided by VIB (the Flanders Institute for Biotechnology)

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