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## **INHIBITOR OF APOPTOSIS PROTEINS DETERMINE GLIOBLASTOMAS STEM- LIKE CELLS FATE IN AN OXYGEN- DEPENDENT MANNER**

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**S**mac mimetics (SMs) are inhibitor of apoptosis proteins (IAPs) antagonists. In glioblastomas (GBs), SMs can trigger apoptotic and non-apoptotic processes<sup>1, 2, 3</sup>. As GBs are highly hypoxic, we investigated SM GDC-0152 effect in GB stem-like cells according to oxygen level. We showed that in an environment rich in oxygen (normoxia), GDC-0152 induced loss of stem-cell properties. Unexpectedly, in an environment deprived of oxygen (hypoxia), it triggered apoptosis and decreased cell proliferation. Analysis of Serine-Threonine Kinases activation upon GDC-0152 treatment revealed involvement of different signaling pathways according to oxygen level. In normoxia, NF- $\kappa$ B pathway was activated and in hypoxia, GDC-0152 efficacy was ATR- and TNF $\alpha$ -dependent. This work shows that GDC-0152 triggers anti-tumoral effects whatever the tumoral oxygen pressure, therefore SMs appear as promising molecules in GBs treatment.

## **BIOGRAPHY**

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