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Hypertonicity-imposed BCL-XL addiction primes colorectal cancer cells for death

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Abstract

Induction of the mitochondria-controlled (intrinsic) apoptosis is a mainstay of current anti-neoplastic chemotherapies. Activation of this death pathway is counteracted by BCL-2-like proteins, which functionally set the threshold for apoptosis and determine whether malignant cells are sensitive or resistant to anti-cancer treatments. Hence, unlocking the intrinsic apoptotic cascade and promoting the cell's commitment to undergo apoptosis concordantly promotes efficacy of anti-cancer treatments. Here, we show that hyperosmotic stress enforces addiction of colorectal cancer cells to BCL-XL, thereby exhausting the protective capacity of BCL-2-like proteins and priming mitochondria for death. Our work identifies osmotic pressure as a cell extrinsic factor that modulates responsiveness of colorectal cancer cells to therapy.

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