Accepted Manuscript

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

Sina Heimer, Gertrud Knoll, Charlotte Steixner, Diana Nicoleta Calance, Dieu Thuy Trinh, Martin Ehrenschwender

PII: S0304-3835(18)30499-3

DOI: 10.1016/j.canlet.2018.07.035

Reference: CAN 14009

To appear in: *Cancer Letters*

Received Date: 15 March 2018

Revised Date: 29 June 2018

Accepted Date: 26 July 2018

Please cite this article as: S. Heimer, G. Knoll, C. Steixner, D.N. Calance, D.T. Trinh, M. Ehrenschwender, Hypertonicity-imposed BCL-XL addiction primes colorectal cancer cells for death, *Cancer Letters* (2018), doi: 10.1016/j.canlet.2018.07.035.

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.