

One-two punch for cancer

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Many cancer cells evade critical DNA surveillance and maintenance by increasing the export—by the Exportin-1 (XPO1) nucleo-cytoplasmic transport protein—of nearly all major tumor suppressor proteins from the nucleus. Thus, overexpression of XPO1 is often an indicator of poor prognosis in numerous malignancies.

Evasion of apoptosis, programmed <u>cell death</u>, is another cancer



hallmark. While studies of venetoclax, a potent and selective inhibitor of the anti-apoptotic protein BCL2, have revealed impressive response rates, some aggressive hematologic malignancies escape through another anti-apoptotic protein, MCL1.

Noting that both BCL2 and MCL1 expression are controlled by an XPO1-regulated protein, and that XPO1 is inactivated by SINE (selective inhibitor of nuclear export) compounds, Michael Savona, MD, and colleagues tested a combination of venetoclax and SINE compounds.

Reporting in the journal *Blood Advances*, they showed the combination enhanced cell killing in both in vitro and in vivo models of aggressive hematologic malignancies. Michael Byrne, DO, currently is leading a clinical trial to test this approach in patients.

More information: Melissa A. Fischer et al. Venetoclax response is enhanced by selective inhibitor of nuclear export compounds in hematologic malignancies, *Blood Advances* (2020). <u>DOI:</u> <u>10.1182/bloodadvances.2019000359</u>

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