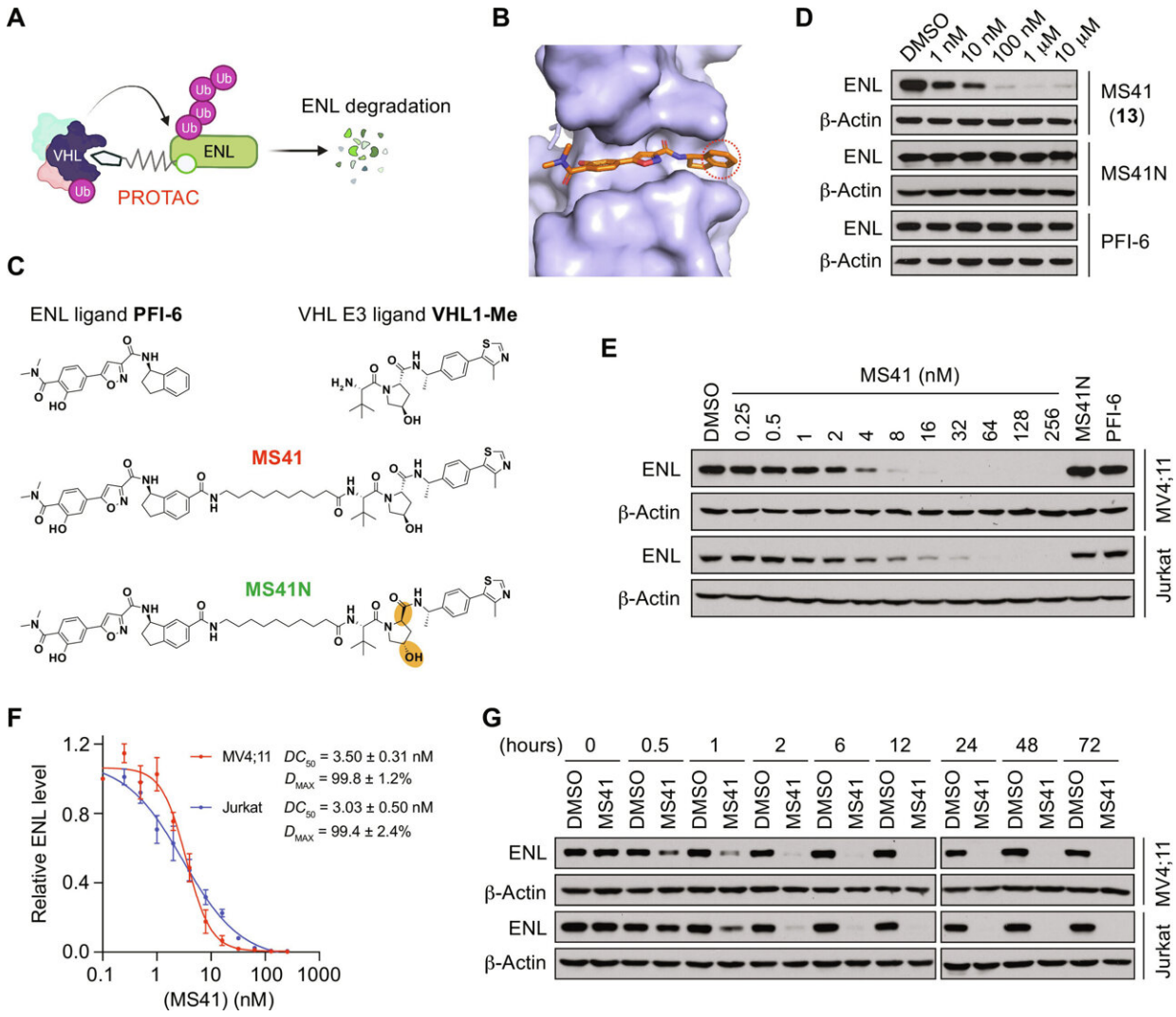
New anti-cancer 'degrader' targets protein essential to infant leukemia

August 30 2024



Discovery of a first-in-class, highly potent VHL-recruiting ENL PROTAC degrader, MS41. Credit: *Science Advances* (2024). DOI: 10.1126/sciadv.ado1432

Scientists at Van Andel Institute and Icahn School of Medicine at Mount Sinai have developed a potent anti-cancer compound that inhibits cancer cell growth in a tough-to-treat type of infant leukemia. The findings are published in the journal *Science Advances*.

The compound, MS-41, targets and destroys ENL, a protein that is essential to the progression of MLL-rearranged leukemia. Without ENL, leukemia cells lose the ability to proliferate and spread.

"Up to 80% of acute leukemias in infants are linked to problems with the MLL gene, yet there are few effective treatments for MLL-rearranged leukemias," said VAI Professor Hong Wen, Ph.D., co-corresponding author of a study describing the findings.

"MS-41 is a new, experimental compound that effectively targets and degrades a central survival mechanism in leukemia cells. Our early results are promising, and we're excited to continue developing MS-41 as a potential leukemia treatment."

MS-41 belongs to a family of cancer-fighting compounds called PROTAC degraders, which are an increasingly popular approach to cancer drug development.

Unlike traditional small-molecule inhibitors, PROTAC degraders completely remove their target proteins, enabling them to deliver robust therapeutic effects at low doses with fewer side-effects. PROTAC degraders also often require less frequent treatment than other currently available cancer medications.

Dr. Hong WenProfessor, Department of EpigeneticsVan Andel Institute. Credit: Van Andel Institute

The findings also reveal that MS-41 did not harm healthy cells when tested in mouse models. Such compounds are desirable as medications because they are less likely to cause side effects.

Moving forward, Wen and her colleagues will investigate MS-41 in additional models to assess if it is applicable in other types of ENL-related acute leukemias and cancer types such as Wilms tumor.

More information: Zhaoyu Xue et al, A potent and selective ENL degrader suppresses oncogenic gene expression and leukemia progression, *Science Advances* (2024). DOI: 10.1126/sciadv.ado1432

Provided by Van Andel Research Institute

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