The roles of USP1 in Ewing sarcoma

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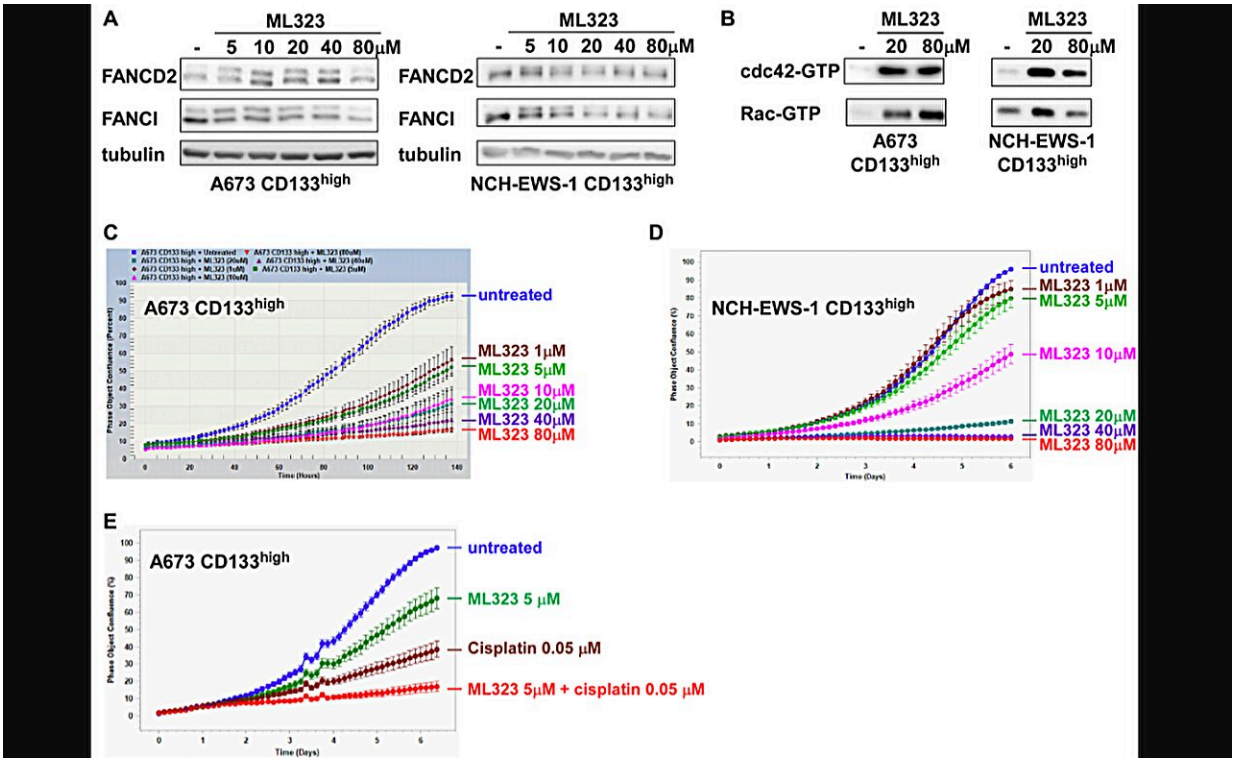

A USP1 inhibitor, ML323, activates cdc42 and inhibits Ewing sarcoma growth. Credit: *Genes & Cancer* (2024). DOI: 10.18632/genesandcancer.235

A new research paper titled "Roles of USP1 in Ewing sarcoma" has been published in *Genes & Cancer*.

Ewing sarcoma is a cancer of bone and soft tissue in children and young adults that is driven by the EWS-ETS fusion transcription factor, most

commonly EWS-FLI1.

Researchers Panneerselvam Jayabal, Xiuye Ma and Yuzuru Shiio from The University of Texas Health Science Center previously reported that Ewing sarcoma harbors two populations of cells, the $CD133^{high}$ population displaying higher growth rate and the $CD133^{low}$ population displaying chemotherapy resistance. In their new study, the researchers now find that the ubiquitin-specific protease 1 (USP1) is a transcriptional target of the EWS-FLI1 fusion oncoprotein, expressed at high and low levels in the $CD133^{high}$ and the $CD133^{low}$ populations, respectively, and determines chemo-sensitivity.

"Ubiquitin-specific protease 1 (USP1) is a deubiquitinating enzyme that plays important roles in DNA damage response," the researchers write.

They also found that USP1 inhibits cdc42, increases EWS-FLI1 transcriptional output, and simulates Ewing sarcoma growth. Results show that chemo-sensitization by USP1 is independent of cdc42. A pharmacological inhibitor of USP1 was able to activate cdc42 and inhibit Ewing sarcoma growth.

"These results uncover critical roles for USP1 in Ewing sarcoma, which regulates growth and chemo-sensitivity via distinct mechanisms," the team concludes.

More information: Panneerselvam Jayabal et al, Roles of USP1 in Ewing sarcoma, *Genes & Cancer* (2024). DOI: 10.18632/genesandcancer.235

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