Sall4 is required for DNA repair in stem cells

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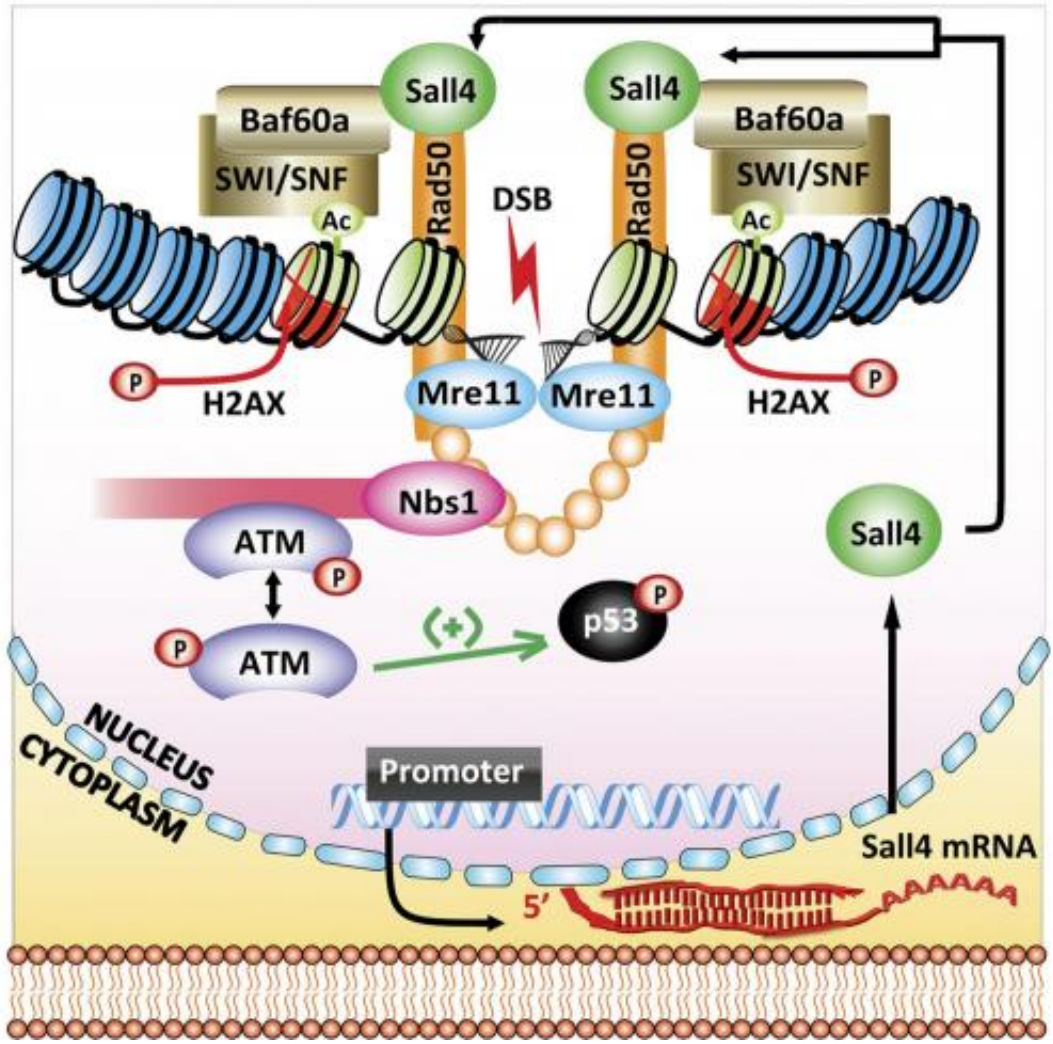

Illustrated model for the role of Sall4 in activating ATM to repair DNA damage in embryonic stem cells. Credit: Xiong et al., 2015

A protein that helps embryonic stem cells (ESCs) retain their identity also promotes DNA repair, according to a study in *The Journal of Cell Biology*. The findings raise the possibility that the protein, Sall4, performs a similar role in cancer cells, helping them fix DNA damage to survive chemotherapy.

Fixing broken DNA is particularly important for ESCs because they will pass on any mutations to their differentiated descendants. Mouse ESCs are adept at making repairs—they carry far fewer mutations than do differentiated cells—but how they achieve this isn't clear. A team of researchers led by Yang Xu, from the University of California, San Diego, tested whether the protein Sall4, which suppresses differentiation of ESCs, has a role in DNA repair.

The researchers found that ESCs lacking Sall4 were poor at mending double-strand breaks, a hazardous form of DNA damage in which both strands of the double helix are severed. They also observed that, after inducing DNA damage in mouse ESCs, Sall4 associated with proteins known to be involved in DNA repair. Overall, their findings support a model for how Sall4 is recruited to the sites of these breaks and activates ATM, a kinase that signals DNA damage and instigates repair. Because tumor cells often overexpress Sall4, the protein might similarly help them repair DNA damage. Sall4 could therefore be considered a target for drug development in cancer biology.

More information: Xiong, J., et al. 2015. *J. Cell Biol.* DOI: 10.1083/jcb.201408106

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