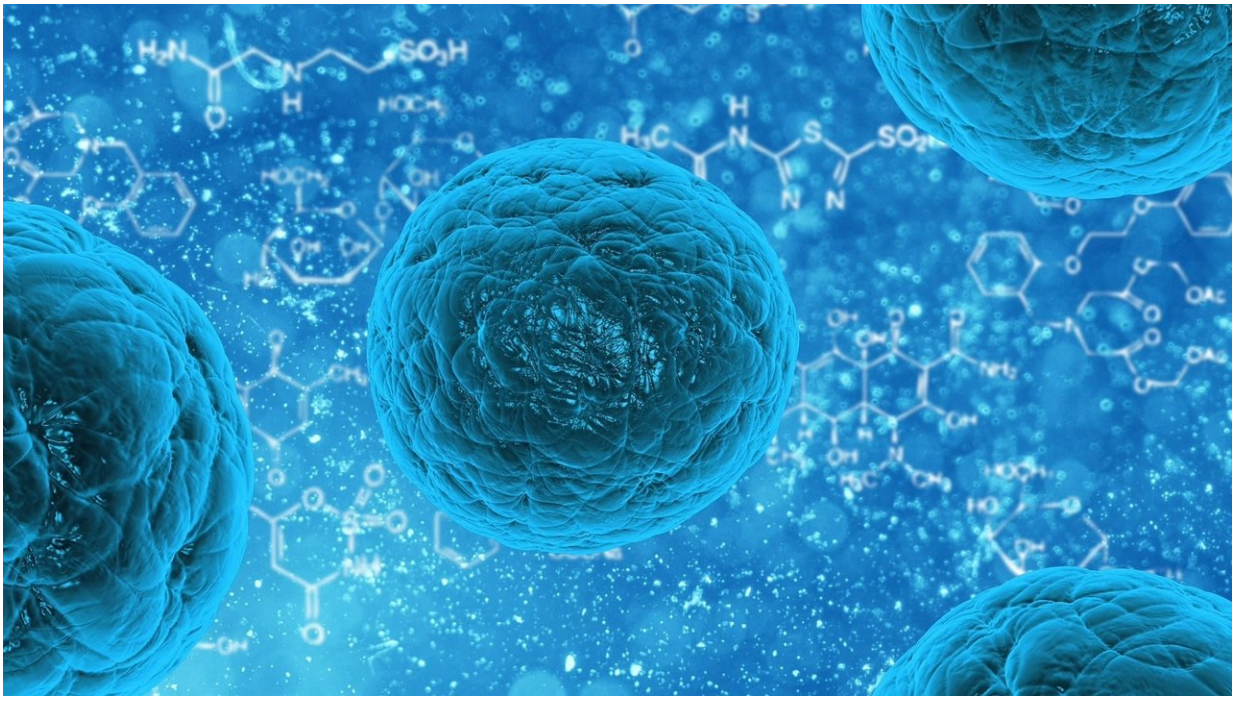
A 'rheostat' for cancer signals

September 2 2019, by Sanjay Mishra



Credit: CC0 Public Domain

WNT signaling pathways play important roles in cell growth, development and cancer. The classical or "canonical" WNT pathway and its atypical, "non-canonical" counterpart share a protein called DVL2 that "transduces" or converts one kind of signal to another.

Now Jason MacGurn, Ph.D., and colleagues have shown that two other proteins, USP9X and WWP1, act on DVL2 to regulate both WNT

signaling pathways.

Whereas WWP1 suppresses DVL2 by tagging it with a protein called ubiquitin that marks it for degradation, USP9X promotes WNT activation by releasing DVL2 from ubiquitin and rescuing it from degradation.

These antagonistic interactions establish a ubiquitylation "rheostat" on DVL2 that is a critical regulator of WNT pathway specification in human breast cancer cells, and which directs its participation in either WNT pathway, the researchers reported in the journal *Cell Reports*.

These findings have important implications for therapeutic targeting of WNT pathways in human cancer.

More information: Casey P. Nielsen et al. USP9X Deubiquitylates DVL2 to Regulate WNT Pathway Specification, *Cell Reports* (2019). DOI: 10.1016/j.celrep.2019.06.083

Provided by Vanderbilt University