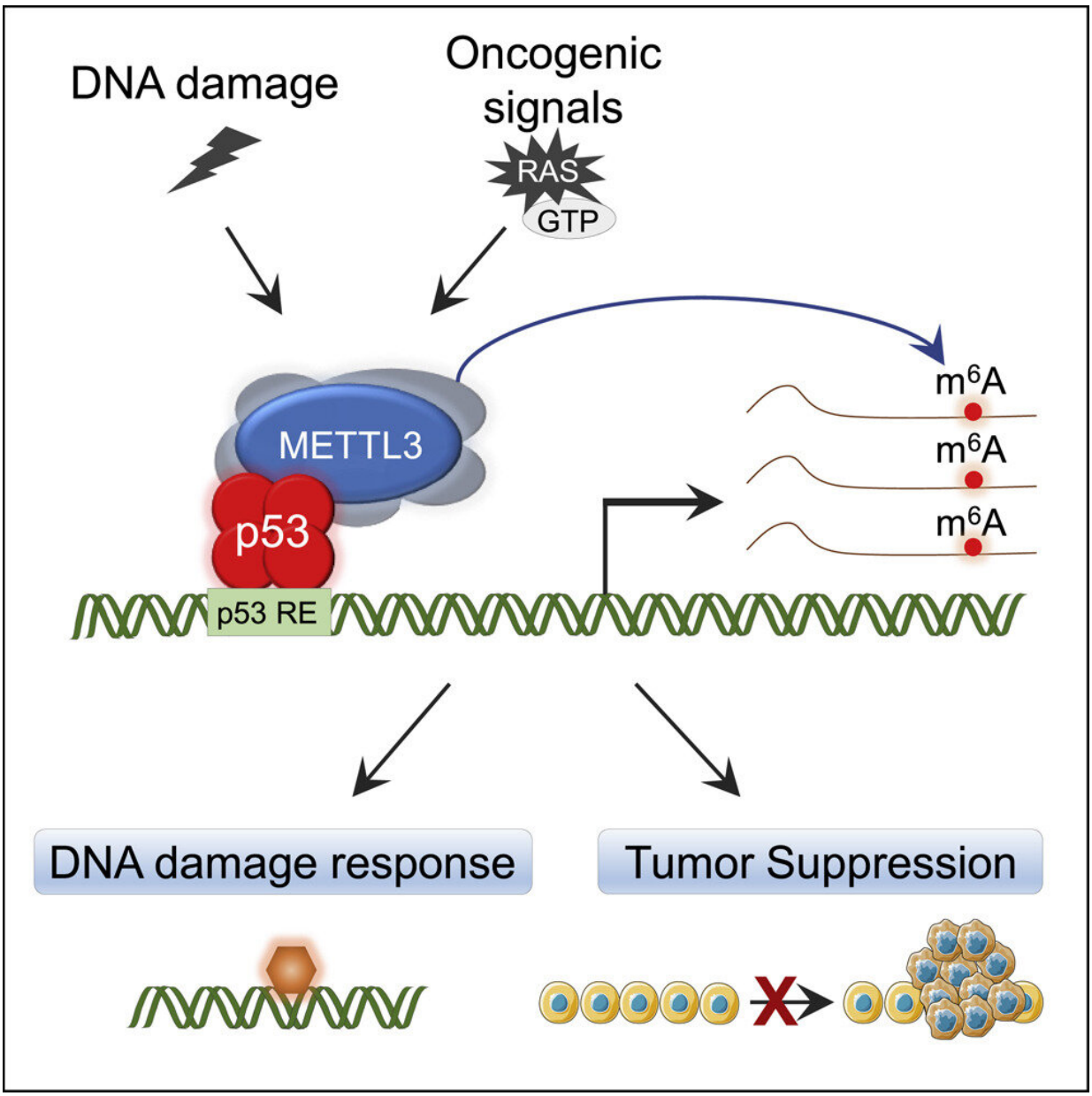
Study identifies new mechanisms that boost p53 signaling and tumor suppression

September 20 2022



Graphical abstract. Credit: *Molecular Cell* (2022). DOI: 10.1016/j.molcel.2022.04.010

A team led by Ludwig Stanford's Laura Attardi explored novel mechanisms by which the p53 protein, often called the guardian of the genome, regulates gene expression by looking for novel proteins that interact with the versatile tumor suppressor in response to cellular stressors. The researchers isolated these proteins based on their binding to p53 and identified them by mass spectroscopy. They reported in a May publication in *Molecular Cell* that METTL3—a key component of an mRNA-modifying protein complex known as M6A RNA methyltransferase complex (MTC) that helps regulate gene expression—amplifies p53 signaling induced by cellular stress.

The researchers showed that METTL3 helps to stabilize p53 and promotes the expression of its target genes in response to DNA damage and oncogenic signaling by more than one mechanism. Indeed, p53 is relatively less stable and adept at inducing its target genes in cells that are deficient in METTL3. Attardi and her colleagues also showed that METTL3 enhances the tumor suppressing activity of p53 in human cancer cells and in mouse models of cancer. Finally, their analysis of human cancer genome data supports a role for MTC in reinforcing p53 function in cancer.

More information: Nitin Raj et al, The Mettl3 epitranscriptomic writer amplifies p53 stress responses, *Molecular Cell* (2022). DOI: 10.1016/j.molcel.2022.04.010

Provided by Ludwig Cancer Research