

Modification of p53 with O-linked N-acetylglucosamine Regulates p53 Activity and Stability

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Post-translational addition of O-linked N-acetylglucosamine (O-GlcNAc) to p53 is known to occur, but the site of O-GlcNAcylation and its effects on p53 are not understood. Here we show that Ser149 of p53 is O-GlcNAcylated and that this modification is associated with decreased phosphorylation of p53 at Thr155, a site targeted by the COP9 signalosome (CSN), resulting in decreased p53 ubiquitination. Accordingly, O-GlcNAcylation at Ser149 stabilizes p53 by blocking ubiquitin-independent proteolysis. Our results suggest that the dynamic interplay between O-GlcNAc and O-phosphate modifications coordinately regulate p53 stability and activity.