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Articles of Significant Interest in This Issue

Mechanism of Suppression of Mdm2 E3 Ligase Activity by Mutant p53

Missense mutations of p53 not only inactivate its tumor suppressor function but also cause its accumulation in tumors and drive progression through gain-of-function activities. Previous studies have suggested that mutant p53 inhibits MDM2 E3 ligase activity, but the underlying mechanisms remain unclear. Yang et al. (e00375-18) show that the mutant p53 core domain binds more tightly to the MDM2 acidic domain than wild-type p53. Consequently, the mutant p53-MDM2 complex is deficient in catalyzing ubiquitin release from the activated E2 conjugating enzyme. These findings suggest that the ability of mutant p53 to impair intramolecular activation of MDM2 contributes to mutant p53 protein accumulation in tumor cells.

Translational Regulation of Fragile X Mental Retardation Protein in Neurons

Loss of fragile X mental retardation protein (FMRP) is the cause of fragile X syndrome, the most common inherited intellectual disability. The function of FMRP as an RNA-binding protein that regulates protein translation is well characterized. However, the mechanisms that control expression of FMRP are incompletely understood. Choi et al. (e00371-18) show that the *fmr1* gene, encoding FMRP, employs both internal ribosome entry site (IRES)-mediated translation and canonical cap-dependent translation. They also reveal a role for heterogeneous nuclear ribonucleoprotein Q (hnRNP-Q) as an IRES-transacting factor for *fmr1* translation in neurons. Excess hnRNP-Q-driven IRES-mediated expression of FMRP is proposed to have detrimental effects on axon growth.

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