LETTER

Effects of EDD on p53 Function Are Context-specific

Ling and Lin (1) define a novel interaction between the E3 ubiquitin ligase EDD and p53, describing various effects of EDD depletion on cell cycle progression. We wish to raise some important points regarding the functional implications of this work.

1. Previous studies examining cell cycle control by EDD (2) showed effects opposite those reported here. Although decreased S-phase was observed following siRNA-mediated EDD knockdown in primary fibroblasts, with no effect in $p53^{-/-}$ cells (Fig. 1 of Ref. 1), increased S-phase following EDD knockdown has previously been observed in HeLa cells (2), which are functionally deficient in p53 activity (3). These effects in HeLa cells are likely mediated through a robust increase in E2F1 expression (2).

2. Not surprisingly, the putative molecular mechanisms underlying these disparate effects are also conflicting. For example, Ling and Lin report changes in p21 transcript following EDD depletion (Fig. 2 of Ref. 1), directly opposite the effects on p21 protein expression observed in HeLa cells (2).

3. Most importantly, the phenotype of EDD-null mice is not altered on a p53-null background (4), providing further evidence that the p53 dependency of effects following EDD depletion are cell type-dependent. These differences in the observed effects of EDD depletion in different cellular models are very relevant to a broader and more comprehensive understanding of the function of both p53 and EDD in various physiological and disease contexts.

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