

**P006** Regulation of protein synthesis initiation factors eIF4GI and 4E-BP1 during recovery of protein synthesis from inhibition by p53  
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Activation of a temperature-sensitive form of p53 in murine erythroleukemia cells rapidly inhibits protein synthesis, with early dephosphorylation and cleavage of both initiation factor eIF4GI and the eIF4E binding protein 4E-BP1. Dephosphorylated 4E-BP1 and the cleaved products of 4E-BP1 and eIF4GI associate with eIF4E, and there is a correspondingly decreased extent of interaction of eIF4E with full-length eIF4GI. When the activation of p53 is reversed within 16h (by returning the cells to the non-permissive temperature) protein synthesis gradually recovers. The recovery correlates with the reappearance and rephosphorylation of intact eIF4GI. These effects are partially blocked by rapamycin. In addition, during recovery full-length 4E-BP1 becomes almost fully rephosphorylated on Ser<sup>64</sup> and Thr<sup>69</sup>, even in the presence of rapamycin, suggesting that mTOR-independent protein kinase(s) are responsible for this. However rapamycin enhances the level of the 4E-BP1 cleavage product, which remains largely unphosphorylated. Thus the ability of rapamycin to impair the recovery of protein synthesis after the inactivation of p53 may be due partly to a delay in the restoration of functional eIF4GI and partly to the continued presence of truncated 4E-BP1, rather than to inhibition of the rephosphorylation of full-length 4E-BP1.