

P011 Mutation of the eukaryotic initiation factor binding sites in eIF4GI results in the inability of eIF4GI to facilitate translation initiation

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Eukaryotic initiation factor (eIF) 4GI is the scaffolding protein in the eIF4F complex. This complex is responsible for recruiting the 40S ribosomal subunit onto the mRNA to allow translation to commence. To act as the scaffolding protein eIF4GI has binding sites for multiple initiation factors located throughout the protein. These include binding sites for eIF4E, eIF4A, eIF3 and poly(A) binding protein (PABP). To determine the importance of the binding sites in the function of eIF4GI during translation initiation, the binding sites for PABP, eIF4A and eIF3 were removed by PCR mutagenesis. The results show that the loss of these binding sites on eIF4GI inhibits the ability of this protein to rescue translation in aphthovirus leader protease treated rabbit reticulocyte lysate (RRL). The reason for the inability of these mutants to direct translation initiation is as yet unknown. However the mutants are able to incorporate into eIF4F complexes and eIF4F complexes associated with polysomes in RRL. Further work to elucidate the mechanism by which the mutations inactivate eIF4GI is underway.