

P050 Translational reprogramming following DNA damage
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Translational control is emerging as a crucial mechanism for coordinating cellular responses to various types of DNA damage. However, for the most part translational reprogramming and mechanisms of selective mRNA translation remain elusive. To explore the affects of genotoxic stress on translational reprogramming, DNA damage was induced in HeLa cells using ethylmethane sulfonate (EMS). We have identified a non-lethal dose of EMS which causes global protein synthesis rates to reduce by 50%, due to phosphorylation of the eukaryotic initiation factor (eIF) 2 on the α subunit, which has the net effect of reducing ternary complex formation (comprising eIF2, GTP and Met-tRNA_i). Furthermore, polysome analysis illustrates that the decrease in protein synthesis correlates to a significant decrease of polysome associated mRNAs. However, a sub-population of existing mRNA is capable of evading global translation inhibition. Therefore, microarray analysis has been used to identify those mRNAs that are selectively recruited to and away from the polysomes. The mechanisms that allow continued translation of specific mRNAs during cellular stress are of immense interest and thus far structural features and regulatory elements in the untranslated regions of mRNA have been implicated. Consequently, we will investigate the signalling pathways and mechanisms responsible for this translational reprogramming.