

P004 The identification of the internal ribosome entry segment (IRES) *trans*-acting factors of the cyclinT1 and set7 apoptotic IRESs

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During apoptosis the rate of protein synthesis is substantially reduced however some mRNAs avoid this translational inhibition. Translational profiling was performed on cells treated with the apoptosis-inducing ligand TRAIL to determine the impact of receptor-mediated cell death on the translational efficiency of a large number of mRNAs. Our data indicated ~3% mRNAs remained associated with the polysomes, particularly transcription, chromatic modification/remodelling and the Notch signalling pathway genes.

Internal ribosome entry segments (IRESs) that function in apoptotic cells were identified in 70% of the mRNAs tested that evade translational inhibition, showing a ~7-fold enrichment of these regulatory elements in this pool. In contrast, the translational repression of certain mRNAs during apoptosis correlated with the inhibition of IRES-mediated translation initiation on these mRNAs. These data demonstrate that mRNAs are subject to differential translational regulation during apoptosis and that the co-ordinated regulation of IRESs plays a pivotal role.

We have focused on the highly active IRESs identified in the cyclinT1 and set7 genes and identified a number of proteins that potentially regulate these IRESs. Crucially, the expression of a number of these proteins is induced following TRAIL-induced apoptosis.