

P029 *Trans*-acting factor requirement in IRES activation during apoptosis

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During the induction of apoptosis extensive changes occur to the translational apparatus. These include cleavage of key factors and changes in phosphorylation status of other factors. This combination leads to a shut down in cap-dependent translation. Microarray analysis of mRNA still retained on polysomes during the induction of apoptosis has shown that 3% of messages are still present. A large number of these are involved in chromatin remodelling and transcription, including Notch2 and SMARCA5. We have now examined the 5'UTRs of a number of these genes and found that 90% of 5'UTRs tested contain IRES. We have shown that these IRESes are sufficient to maintain translation during the induction of apoptosis. Analysis of factors required for IRES function shows that PTB and UNR act synergistically to activate IRES translation in the reticulocyte lysate translation system. Other work in our laboratory has shown that siRNA of PTB *in vivo* is sufficient to inhibit the function of IRESes activated during apoptosis. Interestingly, examination of the cellular levels of PTB during the induction of apoptosis showed a dramatic increase in this protein. We hypothesise that PTB plays a rate limiting step in the initiation of IRES mediated translation during the induction of apoptosis.