

P016 Further Analysis of the BAG-1 IRES and Specific
Trans-Acting Factors

Helen C. Dobbyn, Keith A. Spriggs, Becky M. Pickering,
Jonas Emsley and Anne E. Willis
University of Nottingham, UK

BAG-1 (BCL-2 associated athanogene) enhances the anti-apoptotic behaviour of BCL-2 and is involved in a variety of cellular processes. Notably it acts in conjunction with the 70kDa heat shock proteins as a co-chaperone and interacts with the glucocorticoid receptor. Four BAG-1 protein products are translated from one transcript using alternative translation start sites. Initiation of translation for the predominant p36 isoform occurs by internal ribosome entry in addition to the conventional cap-dependent scanning mechanism. During heat shock, internal ribosome entry maintains translation of BAG-1 when cap-dependent initiation is downregulated. During internal ribosome entry, interaction of the ribosome with the internal ribosome entry segment (IRES) is facilitated by the binding of IRES transacting factors (ITAFs) to the RNA. We have shown that poly r(C) binding protein 1 (PCBP1) and polypyrimidine tract binding protein 1 (PTB1) bind to the BAG-1 IRES and alter its structure. One aim of our current work is to identify additional BAG-1-specific factors that interact with the IRES to further our understanding of IRES regulation. We intend to use x-ray crystallography to elucidate the structure of the BAG-1 IRES in complex with BAG-1-specific ITAFs and characterise the effects of binding on the structure of the RNA.