

P031 Functional Analysis of the Insulin Receptor IRES
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The 5'UTR of the insulin receptor (IR) contains an internal ribosome entry segment and we are investigating how this IRES is involved in controlling expression of the receptor under various physiological conditions.

By deletion analysis we have located the minimal active element and determined the binding sites of various ITAFs on the RNA. In agreement with our recent data, we have been able to show that PTB is critical for the function of this IRES *in vitro*, particularly nPTB. By using chemical and enzymatic modification, a structural model for the IRES in the absence and presence of these binding proteins has been derived.

Transfections into various cell lines have shown that the IR-IRES is especially active in neuronal cell lines. The levels of activity seen can be modulated by various factors, including cell confluence. Furthermore, addition of insulin to subconfluent cells is able to significantly activate the IRES. We have also expressed this IRES in adipocytes and found it to be active. However, we have so far not been able to show any increase in IRES function in these cells upon differentiation in response to the insulin addition. The physiological relevance of this IRES will be discussed.