

The insulin receptor plays a critical role in the maintenance of glucose homeostasis. Regulation of this key function must be under stringent controls. In order to study the regulation of insulin receptor gene expression, we have cloned, sequenced and characterized its promoter. The first exon of the insulin receptor gene is embedded in an unusual segment of DNA composed of Alu repeats. The promoter has the characteristics typical of a housekeeping gene. It is GC-rich and has multiple start sites of transcription. A 574 base pair fragment immediately upstream of the translation initiation site contains promoter activity when transfected into eukaryotic cell lines. Deletion analysis was performed to study promoter function. These studies showed that only 150 base pairs of promoter sequence were necessary for promoter function. This region contains three potential binding sites for the transcription factor, Sp1 and a TC box sequence. Furthermore, the fragment functions equally well in either orientation. We have defined an element in this region with enhancer function for both its homologous and a heterologous promoter. In addition, this region seems to contribute some degree of tissue specificity to insulin receptor gene expression.