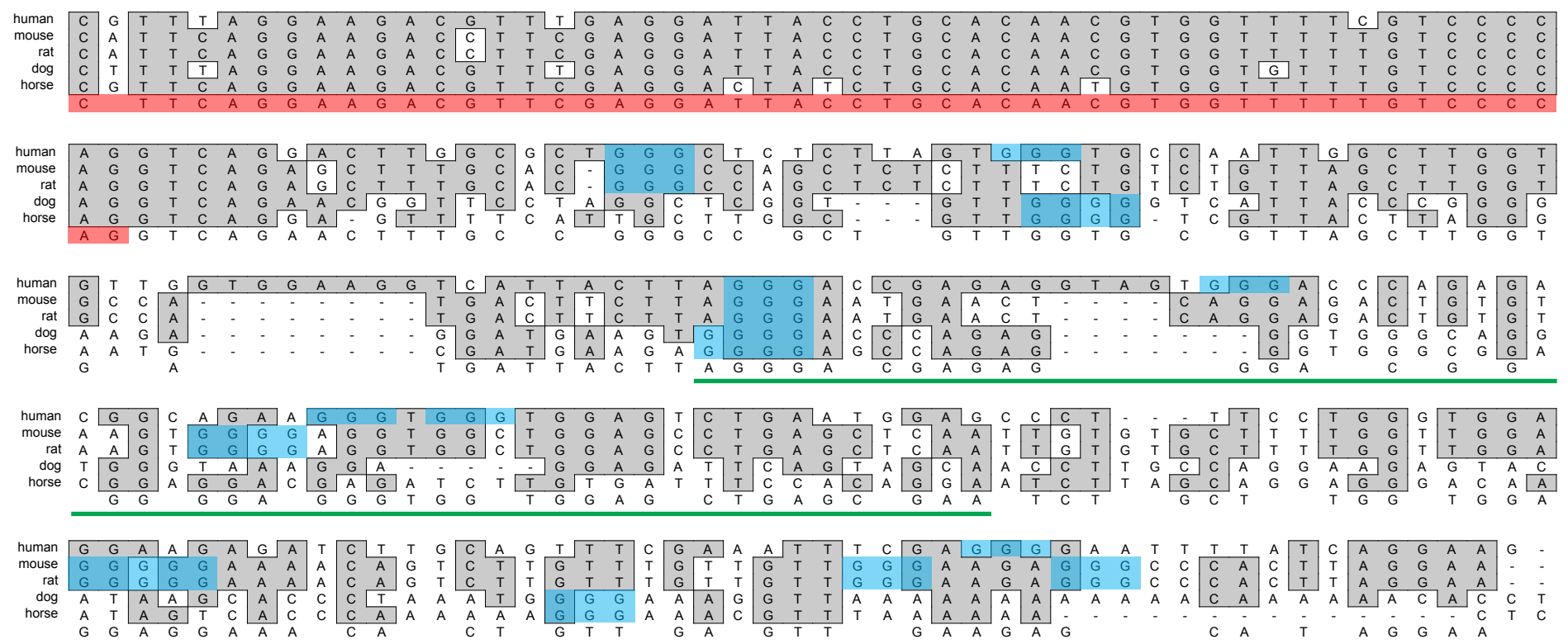

Figure S1. Sequence alignment of the 5' end of intron 10 of the INSR gene from human, mouse, rat, dog and horse is shown. Consensus sequence is shown below the alignment. Sequences were aligned by ClustalW. Shaded blocks show regions of >50% identity. Red highlighted sequence indicates the end of upstream exon 10. Blue highlighted nucleotides indicate conserved GGG motifs. Green underlined sequences indicate the GA rich enhancer sequence identified in the human gene.

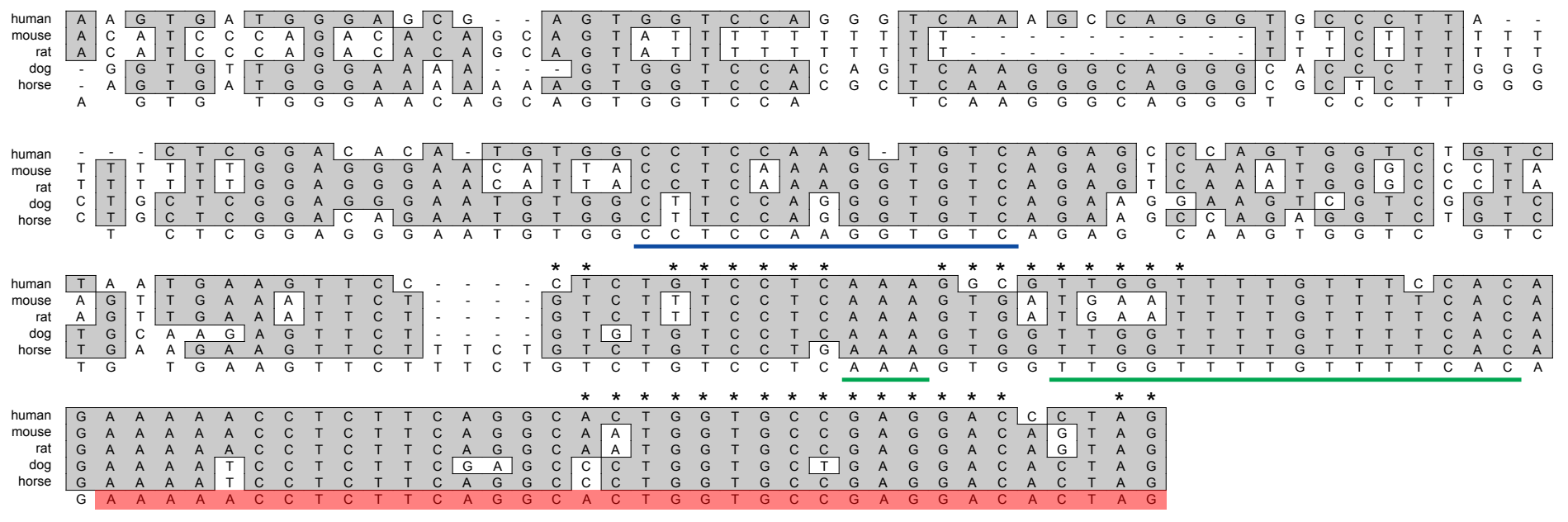

Figure S2. Sequence alignment of the 3' end of intron 10 and exon 11 of the INSR gene from human, mouse, rat, dog and horse is shown. Consensus sequence is shown below the alignment. Sequences were aligned by ClustalW. Shaded blocks show regions of >50% identity. Red highlighted sequence indicates exon 11. Blue underlined nucleotides indicate the silencer sequences including the CUG-BP1 binding site. Green underlined sequences indicate the branch point and poly-pyrimidine tract. Asterisks indicate the nucleotides that are predicted to form a stable stem structure in the human gene.

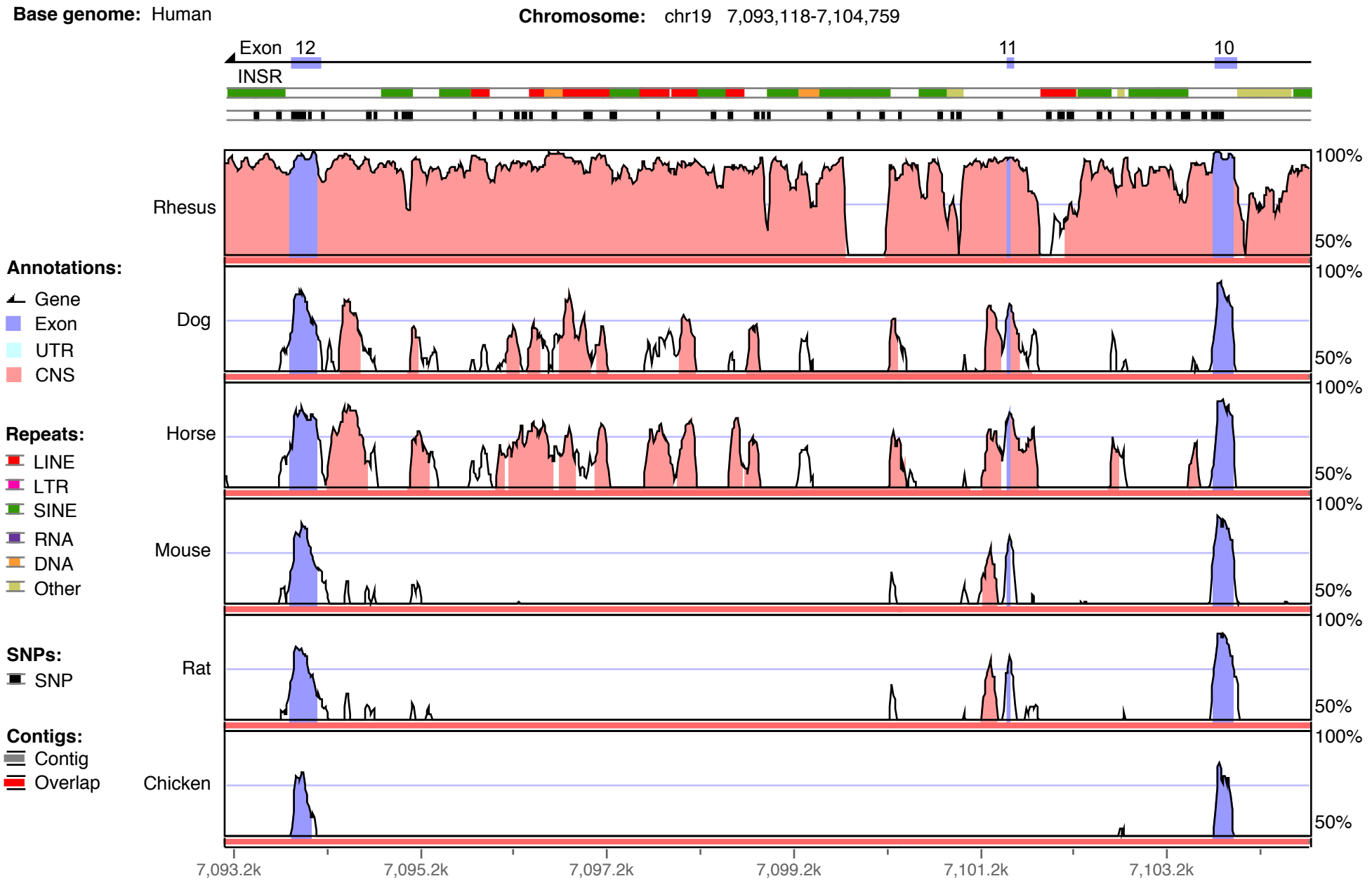

Figure S3. Vista alignment of human, rhesus monkey, dog, horse, rat, mouse and chicken sequences including exons 10, 11 and 12 and the intervening introns. Exonic structure of the human INSR gene is shown at the top. The gene reads from right to left as indicated by the arrow at the top, so intron 11 is to the left of exon 11. Blue areas indicate exon 11, pink areas indicate conserved nucleotide sequence (CNS) between the seven genomes. Conservation in these regions exceeds 50%. The chicken INSR gene does not contain an exon 11 and only encodes a single insulin receptor.

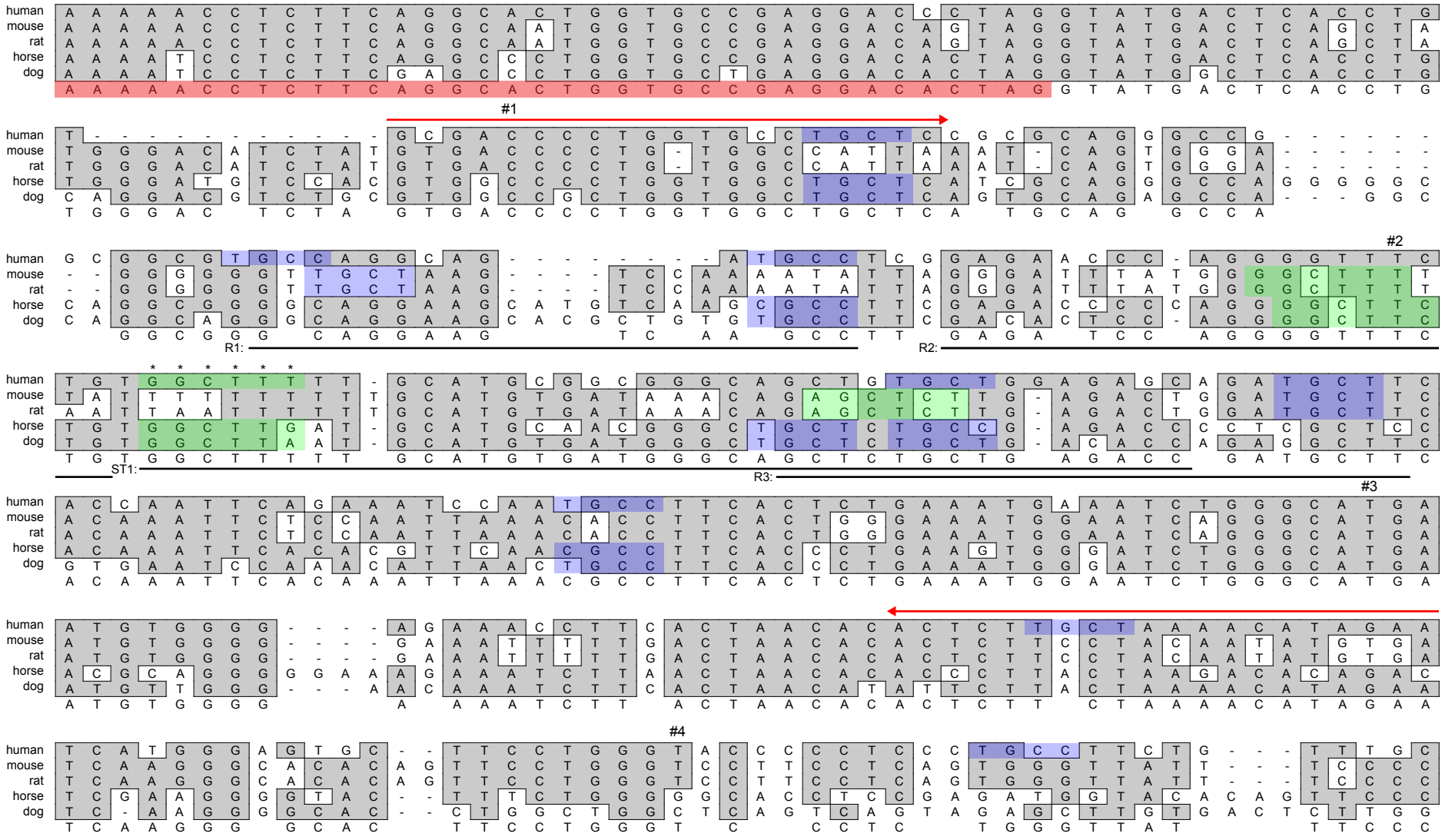

Figure S4. Sequence alignment of 5' end of intron 11 of the INSR gene from human, mouse, rat, dog and horse is shown. Red highlighted sequences indicate the upstream exon 11. Putative MbnI1 binding motifs YGCY and YGCUUY are highlighted with blue and green, respectively. Red arrows above the sequence indicate the primer binding sequence for the RIP assay. Black underlined sequences represent the sequences used for RNA affinity assay. Numbers above the sequence indicate the end points of various deletions: #1 denotes the 5' end of the deletion in human hIRΔ164, #2 denotes the 5' end of the deletion in the rat rIR minigene, #3 denotes the 5' end of the human hIRB and rat rIR5'190, and #4 denotes the 3' end of the conserved enhancer in both the human hIR+enh and the rat rIR+enh.