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.Mutation analysis of the mouse insulin gene promoter in type I diabetes. The insulin gene promoter is known to contain a cluster of E-box sequences, which mediate the transcriptional regulation by members of the helix-loop-helix (HLH) family of transcription factors. Diabetes mellitus arises when beta cells are damaged or destroyed. The genes expressed in beta cells are also required for appropriate development and function of these insulin-producing cells. Therefore, it is reasonable to assume that the mutations in the insulin gene promoter may be associated with diabetes in man. To test this hypothesis, we searched for mutations in the insulin promoter in patients with Type I (insulin-dependent) diabetes mellitus. We performed a scanning mutagenesis analysis of the mouse insulin gene promoter from genomic DNA of Type I diabetic patients and non-diabetic controls. We found no non-sense or missense mutations in the promoter or in the coding region of the gene in patients with Type I diabetes. This result is in agreement with previous studies on the human insulin gene in which no mutations were found in the coding region of the gene in Type I diabetes. However, in contrast to the human insulin gene, we found several non-sense mutations in the promoter of the mouse insulin gene in diabetic patients. Four diabetic patients (including the propositus) and three non-diabetic subjects were heterozygous for a non-sense mutation affecting the sequence 5'-CCAACCTGG-3' in the promoter of the mouse insulin gene. One diabetic patient and one non-diabetic subject were heterozygous for a non-sense mutation affecting the sequence 5'-GGGCCCTGG-3' in the promoter of the mouse insulin gene, while one diabetic patient and one non-diabetic subject were heterozygous for the non-sense mutation affecting the sequence 5'-GGCTGCCTGG-3' in the promoter of the mouse insulin gene. We observed that the non-sense mutations affect the basal transcriptional activity of the insulin gene promoter in transiently transfected beta TC3 cells, a mouse insulin-producing cell line. Reduction in forceps-induced damage in in vitro maturation of the porcine embryo by the use of a single

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