INSULIN RECEPTOR EXPRESSION IN MOUSE PREIMPLANTATION EMBRYOS

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The insulin receptor (IR) mediates the actions of insulin and insulin-like growth factors (IGF-I and II). Two IR isoforms result from alternate splicing of exon 11, IR-A (without exon 11) and IR-B (with exon 11). Exon 11 is 36 bp and encodes 12 amino acids (717-729) in the COOH-terminus of the IR alpha-subunit. IR-A has higher binding affinity for insulin and IGF-II than IR-B. Interestingly, IR-A is predominantly expressed in fetal tissues, adult spleen, brain and tumours, where its expression has been associated with an undifferentiated state. IR-B is expressed primarily in classical insulin sensitive tissues such as adult liver and muscle. In contrast to other species, no evidence existed for IR expression prior to compaction in mice. However, both insulin and IGF-II have been shown to stimulate growth in cleaving embryos (Kaye 1997). We returned to this question using primers flanking exon 11 to detect IR-A and IR-B mRNA. Sequencing confirmed the identity of the amplified PCR products. IR-B mRNA was present in zygotes and all stages to blastocyst, IR-A mRNA was only detected in compacted morulae. Immunofluorescent confocal microsopy using a rabbit polyclonal antibody (against amino acids 128-205 of alpha-subunit) that recognizes both isoforms revealed nuclear IR localization in zygotes and cleavage stage embryos including morulae. The results demonstrate that mice like other species expresses IR throughout preimplantation development in contrast with earlier studies. Nuclear localisation of IR has been observed in hepatocytes and adipocytes and may be associated with transcriptional regulation. IR-A expression in compacted morulae may reflect the change in metabolism that occurs at this time and requires further study.

(1) Kaye, P. L. (1997) Preimplantation growth factor physiology. *Rev. Reprod.* **2**, 121–127.