Insulin/IGF-1 Signals in Zucker Fatty Rats
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Introduction: It is known that ossification of spinal ligament often occurs the abnormal glucose tolerance. This study, the involvement of insulin/IGF-1 signals in spinal ligament cells and leptin signals was investigated under hyperleptinemia and hyperinsulinemia using Zucker Fatty Rat(fa/fa) that had mutation of the leptin receptor gene(fa) and Monosodium Glutamate-treated rats that presents obesity by destroying the hypothalamic ventromedial nucleus.

Materials and Methods: The following rats were used:(1) Zucker Fatty Rats, (2) monosodium glutamate-treated Fa/Fa rats and Fa/Fa rats .Each group consisted of 20 male rats aged 10-12 months. Thoracotomy was performed under general anesthesia, and blood was collected. Fasting blood glucose, insulin, IGF-1, and leptin were measured. The thoracic vertebrae were excised, made the embedding with Paraffin, H.E. staining and Immunohistological staining of IRS-1 and -2 (insulin receptor substrate) was performed using the LsAB method. Moreover the amount of the protein was quantified by the Western Blot Hybridization.

Results: The ZFR and MSG groups developed hyperleptinemia and hyperinsulinemia. On histological staining, bulging of the cartilage endplate, destruction of the fibrous ring accompanied by an increase in the number of chondrocyte-like cells at the ligament attachment site, and hyperplasia of fibrocartilage were significant in the ZFR group. IRS-1-positive cells significantly increased and the appearance of the IRS-1 protein was eminent in the cartilage endplate and the enthesis region in the ZFR group, but IRS-2-positive cells slightly decreased in the ZFR group, compared to those in the MSG and control groups.

Discussion: Insulin/IGF-signals and leptin signals in spinal ligament cells were investigated in ZFR. IRS-1-positive cells increased in the hyperplastic chondrocyte-like cell region, suggesting that IRS-1-mediated signaling for cell proliferation was enhanced.

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