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Xenograft of free or microencapsulated Sertoli cells as a potential therapy for experimental Type 2 Diabetes Mellitus

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Introduction and Aim. Type 2 Diabetes Mellitus (T2DM), one of the world's most important, common and costly diseases associated with devastating complications, is caused by insulin resistance mainly due to a chronic inflammation of the visceral adipose tissue with local and systemic increases in proinflammatory cytokines and adipokines such as tumor necrosis factor-α (TNF-α) and IL-6. Sertoli cells (SC), considered mere mechanical cell aids, have been recently revisited with respect to their functional competence showing that these cells may provide immunomodulatory and trophic factors that are able to ameliorate survival and development of different cell types and constitute an immuno-protective shield for transplantation in many diseases such as Type 1 Diabetes Mellitus. Aim of this work was to verify if the injection of free (subcutaneously) or microencapsulated (intraperitoneally) SC would reverse hyperglycaemia in db/db mice spontaneous T2DM

Materials and Methods. Porcine pre-pubertal SC were isolated, according to previously established methods, after finely chopping the retrieval testicles, with double enzymatic digestion with Collagenase P and a mixed solution of trypsin and DNase I. SC enveloped in Barium alginate-based microcapsules (Ba-SCMCs) were prepared according to our method, by a mono air-jet device system. Free SC and Ba-SCMCs were examined as far as: (a) SC morphology by light microscopy; (b) SC viability, by fluorescence microscopy after staining with ethidium bromide and fluorescein diacetate; (c) SC in vitro function (α-aromatase activity and IGF-I secretion); (d) reversal of T2DM in spontaneous diabetes db/db mice, were concerned.

Results. Ba-SCMCs showed excellent features in terms of size, morphology, sphericity and coalescence. SC viability, both in free and microencapsulated SC, was very high (over 90%). Very good α-aromatase activity and IGF-I secretion were associated with the examined SC preparations. Both subcutaneous free SC injection and intraperitoneal transplantation of Ba-SCMCs demonstrated a significant reduction, in 60% of the treated mice, of HbA1c (6.6 % vs 8.8 %) with a normalization of intraperitoneal glucose tolerance test.

Conclusions. SC may be enveloped in Ba-SCMCs with no loss of their functional properties and morphology. Xenograft of SC, both free and enveloped in barium alginate microcapsules, induced an important reduction of HbA1c blood levels with a normalization of glucose tolerance test (IPGTT). This result might open new perspectives for the future therapy of human T2DM.

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