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Reversal of experimental Laron Syndrome by xenotransplantation of microencapsulated porcine Sertoli cells

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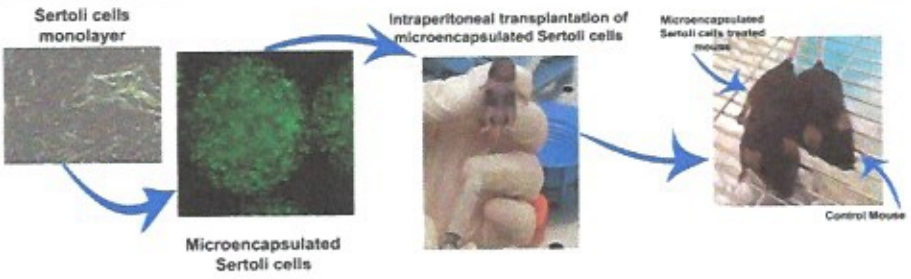
Abstract

Recombinant human IGF-1 currently represents the only available treatment option for the Laron Syndrome, a rare human disorder caused by defects in the gene encoding growth hormone receptor, resulting in irreversibly retarded growth. Unfortunately, this treatment therapy, poorly impacts longitudinal growth (13% in females and 19% in males), while burdening the patients with severe side effects, including hypoglycemia, in association with the unfair chore of taking multiple daily injections that cause local intense pain. In this study, we have demonstrated that a single intraperitoneal graft of microencapsulated pig Sertoli cells, producing pig insulin-like growth factor-1, successfully promoted significant proportional growth in the Laron mouse, a unique animal model of the human Laron Syndrome. These findings indicate a novel, simply, safe and successful method for the cell therapy-based cure of the Laron Syndrome, potentially applicable to humans.

Graphical abstract



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Abbreviations

E-MCs, empty capsules; GH, growth hormone; GHR, growth hormone receptor; hIGF-1, human insulin-like growth factor 1; IGF-1, insulin-like growth factor 1; ITS, insulin-transferrin-selenium; LM, Laron Mouse; LS, Laron Syndrome; pSC-MCs, microencapsulated pig Sertoli cells; mIGF-1, murine insulin-like growth factor 1; MIS, anti-Müllerian inhibiting substance; mRNA, messenger RNA; pIGF-1, pig insulin-like growth factor 1; pSC, porcine Sertoli cells; TRIS, tris(hydroxymethyl)aminomethane hydrochloride

Keywords

Laron Syndrome; Sertoli cells; Xenotransplantation; Microcapsules