Journal of Controlled Release 165 (2013) 90

Contents lists available at SciVerse ScienceDirect

Journal of Controlled Release

journal homepage: www.elsevier.com/locate/jconrel

Cover story

A cell therapy-based cure of the Laron Syndrome

Laron Syndrome (LS) is a rare dwarfism caused by mutations in genes encoding growth hormone receptor (GHR). LS results in GH insensitivity with a severe hindrance of insulin-like growth factor-1 (IGF-1) production, and provokes severe post-natal growth failure, typical craniofacial abnormalities, metabolic modifications, and developmental alterations [1]. Currently, Mecasermin® is the only medical treatment option for patients with LS. Unfortunately, it consists of multiple, intramuscular daily injections, and is associated with extremely limited effects on improvements of longitudinal growth. At the same time, it is burdened with significant, severe side effects such as hypoglycaemia, hypoacusia, intracranial hypertension and intense pain at the injection site [2].

Sertoli cells (SCs), which are originally situated in the male testis, have recently been revisited with respect to their physiologic role and functional competence, based upon production of numerous immunoregulatory and trophic factors. It is known that SCs can ameliorate development, survival, and function of different cell types. It was previously demonstrated that intraperitoneal transplantation of microencapsulated SCs into a stringent murine animal model of type 1 diabetes mellitus, did reverse the disease in the majority of the recipients [3]. In this issue, Professor Calafiore and his colleagues report that porcine pre-pubertal SCs (pSCs), encapsulated in barium alginate-based microcapsules (SCs-MCs), can successfully promote growth in the dwarf GHR−/− "Laron mouse" by secreting pig IGF-1 (pIGF-1) [4].

The study by Professor Calafiore and his team has shown that Laron mouse treated with SCs-MCs significantly increased the body weight and body length (assessed by nose–anus distance), as compared with those of control Laron mouse treated with empty capsules. Moreover, the body weight increased proportionally, as confirmed by weight measurement of any single organ. The X-ray evaluation showed that the length of the femur, tibia and cranium of the mice treated with SCs-MCs increased by 9% as compared with mice treated with empty capsules. To understand the involved mechanisms, the authors measured murine and porcine IGF-1 serum levels that remained low in both control and SCs-MCs treated mice. Only the mice treated with SCs-MCs showed a progressive increase in pIGF-1 serum levels, peaking at 6 months, out of 12 months of post-transplant follow-up. This outcome clearly indicates that the induced growth is related to pIGF-1 secreting SCs-MCs graft.

This work described by Professor Calafiore provides a novel and efficient method for hormone replacement therapy, which is likely to be translated into patients with LS. Although more studies need to be done to translate the successful animal study to clinical applications, the success in the year-long animal study provides a possibility of the long-term cell therapy for treating many other diseases, including diabetes.

References

[1] Z. Laron, Laron syndrome (primary growth hormone resistance or insensitivity): the personal experience 1958–2003, J. Clin. Endocrinol. Metab. 89 (2004) 1031–1044.
[2] D. Fintini, C. Brufani, M. Cappa, Profile of mecasermin for the long-term treatment of growth failure in children and adolescents with severe primary IGF-1 deficiency, Ther. Clin. Risk Manag. 5 (2009) 553–559.
[3] F. Fallarino, G. Luca, M. Calvitti, F. Mancuso, C. Nastruzzi, M.C. Fioretti, U. Grohmann, E. Becchetti, A. Burgevin, R. Kratzer, P. van Endert, L. Boon, P. Puccetti, R. Calafiore, Therapy of experimental type 1 diabetes by isolated Sertoli cell xenografts alone, J. Exp. Med. 11 (2009) 2511–2526.
[4] G. Luca, M. Calvitti, F. Mancuso, G. Falabella, I. Arato, C. Bellucci, E.O. List, E. Bellezza, G. Angeli, C. Lilli, M. Bodo, E. Becchetti, J.J. Kopchick, D.F. Cameron, T. Baroni, R. Calafiore, Reversal of experimental Laron syndrome by xenotransplantation of microencapsulated porcine Sertoli cells, J. Control. Release 165 (2013) 75–81.

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0168-3659/$ – see front matter
http://dx.doi.org/10.1016/j.jconrel.2012.11.018