

Editorial

Prospects for Cell Based Therapy for Type 1 Diabetes

Ming Li* and Susumu Ikehara

Department of Stem Cell Disorders, Kansai Medical University, Japan

EDITORIAL

Type 1 diabetes (T1D) is a chronic autoimmune disease that is usually diagnosed in children and young adults. Immune cells attack the beta cells in the pancreas, resulting in defects in insulin secretion and hyperglycemia. Long-term hyperglycemia affects the major organs, including the heart, eyes, kidneys, and nerves, resulting in organ dysfunction. Thus, maintaining blood glucose levels within the normal range may reduce the risk of these complications. Animal experiments constitute basic research that may provide abundant data for the potential treatment of T1D, and the non-obese diabetic (NOD) mouse, which has characteristics similar to human T1D, is used as a model to study T1D. T cells play an important role in both the early and late stages of T1D, and CD8⁺ T cells infiltrate the islets of NOD mice, injuring the beta cells. Moreover, the number and function of regulatory T cells has been reported to change under hyperglycemic conditions. Furthermore, the other immune cells such as macrophages, DCs and NK cells produce inflammation cytokines such as IFN- α and IFN- γ , which damage beta cells in the pancreata [1].

T1D is a T-cell-mediated autoimmune disease, and autoantibodies have been detected in the peripheral blood after the onset of diabetes in humans. Autoantibodies against beta cell components are used clinically as sensitive markers of this disease, and islet cell autoantibodies, antibodies to insulin, and glutamic acid decarboxylase have been detected in T1D patients [2]. Autoantigen-specific CD4⁺T cells have been studied in T1D patients undergoing pancreas/kidney transplantation [3].

Current therapies for T1D mainly include insulin therapy, antigen-specific intervention therapies and cell based strategies for beta cell regeneration. Insulin therapy helps decrease blood glucose levels, but does not maintain the levels in the normal range over extended periods. Antigen-specific therapies include anti-inflammatory interventions using Omega-3 fatty acid and inducing antigen-specific tolerance using oral insulin. Cell based therapies for T1D include islet and pancreas transplantation, and inducing beta cell regeneration from various stem cells [4]. Although insulin plays an essential role in reducing the hyperglycemia, exogenous insulin injection is unable to replicate the insulin secretion when response to the blood glucose level changes. Researchers have researched on beta cells differentiation from various stem cells, and this may be advances in the treatment of T1D [5]. Stem cells mainly include embryonic stem cells (ESCs), pluripotent stem cells (iPS), and adult tissue stem cells. ESCs are able to differentiate into insulin-producing

*Corresponding author

Ming Li, Department of Stem Cell Disorders, Kansai Medical University, 2-5-1 Shinmachi, Hirakata City, Osaka 573-1010, Japan, Tel: 81-72-804-2450; Fax: 81-72-804-2454; Email: liming@hirakata.kmu.ac.jp

Submitted: 24 October 2014

Accepted: 29 October 2014

Published: 29 October 2014

Copyright

© 2014 Li et al.

OPEN ACCESS

cells and normalize the blood glucose levels in diabetic mice when transplanted into those mice [6]. In contrast, human iPS was induced to differentiate firstly into pancreatic and duodenal homeobox-1 -positive pancreatic progenitors and then into neurogenin 3 -expressing pancreatic endocrine progenitors, while suppressing the differentiation into hepatic or intestinal cells. The differentiated cells were shown to secrete insulin, and to have the potential to treat T1D patients [7]. Tissue stem cells include pancreas-, liver- and bone marrow-derived stem cells, which can also differentiate into beta cells. Furthermore, bone marrow derived-mesenchymal stem cells have significantly suppressed beta cell-specific T cell proliferation in the pancreas, and overcome the autoimmune pathology associated with T1D [8]. Hyperglycemia was normalized in a T1D patient after hematopoietic stem cells and differentiated insulin-producing cells from adipose tissue-derived MSCs were co-transplanted [9].

In conclusion, stem cell-based therapies for T1D may overcome the problem of the lack of donors for islet or pancreas transplantation, and avoid immune destruction when the stem cells are allogeneically transplanted. Thus, cell-based interventions are a potential future strategy for treating T1D.

ACKNOWLEDGMENTS

We would like to thank Mr. Hilary Eastwick-Field and Ms. Keiko Ando for their help in the preparation of the manuscript.

REFERENCES

1. Fairweather D, Rose NR. Type 1 diabetes: virus infection or autoimmune disease? *Nat Immunol.* 2002; 3: 338-340.
2. Taplin CE, Barker JM. Autoantibodies in type 1 diabetes. *Autoimmunity.* 2008; 41: 11-18.
3. Vendrame F, Pileggi A, Laughlin E, Allende G, Martin-Pagola A, Molano RD, et al. Recurrence of type 1 diabetes after simultaneous pancreas-kidney transplantation, despite immunosuppression, is associated with autoantibodies and pathogenic autoreactive CD4 T-cells. *Diabetes.* 2010; 59: 947-957.
4. van Belle TL, Coppieters KT, von Herrath MG. Type 1 diabetes: etiology, immunology, and therapeutic strategies. *Physiol Rev.* 2011; 91: 79-118.
5. Weir GC, Cavelti-Weder C, Bonner-Weir S. Stem cell approaches for diabetes: towards beta cell replacement. *Genome Med.* 2011; 3: 61.

6. Naujok O, Francini F, Picton S, Jorns A, Bailey CJ, Lenzen S. A new experimental protocol for preferential differentiation of mouse embryonic stem cells into insulin-producing cells. *Cell Transplant*. 2008; 17: 1231-1242.
7. Shahjalal HM, Shiraki N, Sakano D, Kikawa K, Ogaki S, Baba H, et al. Generation of insulin-producing beta-like cells from human iPS cells in a defined and completely xeno-free culture system. *J Mol Cell Biol*. 2014.
8. Madec AM, Mallone R, Afonso G, Abou Mrad E, Mesnier A, Eljaafari A, et al. Mesenchymal stem cells protect NOD mice from diabetes by inducing regulatory T cells. *Diabetologia*. 2009; 52: 1391-1399.
9. Dave SD, Vanikar AV, Trivedi HL. Co-infusion of adipose tissue derived mesenchymal stem cell-differentiated insulin-making cells and haematopoietic cells with renal transplantation: a novel therapy for type 1 diabetes mellitus with end-stage renal disease. *BMJ Case Rep*. 2013.

Cite this article

Li M, Ikehara S (2014) Prospects for Cell Based Therapy for Type 1 Diabetes. *Arch Stem Cell Res* 1(1): 1001.