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Name of Journal: *World Journal of Stem Cells*

Manuscript NO: 59128

Manuscript Type: REVIEW

Functional maturation of immature β cells: A roadblock for a ³stem cell therapy to type 1 diabetes

Sun ZY *et al.* Roadblock for stem cell therapy to T1D

Zi-Yi Sun, Ting-Yan Yu, Fang-Xu Jiang, Wei Wang

¹⁵
Abstract

Type 1 diabetes mellitus (T1DM) is a chronic autoimmune disease caused by the specific destruction of pancreatic islet β cells and is characterized as the absolute insufficiency of insulin secretion. Current insulin replacement therapy supplies insulin in a non-physiological way and is associated with devastating complications. Experimental islet transplantation therapy has been proven to restore glucose



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Augsornworawat et al. demonstrate that in vitro human stem-cell-derived islets have immature transcriptome profiles when compared to native human islets. After transplantation, immature SC-islet cells undergo drastic changes in transcriptome and acquire mature gene expression. Grafted SC- β cells express mature β cell genes, including MAFA and G6PC2, resembling native human islets.

Cited by: 1

Author: Punn Augsornworawat, Kristina G. Maxw...

Publish Year: 2020

Claudin 4 in pancreatic β cells is involved in regulating ...

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6943228>

Nov 23, 2019 · Our study suggests a possibility that the highly up-regulated TJ Cldn4 molecule works as a maturation biomarker of postnatal insulin-secreting β cells. Using the biomarker, the fully matured insulin-secreting cells given rise from pluripotent stem cells would be enriched for a regenerative therapy to high-risk type 1 diabetic sufferers 40.

Author: Hongtu Li, Abraham Neelankal John, T...

Publish Year: 2020

Generation of Functional Human Pancreatic β Cells In Vitro ...

[https://www.cell.com/fulltext/S0092-8674\(14\)01228-8](https://www.cell.com/fulltext/S0092-8674(14)01228-8) ▾

Type 1 diabetes results from autoimmune destruction of β cells in the pancreatic islet, whereas the more common type 2 diabetes results from peripheral tissue insulin resistance and β cell dysfunction. Diabetic patients, particularly those suffering from type 1 diabetes, could potentially be cured through transplantation of new β cells.

Cited by: 1348

Author: Felicia W. Pagliuca, Jeffrey R. Millman, ...

Publish Year: 2014

Stem Cell-Derived Islets: Next Steps for ... - Diabetes

<https://diabetes.diabetesjournals.org/content/68/5/901> ▾

May 01, 2019 · Type 1 diabetes (T1D) results from autoimmune destruction of the insulin-producing β -cells in the endocrine pancreatic islets of Langerhans. Patients are thus dependent on exogenous insulin therapy delivered by multiple daily injections or continuous subcutaneous infusion pumps to control elevated glucose levels and prevent the development of life-threatening ketoacidosis.

Cited by: 2

Author: Michael R. Rickels

Publish Year: 2019

Synaptotagmins Tweak Functional β Cell Maturation ...
[https://www.cell.com/developmental-cell/fulltext/S1534-5807\(18\)30324-1](https://www.cell.com/developmental-cell/fulltext/S1534-5807(18)30324-1) ▾
Immature β cells secrete insulin at a lower **glucose threshold** compared to **mature β cells**. In this issue of Developmental Cell, Huang et al. (2018) show that the increase in **glucose threshold** during **β cell maturation** is achieved through balance between the Ca2+-sensitive synaptotagmin 7 and the Ca2+-insensitive synaptotagmin 4.
Cited by: 1 **Author:** Jennifer M. Gilbert, Barak Blum
Publish Year: 2018

Growth and Functional Maturation of β -Cells in ... - Diabetes
<https://diabetes.diabetesjournals.org/content/54/12/3387> ▾
Dec 01, 2005 - The **development** of islet **cell** transplantation as a cure for **diabetes** is limited by the shortage of human donor organs. Moreover, currently used grafts exhibit a marginal **β -cell** mass with an apparently low capacity for **β -cell** renewal and **growth**. Although duct-associated nonendocrine **cells** have often been suggested as a potential source for **β -cell** production, recent work in mice has ...
Cited by: 22 **Author:** Marika Bogdani, Krista Suenens, Troels Bo...
Publish Year: 2005

Towards a Functional Cure for Diabetes Using Stem Cell ...
<https://www.mdpi.com/2073-4409/10/1/191/htm> ▾
Diabetes mellitus is a pandemic metabolic disorder that results from either the autoimmune destruction or the dysfunction of insulin-producing pancreatic beta **cells**. A promising cure is beta **cell** replacement through the transplantation of islets of Langerhans. However, donor shortage hinders the widespread implementation of this **therapy**. Human pluripotent **stem cells**, including embryonic **stem** ...

[PDF] Towards a Functional Cure for Diabetes Using Stem Cell ...
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stem cells and induced pluripotent **stem cells**, represent an attractive alternative beta **cell** source for transplantation. Although major advances over the past two decades have led to the generation of **stem cell**-derived beta-like **cells** that share many features with genuine beta **cells**, producing fully mature beta **cells** remains challenging. Here ...

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Type 1 diabetes results from autoimmune destruction of **β cells** in the pancreatic islet, whereas the more common **type 2 diabetes** results from peripheral tissue insulin resistance and **β cell** dysfunction. Diabetic patients, particularly those suffering from **type 1 diabetes**, could potentially be cured through transplantation of new **β cells**.
Cited by: 1359 **Author:** Felicia W. Pagliuca, Jeffrey R. Millman, Ma...
Publish Year: 2014

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Immature β cells secrete insulin at a lower **glucose threshold** compared to mature β cells. In this issue of Developmental Cell, Huang et al. (2018) show that the increase in **glucose threshold** during β cell maturation is achieved through balance between the Ca^{2+} -sensitive synaptotagmin 7 and the Ca^{2+} -insensitive synaptotagmin 4.

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Author: Jennifer M. Gilbert, Barak Blum

Publish Year: 2018

[m6A mRNA Methylation Controls Functional Maturation in ...](#)

<https://diabetes.diabetesjournals.org/content/69/8/1708> ▾

Aug 01, 2020 · Introduction. Mature β -cells have the unique ability to secrete insulin in response to extracellular glucose concentrations (). Defects in either β -cell number and/or **function** can lead to loss of **functional β -cell** mass and, eventually, to **diabetes** (). Establishment of adequate **functional β -cell** mass is essential for glycemic control in adulthood, which is mainly accomplished during neonatal ...

Cited by: 5

Author: Yanqiu Wang, Jiajun Sun, Zhen Lin, Weizhe...

Publish Year: 2020

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<https://www.mdpi.com/2073-4409/10/1/191/pdf>

stem cells and induced pluripotent **stem cells**, represent an attractive alternative beta **cell** source for transplantation. Although major advances over the past two decades have led to the generation of **stem cell**-derived beta-like **cells** that share many features with genuine beta **cells**, producing fully mature beta **cells** remains challenging. Here ...

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Report SIX2 Regulates Human β Cell Differentiation from **Stem Cells** and **Functional Maturation** In Vitro
Leonardo Velazco-Cruz,¹ Madeleine M. Goedegebuure,¹ Kristina G. Maxwell,^{1,2} Pun
Augsornworawat,^{1,2} Nathaniel J. Hogrebe,¹ and Jeffrey R. Millman^{1,2,3,*} ¹Division of Endocrinology,
Metabolism, and Lipid Research, Washington University School of Medicine, St. Louis, MO 63110, USA

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