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ESPS Peer-review Report
Name of Journal: World Journal of Diabetes
ESPS Manuscript NO: 8043
Title: Adipose stem cell-based regenerative medicine for reversal of diabetic hyperglycemia
Reviewer code: 00498408
Science editor: Ma, Ya-Juan
Date sent for review: 2013-12-13 08:17
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[Y] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	[ ]Rejection
[ ] Grade D (Fair)	[ ] Grade D: rejected	BPG Search:	[Y] Minor revision
[ ] Grade E (Poor)		[ ] Existed	[ ] Major revision
		[ ] No records	

COMMENTS TO AUTHORS

This manuscript by Hyun Joon Paek et al reported a review of adipose stem cells-based studies highlighting their potential effect on reversing diabetic hyperglycemia and their differentiation to insulin-producing cells. However, a few issues, need to be addressed: An important point is regarding the use of mesenchymal stem cells due to their oncogenic potential already reported by different authors who showed the occurrence of neoplasm in autologous MSC-treated NOD mice (Fiorina P et al. J Immunol 2009). However, administration of allogeneic MSC to NOD mice resulted in a temporarily reversal of hyperglycemia in 90% of transplanted NOD mice without any presence of tumors in the treated mice. This pleads for the safety of only allogeneic MSC-based therapies not only for T1D treatment but also for other autoimmune disorders. Although the main potential capacity of insulin produced AD-MSC, two published trials conducted by Trivedi et al included co-transplantation of AD-MSC with hematopoietic stem cells admitting that the addition of HSC was designed to augment the effect of AD-MSC that I think is more convenient to discuss these studies in your last paragraph "challenges and opportunities for ASCs in diabetes". Please include in your table the study of Dave S.D et al (Indian J Endocrinol Metab. 2012 Mar;16 Suppl 1:S65-9. doi: 10.4103/2230-8210.94264. Ex vivo generation of glucose sensitive insulin secreting mesenchymal stem cells derived from human adipose tissue. Dave SD, Vanikar AV, Trivedi HL.) that reported the generation of insulin-secreting human AD-MSC without using xenogenic material. Finally, the paper should be reinforced with many more relevant references: In introduction, paragraph 5 1. Immunological applications of stem cells in type 1 diabetes P Fiorina et al. Endocrine reviews 2011 2. Immunological and regenerative properties of cord blood stem cells. R Francese et al. Clinical Immunology 2010 3. Congenic mesenchymal stem cell therapy reverses hyperglycemia in

experimental type 1 Diabetes M Jurewicz, et al Diabetes 2010 In introduction, paragraph 2 1. Early increase of retinal arterial and venous blood flow velocities at color Doppler imaging in brittle type 1 diabetes after islet transplant alone M Venturini et al. Transplantation 2006 2. Kidney Function After Islet Transplant Alone in Type 1 Diabetes Impact of immunosuppressive therapy on progression of diabetic nephropathy. P Maffi et al. Diabetes Care 2007 3. Determination of asymmetric and symmetric dimethylarginines in plasma of hyperhomocysteinemic subjects R Paroni et al. Amino acids 2005 4. Left ventricular function in insulin-dependent and in non-insulin-dependent diabetic patients: radionuclide assessment E Astorri et al. Cardiology 1997 5. Proteomics reveals novel oxidative and glycolytic mechanisms in type 1 diabetic patients' skin which are normalized by kidney-pancreas transplantation F Folli et al. , PloS one 2010 In introduction, paragraph 1 1. Mechanisms of PDL1-mediated regulation of autoimmune diabetes I Guleria et al. Clinical Immunology 2007 2. Role of ICOS pathway in autoimmune and alloimmune responses in NOD mice MJI Ansari et al. Clinical Immunology 2008 In introduction, paragraph 3 1. A novel clinically relevant strategy to abrogate autoimmunity and regulate alloimmunity in NOD mice A Vergani et al. Diabetes 2010

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[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
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		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS
the paper is good. i would like to see as a physiologist a some illustrations and tables comparing a normal islet cell with its receptor and molecular markers and a stem cell with the markers with regard to their differentiation. a little visual comparisons goes a long way in presenting the information better. they can even be hand drawn if copy right issues are a concern. basically a little bit more structure in taking the reader from known to unknown is required so that as a review paper even an undergraduate can understand the paper's intent.