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PEER-REVIEW REPORT

Name of journal: World Journal of Stem Cells

Manuscript NO: 58129

Title: Adipose-derived stem cells: pathophysiologic implications versus therapeutic potential in systemic sclerosis

Reviewer's code: 05468960
Position: Peer Reviewer
Academic degree: MD, PhD
Professional title: Doctor
Reviewer's Country/Territory: Poland
Author's Country/Territory: Italy

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Reviewer chosen by: Ya-Juan Ma
Reviewer accepted review: 2020-11-12 04:20
Reviewer performed review: 2020-11-16 14:07
Review time: 4 Days and 9 Hours

Scientific quality	[Y] Grade A: Excellent [ ] Grade B: Very good [ ] Grade C: Good [ ] Grade D: Fair [ ] Grade E: Do not publish
Language quality	[Y] Grade A: Priority publishing [ ] Grade B: Minor language polishing [ ] Grade C: A great deal of language polishing [ ] Grade D: Rejection
Conclusion	[Y] Accept (High priority) [ ] Accept (General priority) [ ] Minor revision [ ] Major revision [ ] Rejection
Re-review	[ ] Yes [Y] No
Peer-reviewer statements	Peer-Review: [Y] Anonymous [ ] Onymous Conflicts-of-Interest: [ ] Yes [Y] No

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SPECIFIC COMMENTS TO AUTHORS

Systemic sclerosis (SSc) is a complex multiorgan disease characterized by vascular damage, perivascular inflammation, presence of specific autoantibodies and progressive fibrosis of the skin and internal organs. The initial vascular damage seems to precede and provoke the organ inflammation, followed by accumulation of fibrotic collagen and other extracellular matrix components in vessel walls and interstitial tissue. SSc shows substantial heterogeneity in its clinical symptoms, patterns of organ involvement, and natural history. Skin involvement is a nearly universal feature of SSc. It is characterized by variable extent and severity of skin thickening and hardening. Progressive skin fibrosis has been associated with worsening lung function in patients with dcSSc. The key issue in taking therapeutic decisions in SSc is assessment of inflammatory process activity, and intensity of fibrotic reaction. Generally, patients with SSc are treated with organ-based symptomatic treatment. However, patients with diffuse skin involvement and/or severe inflammatory organ involvement are usually treated more aggressively with systemic immunosuppressive therapy because of the increased risk of complications and organ failure. Unfortunately, current pharmacotherapies are often ineffective, poorly tolerated and associated with many side effects. A number of preclinical and relatively small clinical studies have investigated the efficacy and safety of novel therapy - fat grafting and adipose-derived SVF/ADSC-based treatments in SSc, generally reporting promising therapeutic effects regardless of the type of fat and fat-derived cell preparation and/or purification. For that reason, the importance of the issue researched by the authors is, in my opinion, significant. This manuscript concerns analyses on pathophysiologic implication versus therapeutic potential of adipose-derived stem cells in SSc. This manuscript takes into account many literature reports, therefore data provided in the manuscript are valuable and may have an impact

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on the existing literature. Authors critically describe potential significant differences between ADSCs from SSc patients and healthy donors, which could be significant in the future clinical trials. They thoroughly describe clinical data and implications of white adipose tissue and related ADSCs and mature adipocytes in SSc pathogenesis. Therefore, understanding of the putative role of the adipocytic cell lineage in the development of SSc-related tissue fibrosis may pave the way for the discovery of novel therapeutic targets to prevent or reverse fibrosis by reducing disease progression (which certainly should be confirmed in larger studies). According the reviewer opinion the presented data are worth publishing, as can increase awareness that fat grafting and adipose-derived SVF/ADSC-based treatments in SSc can be a safe and effective therapeutic method.