



**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 43422

**Title:** Circulating factors present in the sera of naturally skinny people may influence cell commitment and adipocyte differentiation of mesenchymal stromal cells

**Reviewer's code:** 02446101

**Reviewer's country:** China

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-11-11

**Date reviewed:** 2018-11-13

**Review time:** 21 Hours, 1 Day

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer's expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Minor revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

1. What the said in the Para 1 and 2 in the Discussion section should be simplified. 2. Place add some results about the identification of BMSCs



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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 43422

**Title:** Circulating factors present in the sera of naturally skinny people may influence cell commitment and adipocyte differentiation of mesenchymal stromal cells

**Reviewer’s code:** 02566952

**Reviewer’s country:** Romania

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-11-11

**Date reviewed:** 2018-11-17

**Review time:** 21 Hours, 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

The manuscript presents an interesting approach in ascertaining the role of circulating molecules extracted from blood stream of lean human healthy subjects, in maintaining metabolic balance and balanced white adipose tissue quantity and function possible



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having a role in converting adipose tissue metabolism to ATP generator brown adipose. Introduction is relevant to the topic and accurately presents state of the art in the field. A minor suggestion, even though it is very interesting, the description of obesity and its classification might be reduced to several phrases in order to allow an increased attention of the reader to the introduction of skinny people (SP) concept and proposed explanatory theories. In a previous work of the team involving the effect of obese and overweight subjects on in vitro differentiation is introduced. Material and methods Are correctly described. Why were only male SP donors used for this study? What was the age group of the donors? Age as well as sex might influence the amount of “ SP factors” and maybe it would be good to mention the choice of a special group (if it was the case) Why did the authors choose to use bFGF for culturing (and priming) of MSCs? Results are very well presented Discussion is well argued to support the hypothesis What authors think about a further study on detecting the exact factors that might have a role in shifting WAT to BAT (or beige) metabolism ? Breaking down results from cytokine array and separately testing their role (for example for the proposed adiponectin or IGFBP-1? This is an important study orienting research towards elucidating the specificity of metabolic balance in a group of individuals, possible generating a modality to treat excess metabolic disorders such as obesity. Study could be extended to provide age and sex related specificity of this feature as well as to identify the exact cytokines involved in keeping metabolic and thermal balance in lean subjects.

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 43422

**Title:** Circulating factors present in the sera of naturally skinny people may influence cell commitment and adipocyte differentiation of mesenchymal stromal cells

**Reviewer’s code:** 02728252

**Reviewer’s country:** Egypt

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-11-11

**Date reviewed:** 2018-11-17

**Review time:** 23 Hours, 5 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input checked="" type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer’s expertise on the
<input type="checkbox"/> Grade E: Do not	language polishing	<input type="checkbox"/> Minor revision	topic of the manuscript:
publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input type="checkbox"/> Advanced
		<input type="checkbox"/> Rejection	<input checked="" type="checkbox"/> General
			<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

It is a well-designed comprehensive in vitro study aimed to evaluate the effect of priming the bone marrow mesenchymal stromal cells with sera obtained from the skinny people compared to those obtained from normal people, regarding proliferation,



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apoptosis, senescence, cell commitment, and differentiation. The authors concluded that sera from skinny people may promote brown adipogenesis rather than white adipocyte differentiation and they hypothesized that some circulating components present in the blood of these individuals may favor brown adipogenesis at expense of white adipocyte production. The study is interesting, well written and has a rational with no further comments.

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 43422

**Title:** Circulating factors present in the sera of naturally skinny people may influence cell commitment and adipocyte differentiation of mesenchymal stromal cells

**Reviewer’s code:** 00504800

**Reviewer’s country:** United States

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-11-11

**Date reviewed:** 2018-11-21

**Review time:** 18 Hours, 9 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	<input type="checkbox"/> Accept	Peer-Review:
<input checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	(High priority)	<input checked="" type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Accept	<input type="checkbox"/> Onymous
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	(General priority)	Peer-reviewer’s expertise on the topic of the manuscript:
<input type="checkbox"/> Grade E: Do not publish	<input type="checkbox"/> Grade D: Rejection	<input checked="" type="checkbox"/> Minor revision	<input checked="" type="checkbox"/> Advanced
		<input type="checkbox"/> Major revision	<input type="checkbox"/> General
		<input type="checkbox"/> Rejection	<input type="checkbox"/> No expertise
			Conflicts-of-Interest:
			<input type="checkbox"/> Yes
			<input checked="" type="checkbox"/> No

**SPECIFIC COMMENTS TO AUTHORS**

The authors desire to demonstrate that circulating factors in the serum of skinny people influence adipocyte differentiation. This is an interesting question and the study here, though preliminary, is well conceived. The main question raised by this manuscript is



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very basic: how do the authors define "skinny people"? Both normal people and skinny people are define as having a BMI of <25. The only criteria used to define skinny people is excess calorie intake, which seems to be 30-40% more caloric intake than normal people while maintaining a BMI <25. Is there precedent for this definition? Did the authors examine serum from individuals with a BMI of <20 compared to 20-25? I understand and appreciate the results presented, but clarification of the definition of skinny is needed. Likewise, bone marrow MSC were used in these experiments. Did the authors perform any experiments or consider using MSC from adipose tissue? Do the authors think there would be significant differences between bone marrow MSC and MSC from other tissues? I think this would be of great interest to the readers. Minor comments: The authors state that a panel of 17 cytokines was examined, but only the ones with significant differences between skinny and normal sera are noted. What are the others? Figure 2C, X axis label should be annexin, not nexin Figure 5F, X axis label of SP is missing In some figures, two asterisks are used to denote statistical significance, but P values for only a single asterisk are provided. I assume \* = P <0.05 and \*\* = P <0.01, but this should be clarified.

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**PEER-REVIEW REPORT**

**Name of journal:** World Journal of Stem Cells

**Manuscript NO:** 43422

**Title:** Circulating factors present in the sera of naturally skinny people may influence cell commitment and adipocyte differentiation of mesenchymal stromal cells

**Reviewer's code:** 02495033

**Reviewer's country:** South Korea

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2018-11-11

**Date reviewed:** 2018-11-21

**Review time:** 11 Hours, 10 Days

SCIENTIFIC QUALITY	LANGUAGE QUALITY	CONCLUSION	PEER-REVIEWER STATEMENTS
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	<input checked="" type="checkbox"/> Accept	Peer-Review:
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<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of	(General priority)	Peer-reviewer's expertise on the
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publish	<input type="checkbox"/> Grade D: Rejection	<input type="checkbox"/> Major revision	<input checked="" type="checkbox"/> Advanced
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**SPECIFIC COMMENTS TO AUTHORS**

WJSC-43422 In the present review, the authors demonstrated that factors from SP sera affect commitment and adipocyte differentiation of MSCs. The results are interesting, and may provide readers and investigators with good information. 1) However, there



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is no clear criteria between NP and SP: i.e., both groups have similar parameters, especially BMI (22.10 vs 20.50) and relatively-high total cholesterol (185.6~190.6 mmol/l). I wonder if the authors did not compare among lean (normal), overweight, and obese people. 2) Please clearly explain the different results of adipogenic genes in Figure 4 and Figure 5c that make readers confused.

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