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ESPS Peer-review Report
Name of Journal: World Journal of Orthopedics
ESPS Manuscript NO: 8396
Title: Inhibition of Rheumatoid Arthritis by Blocking Connective Tissue Growth Factor
Reviewer code: 02446751
Science editor: Song, Xiu-Xia
Date sent for review: 2013-12-28 15:12
Date reviewed: 2014-03-06 21:30

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[Y] Grade A: Priority Publishing	Google Search:	[Y] Accept
[Y] Grade B (Very good)	[ ] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[ ] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS
no comment: the paper is clear and completely satisfying

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ESPS Peer-review Report
Name of Journal: World Journal of Orthopedics
ESPS Manuscript NO: 8396
Title: Inhibition of Rheumatoid Arthritis by Blocking Connective Tissue Growth Factor
Reviewer code: 00505788
Science editor: Song, Xiu-Xia
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A (Excellent)	[ ] Grade A: Priority Publishing	Google Search:	[ ] Accept
[ ] Grade B (Very good)	[Y] Grade B: minor language polishing	[ ] Existed	[ ] High priority for publication
[Y] Grade C (Good)	[ ] Grade C: a great deal of language polishing	[ ] No records	
[ ] Grade D (Fair)		BPG Search:	[ ]Rejection
[ ] Grade E (Poor)	[ ] Grade D: rejected	[ ] Existed	[ ] Minor revision
		[ ] No records	[Y] Major revision

COMMENTS TO AUTHORS

In this paper, the authors propose a possible novel therapeutic target in RA, based mostly in their previous elegant studies on the role of CTGF in the pathogenesis of the disease. I have several comments on this manuscript that should be addressed by the authors: In the Abstract, the statement in lines 7-8 "The binding of …. membrane bound TNFa" should be deleted. Everybody knows that and furthermore, there are anti-TNFa agents that do not act as antibodies. Again in the Abstract, the phrase in lines 10-11 "We present the profile …. using infliximab; several proteins" should be deleted. In this review the authors do not present the profile changes of serum proteins, despite the fact that they have provided a relevant table. They have done that previously. Instead, the phrase "We have previously shown that several proteins, including CTGF" should be added just before "exhibited extensive changes …." in line 12. Although the language of the manuscript is good, there are few points in it where expression is poor and confusing: In the third page of the paper (by the way, pages should be numbered), under the heading "Connective tissue growth factor", in line 7, the phrase "CTGF was discovered …. of a platelet" should read "CTGF was discovered after the detection of cross-reactivity between an antiserum to a platelet". In the same section of the text, in lines 13-14, the statement "Although a number … been defined" does not make any sense the way it is written. It should read as "Although a number of cell surface molecules, such as integrins, have been currently proposed as candidate specific CTGF receptors, such receptors have not yet been definitely documented." In lines 16-18 of the same page "CTGF in the … autocrine system." should read as "In the articular tissue, consisting of different types of cells, CTGF is produced by chondrocytes and maintains cartilage tissue homeostasis via an autocrine process." Again, in the

following sentence, the word "null" does not seem the most appropriate and the word "complete" may fit better, whereas the "osteoclast-like formation" should read as "osteoclast formation" or "osteoclast-like cell formation". The word "system" following "autocrine" should better change to "process" in several points of the text. In the Introduction, page 3, the word "using" in front of "infliximab" should be replaced by "with". In page 6 line 8, the word "distraction" should change to "destruction". Figure 1 should be separated into two distinct figures: Fig. 1 and Fig. 2, instead of consisting of Fig. 1-1 and Fig. 1-2. Consequently, the following figures2, 3 and 4 should become 3, 4 and 5. Most importantly, all the figures should be given a title, besides the relatively extensive legend. Two major comments that relate to Fig. 4 (which should become Fig. 5) and the Discussion and the Conclusions are as follows: Since the two types of cells i.e. synovial fibroblasts and chondrocytes are in close proximity in the inflamed RA joint, and the effect of TNFa on these two cells regarding CTGF is opposite to each other (according to the authors), they should make an appropriate comment, regarding the net result of these effects. The issue they should address is "Why the excess CTGF produced by the fibroblasts does not affect both osteoclasts and chondrocytes in a similar manner, i.e. with a positive effect on chondrocytes as well?" Is the direct inhibition by TNFa of the autocrine mechanism of CTGF production by chondrocytes able to overcome a direct stimulatory effect of the fibroblast produced CTGF on chondrocytes?? This issue should be definitely commented upon. Furthermore, in their Discussion and Conclusions, the authors should give information from their studies referenced #3 and #10, providing any available data on a possible in vivo evidence of CTGF involvement in RA pathogenesis