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ESPS PEER REVIEW REPORT

Name of journal: World Journal of Gastroenterology
ESPS manuscript NO: 12776
Title: The thrombospondin mimetic peptide ABT-898 inhibits inflammation and angiogenesis in a colitis model
Reviewer code: 00109347
Science editor: Jing Yu
Date sent for review: 2014-07-26 13:39
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CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
[ ] Grade A: Excellent	[Y] Grade A: Priority publishing	Google Search:	[ ] Accept
[Y] Grade B: Very good	[ ] Grade B: Minor language polishing	[ ] Existing	[ ] 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	[ ] Existing	[Y] Minor revision
		[ ] No records	[ ] Major revision

COMMENTS TO AUTHORS

This manuscript examines the anti-inflammatory and anti-angiogenic activities of a second generation thrombospondin-1 mimetic ABT-898 in a murine colitis model. Although this drug was designed to be an anti-angiogenic, the data presented indicate that its major model of action is through modulating inflammation, including suppression of IL-6 and STAT3 responses. Several minor issues need to be addressed to complete this study. 1. It is unclear what specific altered parameter relates to the statement on p. 11 regarding Fig 1B that "These results were statistically significant." 2. Panel E in Fig 2 is cited in the Results but not labeled in the figure. 3. In Fig 2 ABT-898 is clearly inhibiting angiogenesis, but endogenous TSP1 appears to not inhibit angiogenesis under the same conditions. Please discuss. 4. The y-axis in Fig 3 needs a better label to indicate that IL-6 is being measured. 5. In Fig 4 p-STAT3 is elevated in the inflamed TSP1-null tissue, but total STAT3 seems also to be elevated. Is the ratio of p-STAT3/total STAT3 constant or elevated in the null? Has the data been replicated? If so, please present a bar graph with statistics. 6. It is interesting that endogenous TSP1 appears to be limiting STAT3 expression and activation because others have reported that STAT3 signaling induces TSP1 expression (Am J Physiol Renal Physiol. 2011 Nov;301(5):F1014-25; Nat Commun. 2014 Jul 11;5:4294). This suggests a negative feedback loop and should be discussed. Minor points: On p. 8 "100 ml of plasma" presumably should read "100 microliters" TSP1-/- is inconsistently superscripted. Technically, to denote the null genotype the

italicized proper murine gene name thbs1-/- should be used.