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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Biological Chemistry

ESPS manuscript NO: 20018

Title: JAK3 inhibitor VI is a mutant specific inhibitor for epidermal growth factor receptor with the gatekeeper mutation T790M

Reviewer's code: 02686084

Reviewer's country: Mexico

Science editor: Yue-Li Tian

Date sent for review: 2015-05-30 11:49

Date reviewed: 2015-06-13 03:24

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	[Y] Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In this manuscript the author demonstrated that of JAK3 inhibitor VI could specifically inhibit EGFR gatekeeper mutation (T790M/L858R) in non-small cell lung cancers and this is the main contribution of actually paper. In the other hand, is necessary included more information and references about of inhibitor-resistant, see for example: 1. J?nne PA, Yang JC, Kim DW, Planchard D, Ohe Y, Ramalingam SS, Ahn MJ, Kim SW, Su WC, Horn L, Haggstrom D, Felip E, Kim JH, Frewer P, Cantarini M, Brown KH, Dickinson PA, Ghiorghiu S, Ranson M. AZD9291 in EGFR inhibitor-resistant non-small-cell lung cancer. *N Engl J Med.* 2015 Apr 30;372(18):1689-99. 2. Jiang T, Zhou C. Clinical activity of the mutant-selective EGFR inhibitor AZD9291 in patients with EGFR inhibitor-resistant non-small cell lung cancer. *Transl Lung Cancer Res.* 2014 Dec; 3(6):370-2. The authors didn't provide pharmacology information, example the IC50 of the inhibitor, please include. Finally, the author will be considerate change the statistical analysis to U Mann-Whitney for not parametric data.



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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Biological Chemistry

ESPS manuscript NO: 20018

Title: JAK3 inhibitor VI is a mutant specific inhibitor for epidermal growth factor receptor with the gatekeeper mutation T790M

Reviewer's code: 02800292

Reviewer's country: Cyprus

Science editor: Yue-Li Tian

Date sent for review: 2015-05-30 11:49

Date reviewed: 2015-06-13 03:32

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" type="checkbox"/> Grade A: Priority publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The authors suggest that JAK3 inhibitor VI can selectively inhibit in-vitro the kinase activation of EGFR with the gatekeeper mutation T790M, which is resistant to EGFR TKIs in NSCLC and suppress cellular proliferation. Their finding indicate that JAK3 inhibitor VI is a mutant selective reversible TKI for EGFR T790M. Although I am not an expert in the field, the experimental approach seems sound and the results appear solid. The writing of the manuscript is solid, as well and explanatory. I tentatively suggest that it can be published to the World Journal of Biological Chemistry.



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Biological Chemistry

ESPS manuscript NO: 20018

Title: JAK3 inhibitor VI is a mutant specific inhibitor for epidermal growth factor receptor with the gatekeeper mutation T790M

Reviewer's code: 02618391

Reviewer's country: United States

Science editor: Yue-Li Tian

Date sent for review: 2015-05-30 11:49

Date reviewed: 2015-06-12 01:35

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input checked="" type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

In current manuscript entitled "JAK3 inhibitor VI is a mutant specific inhibitor for EGFR with gatekeeper mutation T790M", the authors demonstrated that JAK3 inhibitor VI could specifically inhibit EGFR gatekeeper mutation (T790M) in non-small cell lung cancers. There are some major concerns regarding the manuscript: 1. The authors indicated that the JAK3 inhibitor VI was selected by screening a kinase inhibitor library, but didn't give the further details about the library, for example, the size and composition of the library as well as the screening method. 2. The authors didn't provide the fundamental pharmacology information, the IC50 of the inhibitor. Without it, the readers cannot tell the inhibitor's efficacy and potential. 3. In Figure 2 A and B, the variation of total EGFR is too big, the total protein of each sample should be measured and the same amount of protein should be loaded to each lane. Second, the phospho-EGFR should be normalized against control and the results should be shown in a separate bar graph with statistic analysis. Third, there is no indication that how many independent repeats were performed for these experiments.