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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 44742

Title: FGFR4 Single Nucleotide Polymorphism Gly388Arg in Head and Neck Carcinomas

Reviewer's code: 00468686

Reviewer's country: Turkey

Science editor: Ying Dou

Date sent for review: 2018-12-17

Date reviewed: 2018-12-17

Review time: 8 Hours

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 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

None

INITIAL REVIEW OF THE MANUSCRIPT



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PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 44742

Title: FGFR4 Single Nucleotide Polymorphism Gly388Arg in Head and Neck Carcinomas

Reviewer's code: 03478772

Reviewer's country: Taiwan

Science editor: Ying Dou

Date sent for review: 2018-12-17

Date reviewed: 2018-12-17

Review time: 10 Hours

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 type="checkbox"/> Anonymous
<input type="checkbox"/> Grade C: Good	polishing	<input type="checkbox"/> Accept	<input checked="" 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 checked="" 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

My pleasure to review the manuscript about the clinical analysis of FGFR4 SNP in head and neck cancer by Wimmer et al. This is a careful study in the field. I have the following comments. Table 1, Table 3 and Table 4, please remove the column 'Remarks,' that is a



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redundant expression since P-value has the whole story. Table 5, logistic regression, please show the result of odds ratio and corresponding 95% CI. Page 6, Line 4, misspelled word: separated In Methods, Immunohistochemistry: The authors should clearly state that what protein is the target for the IHC staining in this paragraph. Table 3. The details methods and criteria to distinguish low from high expression of FGFR4 should be also explicitly and stated in the Methods section. In the Discussion, the authors jump-started to discuss angiogenesis in the head and neck cancer. However, what all about the angiogenesis is related or linked to FGFR4 were not touched upon and well-referenced. This part should be re-written.

INITIAL REVIEW OF THE MANUSCRIPT

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- ☐ No

PEER-REVIEW REPORT

Name of journal: World Journal of Clinical Oncology

Manuscript NO: 44742

Title: FGFR4 Single Nucleotide Polymorphism Gly388Arg in Head and Neck Carcinomas

Reviewer's code: 03259512

Reviewer's country: Australia

Science editor: Ying Dou

Date sent for review: 2018-12-17

Date reviewed: 2018-12-25

Review time: 4 Hours, 8 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 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 checked="" 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 study addressed the potential clinical significance of FGFR4 Arg388 (single-nucleotide polymorphism) in head and neck carcinoma. The authors tested 284 patient samples using immunohistochemistry and PCR. The tested number is quite large,

thus, supporting the significance of findings. The data indicates that advanced tumor stage and local metastasis are significantly associated with reduced disease-free survival in mutant FGFR4 Arg388 carriers (patients). Furthermore, increased expression of FGFR4 correlated significantly with worse overall survival in the tested cancer patients. The authors suggested that FGFR4 Arg388 represents a useful target for future multimodal therapeutic interventions. The study is an interesting and well-written. There are several minor questions to address. 1. It is necessary to indicate (Methods section) whether the study was approved by a relevant Human Ethics committee. 2. Immunohistochemistry (IHC) section, page 5: "...incubated with 1:100 pre-diluted primary antibodies (clone 16; Santa Cruz,..." it is necessary to add "FGFR" before primary abs, and if possible it is necessary to include cat# for the used abs. 3. Authors wrote; "Staining intensity was differentiated into three groups: 1. + (weak), 2. ++ (moderate), and 3. +++ (high)." It is necessary to include exemplary photographs to illustrate each group. Fig.2 is supposed to present all categories, however the 'moderate' category is missing. The "low" category looks not so very low. 4. How the categorization was done? It is unclear. Was it manually categorized/ how many people were involved into categorization? Was it done blindly (the researchers were not supposed to know the patient's name, conditions etc). The methods section should include more detailed description of IHC as it is one of the main parts of the study. 5. Reference section can be improved and should include the following papers: Choi KY, Rho YS, Kwon KH, Chung EJ, Kim JH, Park IS, Lee DJ. ECRG1 and FGFR4 single nucleotide polymorphism as predictive factors for nodal metastasis in oral squamous cell carcinoma. Cancer Biomark. 2012-2013;12(3):115-24. doi:10.3233/CBM-130299. Gao L, Lang L, Zhao X, Shay C, Shull AY, Teng Y. FGF19 amplification reveals an oncogenic dependency upon autocrine FGF19/FGFR4 signaling in head and neck squamous cell carcinoma. Oncogene. 2018 Dec 5. doi: 10.1038/s41388-018-0591-7. 6. Discussion section should be



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also extended and describe potential mechanisms of FGFR4 signaling (shortly, anti-apoptotic , pro-angiogenic effects etc)/ the authors might include a schematic presentation of FGFR4 signaling in head in neck cancers.

INITIAL REVIEW OF THE MANUSCRIPT

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