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ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Biological Chemistry
ESPS manuscript NO: 19999
Title: Targeting amino acid metabolism in cancer growth and anti-tumor immune response
Reviewer's code: 03283891
Reviewer's country: United States
Science editor: Yue-Li Tian
Date sent for review: 2015-05-29 13:43
Date reviewed: 2015-06-12 21:13

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

COMMENTS TO AUTHORS

?Overall this is a well written review with targeted therapies in cancer being a very timely topic. ?There are several times that preclinical studies are mentioned and listed the references. The table provides are a great summary of these, but as a review article it would be good to take a more consistent and comprehensive approach. For example, under arginine you list preclinical studies in hepatocellular carcinoma and pancreatic cancer- without having to look up the references it would be nice to know what model was used (in vivo/in vitro). Then under tryptophan you list the actual cell line P815B- what tumor site it this? oConsider revising the table to include the disease site and the model for each study. ?It is mentioned under tryptophan and glutamine that there are safety cancers/ and general toxicity. Again, as a review article this should be a comprehensive source where the reader can easily identify the issues. As a clinical provider involved in both cytotoxic chemotherapy trials and targeted trials I am continually amazed what patients are willing to endure for the chance at more time alive. Are the toxicities in these clinical studies grade 3 or 4? What about in the preclinical studies, is it animal weight that is monitored, or are they resulting in animal fatality?

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ESPS PEER-REVIEW REPORT

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[ ] Grade B: Very good	[Y] Grade B: Minor language polishing	[ ] The same title	[ ] High priority for publication
[Y] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
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		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This is brief review article that nicely describes the potential role of amino acid metabolism in cancer growth and immune response. Recent studies indicate that amino acid metabolism plays a significant role in the pathophysiology of cancer cachexia. Authors have done careful job in describing how some of the essential amino acids involved in the cancer growth. Few minor comments are given below to improve the manuscript. Some of the sentences are too long and not clear. For example; Page 4; the sentence that starts with "It is hypothesized….deprivation" Page 5; the sentence that starts with "As a result…..died". Page 8"the sentence that starts with "The cytoplasmic….activation" A schematic diagram showing the links between amino acid metabolism, inflammation and cancer will be great help for the readers.

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[ ] Grade C: Good	[ ] Grade C: A great deal of language polishing	[ ] Duplicate publication	[ ] Rejection
[ ] Grade D: Fair	[ ] Grade D: Rejected	[ ] Plagiarism	[Y] Minor revision
[ ] Grade E: Poor		[Y] No	[ ] Major revision
		BPG Search:	
		[ ] The same title	
		[ ] Duplicate publication	
		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

This manuscript provides up-to-date information of amino acid metabolism in cancer development. Dr. Ananieva discussed four main types of amino acid metabolism including arginine and tryptophan, serine and glycine, glutamine, and branched chain amino acids; also presented several lines of drug evidence that currently targets these metabolic pathways in clinical trials. The paper focuses primarily on amino acid metabolism by which both cancer cells and immune cells grow and differentiate, indicating the potential competition for sharing same nutrients. In general, the paper has a clear objective and is a well-written review in which the organization of the manuscript makes the material easy to follow. A few minor concerns may be addressed. 1) These amino acids are essential for almost all of different types of body cells in biological, physiological and pathological development. Abnormal regulations of these metabolic processes must occur in a variety of human diseases, not limited to cancer; therefore, the other diseases associated with dysfunction of these metabolic pathways should be briefly discussed. Indeed, some diseases are largely connected with carcinogenesis such as inflammation and cancer. 2) The paper discussed some clinical results that

unveil differential expression levels of amino acid metabolic enzymes in cancer such as PHGDH, IDO, TDO, etc. Are there studies or data that evaluate abnormal levels (either up or down regulation) of corresponding amino acids in tumor or blood? These kinds of evidence may hold great value for establishing cancer biomarkers. 3) It is nice to have a summery table listing a number of drugs used in clinical trials, which specifically target individual amino acid metabolism. Are these drugs limited to cancer patient treatment? As stated earlier, other cells like immune cells also share the same material for cell metabolism. As such, it is curious to know if some of these drugs are engaged in clinical practice for immune disorders or others.

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		[ ] Plagiarism	
		[Y] No	

COMMENTS TO AUTHORS

The review manuscript, "Targeting Amino Acid Metabolism in Cancer growth and Anti-Tumor Immune Response" (Manuscript #20150527103026), authored by Dr. Ananieva describes targeting of amino acid metabolism and the potential use of that targeting as a cancer treatment by developing more effective immunotherapies. The author describes links that exist between the immune system and amino acids that either have been or have the potential to be exploited for therapeutic purposes. The brief review provides insight into the role of the immune system and targeting of tumors using inhibitors of metabolic enzymes. This is a promising area in which to develop new therapeutic agents and the role of immune system cells is discussed. Overall, the manuscript is well-written. Minor issues that the author should consider addressing: 1. The author should consider adding a figure or figures showing some of the metabolic pathways that are described in the text. 2. Page 4. "…by being source of arginine…", is better as "…by being a source of arginine…". 3. Page 7. The review paper by Mider cited does not "show", because it is a review paper. Manuscripts concerning glutamine metabolism and cancer actually appeared prior to the review manuscript. 4. Page 7.

Although glutamine is not essential, it can become a conditionally essential amino acid, which is later discussed. That conditionality may be important to mention in the same sentence.