

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6889

Title: A complex role for the immune system in initiation and progression of pancreatic cancer

Reviewer code: 00506409

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-04 14:55

Date reviewed: 2013-11-07 19:02

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	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"/> Existed	<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"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)		BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

This is an interesting review on the role of the immune system in the emergence of pancreatic ductal adenocarcinoma, a horrible type of cancer with very low actual survival. A major aspect in the pathogenesis of this cancer is the development of chronic pancreatitis, in which components of the innate and acquired immune system are involved. The authors present a comprehensive review of the literature of the clinical condition, and related data from studies in experimental small animal models. The manuscript is well written, and the figures are of good quality. The authors have not included page numbers and line numbers in their manuscript which complicates the writing of this review. In the following, reference is made to page numbers in the pdf file in which the body text is on page 2-19, references on page 19-33, and figures plus figure legends on page 34-39. There are a number of points that are recommended to be addressed in improvement of the manuscript. Major points ? There is no abstract in the manuscript (it is there on the website). ? There is no list of abbreviations in the manuscript. Many abbreviations in the text are not explained. ? The first part of the manuscript is a description of the immune system. This is essentially the same as a text book of Immunology, and could easily be deleted. This also applies to figure 1. This comment is perfectly in balance with the fact that there is no section on pancreas function, or consequences of pancreas dysfunction because of (acute/chronic) pancreatitis or pancreas carcinoma. ? An exception to the previous point might be the introduction of M1-polarized and M2-polarized macrophages on page 3, and specific aspects of the immune system function as it relates to cancer. ? Page 8 "Rodent models are used most often because of their cost-effectiveness and ease of characterization and genetic manipulation;": this statement is correct, but what is neglected in this review is the fact that the immune system in rodents differs largely from that in humans. Also, antigen exposure related to

housing adds to this difference. Therefore, in a review on the relation between the immune system and pancreatic adenocarcinoma, it seems very appropriate to mention this difference as a limitation of modeling pathogenetic processes in rodents. See also the statement on page 12 “Because of this, the immune response in animals may not mirror that of studies using human tissue.”: it is essentially not “Because of this”, but rather “This is because”. ? Instead of figure 1 (that is just a copy of an immunology textbook), it is recommended to present those components of the immune system (including their cells and products like cytokines and lymphokines) that may play a role in the interaction between the immune system and development of pancreatic adenocarcinoma in a table with reference to the basis of the suggested role. Also, it is recommended to prepare a figure that presents all mechanisms involved (including the immune mechanisms but also those intrinsic pancreatic stimulants) at various steps in the process of developing from a normal pancreas into acute pancreatitis into chronic pancreatitis into pancreas carcinoma. This will highly help the reader to ingest and digest the information in the various sections of the manuscript and understand the conclusions. Minor points ? Page 2: the abbreviation ‘PanINs’ is not explained. See page 12 for explanation. ? In the description of immunity to cancer cells, the term ‘immune surveillance’ is lacking. See also page 12 “The immune system has the ability to protect a host from tumor growth as well as promote cancer progression through editing tumor immunogenicity.”, and subsequent sentences. The term ‘immune surveillance’ first appears on page 17. ? Page 5 “B-lymphocytes are largely responsible for body’s ability to mount a long-term pathogen-specific response.”: this is an incomplete statement, because T-lymphocytes have a similar role i

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Title: A complex role for the immune system in initiation and progression of pancreatic cancer

Reviewer code: 01779392

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-04 14:55

Date reviewed: 2013-12-15 00:37

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input checked="" type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input type="checkbox"/> Major revision
		<input type="checkbox"/> No records	

COMMENTS TO AUTHORS

The review tried to study a complex role of the immune system in initiation and progression of pancreatic cancer via the data from clinical studies and rodent models. Many studies showed that the development and progression of pancreatic ductal adenocarcinoma (PDAC) is strongly influenced by the presence of inflammation (acute and chronic pancreatitis). This review will highlight the roles of the immune response, focusing primarily on inflammation, in the development of PDAC. The major problems are that authors spent great length to describe the immune system, acute pancreatitis and chronic pancreatitis, immune cells in PDAC, but can not explain clearly the roles of those immune cells. Therefore, the suggestive comments are to cut down contents of the immune system, acute pancreatitis and chronic pancreatitis, and increase contents of roles of the immune cells in PDAC.

ESPS Peer-review Report

Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6889

Title: A complex role for the immune system in initiation and progression of pancreatic cancer

Reviewer code: 01808896

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-04 14:55

Date reviewed: 2013-12-23 23:41

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C (Good)	<input type="checkbox"/> Grade C: a great deal of	<input type="checkbox"/> No records	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D (Fair)	language polishing	BPG Search:	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E (Poor)	<input type="checkbox"/> Grade D: rejected	<input type="checkbox"/> Existed	<input checked="" type="checkbox"/> Minor revision
		<input type="checkbox"/> No records	<input type="checkbox"/> Major revision

COMMENTS TO AUTHORS

Smith et al. reviewed the role of the immune system in initiation and progression of pancreatic duct cancer. This review is organized properly and worthy to be published in World Journal of Gastroenterology. Some minor revisions might be more informative for the readers, as shown below.

1) As is well known, such immune system is generally associated with in vivo carcinogenesis and progression of various cancers. The specificity of pancreatic cancer should be mentioned. 2) Recent studies revealed pancreatic cancer stem cells (CSCs) might be derived from acinar-to-ductal metaplasia (ADM). The role of immune system in ADM and CSCs should be mentioned in more detail. 3) More schematic figures might be required to illustrate the cellular functions and cytokine cascades, including TAMs, MDSC, Treg, IL1 β , TNF α and IL6.

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Name of Journal: World Journal of Gastroenterology

ESPS Manuscript NO: 6889

Title: A complex role for the immune system in initiation and progression of pancreatic cancer

Reviewer code: 01573525

Science editor: Zhai, Huan-Huan

Date sent for review: 2013-11-04 14:55

Date reviewed: 2013-12-24 01:10

CLASSIFICATION	LANGUAGE EVALUATION	RECOMMENDATION	CONCLUSION
<input type="checkbox"/> Grade A (Excellent)	<input checked="" type="checkbox"/> Grade A: Priority Publishing	Google Search:	<input checked="" type="checkbox"/> Accept
<input checked="" type="checkbox"/> Grade B (Very good)	<input type="checkbox"/> Grade B: minor language polishing	<input type="checkbox"/> Existed	<input type="checkbox"/> High priority for publication
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COMMENTS TO AUTHORS

The authors comprehensively overview the current understanding of the complex role of the immune system in the development and progression of pancreatic cancer. Drawing from both clinical and pre-clinical data, they present the current understanding of the immune response to acute and chronic pancreatitis, as well as to pancreatic cancer and the immunosuppressive environment often produced. They review the cells of the immune system, their functions, and the interactions that drive their recruitment and activation at the tumor site. They also discuss the possibility of using the immune response to assist in targeting pancreatic cancer. I have no comments to add to this comprehensive and well written review.