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8226 Regency Drive, Pleasanton, CA 94588, USA

Telephone: +1-925-223-8242

Fax: +1-925-223-8243

E-mail: bpgoffice@wjgnet.com

<http://www.wjgnet.com>

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Answering reviewers

In response to reviewers 00001832 and 00043819 the abstract has been shortened and focused, while the table has been trimmed in its content to include PMID as identifiers. Within the table targets have been grouped for ease of identification and interpretation. Furthermore following very helpful comments from reviewer 00001832 we have included the largest randomised controlled trials assessing tumour vaccines in pancreatic cancer within the tumour immunology section. While, within the tumour stroma section we agree that recently published findings on failure of Sonic Hedgehog antagonists in multicentre trial by Catenacci et al is worthy of inclusion and discussion. In response to both reviewers 01212501 and 00724450 we have edited the grammar within the manuscript. We have made every effort while improving the grammar of the manuscript to be concise thus making our work more compact. To summarise possible targets for therapy within the microenvironment of pancreatic cancer we have included a diagram identifying the major changes in immune cell distribution, stroma accumulation and inflammatory signalling pathways as pancreatic cancer forms as requested by reviewer 01212501. Furthermore we have included a section highlighting the considerations for surgeons treating this disease and consider whether peri-operative care may impact on outcome via inflammatory insults as raised by reviewer 01212501. Reviewer 00052339 makes a very valid point regarding mechanisms for resistance of pancreatic cancer cells to the effects of anti-PD1 therapies while other tumours have been observed to respond. We have made an attempt to explain resistance mechanisms within the text.

We are very grateful for your consideration of this manuscript in its final format and hope we have thoroughly addressed the issues raised by the reviewers.

Yours sincerely

Dr Colin Steele
PhD, MRCS(Glasgow)