Format for ANSWERING REVIEWERS

July 28, 2015

To Whom It May Concern,

Please find enclosed the revised manuscript in Word format (file name: 19260-Revised manuscript.docx)

Title: Genomic alterations in pancreatic cancer and their relevance to therapy

Authors: Erina Takai, Shinichi Yachida

Name of Journal: *World Journal of Gastrointestinal Oncology*

ESPS manuscript NO: 19260

We thank the reviewers for their insightful comments and have incorporated them into our manuscript as recommended. Our detailed comments are listed below.

REVIEWER 1 (00069406). Figure 1 contains less information than which is already published in the literature.	According to the reviewer's comment, we have excluded Figure 1.
REVIEWER 2 (00224612). Comment 1. The authors state that "although great efforts have been made to develop small-molecular inhibitors of mutant *KRAS*, no clinically effective antagonist has yet been identified". In this context, the authors should cite and include: The Ras renaissance. PMID: 25877186.	According to the reviewer's comment, we have cited the review article (ref 42).
Comment 2. The authors state that "activation of the PI3K/Akt/mTOR pathway also plays an important role in maintenance of pancreatic cancer". In this context, the authors might also want to cite and include: A subset of metastatic pancreatic ductal adenocarcinomas depends quantitatively on oncogenic Kras/Mek/Erk-induced hyperactive mTOR signalling. PMID: 25601637	According to the reviewer's comment, we have cited the article (ref 57).
Comment 3. The authors state that	According to the reviewer's comment,

"interestingly, blockade of Hedgehog pathway has also been proposed as a mean to target the tumor stroma and improve delivery of gemcitabine in vivo". The authors should also state and cite that the Saridegib trial failed.	we have added the following sentence: Small-molecular inhibitor Saridegib (IPI-926) was tested in combination with gemcitabine in patients with pancreatic cancer. However, the Phase I/IIb trial was stopped because patients receiving the combination had higher rates of progressive disease and lower overall survival in 2012 [ref 72].
Comment 4. Figure 1 should be omitted since the authors do not review in depth pancreatic cancer progression models.	According to the reviewer's comment, we have excluded Figure 1.

Kindest regards,

Erina Takai, PhD