Author's response to reviews

Title: BRAF V600E mutation and KRAS codon 13 mutations predict poor survival in Chinese colorectal cancer patients

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Author's response to reviews: see over
Dear Editor,

Hereby we would like to submit to the Editorial Office of "BMC Cancer" the manuscript titled: "BRAF V600E mutation and KRAS codon 13 mutations predict poor survival in Chinese colorectal cancer patients”. We have initially submitted this manuscript to Molecular Cancer, the editorial team recommended that BMC Cancer would be more appropriate for our research. Therefore, we accepted the transfer to BMC Cancer.

In this manuscript we identified the mutation frequencies of KRAS, BRAF and PIK3CA genes in Chinese colorectal cancer patients and investigated their impact on prognosis. So far, data has been largely available for western countries patients, whereas there is a lack of agreement in mutation frequencies in Chinese CRC patients, especially for BRAF and PIK3CA, because they were reported differently in limited data published. More importantly, little is known about their prognostic values in Chinese CRC patients since few studies had follow-up data.

A study-cohort of 214 Chinese patients enabled us to perform multivariate analyses, revealing that BRAF V600E mutation can be used as a prognostic factor for colon cancer, independent of TNM stage; and KRAS codon 13 mutations ((in particular, c.38G>A, p.G13D) can be used as a prognostic factor for colorectal cancer. In conclusion, our study, to the best of our knowledge, assessed for the first time, the impact of KRAS mutations, including distinguished mutation subtypes, on prognosis in the Chinese CRC patients when the confounding effector of BRAF mutation was controlled. Currently, our observation indicates us to attach importance to molecular features in CRC patients and control confounding effects in future clinical trials. Actually, among studies from western countries, only a small and very recent detailed analysis estimated the effect of KRAS mutations on prognosis when codon 12 and 13 are counted separately. Since we believe that our findings emphasize the importance of prospective evaluation of molecular features, not only for Chinese patients but also for all CRC patients, and may lead to a change in treatment strategies in near future, we think that this manuscript is suitable for publication in the "BMC Cancer”.

We state that the manuscript is original, is not under consideration or has not been published elsewhere. Its content has not been anticipated by any previous publication and the authors have no financial interest in its contents.
Thank you very much for your time and consideration. And we will appreciate greatly if we would receive your reply in your earliest convenience.

Yours sincerely,

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Brief CV of Youji He
Youji He studied Medicine (MD, 1994) at the Medical School of Southeast University in Nanjing, China. She obtained her Master degree in Medical genetics in 1997 from the same university. In 1998-2000, she was a visiting scientist in INSERM (National Institute of Health and Medical Research), UNIT 344-Molecular Endocrinology, Necker Medicine Faculty, in Paris, France. Afterwards, she studied Molecular biology at the Academic Medical Centre, University of Amsterdam and obtained her Ph.D in 2007. In 2007-2011, she joined Prof. Laura van’t Veer’s research group in the Netherlands Cancer Institute in Amsterdam as a Postdoctoral fellow, working on the development of prognostic and predictive biomarkers for colorectal cancer. In Sept. 2011, she returned to China and accepted a position of Professor at the Medical School of Southeast University. In 2012, she received a grant from National Natural Science Foundation of China for a translational research project on colorectal cancer. In 2013, she received another grant from Research Fund for the Doctoral Program of Higher Education of China, Ministry of Education of China.