Author's response to reviews

Title: Incarvine C suppresses proliferation and vasculogenic mimicry of hepatocellular carcinoma cells via targeting ROCK inhibition

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Version: 2 Date: 4 June 2015

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

We are submitting our original manuscript entitled “**Incarvine C suppresses proliferation and vasculogenic mimicry of hepatocellular carcinoma cells via targeting ROCK inhibition**” by Ji-Gang Zhang, Dan-Dan Zhang, Xin Wu, Yu-Zhu Wang, Sheng-Ying Gu, Guan-Hua Zhu, Xiao-Yu Li, Qin Li and Gao-Lin Liu.

In this study, we explored an antimetastatic HCC agent derived from traditional Chinese medicinal herbs and found that Incarvine C (IVC), an active component of Incarvillea sinensis Lam, had remarkable inhibitory effects on the survival, proliferation, migration and vasculogenic mimicry (VM) of HCC cells. IVC dose-dependently inhibited the growth of MHCC97H cells. Mechanistic studies showed that IVC induced MHCC97H cell cycle arrest at G1 transition, which was associated with cyclin-dependent kinase 2 (CDK-2)/cyclin-E1 degradation and p21/p53 up-regulation. Meanwhile, IVC induced apoptotic death of MHCC97H cells. Furthermore, IVC strongly suppressed the phosphorylation of the ROCK substrate: myosin phosphatase target subunit-1 (MYPT-1) and ROCK-mediated actin fiber formation. In addition, IVC inhibited MHCC97H cell migration and cell-dominant tube formation in vitro, which was accompanied with the down-regulation of VE-cadherin, EphA2, PI3K, MMP-14, MMP-2, MMP-9 and LAMC2 as detected by real-time qPCR, Western blot and immunofluorescence. Taken together, the effective inhibitory effect of IVC on MHCC97H cell proliferation and neovascularization was associated with ROCK inhibition, suggesting that IVC may be a new potential drug candidate for the treatment of HCC.

We feel that a wide range of readers will be interested in this manuscript, and wish it is suitable for publication in the **BMC Cancer**. The manuscript was prepared according
to the requirements of the journal. All the results in the current manuscript have never been published or submitted elsewhere. And all authors read and approved the final manuscript.

Sincerely yours,

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Jun 2, 2015

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