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A novel fully human IgG1 antibody targeting VEGFR2 pathway blockade angiogenesis both *in vitro* and *in vivo*

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Abstract

Vascular endothelial growth factor (VEGF) and its receptors, especially receptor 2 (VEGFR2, or KDR), are implicated to play a critical role in angiogenesis under both physiological and pathological conditions. Inhibition of angiogenesis with antagonists to either VEGF or KDR has led to significant therapeutic efficiency both in preclinical animal models and in clinical trials. However, the only neutralizing antibody in this pathway currently available is Bevacizumab (Avastin). Our research was focused on the development of a fully human monoclonal antibody (mAb) targeting VEGFR. Firstly, we generated two groups of recombinant vectors using a phage display based single chain antibody fragment (scFv), which was previously generated in our lab. The vectors were then introduced to CHO-s cells and clones with higher yield were picked accordingly. After an optimal fermentation condition was determined, fed-batch fermentation was performed in 5L bioreactor. Affinity and kinetic assay by Biacore system revealed that the mAb could specifically bind to KDR with high affinity. Plus, we also investigated the potential antiangiogenic activity both in vitro and in vivo. The mAb could inhibit VEGF-stimulated human umbilical vein endothelial cell (HUVEC) proliferation, migration and tube formation, prevent micro-vessel outgrowth from rat aortic rings and suppress neovascularization of CAM. Signal pathway protein study exhibited the mAb could attenuate VEGF-stimulated phosphorylation of KDR and related signal proteins in the proliferation and survival of HUVECs. In conclusion, the overall data proved that the given mAb, thereby, has potential clinical applications in the treatment of cancer and other diseases where pathological angiogenesis is involved.

Biography

Professor Juan Zhang has completed her Ph.D from China Pharmaceutical University and has been involved in a co-supervised ph.D student project Imperial College London in 2007. She is currently a visiting scholar in University of California, Los Angeles. Dr Zhang has published more than 30 papers in reputed journals and serving as reviewer for number of international journals