Editorial

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Finding a New Prognostic Biomarker for Metastatic Colorectal Cancer

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For detecting new biomarkers in colorectal cancer, whether they are prognostic or predictive, we should understand the mechanism of the metastatic process at the gene expression level. This article presents a new prognostic biomarker, 'placental growth factor (PlGF)' to the clinical field. PlGF, which is a member of the vascular endothelial growth factor (VEGF) family in conjunction with VEGF-A and VEGF-B, is a ligand for VEGF receptor-1, which is expressed on endothelial cells, monocytes/macrophages, and some tumor cells. PlGF was isolated in 1991 from the placenta and was found only in very low levels under physiological conditions, but it was up-regulated in pathological circumstances such as wound healing, ischemia and tumor growth [1].

PlGF up-regulation has been found in human meningiomas, hemangioblastomas, melanomas, and cervical squamous cell carcinomas and is associated with angiogenesis in renal cell carcinomas. On the contrary, PlGF is down-regulated in thyroid carcinomas, germ cell tumors and cervical adenocarcinomas. Chen et al. [2] reported that PlGF was significantly up-regulated in gastric cancer tissue and was significantly correlated with microvessel density-evaluated angiogenesis and tumor stage. In this research, the authors found that the PlGF protein expression level in colorectal cancer tissue was significantly correlated with microvessel density, overall patient survival, and clinicopathological factors such as lymph-node metastasis, tumor stage, and lymphovascular invasion. According to the authors, PlGF seems to be an independent surrogate prognostic factor for colorectal cancer progression. However, for these results to be adopted in the clinical filed, it is very important that a large-sample-size study be brought conducted in a validation setting.

The findings of this research finding suggest that PlGF may constitute a novel approach to colorectal cancer treatment. Several agents against PlGF have already developed or are currently under development. Among these agents, two novel agents against PlGF will be briefly discussed. Firstly, aflibercept (ZALTRAP) is a recombinant fusion protein that acts as a soluble receptor that binds to VEGF-A, VEGF-B and PlGF. In April 2011, Van Cutsem et al. [3] reported that aflibercept improved the primary endpoint of overall survival in the Velour phase III clinical trial for second-line treatment for metastatic colorectal cancer. Secondly, the humanized anti-PlGF mAb (TB-403) is directed against PlGF. A trial with TB-403 has only completed its first phase. Antitumor activity has been demonstrated with TB-403 in human tumor xenograft models of renal cell carcinomas and hepatocellular carcinomas. The mechanism of action for TB-403 is currently under investigation; preclinical studies suggest its effects may include blocking tumor angiogenesis and primary tumor growth, as well as inhibition of metastasis. In addition, PlGF inhibition may complement and potentiate the antitumor effects of VEGF inhibition, in part by inhibiting macrophage recruitment [4].

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