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The dual effects of a novel peptibody on angiogenesis inhibition and M2 macrophage polarization on sarcoma

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Abstract :

Inhibition of the VEGF/VEGF receptor (VEGFR) and angiopoietin-2 (Ang-2)/TEK receptor tyrosine kinase (Tie-2) pathway is a potential target for tumor angiogenesis. We previously showed that a peptide AS16 which dually inhibits VEGFR/Ang-2 could reduce the tumor growth and decrease the number of microvessels in tumor. However, its short circulating half-life in the serum limits its clinical applications. In this study, as an effort to prolong the short in vivo half-life of AS16, we designed a fusion protein containing peptide AS16 and an IgG Fc fragment. Pharmacokinetic study also revealed that AS16-Fc has a prolonged circulating half-life of about 231 minutes in rats. We examined the effects of treatment on the tumor vasculature and immune cell populations, tumor growth, in both the MCA-205 and S180 tumor models. We found that AS16-Fc dramatically reduced tumor volume, vascular density and tumor-associated macrophages. Macrophages were identified as potential novel targets following anti-angiogenic therapy, our findings imply a novel role for anti-angiogenic peptide AS16-Fc. These findings indicate that AS16-Fc could be more effective on inhibiting tumor growth angiogenesis and tumor immune microenvironment than that of peptide AS16.