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Development of an anti-VEGF Fc-fusion angiogenesis-inhibiting protein

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Angiogenesis is a hallmark of cancer and VEGF is the most potent pro-angiogenic factor that stimulates angiogenesis in diseases such as cancer metastasis, age-related macular degeneration, diabetic retinopathies, psoriasis and rheumatoid arthritis. Hence, blocking VEGF is the best way to prevent angiogenesis. An anti-VEGF, Fc-fusion protein, VEGFR1(D1-D3)-Fc, was developed in-house, using recombinant DNA technology. VEGFR1(D1-D3)-Fc fusion gene was generated by PCR amplification, followed by fusion of genes encoding the first three extracellular domains of VEGFR1 and human IgG1-Fc region. The fusion gene was cloned in expression vector, pXC17.4, following which it was used to transfect mammalian cell line, CHOK1SV GS-KO. However, protein degradation was observed during production of indigenous VEGFR1(D1-D3)-Fc and measures were taken to inhibit proteolytic cleavage of the fusion trap. The Fc-fusion protein was characterized in terms of molecular weight, secondary and tertiary structure, thermal stability, purity, isoelectric point and glycosylation profiling. Strong binding affinity of the fusion traps for VEGF-A was demonstrated and the angiogenesis-inhibitory functions were confirmed, both in cell-based assays as well as a xenograft animal model. VEGFR1(D1-D3)-Fc was demonstrated to have potential in advancing in the pipeline of anti-cancer drug development. Since the VEGFR1(D1-D3)-Fc protein has high binding affinity for VEGF, it will remove circulating VEGF from the system, thus inhibiting the downstream signaling giving rise to cell survival and proliferation. Hence, this anti-VEGF molecule will act as a very effective anti-angiogenic agent, as has already been shown in in vitro and in vivo experiments.

Biography

Sanjukta Chakrabarti is currently pursuing her PhD from Deakin University, Australia. She has completed MSc in Biochemistry from Calcutta University, followed by MTech in Biomedical Engineering from Indian Institute of Technology Mumbai, India. She is a Senior Scientist working with Reliance Life Sciences, a premier organization dealing with pharmaceuticals, biopharmaceuticals, molecular medicine, regenerative medicine and clinical research in Mumbai, India. She has published 4 papers in reputed journals and has been working in biopharmaceutical industry for the last 15 years.

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