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Expression of *Shiga like* toxin (SLT) fused to vascular endothelial growth factor (VEGF) in *E. coli* for targeting angiogenesis

Osama O Ibrahim
Bio Innovation LLC, USA

Angiogenesis is a highly controlled process of growing new blood vessels under normal circumstances. However, in a large number of pathologies, such as solid tumor growth, angiogenesis is a crucial component of the disease process. Therefore, inhibitors of angiogenesis are being investigated as potential therapeutics for tumor growth. During angiogenesis endothelial cells of existing blood vessels undergo a complex process of reshaping, migration, growth and organizing into new vessels. Vascular Endothelial Growth Factor (VEGF) is a central mediator of this process and acts via receptors whose expression is restricted almost exclusively to endothelial cells. Because of its selectivity, VEGF represents a unique vehicle for delivery of inhibitors of angiogenesis to endothelial cells. Among potential inhibitors of angiogenesis, the *shiga-like* toxin-1 (SLT-I) produced by *E. coli* (O157:H7) has the advantage that endothelial cells appear to be particularly sensitive to its action. The hypothesis that combining an SLT-I toxin with VEGF as a delivery vehicle would serve as a highly selective and active inhibitor of angiogenesis. To this end, fusion proteins containing VEGF121 and two forms of *shiga-like* toxin-I (SLT-I) were developed and tested in vitro for activities that have the potential to inhibit angiogenesis in vivo. Plasmids encoding the fusion proteins VEGF121/A1 containing the catalytically active fragment of the SLT-I A subunit and VEGF121/A containing the full length A subunit of SLT-I were constructed in pET-29a and pET-32a systems. *Escherichia coli* BL21 (DE3) pLysS bacteria were transformed with the plasmid constructs for the expression of these two fusion proteins. Both purified fusion proteins inhibited the translation of luciferase mRNA as a reporter gene *in vitro* translation system, indicating that both fusion proteins retain the N-glycosidase activity of SLT-I. However, only VEGF121/A1 fusion proteins displayed the ability to induce auto-phosphorylation of the VEGF receptor KDR/FLK-1 and displayed a strong, selective growth inhibition of cultured cells expressing KDR/FLK-1 receptors. These results indicated that VEGF/SLT fusion proteins are promising therapeutic agents that can be developed into powerful and selective inhibitors of angiogenesis.

Biography

Osama Ibrahim is a highly-experienced Principal Research Scientist with particular expertise in the field of microbiology, molecular biology, food safety, and bioprocessing for both pharmaceutical and food ingredients. He is knowledgeable in microbial testing, microbial screening, culture improvement, molecular biology and fermentation research for antibiotics, enzymes, therapeutic proteins, organic acids and food flavors.Since 1979 he is a member of American Chemical Society, American Society of Microbiology, and Society of Industrial Microbiology.

bioinnovation04@yahoo.com

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