Osama O Ibrahim, Pharm Anal Acta 2016, 7:1 (Suppl)
http://dx.doi.org/10.4172/2153-2435.C1.027

OMICS International
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8th International Conference and Exhibition on

Pharmaceutics & Novel Drug Delivery Systems

March 07-09, 2016 Madrid, Spain

Expression of Shiga-like toxin fused to Vascular Endothelial Growth Factor (VEGF/SLT) in *E. coli* for targeting angiogenesis

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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 a 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 O Ibrahim is a highly-experienced Principle Research Scientist with particular expertise in the fields of biochemistry, microbiology, molecular biology, and bioprocessing for both pharmaceutical and food ingredients. He was external research liaison for Kraft Foods with Universities for research projects related to bioprocessing and molecular biology. In the 2005, he accepted an early retirement offer from Kraft Foods and formed his own biotechnology company (Bio Innovation) providing technical and marketing consultation for new start-up biotechnology and food companies. He holds three bioprocessing patents and received his PhD in basic medical science (Microbiology, Immunology and Molecular biology) from New York Medical College. He is a Member of American Chemical Society, American Society of Microbiology, and Society of Industrial Microbiology since 1979.

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