A novel bacterial protein as a therapeutic angiogenesis inhibitor

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Technology description

Summary

Background The development of specific anti-angiogenic agents is an attractive therapeutic approach for the treatment of angiogenesis-dependent diseases such as cancer progression, metastasis, hemangioma, arthritis, psoriasis and atherosclerosis1. However, there are diseases that result in excessive or insufficient blood vessel formation. Angiogenesis is vital to the progression of small, localized neoplasms to larger, growing, and potentially metastatic tumors. The principle cells involved in angiogenesis are endothelial cells that line all blood vessels; in the process of angiogenesis, endothelial cells go through a series of steps, including activation, basement membrane degradation, migration, extracellular matrix invasion, proliferation, and vessel formation. While it was proposed in 1971 that inhibition of angiogenesis could be an effective way to treat human cancer, there are still only a limited number of effective and safe angiogenesis inhibitors that are currently used to treat the vascularization of tumors. There are a variety of issues with current angiogenesis inhibitors, including safety, efficacy, and the development of resistance to anti-angiogenic compounds. Technology Bacterial toxins have been used for nearly two decades to successfully treat various types of cancers. A University of Colorado research team has identified a novel extracellular bacterial protein which was found to specifically kill, through a receptor-mediated mechanism, human vascular endothelial cells (HUVEC) derived from human placenta at extremely low concentrations (picomolar). Subsequent testing of a highly purified protein preparations revealed that this protein inhibits the proliferation of endothelial cells, and inhibits angiogenesis in a chick chorioallantoic membrane (CAM) assay. These data indicate that the protein, or a portion thereof, could be used as an angiogenesis inhibitor for therapeutic purposes to inhibit the vascularization of tissues associated with disease states. The research team has also performed Zebrafish experiments (a widely used antiangiogenic model) demonstrating that this protein is a powerful angiogenesis inhibitor within a safe therapeutic range (data available under CDA). Applications In addition to its usefulness as an anti-tumor agent, inhibition of angiogenesis may have other applications such as eye disease, and the relief of arthritic pain caused by invading blood vessels. This compound is unique in that it targets endothelial cells directly, and so may not cause the side effects associated with current angiogenesis inhibitors. Furthermore, it has not yet been used as a therapeutic agent, so resistance is not yet a concern.

Institution

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