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175: Scaffold Peptide for Anti-Angiogenic Therapy

- ✓ **Growth inhibition of VEGF treatment resistant tumors**
- ✓ **Peptides as alternative to antibodies with similar binding affinities**
- ✓ **increased serum stability and target affinity**

The Technology

The technology relates to a scaffold polypeptide positions at an exposed surface for use in diagnosing, treating or preventing disorders associated with angiogenesis.

Peptides represent a promising alternative to antibodies. Due to their small size their diffusion is not limited and they offer similar binding affinities as antibodies and the synthesis of peptides is easier and less expensive. The application of scaffold proteins instead of linear peptides solves the problem of serum stability. Scaffold proteins are small, stable and characterized by a conformational constrained structure. Two representatives are the scaffold proteins Min23 and the sunflower trypsin inhibitor I (SFTI). The trypsin inhibitor Min23 is composed of 23 amino acids, stabilized by two disulfide bonds and permissive for loop insertions whereas SFTI consists of 14 amino acids and is stabilized by one disulfide bond. In contrast to linear peptides which offer generally a half-live of few minutes in human serum, the half-live of SFTI is 34.5 hours in open and 75.8 hours in cyclic conformation. Other Scaffold Peptides, using Delta-like 4 (DII4), are available!

Background

Angiogenesis is a normal physiological process of the human body involving the formation of new blood vessels from pre-existing ones. However, angiogenesis is also a fundamental step in tumor development as well as for metastasis and regarded as one major hallmark of cancer. Consequently, anti-angiogenic antibodies (e.g. bevacizumab) address vascular endothelial growth factor (VEGF) for treatment of metastatic colon cancer, non-small lung cancer, breast cancer, renal cancer and glioblastome. Unfortunately, several tumors are insensitive or resistant towards VEGF. Besides VEGF and bFGF, the membrane protein Delta-like 4 (Dll4) is involved in the regulation of angiogenesis by binding to a Notch receptor. In contrast to the VEGF-mediated pro-angiogenic signal the interaction between Dll4 and Notch receptor initiates the formation of unproductive increased sprouting of new blood vessels which results, in growth inhibition of tumors.

Advantages

- ✓ high serum stability
- ✓ less side effects compared with antibodies
- ✓ easy to synthesis
- ✓ less expensive

Commercial Opportunity

- ✓ cancer drug development
- ✓ regulation of angiogenesis

Intellectual Property

Patent application EP 12 159 272.9
EP 12 159 274.5

Reference:

Zoller et al. Molecules 01/2011; 16(3):2467-85.

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Dynamic PET-images in AR42J tumor-bearing rat after injection of 25 MBq of ^{125}J-(Tyr^{19}) DII-Rib. Tumor lesions is marked. Summation imaged was required over a 20-min frame.