Peptides and Binding Antibodies targeting EMMPRIN for the treatment of Cancer & Autoimmune Diseases (BioRap)

The identification of a specific epitope in EMMPRIN that has a role in the induction of both MMP-9 and VEGF, has brought about the development of two novel immunotherapy approached targeting EMMPRIN - A multiple antigenic peptide and a binding antibody.

Macrophages heavily infiltrate solid tumors, and are subjected to the influence of the tumor microenvironment that activates them in an alternative/M2 way. Although tumor cells secrete the pro-angiogenic factors vascular endothelial growth factor (VEGF) and matrix metalloproteinases (MMPs), macrophages quickly become the main cell type to secrete high amounts of them. VEGF and MMPs, particularly MMP-9, are crucial for tumor angiogenesis, progression, invasiveness, and metastasis.

MMP-9 releases and activates VEGF that is trapped in the ECM, and enhances migration of leukocytes, metastatic cells and endothelial cells. VEGF is a chemoattractant for macrophages, and induces MMP-9. Thus, these two factors form a positive feedback loop that dramatically accelerates tumor growth.

The Extracellular Matrix MetalloProteinase INducer (EMMPRIN, also known as CD147, or basigin) was found to be over-expressed in many types of tumors, and was shown to enhance the expression of both VEGF and MMPs. Since clinical trials that used a wide range of MMPs inhibitors failed to inhibit tumor progression, and anti-VEGF antibodies provide only temporary relief with a risk of a rebound effect', EMMPRIN may provide an attractive therapeutic target.

Previous studies showed that many types of cancer cells overexpress EMMPRIN, which is found in positive correlation to increased invasiveness, whereas an anti-EMMPRIN neutralizing antibody reduces MMP-9 and VEGF expression and tumor invasiveness. Furthermore, EMMPRIN overexpression was also demonstrated in several autoimmune diseases (e.g. Rheumatoid Arthritis), linking those conditions to tissue destruction and angiogenesis. EMMPRIN's ability to induce MMP-9 expression was mapped to the first of its two heavily glycosylated extracellular domains (EC-I, EC-II), but the precise epitopes are not known, nor is the region that regulates VEGF induction.

The group of Drs. Rahat, Lahat and Bitterman has identified a specific epitope in EMMPRIN that has a role in the induction of both MMP-9 and VEGF. This allowed the development of two new immunotherapy approaches to target EMMPRIN: one that is based on the use of epitope-specific poly- and monoclonal antibodies, and the other that stimulates a specific immune response using a multiple antigenic peptide (MAP) with the specific epitope sequence. These two types of molecules can be used as immunotherapy strategies in the treatment of cancer and autoimmune diseases. Furthermore, the group has already demonstrated that immunization of tumor-bearing mice with the specific MAP resulted in (a) reduced or even regression of tumors; (b) inhibition of lung metastases; (c) increased the survival time of the animals; (d) prevention of tumor recurrence. All this was achieved by mounting a specific immune response that reduced angiogenesis and produced specific anti-EMMPRIN antibodies in the immunized mice.

Disease	Target	Type of Molecule	Commercialization Status	Link to molecule description
Cancer, autoimmune diseases	EMMPRIN	Antibody	Available for licensing	Read more
Cancer, autoimmune diseases	EMMPRIN	Multiple antigenic peptide (MAP)	Available for licensing	Read more

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