

Protease Activated Receptors (PAR) Mimetics for Cancer Treatment. (Hadasit)

code: 8-2010-165

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Need:

Target-specific approaches are recognized as the basis for novel cancer therapeutics. Protease-Activated-Receptors (PARs), a G Protein-Coupled Receptor, play central roles in tumor progression. PARs are over-expressed in a wide range of epithelial malignancies relative to normal epithelium, thus offering the opportunity for a tumor-specific drug. The PAR C-terminal PH domain binds to other proteins that have a key role in tumorigenesis, suggesting that this domain might be effectively targeted by a novel therapeutic.

Breast cancer, as the leading indication, is treated with monoclonal antibodies (Herceptin for Her2⁺ tumors), hormone-blocking therapy & chemotherapy. The estimated market is ~\$10B (mostly Herceptin) and growing with increased disease incidence. Given PAR expression in epithelial tumors, additional cancer indications include ovary, prostate, colon & melanoma - each a growing >\$1B market and in some cases \$10B in the future. Since the mechanism of action of the PAR peptide is orthogonal to that of other drugs, the new drug is expected to be used in combination with other available drugs.

Innovation:

Peptides mimicking the primary binding site on the PAR₂ C-terminal PH-domain as a potential therapeutic for epithelial cell tumors.

Findings:

PAR₁ or PAR₂ overexpression enhances breast tumor growth in a mouse xenograft model of breast cancer.

PAR₁ and PAR₂ act as a functional heterodimeric unit during tumor development.

Inhibition of PAR₂ expression or activity either by a non-functional PAR₂ protein or by knocking-down of PAR₂ expression attenuates the activity of both PAR₁ and PAR₂.

A peptide from the PAR₂ PH domain inhibits the growth of tumors driven by PAR₁/PAR₂ overexpression.

Indications/Applications:

A novel tumor-specific therapeutic for epithelial malignancies.

Competitive Advantages:

Specific targeting of a biologically key protein for tumor progression as a therapeutic for a wide range of epithelial malignancies.

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