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Anti-Angiogenic Peptides from an Endogenous Protein

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Keywords: Prostate Specific Antigen (PSA), cancer, peptide, angiogenesis, serine protease, Zn^{2+} .

Collaboration Research Opportunity: Roswell Park Cancer Institute is seeking partners to help co-develop peptides derived from human PSA as possible therapeutic agents.

Summary: Angiogenesis is critical in tumor progression and metastasis in most, if not all, solid tumors; especially since a functional vascular supply is required for the continued growth of solid tumors and the spread of cancer cells. Small non-growing tumors may remain dormant for years and the angiogenic switch to aggressive metastatic phenotype involves a change in the local equilibrium between factors inducing blood vessel formation and those inhibiting the process.

There is an ongoing and unmet need to develop compositions and methods for inhibiting angiogenesis as a therapeutic modality for treating solid tumors, and in particular, for prophylaxis and/or therapy of prostate tumors.

Technology: Prior research has shown that peptides derived from PSA (human prostate specific antigen) are anti-angiogenic, and that the loss of PSA expression in multiple human tumors including prostate, breast, endometrial, cervical, and parotid cancers is correlated with poorer prognosis. Peptides derived from PSA represent an ideal therapeutic agent if they maintain the anti-angiogenic activity of the intact parent molecule because they would be less expensive to synthesize than to purify and because PSA as an endogenously produced molecule should be non-immunogenic.

In this invention, researchers at Roswell Park Cancer Institute have demonstrated that PSA in which the serine-protease enzymatic activity has been completely ablated by incubation with Zn^{2+} is equally anti-angiogenic as enzymatically intact PSA. Furthermore, two of the five synthetic peptides that were based upon hydrophilic regions of native human PSA demonstrated approximately 40% of the anti-angiogenic activity of native PSA. Thus, this invention also provides evidence that the transcriptional, regulatory, anti-tumorigenic, and anti-angiogenic activity of human PSA are independent of the enzymatic activity of PSA.

Potential Commercial Applications:

- Peptides would be a powerful non-immunogenic, anti-angiogenesis therapy for multiple cancers, particularly in those in which PSA has been shown to be expressed and correlated with better prognosis.
- Small synthetic peptides can be synthesized and systematically altered to improve activity and bioavailability while minimizing non-specific effects at a fraction of the cost.
- Invention provides a method of inhibiting human endothelial cell migration as well as inhibiting angiogenesis, tumor growth, and/or metastasis.

Competitive Advantages:

- Replacement of PSA should restore endogenous anti-angiogenic activity.
- Peptides derived from PSA should not be antigenic, minimizing the production of inhibitors that would necessitate ever increasing doses of the agent.

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- Synthetic production of peptides derived from PSA offers a significant cost savings compared to the cost of isolating PSA from human seminal plasma, allowing easier identification of the portion of the PSA that is the active moiety in the anti-angiogenic effect.

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