Use of Inhibitors of P-Selectin in Inhibition of Angiogenesis in Diseases Characterized by Female Preponderance

(VA Reference No. 06-123)

Attractive therapeutic target for cancer and inflammatory diseases in female patients

Technology
The Department of Veterans Affairs has identified that the protein P-selectin is a critical component of estradiol-induced angiogenesis. Based on the identification, P-selectin is a potential novel, attractive therapeutic target for cancer and inflammatory diseases in female patients.

Description
This therapeutic target for cancer demonstrates that P-selectin is involved in angiogenesis, and that regulation of P-selectin has an impact in hyper-proliferative disease related angiogenesis.

The VA inventors have elucidated a mechanism in which P-selectin mediates estradiol-induced angiogenesis and have demonstrated that decreased expression of P-selectin by siRNA leads to inhibition of tumor growth for estrogen receptor positive cells in mouse models.

P-selectin is a member of the selectin family of adhesion molecules and is expressed in endothelial cells and activated platelets. It plays an essential role in recruiting leukocytes to the site of injury during inflammation. Increased P-selectin and soluble P-selectin have been detected on several human carcinomas including colon, lung, and breast, and P-selectin deficiency decreases tumor growth and metastasis in an animal model using human colorectal carcinoma cell lines. In addition P-selectin expression is also increased in a number of chronic inflammatory diseases, such as rheumatoid arthritis, where several cytokines are known to increase P-selectin expression in mouse endothelial cells in vitro and in vivo.

Competitive Advantage
P-selectin has the potential to be a very attractive therapeutic target for cancer and inflammatory diseases in female patient and the identification of the therapeutic target should be of interest in advancing cancer therapy.

This therapy:
- Could lead to a therapeutic compound that inhibits P-selectin and inhibits estrogen dependent cancer growth, therefore eliminating the necessity of estrogen antagonists for breast cancer therapy
- Has the potential to inhibit angiogenesis more effectively which will improve disease prognosis and potentially limit common side effects

Status
The Department of Veterans Affairs is looking for a partner for further development and commercialization of this technology through a license and the VA inventors are available to collaborate with interested companies through a Cooperative Research and Development Agreement (CRADA).