NOVEL MODULATORS OF THE ACTIVITIES OF HEPARIN AND EXTRACELLULAR MATRIX PROTEINS

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The inventors, in the Division of Hematology here at Thomas Jefferson University (TJU), have designed a novel class of peptides with high affinity for glycosaminoglycans (GAG) and proteoglycans (PG) of the extracellular matrix (ECM). The peptides counteract excessive bleeding following heparin anticoagulation treatment. Excessive bleeding is a serious complication of all anticoagulants currently available for thromboembolism therapy or thromboprophylaxis. The anticoagulant market, estimated at $1.5 billion in 2001, is expected to expand significantly over the next ten years, as will the need for safe and effective reversal agents.

Protamine is the only FDA-approved agent currently available to neutralize heparin, but its usage must be carefully monitored because of associated toxicity. The TJU heparin-reversal peptides can neutralize low molecular weight and unfractionated heparin in blood samples from treated patients. Importantly, they show no or minimal hemodynamic toxicity in rats. Another disadvantage of Protamine is that it can sensitize patients and cause a potentially life-threatening anaphylactic reaction when re-administered during subsequent procedures requiring anticoagulation. The TJU heparin-reversal peptides do not appear to be immunogenic.

In addition to reversal of excess anticoagulant to prevent hemorrhage, the therapeutic peptides have broader clinical application, including:

- Promotion of cartilage development during tissue transplantation/replacement orthopedic surgery.
- Inhibition of proteoglycan-mediated angiogenesis to prevent tumor growth
- Promotion of endothelial cell attachment in synthetic graft treatment of vascular diseases, such as atherosclerosis, thrombosis, restenosis, and aneurysms
- Targeted drug delivery to the ECM or cell surfaces expressing proteoglycans or glycosaminoglycans, such as cartilage or the vascular wall

We would appreciate the opportunity to share additional information about this promising therapeutic peptide technology with you. A US patent has issued (6,885,801) on this technology and a second patent application is pending. Please find the issued US patent attached for your review. To arrange a meeting with the inventors, or to obtain related information, please contact Michael Caggiano (michael.caggiano@jefferson.edu) in the TJU Office of Technology Transfer (OTT), citing TJU Reference Numbers SAN_JAM.001 and SAN_JAM.002.