

EASTERN MICHIGAN UNIVERSITY

Chemistry Department

M. S. Thesis Seminar

Sarah Burke

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Monday, Nov. 2nd, 4:00 pm

Science Complex Room 158



Progress Toward a Structure-Function Relationship for Novel, Small-Molecule Inhibitors of Plasminogen Activator Inhibitor-1

Plasminogen activator inhibitor-1 (PAI-1) is a serpin protein whose function is to inhibit tissue-type plasminogen activator (tPA) and urokinase-type plasminogen activator (uPA), and hence, fibrinolysis. This inhibition leads to decreased plasminogen to plasmin conversion, which results in deleterious effects on the organism, such as blood clots. Elevated levels of PAI-1 are implicated in a variety of diseases and conditions. We have synthesized a variety of novel, small-molecule PAI-1 inhibitors in order to establish a structure-function relationship throughout the compounds. This goal was accomplished through an iterative process in which only one aspect of the molecule was altered at a time. Knowledge of this structure-function relationship will help to guide future endeavors in PAI-1 inhibitors, which will eventually lead to a decrease in symptoms of conditions such as atherosclerosis, diabetes, and cancer.