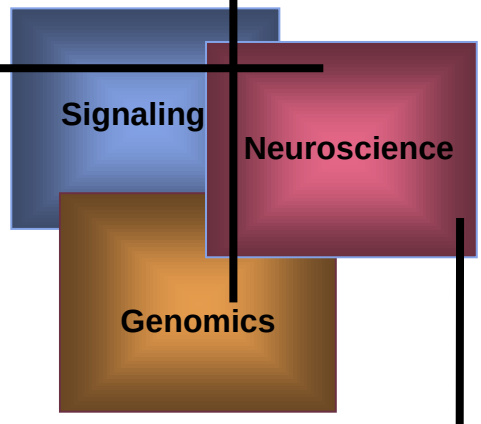
The Department of Pharmacology

Proudly Presents the Seminar Series:



Frontiers in Pharmacology

John Morser, PhD

Cardiovascular Institute, Stanford School of Medicine

Role of Thrombin Activatable Fibrinolysis Inhibitor (TAFI)

TAFI is a circulating zymogen that upon activation by the thrombin/thrombomodulin complex or plasmin becomes a basic carboxypeptidase. In vitro, substrates include fibrin, bradykinin, osteopontin, C5a and chemerin. After treatment with activated TAFI the biological activity of these compounds is modified. In vivo, inhibition of TAFI accelerates fibrinolysis. TAFI deficient mice are protected from lung fibrosis, pulmonary hypertension and glomerular nephritis but have exacerbated abdominal aortic aneurysm, bronchial asthma and fibrosis due to unilateral urether obstruction. Thus the effect of TAFI depends on context. A TAFIa inhibitor (BX528) was discovered based on structure based drug design and its pharmacokinetics and pharmacodynamics were determined. It was active in 4 independent models of thrombosis in 3 different species, suggesting its use in thrombotic disease.

Friday, January 22th
10:00 am
GBSF Auditorium
(Rm. # 1005)