

# WINTER 2005 SEMINAR SERIES

## F21C BIOPROCESSING & BIOSENSING CENTER

• DIVISION OF FOOD SYSTEMS & BIOENGINEERING •

### PRESENTER

**Dr. John Diener, Archemix, Cambridge, MA**

### TITLE

**Allosteric Ribozymes and Aptamers from High Throughput Screen to Novel Therapies**

### ABSTRACT

At Archemix, we are using the power of our in vitro selection (SELEX) technology both for the generation of molecular sensors as well as for the discovery of molecular therapeutics. Two RNA based, molecular sensors that specifically recognize ADP in a background of over 100-fold molar excess of ATP have been generated. These sensors are nucleic-acid based and comprise a general method for monitoring protein kinase activity. Both systems perform well when configured for high throughput screening, and have been used to re-discover a known protein kinase inhibitor in a high throughput screening format. Additionally, we have identified a DNA aptamer that binds to the A1 domain of vWF and blocks the interaction of vWF with platelets. The DNA aptamer has been rendered highly resistant to plasma nucleases in vitro through an extensive structure activity relationship (SAR) study involving the systematic replacement of standard deoxy-nucleotides with stabilizing nucleotides. In binding assays, the aptamer has high affinity for vWF (KD ~ 1 nM. Functionally, the anti-vWF aptamer inhibits botrocetin-induced platelet aggregation (BIPA) in human platelet rich plasma (IC90 ~ 100-300 nM). Finally, stabilized aptamer has been dosed in cynomolgus macaques and inhibits platelet function as assessed by BIPA. Thus the anti-vWF aptamer may be useful as a novel anti-platelet agent for the treatment of ACS patients.

### DATE • TIME • LOCATION

**Tuesday, April 19, 10:00am**  
**Monsanto Auditorium, Life Science Center**  
**• Refreshments**