

Public Abstract

First Name:Dipti

Middle Name:Narayan

Last Name:Barman

Adviser's First Name:Dr. Timothy E

Adviser's Last Name:Glass

Co-Adviser's First Name:

Co-Adviser's Last Name:

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Department:Chemistry

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Title:pH Sensitive Fluorescent Sensors

Pheochromocytoma is a cancer of the adrenal gland. Pheochromocytomas produce a variety of catecholamines, including norepinephrine. The result is high blood pressure which is caused by the release of catecholamines into the bloodstream (i.e. elevated concentration of plasma or urinary catecholamines). Detecting this cancer by measurement of catecholamine concentrations in serum can be challenging for the clinician.

Fluorescence probes are becoming useful tools for investigating cellular events by fluorescence microscopy. Our group has developed a dopamine/norepinephrine sensor which binds norepinephrine in the vesicles of chromaffin cells. We have designed and synthesized both coumarin and quinolone based sensors that reversibly covalently bind with both the amine and catechol moieties of catecholamines via the formation of an iminium ion and boronate ester respectively. With the fluorescence response of the binding process we can then accurately determine the concentration of catecholamines, thereby facilitating diagnosis. However the binding rate is slow; making synaptic measurements difficult (synapse firing takes 10 milliseconds). My goal is to modify these sensors to be pH sensitive. Then the probe can bind neurotransmitter in the vesicle and remain off (pH=5.5). When stimulated the cell will exocytose the sensor and at pH=7.4, the sensor will fluoresce. The synthesis of pH sensitive fluorescent chemosensors for amines and their properties is described.