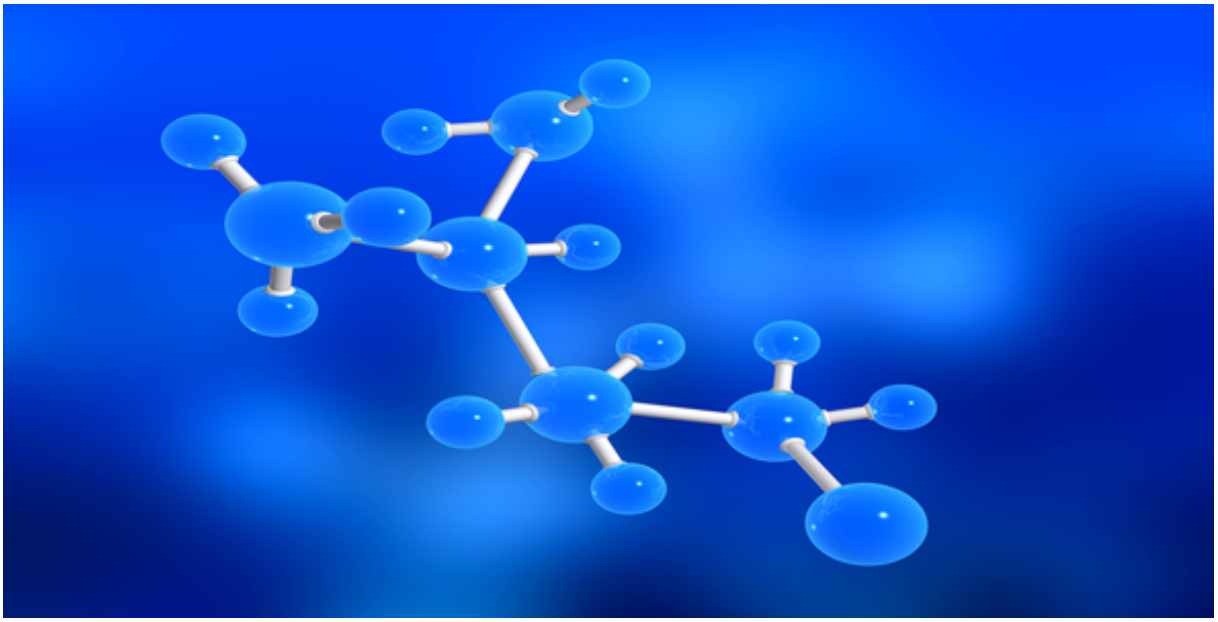
THE UNIVERSITY of NORTH CAROLINA at CHAPEL HILL

Research Reagents/Methodology/Tools

Fluorogenic Sensor of Mammalian

Phosphatidylinositol-Specific Phospholipase C



Dysregulation of phosphatidylinositol-specific phospholipase C isozymes (PI-PLCs) have been implicated in various diseases including cancer and Alzheimer's disease. However, two limitations for understanding PI-PLC regulation remain: 1) it is difficult to monitor PI-PLC activity in living cells; and 2) selective small molecule PI-PLC inhibitors are lacking. Researchers at UNC have addressed these two limitations through the development of a fluorogenic PI-PLC sensor. This sensor can be used for general research or can be used to screen libraries of small molecules for inhibitor development.

Benefits

- Real-time monitoring of cellular activity of PI-PLCs
- Eliminates need for current radiolabeled protocols
- Can be used to profile different cell types and disease states
- Small molecule PI-PLC inhibitor development though high throughput screen

carolina blue™ opportunity

For More Information

If you would like more information about this technology or UNC - Chapel Hill's technology transfer program, please contact:

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The Technology

Phophatidylinositol-specific phospholipase C (PI-PLC) isozymes are key signaling proteins that regulate the physiological responses of many extracellular stimuli such as hormones, neurotransmitters, and growth factors. Aberrant regulation of PI-PLCs has been implicated in various diseases including cancer and Alzheimer's disease. Therefore, PI-PLCs are considered to be interesting drug targets. How, when, and where PI-PLCs are activated under different cellular contexts is largely unknown.

There are still limitations to understanding and targeting PI-PLCs. The development of fluorogenic PI-PLC reporters will address a number of the issues associated with studying PI-PLCs. Currently available fluorogenic assay kits are specific for phosphatidylcholine-specific PLC s(PC-PLCs) and do not recognize PI-PLCs found to be important in disease. Secondly, there have been several efforts to attach fluorophores directly to PI-PLC substrates to generate fluorogenic PI-PLC reporters, but these reporters are mainly for bacterial PLCs and demonstrate low signal-to-background ratios. Unfortunately, the most reliable methods that are currently available for detecting PI-PLCs require radioactive labeling.

Dr. Qisheng Zhang and colleagues at UNC – Chapel Hill have developed a fluorogenic reporter for mammalian PI- PLCs that can be cleaved in tandem to generate inositol phosphate 1, quinomethide 2, and 6-aminoquinoline 3. When applied in enzymatic assays with either PI-PLCs or cell lysates, this reporter displays more than 10-fold fluorescence enhancement in response to PI-PLC activities. This sensor can be used to screen large collections of small molecules for inhibitor development, and monitor PI-PLC activity in living cells in real-time.

Opportunity

UNC's Office of Technology Development seeks to stimulate development and commercial use of UNC-developed technologies. UNC is flexible in its agreements, and opportunities exist for joint development, academic or commercial licensing (exclusive, non-exclusive, and field-of-use), publishing, or other mutually beneficial relationships. UNC is pursuing intellectual property protection for this innovation.