CENTER FOR CANCER RESEARCH

Connecting the Cancer Community

Mimetic Peptide as a Cancer Therapeutic

TECH Council MD

Maryland TEDCO Technology Development Corporation

TEDCO/NIH/NCI Technology Showcase

Kyung Lee, Ph.D., Lab of Metabolism

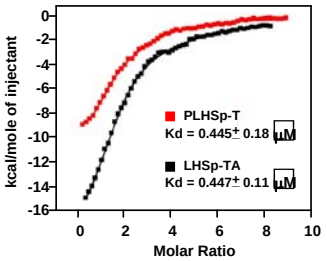
September 25, 2007

National Institutes of Health — National Cancer Institute

Technology

CENTER FOR CANCER RESEARCH

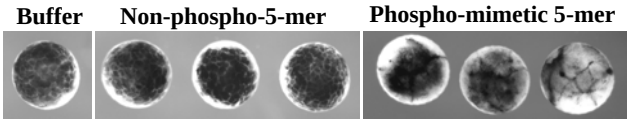
- **Polo-like kinase 1 (Plk1) is upregulated in various origins of human cancers and thought to be a promising cancer drug target.**
- **The non-catalytic polo-box domain is essential for the mitotic function of Plk1.**
- **We identified 5-mer peptides that bind to the Plk1 PBD in a phospho-specific manner.**
- **The 5-mer specifically binds to Plk1 as the only apparent binding protein, but does not bind to the two-closely related kinases, Plk2 and Plk3.**



(S. Kurian and J. McMahon)

Technology

- **Provision of a phospho-mimetic peptide into cultured HeLa cells or Xenopus embryos inhibits cell proliferation and induces apoptosis.**



- **Co-crystal structure for the 5-mer phospho-peptide and the Plk1 PBD has been determined (T. Moulaei and A. Wlodawer).**

Technology Applications

Based on the specific and high affinity interaction between the 5-mer peptide and the Plk1 PBD:

- Isolation of PBD inhibitors by *in vitro* HTS

- Virtual screening and structure-based drug design

- Further development of 5-mer-based mimetic peptide

Commercial Applications

The 5-mer peptide can be used to develop:

- **anti-Plk1 PBD agent that specifically inhibits the mitotic functions of Plk1**
- **anti-Plk1 therapeutic agent to treat various cancers in humans**

Collaboration Opportunities

CRADA opportunities:

- **Further development of 5-mer p-Thr mimetic peptide that specifically binds to and interferes with the function of Plk1**
- **Screening of Plk1 PBD inhibitors using the peptide-PBD interaction**

Available in the Laboratory of Metabolism, CCR:

- **Plk1 PBD-binding (ELISA assay and ITC) and ELISA-based Plk1 kinase assay for activity measurement**
- **Plk1 inhibition assays in cultured cells (activity, immuno-fluorescence, flow cytometry, apoptosis assays, etc)**
- **Co-crystal structure for the 5-mer peptide and the Plk1 PBD**

Contact Information

<u>For further information contact</u>:

Kyung S. Lee, Ph.D.
Laboratory of Metabolism
Center for Cancer Research
NCI, NIH
Bethesda, MD 20892

Email: kyunglee@mail.nih.gov
Phone: 301-496-9635