Abstract Submitted
for the MAR12 Meeting of
The American Physical Society

Computational Design of Druglike Small Molecule Plk1 PBD Inhibitors SEAN VANADIA, The College of New Jersey (TCNJ) Undergraduate — Polo-like Kinase 1 (Plk1) participates in regulation of the cell cycle and is often overexpressed in cancers. Inhibition of Plk1 was found to suppress cancer development. Most known kinase inhibitors interact with highly conserved ATP binding sites of the kinases. This makes the design of Plk1-specific inhibitors difficult. However, Plk1 has another active site, the Polo-Box Domain (PBD). PBD is not present in other kinases that were studied here. In this research, the PBD site of Plk1 was used as a target for designing small molecules that could potentially bind Plk1. A previously designed small molecule, Purpurogallin (PPG), was found to bind only the PBD of Plk1 and a highly similar site of LYN kinase, but no other kinases. The PPG structure was used as a template to design new putative Plk1-specific inhibitors. Druglike properties of the new molecules were evaluated with the Osiris Property Explorer program. Interactions of the molecules with Plk1, LYN, and eight other kinases were studied using the Argus Lab docking program. Further search for Plk1-specific inhibitors that could potentially target cancers with overexpressed Plk1 is discussed.

Sean Vanadia
The College of New Jersey (TCNJ) Undergraduate

Date submitted: 11 Nov 2011 Electronic form version 1.4