Abstract Submitted
for the MAR16 Meeting of
The American Physical Society

Allosteric Small-Molecule Inhibitors of the AKT Kinase D. S. DALAFAVE, The College of New Jersey — This research addresses computational design of small druglike molecules for possible anticancer applications. AKT and SGK are kinases that control important cellular functions. They are highly homologous, having similar activators and targets. Cancers with increased SGK activity may develop resistance to AKT-specific inhibitors. Our goal was to design new molecules that would bind both AKT and SGK, thus preventing the development of drug resistance. Most kinase inhibitors target the kinase ATP-binding site. However, the high similarity in this site among kinases makes it difficult to target specifically. Furthermore, mutations in this site can cause resistance to ATP-competitive kinase inhibitors. We used existing AKT inhibitors as initial templates to design molecules that could potentially bind the allosteric sites of both AKT and SGK. Molecules with no implicit toxicities and optimal drug-like properties were used for docking studies. Binding energies of the stable complexes that the designed molecules formed with AKT and SGK were calculated. Possible applications of the designed putative inhibitors against cancers with overexpressed AKT/SGK is discussed.

Danielle Dalafave
The College of New Jersey

Date submitted: 02 Dec 2015 Electronic form version 1.4