Background: Pharmacological inhibition of PDK1 (POK), is a kinase that activates members of the AKT/PKB and GSK3β family. PDK1 inhibition has shown anti-cancer effects in multiple preclinical and clinical settings. 

POK can interact with substrates through PDK1 (PDP)-mediated or PDK1-independent mechanisms. PDK1 has been used as a model system for understanding and validating the mechanisms of POK.

Results: Here we report characterization of two panel POK kinase inhibitors, GSK-2234470 and SNS-510 (Fig 2). First, screen POK-mediated AKT phosphorylation in cell lines and showed strong and prolactivity activity against both AKT and other AKT-related kinases, including GSK-3β. 

IC50 of POK activity was assessed by inhibition of phosphorylation of AKT in human cell lines, including breast cancer cell lines and prostate cancer cell lines. Similarly, inhibition of AKT activity was observed in both cell lines. POK activity was further assessed by inhibition of phosphorylation of AKT in primary breast cancer tumors. POK activity was observed in both breast cancer tumor types.

Conclusions: POK inhibition shows promise for the treatment of cancer. POK activity was observed in both breast cancer tumor types.