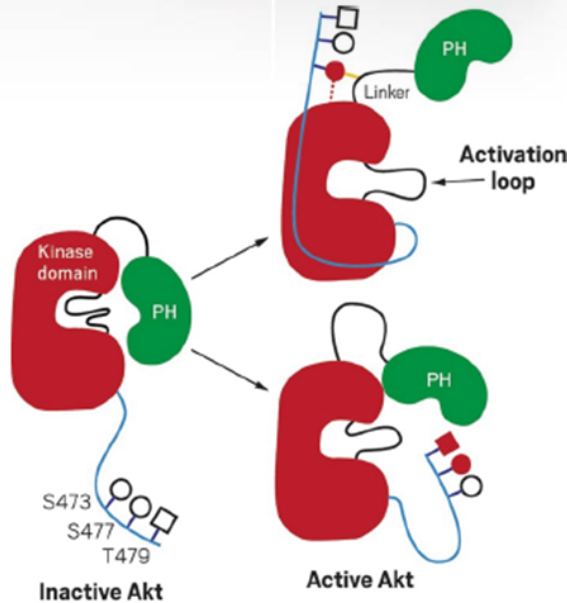


Revealed Activation Mechanism Could Help Cancer Research



Inactive Akt1 can be activated by two mechanisms. In one mechanism, phosphorylated serine 473 interacts with the linker between the kinase and PH domain. In the other, phosphorylated serine 477 and threonine 479 result in the displacement of the PH domain.

N. Chu, A. L. Salguero, A. Z. Liu, Z. Chen, D. R. Dempsey, S. B. Ficarro, W. M. Alexander, J. A. Marto, Y. Li, L. M. Amzel, S. B. Gabelli, P. A. Cole. *Cell* **174**(4):897-907 (2018).

Work was performed in part at Brookhaven National Laboratory

Scientific Achievement

Scientists revealed the activation mechanism of Akt1 protein kinase, which modulates metabolism and cancer proliferation.

Significance and Impact

Akt 1 protein kinase plays an essential role in cancer proliferation, which defines cancer aggressiveness. Understanding the full functions of the protein could help advance cancer therapies.

Research Details

- Previous studies showed a different activation mechanism for Akt1 kinase; however, the studies were performed on the protein in a different state.
- Using biochemical, x-ray crystallographic, and cellular approaches, the team determined that pSer473-Akt activation is driven by an intramolecular interaction.
- The x-ray crystallographic data were taken at NSLS-II AMX and FMX beamlines and at APS sector 31.