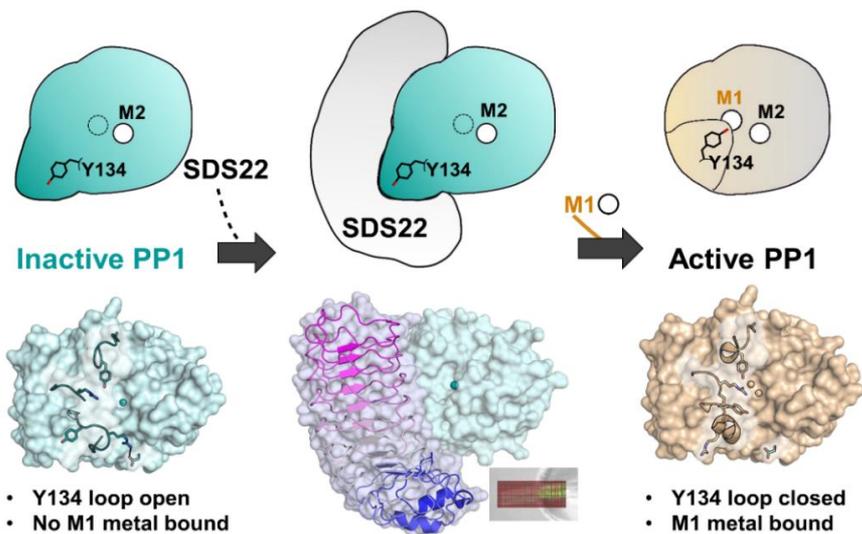


Inhibitor or Activator: Why not Both?



To activate PP1, SDS22 needs to bind and stabilize it. Then, through an unknown mechanism, a zinc ion (Zn^{2+}) is loaded into PP1's metal site, M1. Only then can SDS22 release from the now active PP1.

M. S. Choy, T. M. Moon, R. Ravindran, J. A. Bray, L. C. Robinson, T. L. Archuleta, W. Shi, W. Peti, K. Tatchell, R. Page. *PNAS* **116** (41) 20472-20481 (2019).

Work was performed in part at Brookhaven National Laboratory

Scientific Achievement

Scientists discovered how the regulatory protein, SDS22, acts as both inhibitor and activator for protein phosphatase 1 (PP1).

Significance and Impact

PP1, with PP2A, accounts for more than 90% of the phosphatase activity in eukaryotes. Understanding how PP1 is activated will lead to new treatments for PP1-related diseases, such as cancer.

Research Details

- Previous studies showed the conundrum of SDS22 being both an inhibitor and activator of PP1.
- Using biophysical, x-ray crystallographic & cellular studies, the team discovered that SDS22 first binds to inactive PP1. But in order to activate PP1, Zn binding to PP1 is necessary, which results in SDS22 dissociation and the release of active PP1.
- X-ray crystallographic data were collected at NSLS-II's FMX beamline.