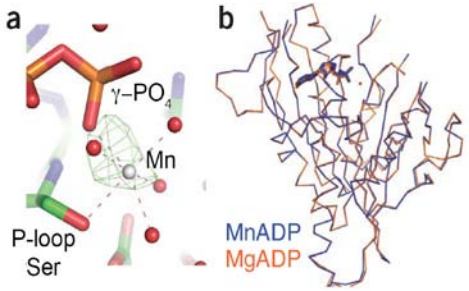
A Metal Switch for Controlling Molecular Motor Proteins

Scientific Achievement

Engineered a cysteine substitution for kinesins – motor proteins that require a divalent metal ion to convert the energy of ATP hydrolysis into force generation – to render them able to use manganese instead of magnesium, which inactivates motor processes.



Crystal structure of kinesin-MnADP. (a) The active site of kinesin-MnADP is shown. Water molecules are shown as red spheres and Mn2+ as gray sphere. The green cage represents the positive peak in the FoFc map (3 σ) with the MnADP data being refined with the kinesin-MgADP structure (3DC4). (b) Alignment of main chain atoms of kinesin-MnADP with kinesin-MgADP.

Significance and Impact

By controlling the ratio of manganese and magnesium, researchers can "switch on and off" the processes of the enzyme. This method is a tool for selectively turning off a motor protein and provides a method for further research into P-loop hydrolase enzymes.

Research Details

- Researchers solved the structure of these proteins using X-ray diffraction at NSLS, helping them identify which metals would serve as 'on' and 'off' switches.
- The metal switch can also adjust the speed of catalysis. Similar to a dimmer light switch, catalysis can be turned on, off, or slowly turned on.
- The discovery allowed for dissection of the kinetic cycle of the kinesin motor, which is not easy to determine otherwise. Researchers can now know which steps of the cycle slow down or speed up with introduction of Mg and Mn.

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Work was performed at Brookhaven National Laboratory

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