Sunyoung Kim et al., J Proteomics Bioinform 2016, 9:10(Suppl)
http://dx.doi.org/10.4172/0974-276X.C1.088

Proton tunneling accelerates ATP hydrolysis in Eg5 kinesin

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ATP hydrolysis requires that a proton from the water nucleophile must be abstracted and transferred in order to create a hydroxide capable of attacking the substrate. In crystallographic capture of ATP hydrolysis, a two-water cluster is found in the active site of two different kinesin isoforms. These data suggest that a proton is shared between the lytic water, positioned for gamma-phosphate attack, and the second water that serves as a general base. The unusual short distance between the two orthosteric water molecules, observed by crystallography, is confirmed by solvent kinetic isotope experiments. The positive kinetic isotope effect (KIE) confirms proton abstraction from water commits kinesin to catalysis and its pH-dependence verifies that switch salt-bridge residues direct chemotransduction. Additionally, a classical description for this proton transfer is refuted by the KIE magnitude, temperature-independent Arrhenius pre-exponential factor ratios, and activation energy differences. Taken together, we conclude that the first step in kinesin catalysis has a tunneling component, a quantum mechanical event by which a particle transfers through a reaction barrier. This first detection of tunneling in an ATPase is of consequence for two reasons. First, proton tunneling is likely widespread in biomolecules, rather than solely a characteristic of metalloenzymes. Second, energy barrier penetration by proton tunneling is an alternate explanation to classical transition-state stabilization theory for the fast reactivities of motor proteins.

Biography

Sunyoung Kim has completed her PhD at the University of Michigan and the University of Padova, Italy and Post-doctoral studies at the University of Minnesota. She is a Member of the Louisiana Cancer Research Consortium and Founder of a spin-out company to personalize medicine with structural biomarkers. She leads a collaborative, multilab nanomotor research program. She has published more than 25 papers and serves as an Editorial Board Member of the *Journal of Biological Chemistry*. In addition, she has performed a variety of administrative roles at the departmental, institutional and state levels, as well as held elected positions for national scientific societies.

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