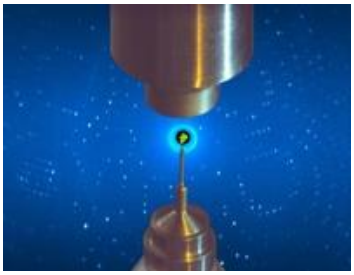

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High-resolution structure studies of NADH-cytochrome b5 reductase

Wednesday, 9 June 2021 10:50 (20 minutes)

NADH-cytochrome b5 reductase (b5R) on endoplasmic reticulum membrane in mammalian liver cell plays a variety of roles concerning lipid unsaturation and xenobiotic metabolism. b5R transfers electrons from two-electron carrier of NADH to one-electron donor of cytochrome b5. In the redox cycle of b5R, a hydride transfer from NADH to oxidized FAD and deprotonation from the reduced FADH take place in b5R. Therefore, high-resolution structure analyses including the information about hydrogen atoms and valence electron densities are required for understanding molecular mechanisms of the b5R redox reaction. High-resolution X-ray crystal structures were previously determined using the oxidized form of b5R (M. Yamada et al., J. Mol. Biol., 2013; K. Takaba et al., Sci. Rep., 2017). In this work, the neutron crystal structures of the oxidized form of b5R were determined including hydrogen atoms of solvent molecules, and the X-ray crystal structures of the reduced form of b5R were determined including hydrogen atoms of the NADH cofactor. Recently, neutron diffraction data sets of the reduced form have been collected at BIODIFF of FRM II. The neutron structure analysis of the oxidized form clearly shows the hydrogen-bonding network from the FAD cofactor to the protein surface. The X-ray structure analysis of the reduced form reveals the NAD+ and NADH bound states using wildtype and T66V mutant. These structural features indicate a proton transfer pathway from FAD to the protein exterior.

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