Vibrational Spectroscopic Investigation of Molecular Mechanisms of Aerobic Respiration

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In the mitochondrial respiratory chain of aerobic organisms, three membrane protein complexes couple electron transfer with proton pumping. The proton motive force thus generated across the inner mitochondrial membrane is utilized to synthesize ATP, the energy currency of the cell.

Cytochrome *c* oxidase (CcO) is one of such molecular machineries and reduces dioxygen to water. This reaction is the reverse reaction of the photosynthetic oxygen evolution. The dioxygen reduction by CcO is coupled with proton pumping. X-ray crystallography has determined the three dimensional structures of bovine CcO at a resolution of 1.8Å. Vibrational spectroscopy, on the other hand, has revealed the reactivity of functional groups in the protein and also provided pieces of information with respect to the protein dynamics. Actually, time-resolved resonance Raman spectroscopy has been applied to study the dioxygen reduction reaction and the protein dynamics after ligand dissociation from the heme. This is based on the high selectivity of the technique to reveal vibrational spectra of the heme and its vicinity. A high-sensitivity infrared spectroscopy developed in our laboratory has enabled us to reveal dynamics of the metal centers and protein main chain after ligand dissociation. The results show the presence of "a conformational relay system", between the dioxygen reducing site and proton gate site in the protein, by which an efficient proton pumping is realized.

Reference: Kubo, M., Nakashima, S. *et al.* (2013) *J. Biol. Chem. 288*, 30259 – 30269.