# BK21 Plus Seminar

## "Protein oxidation in the bacterial envelope is reversed by the two different electron transport systems: from the structure to the discovery of a new system"

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**Structure and multistate function of the transmembrane electron transporter CcdA.**
The mechanism by which transmembrane reductases use a single pair of cysteine residues to relay electrons between protein substrates across biological membranes is a long-standing mystery in thiol-redox biochemistry. Here we show the NMR structure of a reduced-state mimic of archaeal CcdA, a protein that transfers electrons across the inner membrane, by using a redox-active NMR sample. The two cysteine positions in CcdA are separated by 20 Å. Whereas one is accessible to the cytoplasm, the other resides in the protein core, thus implying that conformational exchange is required for periplasmic accessibility. In vivo mixed disulfide-trapping experiments validated the functional positioning of the cysteines, and in vitro accessibility results confirmed conformational exchange. Our NMR and functional data together show the existence of multiple conformational states and suggest a four-state model for relaying electrons from cytosolic to periplasmic redox substrates

**Repairing oxidized proteins in the bacterial envelope using respiratory chain electrons.**
The reactive species of oxygen and chlorine damage cellular components, potentially leading to cell death. In proteins, the sulfur-containing amino acid methionine is converted to methionine sulfoxide, which can cause a loss of biological activity. To rescue proteins with methionine sulfoxide residues, living cells express methionine sulfoxide reductases (Msrs) in most subcellular compartments, including the cytosol, mitochondria and chloroplasts. Here we report the identification of an enzymatic system, MsrPQ, repairing proteins containing methionine sulfoxide in the bacterial cell envelope, a compartment particularly exposed to the reactive species of oxygen and chlorine generated by the host defence mechanisms. MsrP, a molybdo-enzyme, and MsrQ, a haem-binding membrane protein, are widely conserved throughout Gram-negative bacteria, including major human pathogens. MsrPQ synthesis is induced by hypochlorous acid, a powerful antimicrobial released by neutrophils. Consistently, MsrPQ is essential for the maintenance of envelope integrity under bleach stress, rescuing a wide series of structurally unrelated periplasmic proteins from methionine oxidation, including the primary periplasmic chaperone SurA. For this activity, MsrPQ uses electrons from the respiratory chain, which represents a novel mechanism to import reducing equivalents into the bacterial cell envelope. A remarkable feature of MsrPQ is its capacity to reduce both rectus (R-) and sinister (S-) diastereoisomers of methionine sulfoxide, making this oxidoreductase complex functionally different from previously identified Msrs. The discovery that a large class of bacteria contain a single, non-stereospecific enzymatic complex fully protecting methionine residues from oxidation should prompt a search for similar systems in eukaryotic subcellular oxidizing compartments, including the endoplasmic reticulum.

- **Date: 4:00PM/Aug, 8(Tue.)/2017**
- **Place: Room 401, Chemistry Bldg.**
- **Inquiry: Prof. Seung-Jae Lee, Cheol-Sang Hwang (279-2352)**

*** This seminar will be given in Korean.**
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