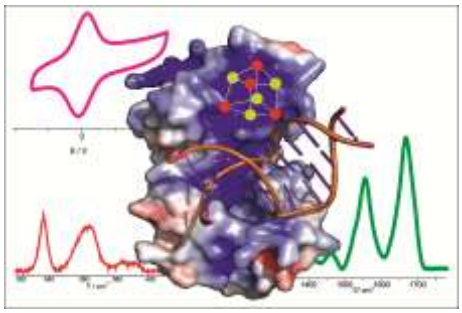
Project:



Targeting the metal cluster in DNA repair enzymes

Deinococcus radiodurans is an extremely radiation and desiccation resistant bacterium, which can withstand 200-fold higher irradiation doses than other bacteria. The resistance mechanism is not known, but an efficient DNA repair machinery, is considered to play a key role in it. Endonuclease III (EndoIII) is an [4Fe-4S] cluster containing DNA repair enzyme from the helix-hairpin-helix family of DNA glycosylases, crucial for removal of oxidation damaged bases in DNA. Early evidence indicated that Fe-S clusters in these enzymes are not amenable to oxidation or reduction in solution and suggested structural or regulatory role of the cofactor. More recent electrochemical studies of glycosylases immobilized on DNA-modified electrodes indicated that the [4Fe-4S] cluster is activated towards oxidation upon binding to DNA. We have recently demonstrated that the cluster of the immobilized EndoIII from *D. radiodurans* (*Dr*EndoIII) is prone to reduction, which is not necessarily DNA-mediated (1).

This Master project envisages further studies of the cluster in *Dr*EndoIII, which will lead to establishment of its role in DNA glycosylases. In particular, we will utilize novel transparent and conductive electrodes (e.g. indium tin oxide, ITO) for immobilization of *Dr*EndoIII and UV-Vis spectro-electrochemistry for its characterization, in the presence / absence of normal / damaged DNA. The candidate will have an opportunity to learn a wide range of experimental approaches, from protein purification to spectroscopic and electrochemical techniques.

Supervisors:

Elin Moe and Smilja Todorovic

(1) Moe, E., Sezer, M., Hildebrandt, P., Todorovic, S. (2015) Surface enhanced vibrational spectroscopic evidence for an alternative DNA-independent redox activation of endonuclease III *Chem. Comm.* DOI: 10.1039/C4CC09498K