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NMR and Electron Microscopy Structural Studies of the *E. coli* Class Ia Ribonucleotide Reductase

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Ribonucleotide reductase (RNR) catalyzes the conversion of ribonucleotides into deoxyribonucleotides. RNR is thus an essential component of life in all organisms and serves as a drug target for a wide range of diseases including cancer. Despite its medical relevance an atomic resolution structure of the active complex has yet to be achieved. Here a dual NMR (Nuclear Magnetic Resonance) and electron microscopy approach is undertaken to investigate the molecular structures of the active ($\alpha_2\beta_2$) and inactive ($\alpha_4\beta_4$) forms of the *E. coli* class Ia RNR. A special double mutant $E_{52}Q/F_3Y_{122}$ is shown to stabilize $\alpha_2\beta_2$ for at least 2 hours. The $E_{52}Q/F_3Y_{122}$construct allows for a negative stain electron microscopy map to be obtained at sub-20 Å resolution for the first time. The $\alpha_2\beta_2$ active complex is found to have an asymmetric mode of binding, contrary to the previously proposed symmetric docking model. DNP (Dynamic Nuclear Polarization) enhanced solid-state NMR measurements on mixed labeled samples reveal atomic resolution distance constraints at the α/β interface. The assignment of these NMR resonances requires MD (Molecular Dynamics) simulations constrained to the electron microscopy map.

Biography:

Alexander T. Taguchi career as a magnetic resonance spectroscopist began at the University of Illinois at Urbana-Champaign (USA) Biophysics graduate program. He studied photosynthetic reaction centers using pulsed Electron Paramagnetic Resonance to obtain high-resolution insight into the structure-function relationships of the electron transport processes. He then transitioned into the field of iron-sulfur clusters as a postdoctoral fellow at the Nippon Medical School in Tokyo, Japan. Currently he has been working as an NIH postdoctoral fellow on solid-state Nuclear Magnetic Resonance fast magic angle spinning on protein complexes at the Massachusetts Institute of Technology.