Poster Presentation

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Complex structure of NADPH-cytochrome P450 reductase and heme oxygenase-1

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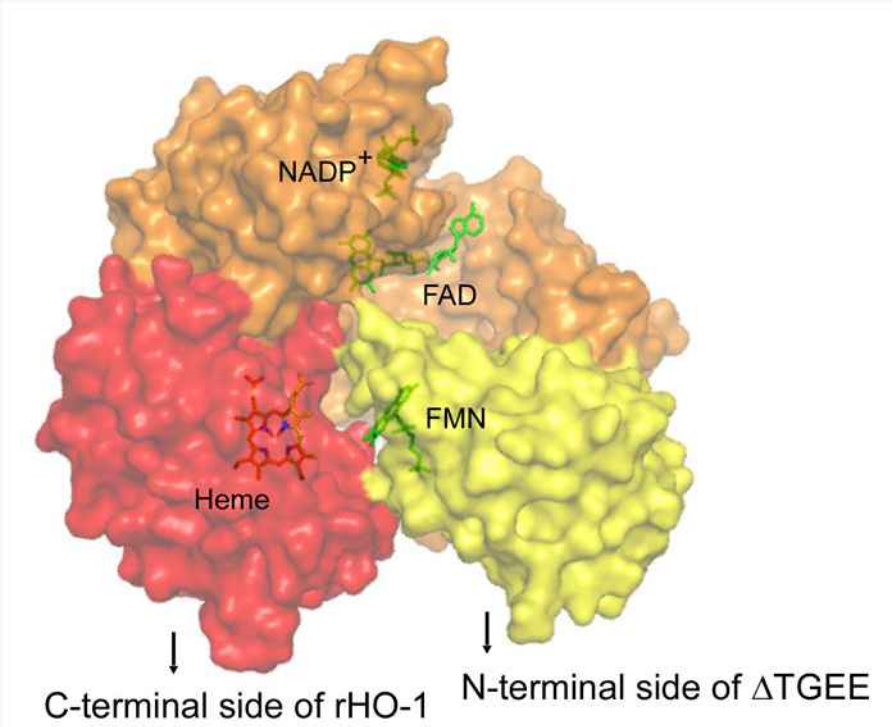
NADPH-cytochrome P450 oxidoreductase (CPR) supplies electrons to various heme proteins including heme oxygenase (HO), which is a key enzyme for heme degradation. Electrons from NADPH flow first to FAD in CPR, then to FMN in CPR, and finally to heme in the redox partner. For electron transfer from CPR to its redox partner, ''closed-open transition'' of CPR is indispensable because FMN in the closed conformation of CPR is covered by FAD-binding domain, thus FMN is not exposed to the surface in the closed conformation. Recently, Hamdane et al. determined the crystal structures of a hinge-shortened rat CPR variant (ΔTGEE), which favors an open conformation [1]. In the open conformation of CPR, FMN is exposed to the surface, thus this conformation appears to be favorable to interact with the redox partners, though no complex structure of CPR and its redox partner has been determined. Here, we demonstrate that ΔTGEE makes a stable complex with heme-rat HO-1 (rHO-1) complex and can support HO reaction, though its efficiency is extremely limited. Further we determine the crystal structure of ΔTGEE in complex with heme-rHO-1 at 4.3 Å resolution [2]. X-ray scattering and biochemical data suggest that the complex structure of ΔTGEE and heme-rHO-1 is similar to that of wild type CPR and heme-rHO-1. Distance between heme and FMN in this complex (6 Å) implies direct electron transfer from FMN to heme. On the other hand, FAD is far from FMN and heme, indicating that the ''closed-open transition'' of CPR is required for electron transfer from FAD to FMN.

[1] *D. Hamdane, C. Xia, S. C. Im, et al., J. Biol. Chem., 2009, 284, 11374-11384.,* ***[2]*** *M. Sugishima, H. Sato, Y. Higashimoto, et al., Proc. Natl. Acad. Sci. USA, 2014, 111, 2524-2529.*



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