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Structural characterization of bacterial NAD(P)H oxidase: highlighting the origin and mechanism of eukaryotic NOX

For a long time NOX enzymes have been thought to be a landmark of pluricellular organisms where the production of reactive oxygen species could be associated to physiological function related to the multicellularity (immune defense, vascular tone regulation, hormone synthesis, etc..).
However, our group identified in 2017, a first ancestor to eukaryotic NOX in bacteria with the identification of the two component MsrQ/Fre enzymatic complex in which the MsrQ protein was evolutionary connected to the transmembrane domain of NOXes while the Fre protein was an analog of the NOX dehydrogenase domain (DH). Later, we demonstrated also the existence, in the bacterial world, of a large family of real NOX enzymes, membrane protein containing both TM and DH domain. Among the hundreds of sequences discovered, we biochemically characterized the NOX from Streptoccus pneumoniae, SpNOX, and demonstrate that it shares many of the biochemical features of eukaryotic NOX. However some difference, modulation exist between bacterial and eukaryotic NOX enzyme regarding the selectivity toward cofactors and regulation of the activity (constitutive vs regulated activity).
Here, through additional biochemical characterization as well as several new X-ray structures of an entire bacterial NOX and also isolated bacterial DH domains, we will bring new insight on the origin as well as the evolution of the enzymatic mechanism from the primitive MsrQ/Fre system up to the eukaryotic NOX enzymes.

Session

Structural biology

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