New Enzyme Mechanism Elucidated for Carbon–Carbon Bond Cleavage in a Lignin Dimer Compound

Background

- The viability of biological conversion of lignin-derived aromatic compounds is predicated on access to biologically available aromatic substrates.
- Refractory carbon–carbon linkages in lignin inherently limit the yield of lignin-derived aromatic monomers for biological conversion, but microbial pathways for the cleavage of these linkages are emerging.

Approach

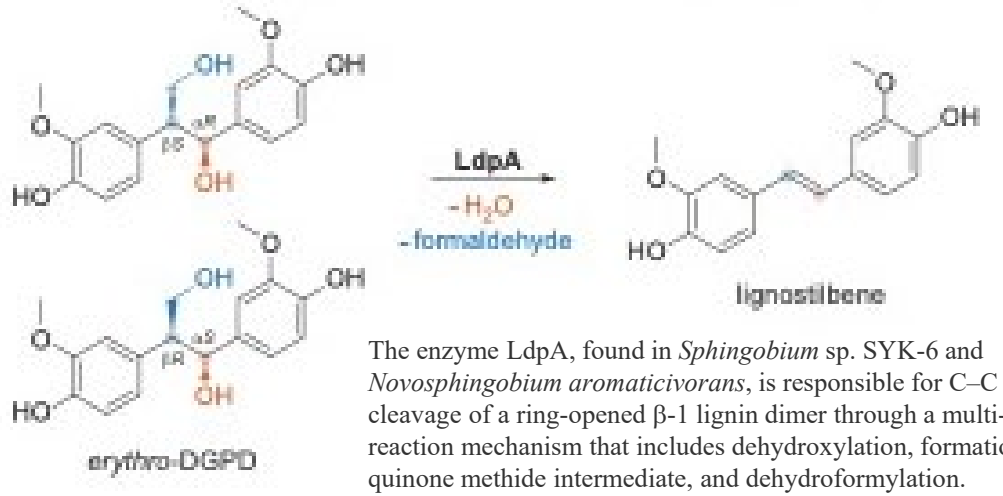
- Here, we examined an enzyme, LdpA, that can cleave C–C linkages in a ring-opened β-1 lignin dimer compound, *erythro*-DGPD.
- We used biochemical, structural, and computational methods to elucidate the reaction mechanism and structure of LdpA.

Results

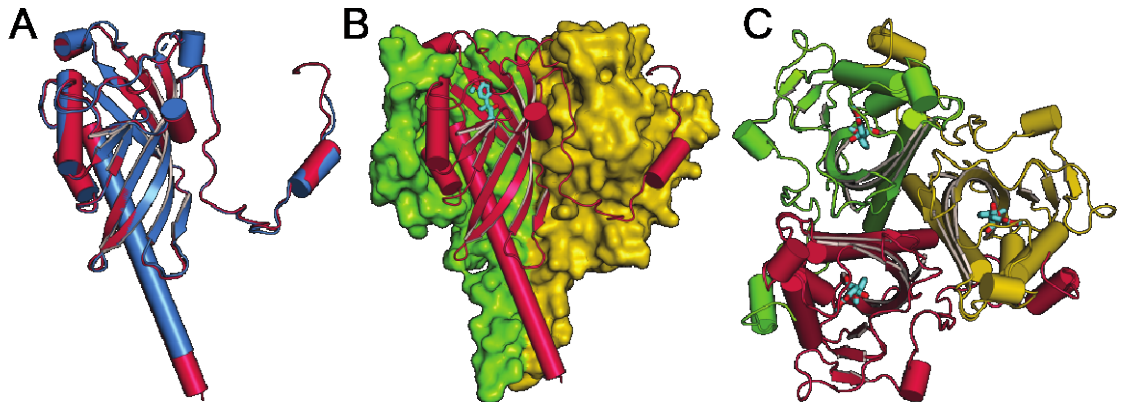
- LdpA variants from two bacteria were shown to convert *erythro*-DGPD to lignostilbene, which can be further converted in vivo to 2 molar equivalents of vanillin via lignostilbene dioxygenase.
- The reaction was shown to proceed through a unique, multi-step reaction mechanism for enzymes from the NTF-2 family that includes dehydroxylation, formation of a quinone methide intermediate, and deformylation.

Significance

- This work elucidates a new reaction for NTF-2 family enzymes generally and for cleavage of an abundant lignin dimer compound for biological funneling.



The enzyme LdpA, found in *Sphingobium* sp. SYK-6 and *Novosphingobium aromaticivorans*, is responsible for C–C bond cleavage of a ring-opened β-1 lignin dimer through a multi-step reaction mechanism that includes dehydroxylation, formation of a quinone methide intermediate, and dehydroformylation.



Structural architecture of LdpA. (A) Superposition of *Sp*LdpA (magenta) with *Na*LdpA (teal). (B) Side view of the *Sp*LdpA trimer. Two protein chains are shown as surfaces (yellow and green) and one protein chain is shown in cartoon mode (red) with bound substrate erythro-DGPD (light blue). (C) Top view of the *Sp*LdpA trimer.

Kuatsjah, E. *et al*. Biochemical and structural characterization of a sphingomonad diarylpropane lyase for cofactorless deformylation. *PNAS* (2023) in press https://www.pnas.org/doi/10.1073/pnas.2212246120