Cytochromes P450 are effective biocatalysts for aromatic O-demethylation of alkylguaiacol substrates from lignin-first biorefining

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Background

- Aromatic O-demethylation is a key, often rate-limiting biocatalytic step in biological funneling of lignin-derived compounds.
- CBI researchers (with collaborators) have described a cytochrome P450-based paradigm for this key reaction previously (Tumen-Velasquez, Johnson *et al., PNAS* 2018; Mallinson *et al. Nature Comm.* 2018; Machovina *et al. PNAS* 2019) with a focus on guaiacol as a substrate.

Approach

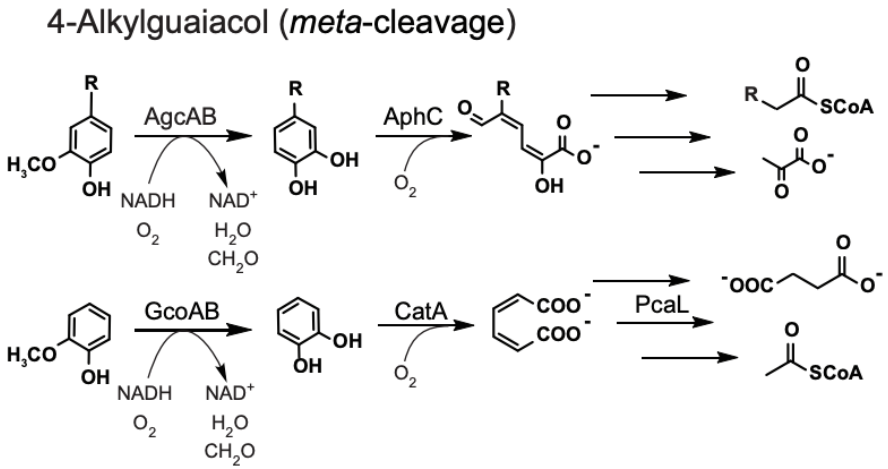
- This study examined the potential for cytochrome P450 enzymes to demethylate alkylguaiacol substrates using a transcriptomics-based approach in work led from the University of British Columbia (Lindsay Eltis).
- Detailed biochemical assays were performed to verify enzyme function.

Outcome

- This work describes the ability of two cytochromes P450 from the *Rhodococcus* genus to demethylate 4-propyl guaiacol.
- This study expands the membership of the CYP255A subfamily of enzymes relevant for biocatalytic valorization of lignin.

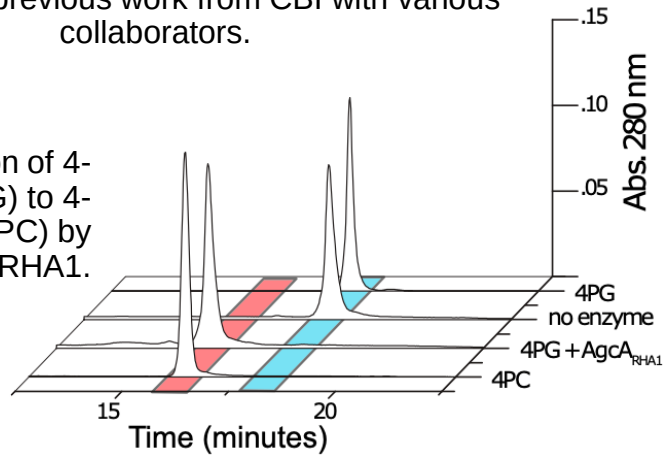
Significance

- Biological funneling can convert lignin-derived mixtures to single value-added co-products and to add substantial value to the lignocellulosic biorefinery.
- This work demonstrates for the first time the bioconversion of primary substrates derived from a target lignin-first biorefining method, reductive catalytic fractionation.



Relationship between the Rhodococcal CYP255A enzymes. AgcAB was described in the present study. GcoAB was described in previous work from CBI with various collaborators.

Transformation of 4-propylguaiacol (4PG) to 4-propylcatechol (4PC) by AgcA from *R. jostii* RHA1.



MM Fetherolf, DJ Levy-Booth, LE Navas, J Liu, JC Grigg, A Wilson, R Katahira, GT Beckham, WW Mohn, LD Eltis. Characterization of alkylguaiacol-degrading cytochromes P450 for the biocatalytic valorization of lignin. *PNAS* (2020) 117 (41) 25771-25778. doi.org/10.1073/pnas.1916349117

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