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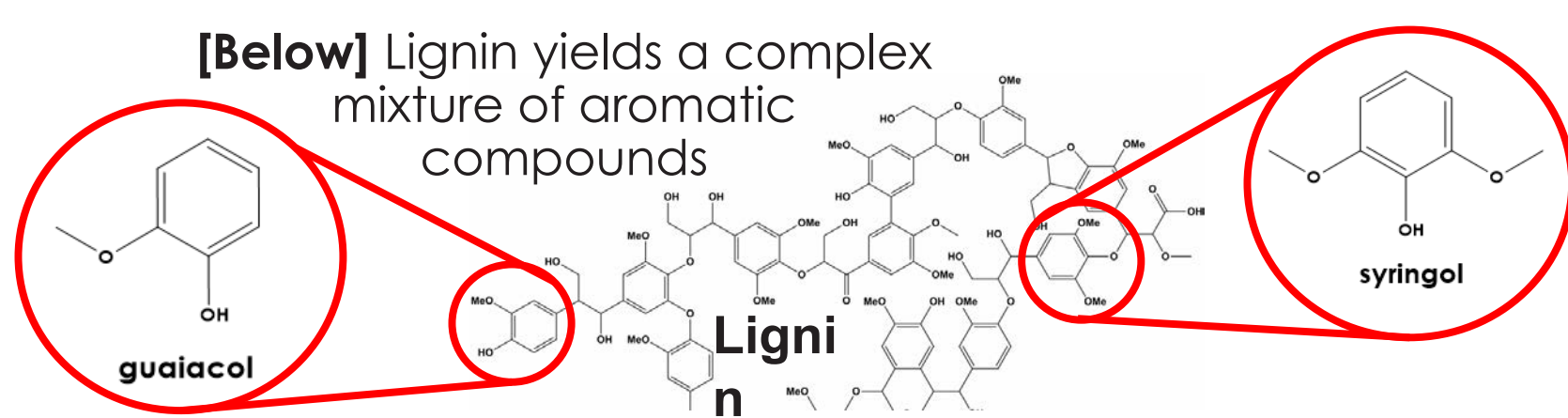
Modular Pathway Expansion in *Acinetobacter baylyi* ADP1 to Exploit Aromatic Compound Metabolism for Biotechnology

Bacterial pathways for aromatic compound metabolism have diverse biotechnology applications including lignin valorization. This project exploits the genetic system of a soil bacterium, *Acinetobacter baylyi* ADP1, for the development of synthetic biology methods to create new biochemical pathways. This approach builds on the modular nature of pathways that funnel diverse aromatic compounds to central metabolism. The goals of this project are threefold: (1) design and modify novel pathways for biotechnology, (2) generate enzymes for metabolic engineering or in vitro catalysis, and (3) analyze mutations to characterize their metabolic effects.

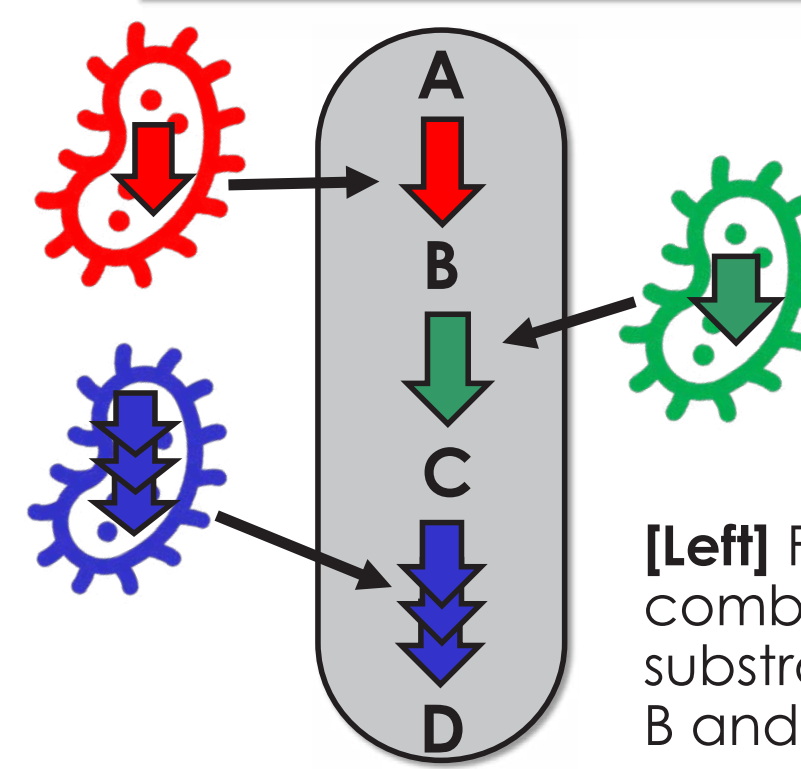
Lignin is a renewable resource made of a heterogeneous mixture of aromatics

- Lignin degradation is slow and microbially collaborative
- A goal is to funnel these aromatic compounds through bacterial central metabolism and into a desired product

[Below] Lignin yields a complex mixture of aromatic compounds



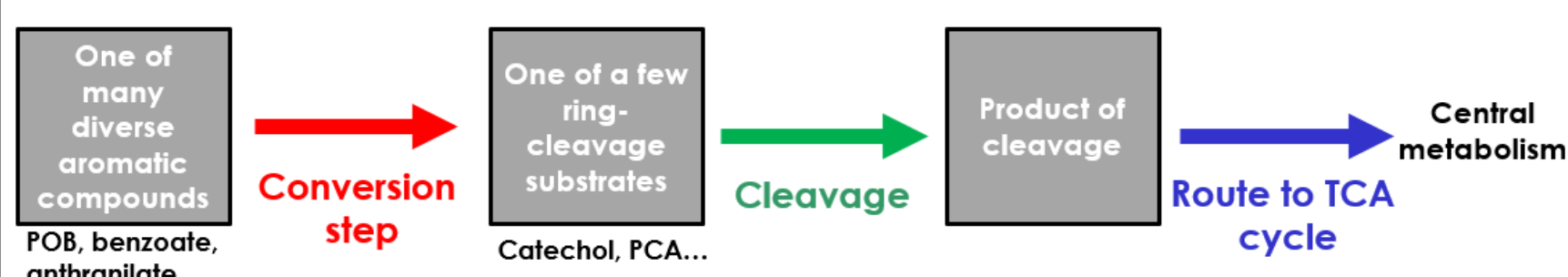
Pathway design in ADP1 aims to combine genetic modules from diverse organisms



- The soil bacterium *Acinetobacter baylyi* ADP1 is genetically facile, making it an ideal host for designing and evolving new metabolic pathways

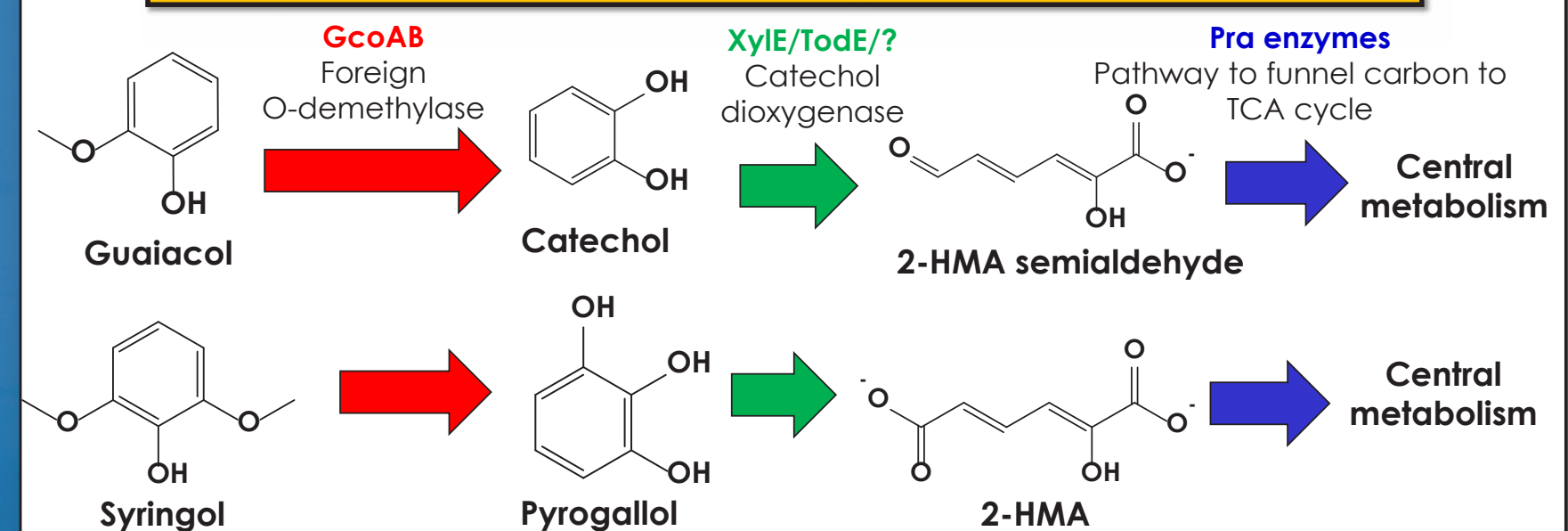
[Left] Foreign modules are combined in ADP1 to metabolize a substrate, A, through intermediated B and C, to a product, D.

Aromatic compound catabolic pathways can be generalized into three steps



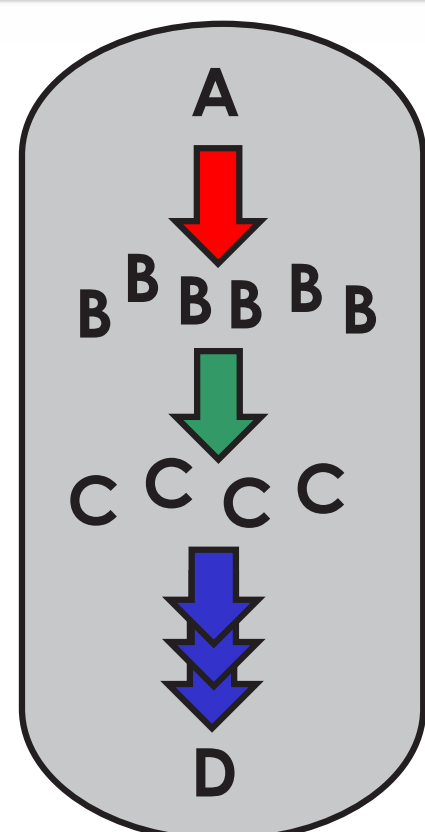
- Previous work integrated individual genetic modules into the ADP1 metabolic network [Above: conversion, cleavage, route to TCA cycle]

Foreign modules are combined in ADP1 to expand aromatic compound catabolism



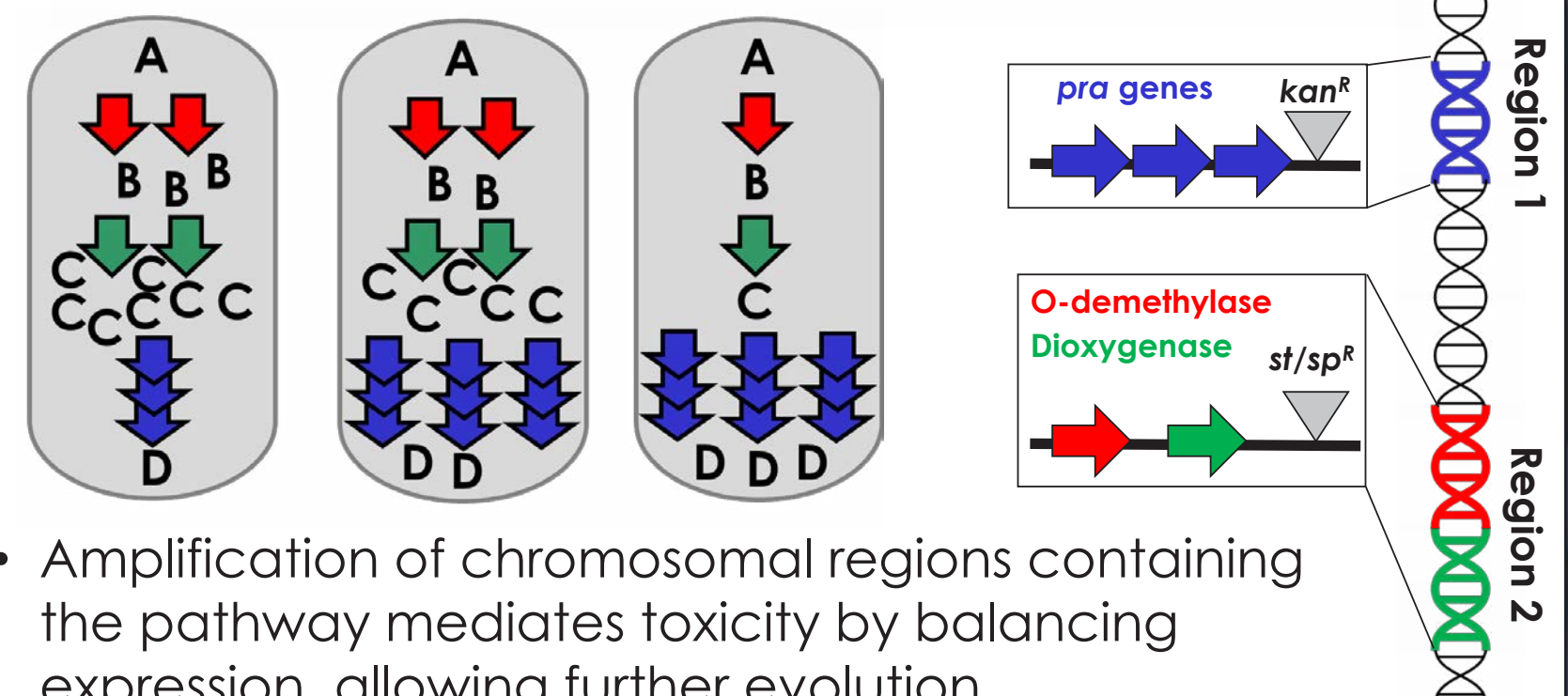
- Guaiacol is not natively degraded by ADP1. The degradative route for syringol in nature is unknown.

Toxic intermediates may prevent growth when modules have not coevolved



- Pyrogallol and catechol are toxins as well as carbon sources: imbalanced metabolism leads to toxin accumulation.
- Death of productive cells prevents evolution for improved function.

Independent chromosomal amplification of module genes accelerates evolution



- Amplification of chromosomal regions containing the pathway mediates toxicity by balancing expression, allowing further evolution.