Computationally Designed Peroxygenases for Selective Terpene Oxyfunctionalization

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Overview

Terpenes represent the largest class of secondary plant metabolites. Their oxyfunctionalized derivatives, terpenoids, are widely used in the pharmaceutical, flavor, and fragrance industries due to their aromatic properties. However, the selective oxidation of terpenes remains a longstanding challenge, given their multiple, similarly reactive sites. This technology leverages the FuncLib computational platform to create a ready-to-use library of 50 diverse and functional peroxygenase variants, each engineered to enable precise oxyfunctionalization across a broad spectrum of terpene substrates.

Applications

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- Biocatalysis for the flavor and fragrance industry - producing compounds, including key aroma components (e.g., citral, carveol)
- Synthesis of vitamin A intermediates and other terpenoid-based drugs
- Selective late-stage oxidation in pharmaceutical development
- Sustainable green chemistry alternatives to metal-based oxidations

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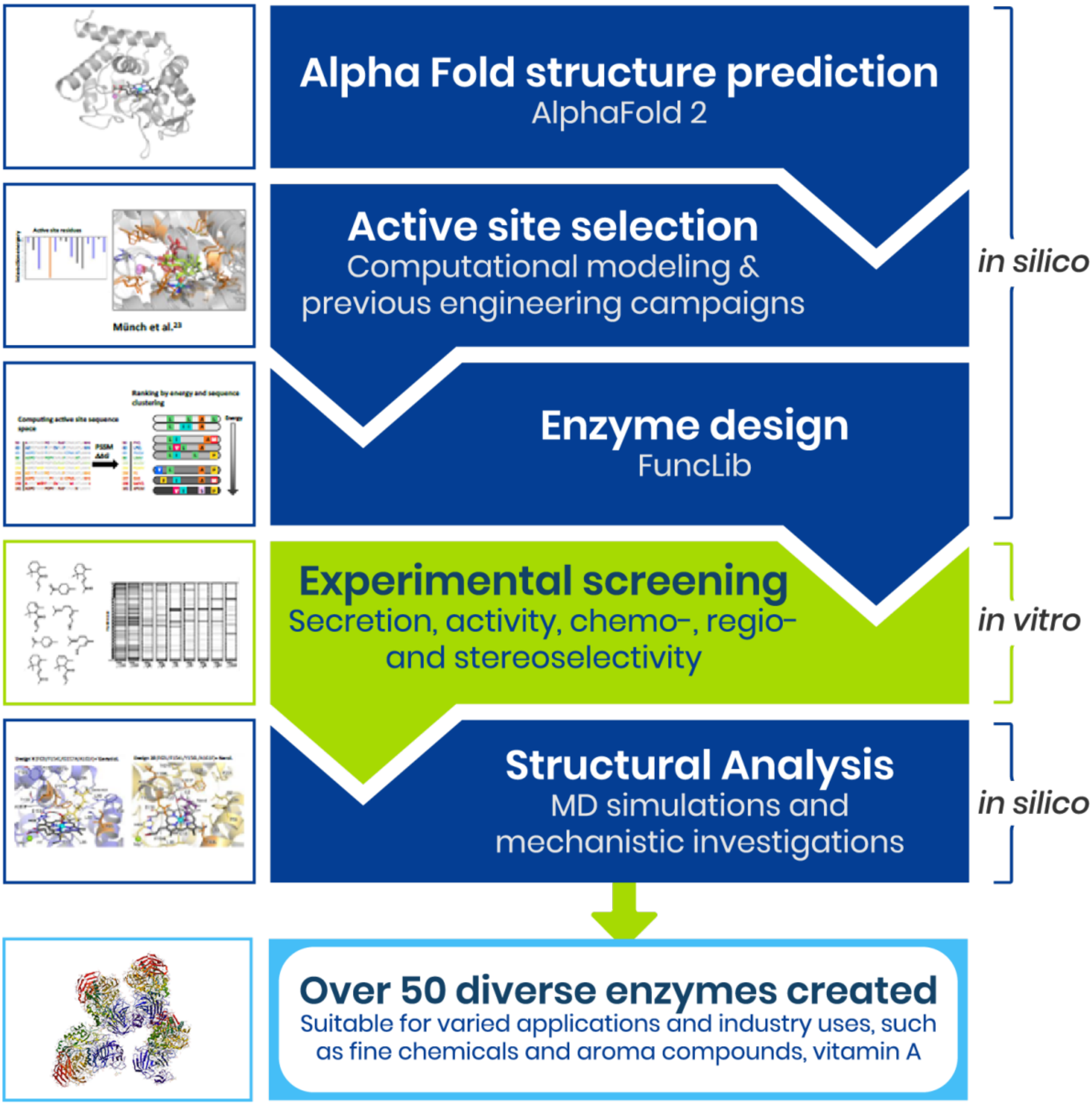
Differentiation

- High diversity: All 50 designed enzyme variants were functional, covering a broad substrate scope
- Activity increases up to 1880-fold on selected substrates
- Enhanced selectivity, High regio- and enantioselectivity; access to new product profiles
- Enables rapid screening of small libraries instead of thousands of variants
- Scalable: successful upscaling of reactions for product isolation.

Development Stage

Fifty computationally designed variants of MthUPO were experimentally validated. Multiple variants demonstrated improved activity and selectivity for diverse terpene substrates. Selected variants were scaled for product isolation (e.g., >150 mg of 2,3-nerolepoxide produced), with a strong correlation between structural modeling and functional outcomes.



Overview of the different steps of the work protocol