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Harnessing the Potential of Fusion Enzymes in Multi-enzymatic Cascades

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PURPOSE OF THE ABSTRACT

The concept of enzyme cascades, where multiple enzymatic reactions are interconnected, has gained substantial interest due to its ability to streamline complex chemical transformations. To mediate redox transformations, Oxidoreductases, a class of enzymes involved in electron transfer reactions, play a crucial role. However, their integration into biocatalytic transformations and multi-enzymatic cascades often presents challenges e.g. the reliance on costly and limited cofactors. To address this issue, fusion enzymes that regenerate their cofactors have emerged as promising tools for cofactor-dependent biocatalysis [1].

In this work, we present a comprehensive overview of the process involved in designing fusion enzymes for cascade applications, namely with the established cascade for the conversion of glucose to isobutanol [2]. In-silico modeling is employed to aid with the creation of fusion enzymes to control the spatial arrangement of catalytic domains and identify cofactor-binding sites. The enzymes are modified to produce chimeric proteins that combine catalytic functions with the capacity to recycle cofactors while retaining the oxidized/reduced cofactor in a confined microenvironment that benefits from the fusion pattern. The approaches used to choose suitable fusion partners are reviewed, and the importance of structural compatibility for preserving catalytic functions is emphasized. Moreover, we want to delve into the challenges and opportunities associated with fusion enzymes, including limitations in in-silico accuracy and the potential for experimental validation. These include optimization of fusion enzyme design, scalability, and compatibility with different cofactors. We aim to highlight possible challenges, concerns, and recent advances in the use of fusion enzymes, as well as to forecast future directions in the field of cofactor regeneration.

FIGURES

FIGURE 1

FIGURE 2

KEYWORDS

BIBLIOGRAPHY

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