ALMAC

Partnering to Advance Human Health

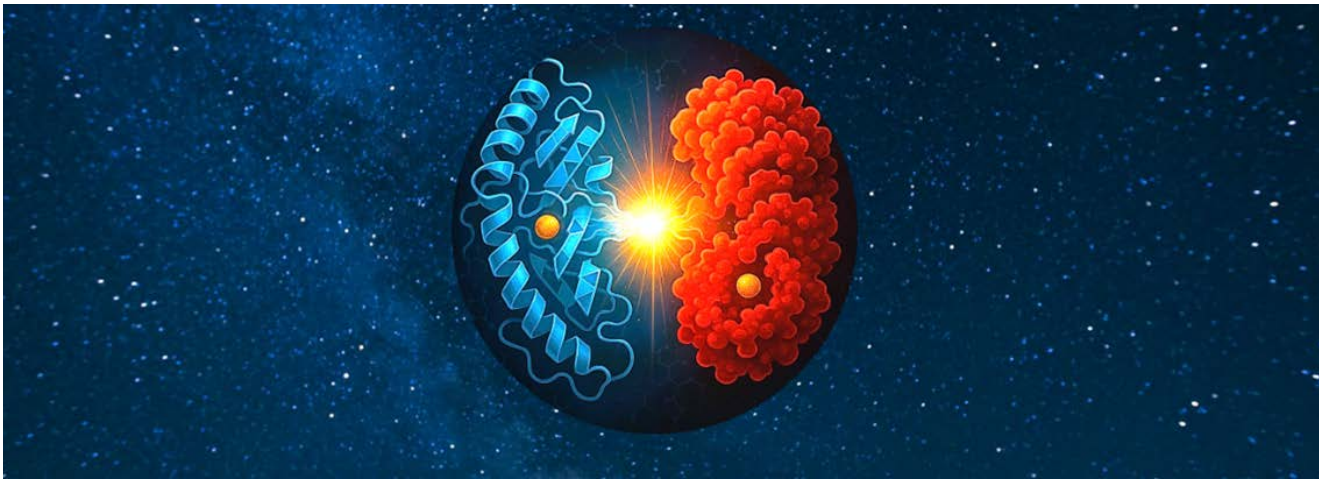
Almac Voice

Fusion Enzymes: Innovating Biocatalysis

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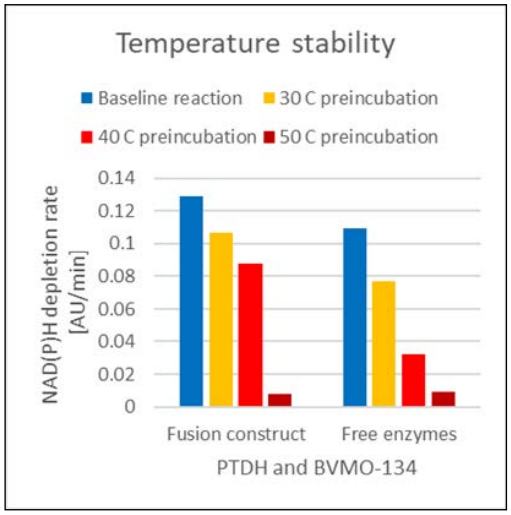
Introduction

Fusion enzymes represent a powerful innovation in biocatalysis, combining multiple enzymatic functions into a single, efficient catalyst. One such example is the fusion which merges phosphite dehydrogenase (PTDH) with Baeyer-Villiger monooxygenase (BVMO).

Advantages of Fusion Enzymes:

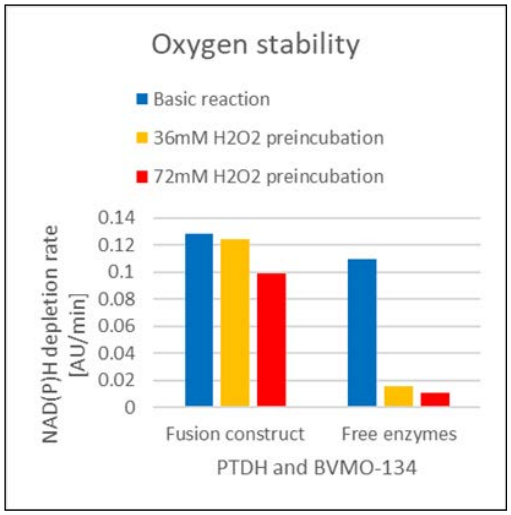
- Only one catalyst is required, simplifying the reaction setup.
- Soluble expression of tricky enzymes can be improved by a more soluble N-terminal fusion partner.
- Thermostability may be enhanced through a thermostable fusion partner.
- Increased efficiency in mass transfer due to closer proximity of cofactor-producing and cofactor-using enzymes.

Activity highlights



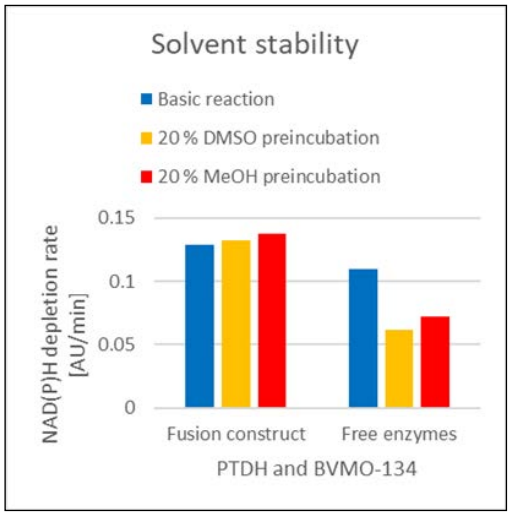
Temperature stability

The BVMO fusion partner was engineered to improve temperature stability, which consequently benefited the BVMO. The data to the left shows the kinetic profile for BVMO-134. The fusion construct of BVMO-134 was shown to have increased resilience at elevated reaction temperatures, which has the potential to widen BVMO use in pharmaceuticals, green chemistry, and specialty chemicals. Enhanced thermal stability allows longer reactions often resulting in higher yields. Therefore, continued development of the fusion partner may drive further improvements in future biocatalysts.



Oxygen stability

BVMOs, like other oxidising enzymes, are prone to oxygen inactivation during biotransformations. This susceptibility often limits their use in large-scale industrial applications, as enzyme deactivation can compromise overall process efficiency. The engineered fusion partner improved the wild-type BVMO's stability, yielding a more resilient fusion construct. As a result, the fusion enzyme demonstrates increased robustness under operational conditions, enabling broader utility in biocatalytic processes.



Solvent stability

Solvent stability can often be the serendipitous by-product of increased temperature stability. Shown here is an example of reaction kinetics of BVMO-134 with the fusion construct displaying enhanced activity in the presence of 20% organic solvent compared to the free enzyme. This improved tolerance enables the enzyme to function efficiently even in the presence of otherwise inhibitive organic solvents. As a result, the fusion BVMO is better suited for challenging industrial environments, for example, where elevated concentrations of organic solvent are required to enhance substrate solubility.

Conclusion

The PTDH-BVMO fusion exemplifies the benefits of enzyme fusion technology, offering improved stability, expression, and catalytic efficiency. These attributes make it a promising tool for industrial and research applications in biocatalysis.

Almac's new self-sufficient BVMO kit

Almac has developed a new self-sufficient BVMO fusion enzyme kit by combining twelve of Almac's best BVMOs with a recycling enzyme partner. The fusion constructs enhanced the stability of certain BVMOs that previously exhibited limited tolerance to high temperatures and oxygen, while others demonstrated increased reaction rates compared to their non-fused enzyme counterparts. Although this technology is not a comprehensive solution for all biocatalysis challenges, it represents a meaningful advancement in the field.



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