Enzymes and Enzyme Mimics for Nitric Oxide Delivery

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Nitric oxide (NO) is a free radical with an incredible breadth of biological functionalities.[1] NO plays essential roles in modulating vascular homeostasis, neuronal activity, wound healing, and participates in immune responses to pathogens. However, the full potential of NO as therapeutic agents is complicated by its short half-life and limited diffusion distance in human tissues. Current strategies for NO delivery focus on the encapsulation of NO donors into scaffolds, but this approach is limited by the finite reservoir of NO donors that can be loaded within the materials. Alternatively, NO can be generated from NO prodrugs using an enzyme-prodrug therapy approach. We recently reported an enzyme−prodrug therapy approach for controlled and localized NO delivery via β-galactosidase−β-gal-NONOate enzyme−prodrug pair.[2,3] In this approach, β-galactosidase was embedded in implantable materials, which thus became biocatalytic, to locally convert externally administered β-gal-NONOate to active NO at the desired site. NO delivery could be initiated when needed by external administration of the prodrug and NO dosing was controlled by the concentration of administered β-gal-NONOate. NO generated using these biomaterials were able to elicit physiologically relevant effects such as to induce vasodilation[3] and reduce intraocular pressure[2] in *ex vivo* animal models.

This talk will also highlight examples of enzyme mimics we recently developed that catalytically decompose NO donors to generate NO at physiological conditions.[4] We reported that zinc oxide (ZnO) particles[5] mimicked the activities of β-galactosidase and glutathione peroxidase, and catalyzed both exogenous (β-gal-NONOate) and endogenous (S-nitrosoglutathione) NO donors to generate NO.[6] We achieved physiologically relevant NO levels by simply modulating the concentrations of ZnO and NO donors. After 6-month, ZnO particles preserved their catalytic potency, which is highly beneficial towards long-term biomedical applications. Our findings may open new routes to the next generation of NO-releasing biomaterials and devices in diverse biomedical applications.

References:

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