Evaluating Lysyl Oxidase Activity with Turn-On Fluorescent Probes

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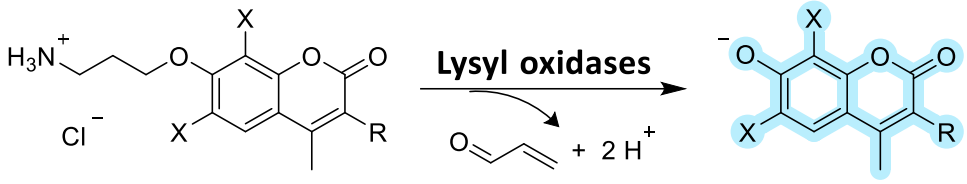
Remodelling and maturation of collagen, the dominant structural protein in mammals, is crucial for the integrity of organs and wound healing.[1,2] These processes include post-translational cross-linking of collagen strands triggered by the oxidation of lysine residues through lysyl oxidases (LOXs). This enzyme family consists of five isoforms - lysyl oxidase and four lysyl oxidase-like enzymes. LOXs catalyze the oxidative deamination of lysine residues in the telopeptide domain of collagen and are important for the mechanical properties of the extracellular matrix (ECM).[1] Excessive LOX activity is, however, associated with fibrotic and malignant diseases which are estimated to account for around 45% of deaths in developed countries.[3]

A comprehensive investigation of LOX activity is therefore important for a deeper understanding of normal physiological versus pathological processes. The current standard activity assay detects hydrogen peroxide, the by-product of the oxidative deamination reaction, and lacks specificity.[4] Our group has recently developed an enzyme-reactive sensor that detects LOX *in vitro*, *in vivo* and in tissue sections.[5]



In this work, we developed a quick and straightforward assay for measuring LOX activity, based on the turn-on of a coumarin-based sensor. We have examined various analogs of the activity-based probe and evaluated their selectivity for LOX isoforms over related amine oxidases. We anticipate that our tools will be valuable for the screening of drug candidates targeting LOXs and deciphering the role of LOXs' in healthy and diseased states.

References:

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