Sequence and Structure Selectivity of Human Lysyl Oxidase-Like 2 (LOXL2)

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Collagen is the dominant structural protein in mammals and its maturation is vital for the integrity of organs and wound healing.[1,2] A key intermediate of collagen biosynthesis and maturation is the so-called tropocollagen.[1] The collagen assembly comprises a proline-rich triple-helical domain and two terminal telopeptide domains which are not assembled into higher-order structures.[1] Tropocollagen undergoes cross-linking into fibrils and fibers. The cross-linking process is induced by the lysyl oxidase enzyme family (LOX and four LOX-like enzymes).[1,2] These copper amine oxidases catalyze the conversion of lysine residues (Lys) to aldehyde-containing allysines that spontaneously undergo aldol and related reactions to form cross-links.[2,3] While the LOX-mediated cross-linking is crucial for the mechanical properties of the extracellular matrix, excessive LOX activity is associated with fibrotic and malignant diseases.[2,3] The isoform LOXL2 is of particular interest as a therapeutic target as it is over-expressed in many types of cancers.[3] In this work, we decipher the sequence and structure selectivity of LOXL2. We will present the selectivity of LOXL2 for Lys derivatives, including Lys-containing single-stranded and triple-helical collagen model peptides.

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[3] Philip C. Trackman, *Expert Opinion on Therapeutic Targets*, **2016**, 20, 935-945.