Role of SRCR Domains in Collagen IV-Crosslinking Activity of LOXL2

Pena, Abner

Lysyl oxidases are a family of enzymes that oxidize lysine residues, regulating many biological processes including extracellular matrix stabilization. In this project we focused on lysyl oxidase 2 (LOXL2) which is an essential enzyme to the biogenesis of connective tissue (1) and crosslinks to the domain of the 7S found in Collagen IV (2). Since this enzyme is known to be overexpressed in Chronic Kidney Diseases (CKD) (3) and in liver fibrosis (4), it could be an interesting target for pharmacological treatment. In order to reach a further understanding of the activity of this enzyme, we studied the role of the Scavenger Receptor Cysteine-Rich (SRCR) domains which function is still misunderstood. All SRCR domains were taken out of the Myc-tagged-LOXL2 cDNA by PCR and then, the resulting product was cloned into a vector and transfected in HEK293 cells in order to determine its effect over enzymatic function and localization. It was hypothesized that if all of the four domains were taken away from the LOXL2, the enzyme would still work. This hypothesis was proven as the enzyme did not show any activity of luminescence and was not secreted by the cell, seen in the Western Blot. It can be inferred that the LOXL2 expression depends on SRCR and so does its' activity. This information can be used, so that a drug can be synthesized that inhibits the function of the SRCR domain, stopping the cell from secreting the enzyme, thus having a better control over CKD and liver fibrosis.

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