Lysyl Oxidases as Targets for Cancer Therapy and Diagnostic Imaging

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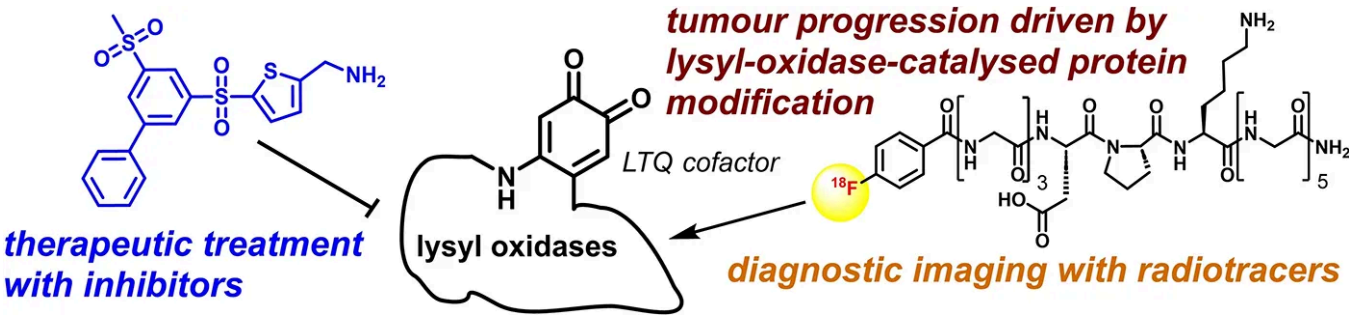
PUBLIZIERT AM
2023-09-15

JOURNAL
ChemMedChem

LINK
https://doi.org/10.1002/cmdc.202300331

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Graphical Abstract

Over the past two decades, lysyl oxidases have been recognised as key enzymes in tumour invasion and metastasis, which has spurred efforts to develop inhibitors and molecular probes for therapeutic and imaging purposes, respectively. This review summarises the structural and functional aspects of these unique enzymes in relation to tumour progression and highlights recent developments in inhibitors and imaging probes.

Abstract

The understanding of the contribution of the tumour microenvironment to cancer progression and metastasis, in particular the interplay between tumour cells, fibroblasts and the extracellular matrix has grown tremendously over the last years. Lysyl oxidases are increasingly recognised as key players in this context, in addition to their function as drivers of fibrotic diseases. These insights have considerably stimulated drug discovery efforts towards lysyl oxidases as targets over the last decade. This review article summarises the biochemical and structural properties of theses enzymes. Their involvement in tumour progression and metastasis is highlighted from a biochemical point of view, taking into consideration both the extracellular and intracellular action of lysyl oxidases. More recently reported inhibitor compounds are discussed with an emphasis on their discovery, structure-activity relationships and the results of their biological characterisation. Molecular probes developed for imaging of lysyl oxidase activity are reviewed from the perspective of their detection principles, performance and biomedical applications.