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Long Non-Coding RNA *MALAT1* Inhibition via Antisense Oligonucleotides Attenuates Diabetic Kidney Disease Progression Through Regulation of Endothelial-Mesenchymal Transition

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Abstract

Endothelial-mesenchymal transition (EndMT) contributes to renal fibrosis in diabetic kidney disease (DKD). We identified the long non-coding RNA *MALAT1* as a key regulator of EndMT in high glucose-stimulated human glomerular endothelial cells. *MALAT1* sponged miR-145, thereby derepressing ZEB2 and promoting endothelial dysfunction. Systemic administration of gapmer antisense oligonucleotides (ASOs) targeting *MALAT1* in db/db diabetic mice reduced albuminuria by 50%, preserved glomerular endothelial marker expression, and attenuated interstitial fibrosis. RNA-immunoprecipitation confirmed direct *MALAT1*-miR-145-ZEB2 axis regulation. LncRNA-targeted therapies represent a novel approach to halt DKD progression.

Keywords: long non-coding RNA, MALAT1, diabetic kidney disease, endothelial-mesenchymal transition, antisense oligonucleotides, miR-145