Exploring the effect of LncRNA DANCR to regulate the Keap1-Nrf2/ARE pathway on oxidative stress in Rheumatoid Arthritis

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Abstract

Introduction:This study focused on investigating the effects of LncRNA DANCR regulation of Keap1-Nrf2/ARE pathway on inflammation and oxidative stress in RA. Methods:The levels of LncRNA DANCR/miR-486-3p/ Keap1 in peripheral blood of 30 RA groups and 30 normal subjects were examined, and the association of LncRNA DANCR with inflammatory indicators of rheumatoid arthritis was investigated. We construct overexpression plasmids and small interfering RNAs of LncRNA DANCR to investigate the relationship between LncRNA DANCR and FLSs viability and migration in rheumatoid arthritis, as well as the effects on cellular oxidative stress factors and Keap1-Nrf2/ARE pathway; molecular biology analysis was used to predict microRNAs that can bind LncRNA DANCR, and luciferase verified the binding sites of LncRNA DANCR with Keap1 and miR-486-3p; to further refine the gene and protein expression results, we used RT- qPCR and immunoblotting assays . Results: In both groups of PBMCs, the expression levels of LncRNA DANCR and Keap1 mRNA were higher in the rheumatoid arthritis group than in the normal control group, and the opposite was true for miR-486-3p; LncRNA DANCR was positively correlated with TAOC, IL6, RF, IL17, anti-CCP, MDA, and SOD, but not with ESR, DAS28, IL11, and SOD, DAS28, IL11, ROS, CRP were negatively correlated; overexpression of lncRNA DANCR stimulated the Keap1-Nrf2/ARE pathway, decreased the expression of IL10, SOD, TAOC, and increased the expression levels of MDA, IL11, IL-17, PD-L1, and silencing of lncRNA DANCR was the opposite, but knockdown of miR- 486-3p or overexpression of keap1 reversed the expression of the above-mentioned inflammatory and oxidative factors. In addition, pcDNA-DANCR clearly showed stronger cell invasion and migration ability and exacerbated its inflammatory response, we verified their targeting relationship using dual luciferase. Conclusion: The low-expressed lncRNA DANCR may regulate the Keap1-Nrf2/ARE pathway and suppress the inflammatory and oxidative responses in RA patients.

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