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Theranostic value of miR-499a seed region variant in Bronchial asthma

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Background: Small non-coding RNAs (microRNAs) have been evolved to master numerous cellular processes. Genetic variants within microRNA seed region might influence microRNA biogenesis and function. The study aimed at determining the role of microRNA-499 (miR-499) gene family polymorphism as a marker for susceptibility and progression of bronchial asthma and to analyse the structural and functional impact of rs3746444 within the seed region.

Methods: Genotyping for 192 participants (96 patients and 96 controls) in the discovery phase and 319 subjects (115 patients and 204 controls) in the replication phase was performed via Real Time-Polymerase Chain Reaction technology. Patients underwent the methacholine challenge test and biochemical analysis. Gene structural and functional analysis, target prediction, annotation clustering, and pathway enrichment analysis were executed. Predicted functional effect of rs37464443 SNP was analysed.

Results: miR-499 gene family is highly implicated in inflammation-related signalling pathways. Rs374644 (A>G) in MIR499A and MIR499B within the seed region could disrupt target genes and create new genes. The G variant was associated with high risk of developing asthma under all genetic association models (G versus A: OR = 3.27, 95% CI = 2.53-4.22; GG versus AA: OR = 9.52, 95% CI = 5.61-16.5; AG versus AA: OR = 2.13, 95% CI = 1.24-3.46; GG + AG versus AA: OR = 4.43, 95% CI = 2.88-6.82). GG genotype was associated with poor pre-bronchodilator FEV1 (p=0.047) and the worst bronchodilator response after Salbutamol inhalation, represented in low peaked expiratory flow rate (p = 0.035).

Conclusions: miR-499 rs3746444 (A>G) polymorphism was associated with asthma susceptibility and bronchodilator response in Egyptian children and adolescents. Further functional analysis is warranted to develop more specific theragnostic agents for selecting targeted therapy.

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