ASSOCIATION OF MICRORNA-146A RS57095329 POLYMORPHISM WITH SUSCEPTIBILITY TO GOUT TOPHI IN A CHINESE HAN POPULATION

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Background: MicroRNA-146a (miR-146a) plays an important role in regulation of autoinflammatory diseases including gout[1]. Growing evidences have demonstrated that association of miR-146a gene single nucleotide polymorphisms (SNPs) with risk of several diseases[2], but no genetic relevance studies of miR-146a gene polymorphisms to gout have been reported by now.

Objectives: To investigate the potential association of gout and the functional rs57095329 SNP of miR-146a in the Chinese Han population.

Methods: The rs57095329 SNP was detected in 448 primary gout patients (containing 76 tophi patients) and 418 healthy control subjects. Peripheral blood mononuclear cells (PBMCs) miR-146a expression was measured in 81 gout patients (including 32 tophi patients and 49 non-tophi patients) and 47 healthy subjects.

Results: No significant difference was detected in the distribution of miR-146a rs57095329 between 448 gout patients and 418 healthy subjects (P>0.05). However, significant differences were observed between 76 gout with tophi patients and 418 healthy subjects, between gout with tophi (76) and with no tophi patients (372) both in genotypes and allele distributions (P<0.01, respectively). Gout patients carrying AG/GG genotypes had a 0.323-fold reduced risk for tophi than those carrying AA genotype, and the G allele carrier of gout patients had a 0.362-fold reduced risk for tophi. Additionally, GG genotype was significantly associated with increased expression of miR-146a in 32 tophi patients (Figure).

Conclusion: Our study shows a novel, significant association between the miR-146a rs57095329 polymorphism and a lower risk of tophi in gout patients. Furthermore, our findings suggest that this gene polymorphism might affect the genetic predisposition to tophi development and modulate the expression of miR-146a level in tophi patients. This new knowledge about miR-146a may be clinically important and confirms a role for miR-146a in the pathophysiology of tophi, with potentially important therapeutic implications.

REFERENCES:

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URINARY TRANSCRIPTS AS BIOMARKERS OF LUPUS NEPHRITIS

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Background: Children with systemic lupus erythematosus (cSLE) with kidney involvement face considerable morbidity and mortality. Commonly used methods for assessing kidney involvement in cSLE, such as renal function tests, are non-specific and provide a limited picture of disease activity. Kidney biopsy, the mainstay to assess disease class and chronicity as well as response to treatment, is an invasive procedure. The field of transcriptomics has identified markers that have helped our understanding of cSLE pathogenesis.

Objectives: Transcriptional profiling of urinary cells has the potential to provide us with non-invasive biomarkers and has not been studied thus far. Our aim is to evaluate intracellular urinary transcripts in cSLE.

Methods: Using the Human Inflammation v2 panel on the nanoString nCounter platform, expression of 255 genes was profiled from 82 urinary pellets (all from 43 cSLE with different classes of lupus nephritis).

Results: Healthy control samples yielded low quantities of RNA and were excluded from further analysis. The patient's raw transcript counts were normalized and the use of unsupervised learning analysis revealed robustness among classes with higher disease activity (higher SLE Disease Activity Index (SLEDAI) scoring). Statistical analysis (ANOVA) showed that Classes III or IV + V (mixed nephritis; highest average SLEDAI) display robust interferon and inflammasome-related signatures in comparison to other classes. Interestingly, samples from cSLE with no known nephritis also displayed an interferon signature, although less intense than the mixed class. Some transcripts such as C3 (complement 3) were uniquely dysregulated in the mesangial class. Therapeutically targetable pathways were identified in a number of patients (specifically in the mixed class).

Conclusion: These studies are currently being extended in order to confirm the value of urinary transcriptional profiling as a source of biomarkers and to identify potential therapeutic targets in cSLE.

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