

Whole Blood microRNA Signature for Primary Sjögren's Syndrome-Related Lymphoma.

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Background/Purpose: Micro RNAs (miRNAs) are 18–25nt non-coding RNAs that bind target/complementary sequences within the 3'UTR of RNA molecules steering them towards degradation or translational repression, and play a key role in the regulation of gene expression. Better understanding of the expression pattern of miRNAs in diseases may improve our understanding of the biological basis of the disease and identify potential biomarkers. The role of miRNAs in primary Sjögren's syndrome (PSS) and PSS-related lymphoma remains poorly understood. The aim of this project is to identify a miRNA signature for PSS-related lymphoma.

Methods: We profiled the expression of miRNAs in whole blood (PaxGene) total RNA preparations using the Exiqon miRCURY LNA array which encompasses 1400 miRNAs and other small non-coding RNAs. A discovery cohort comprised of 36 samples from the United Kingdom Primary Sjögren's Syndrome Registry (UKPSSR) (12 PSS patients with lymphoma, 12 PSS patients without lymphoma, 12 healthy controls) were used in the initial analysis. We also explored different normalisation strategies and developed an approach which we considered most appropriate for analyzing these data. Real-Time PCR was used to validate the most highly differentially expressed miRNAs between groups. A miRNA signature for PSS-related lymphoma was identified using cluster analysis followed by validation with a second independent cohort of 36 patients and controls.

Results: The initial miRNA array profiling revealed a clear clustering of the 3 subject groups. Between the 'High Function' and 'Lymphoma' patient groups, 44 miRNAs were found to be differentially expressed. The differential expressions of these miRNAs were validated by RT-PCR in 3 out of 9 miRNAs with the highest fold-changes between the two groups. Indeed, based on the expression levels of these 3 miRNAs were sufficient to distinguish PSS patients with lymphoma from those without. Two out of these 3 miRNAs were also differentially expressed between the same two groups in the validation cohort.

Conclusion: We have identified 2 miRNAs that are differentially expressed in peripheral blood between PSS patients with lymphoma and those without lymphoma. Identifying the mRNA targets of these miRNAs in PSS may improve our understanding of the pathogenesis of PSS-related lymphoma. Furthermore, miRNAs may be useful biomarkers for PSS-related lymphoma.

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