PLoS One. 2015 Mar 24;10(3):e0121903. doi: 10.1371/journal.pone.0121903. eCollection 2015.

Identification of a MicroRNA Signature for the Diagnosis of Fibromyalgia.

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Abstract

BACKGROUND:

Diagnosis of fibromyalgia (FM), a chronic musculoskeletal pain syndrome characterized by generalized body pain, hyperalgesia and other functional and emotional comorbidities, is a challenging process hindered by symptom heterogeneity and clinical overlap with other disorders. No objective diagnostic method exists at present. The aim of this study was to identify changes in miRNA expression profiles (miRNome) of these patients for the development of a quantitative diagnostic method of FM. In addition, knowledge of FM patient miRNomes should lead to a deeper understanding of the etiology and/or symptom severity of this complex disease.

METHODS:

Genome-wide expression profiling of miRNAs was assessed in Peripheral Blood Mononuclear Cells (PBMCs) of FM patients (N=11) and population-age-matched controls (N=10) using human v16-miRbase 3D-Gene microarrays (Toray Industries, Japan). Selected miRNAs from the screen were further validated by RT-qPCR. Participating patients were long term sufferers (over 10 years) diagnosed by more than one specialist under 1990 American College of Rheumatology criteria.

RESULTS:

Microarray analysis of FM patient PBMCs evidenced a marked downregulation of hsa-miR223-3p, hsa-miR451a, hsa-miR338-3p, hsa-miR143-3p, hsa-miR145-5p and hsa-miR-21-5p (4-fold or more). All but the mildest inhibited miRNA, hsa-miR-21-5p, were validated by RT-qPCR. Globally, 20% of the miRNAs analyzed (233/1212) showed downregulation of at least 2-fold in patients. This might indicate a general de-regulation of the miRNA synthetic pathway in FM. No significant correlations between miRNA inhibition and FM cardinal symptoms could be identified. However, the patient with the lowest score for mental fatigue coincided with the mildest inhibition in four of the five miRNAs associated with the FM-group.

CONCLUSIONS:

We propose a signature of five strikingly downregulated miRNAs (hsa-miR223-3p, hsa-miR451a, hsa-miR338-3p, hsa-miR143-3p and hsa-miR145-5p) to be used as biomarkers of FM. Validation in larger study groups is required before the results can be transferred to the clinic