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Transcriptional Analysis of Blood Lymphocytes and Skin Fibroblasts, Keratinocytes, and Endothelial Cells as a Potential Biomarker for Alzheimer's Disease

Mukhamedyarov M., Rizvanov A., Yakupov E., Zefirov A., Kiyasov A., Reis H., Teixeira A., Vieira L., Lima L., Salafutdinov I., Petukhova E., Khaiboullina S., Schlauch K., Lombardi V., Palotás A.
Kazan Federal University, 420008, Kremlevskaya 18, Kazan, Russia

Abstract

© 2016 - IOS Press and the authors. All rights reserved.Alzheimer's disease (AD) is a devastating and progressive form of dementia that is typically associated with a build-up of amyloid-β plaques and hyperphosphorylated and misfolded tau protein in the brain. Presently, there is no single test that confirms AD; therefore, a definitive diagnosis is only made after a comprehensive medical evaluation, which includes medical history, cognitive tests, and a neurological examination and/or brain imaging. Additionally, the protracted prodromal phase of the disease makes selection of control subjects for clinical trials challenging. In this study we have utilized a gene-expression array to screen blood and skin punch biopsy (fibroblasts, keratinocytes, and endothelial cells) for transcriptional differences that may lead to a greater understanding of AD as well as identify potential biomarkers. Our analysis identified 129 differentially expressed genes from blood of dementia cases when compared to healthy individuals, and four differentially expressed punch biopsy genes between AD subjects and controls. Additionally, we identified a set of genes in both tissue compartments that showed transcriptional variation in AD but were largely stable in controls. The translational products of these variable genes are involved in the maintenance of the Golgi structure, regulation of lipid metabolism, DNA repair, and chromatin remodeling. Our analysis potentially identifies specific genes in both tissue compartments that may ultimately lead to useful biomarkers and may provide new insight into the pathophysiology of AD.

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Keywords

Alzheimer's disease, amyloid, biomarker, diagnostics, early diagnosis, endothelial cell, fibroblast, inflammation, keratinocyte, lymphocyte, mild cognitive impairment, neurodegeneration, oxidative stress, skin biopsy