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The microRNA expression signature of CD4+ T cells in the transition of brucellosis into chronicity

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Abstract

 Brucellosis is a serious infectious disease that continues to be a significant cause of morbidity worldwide and across all ages. Despite early diagnosis and treatment, 10±30% of patients develop chronic brucellosis. Although there have been recent advances in our knowledge of Brucella virulence factors and hosts' immune response to the infection, there is a lack of clear data regarding how the infection bypasses the immune system and becomes chronic. The present study investigated immunological factors and their roles in the transition of brucellosis from an acute to a chronic infection in CD4+ T cells. CD4+ T cells sorted from peripheral blood samples of patients with acute or chronic brucellosis and healthy controls using flow cytometry as well as more than 2000 miRNAs were screened using the GeneSpring GX (Agilent) 13.0 miRNA microarray software and were validated using reverse transcription polymerase chain reaction (RT-qPCR). Compared to acute cases, the expression levels of 28 miRNAs were significantly altered in chronic cases. Apart from one miRNA (miR-4649-3p), 27 miRNAs were not expressed in the acute cases (p <0.05, fold change> 2). According to KEGG pathway analysis, these miRNAs are involved in the regulation of target genes that were previously involved in the MAPK signalling pathway, regulation of the actin cytoskeleton, endocytosis, and protein processing in the endoplasmic reticulum. This indicates the potential role of these miRNAs in the development of chronic brucellosis. We suggest that these miRNAs can be used as markers to determine the transition of the disease into chronicity. This is the first study of miRNA expression that analyses human CD4+ T cells to clarify the mechanism of chronicity in brucellosis.

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