Novel potential marker for Sézary syndrome diagnosis: *TMEM244* gene

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Sézary syndrome (SS) is a leukemic form of cutaneous T-cell lymphoma (CTCL). Diagnosis of SS still causes many problems and requires wide interdisciplinary knowledge. What's more, SS can resemble inflammatory dermatoses as well as another CTCL type mycosis fungoides (MF). Therefore, there is a need for a relevant diagnostic tool, that will also allow sensitive disease monitoring and accurate assessment of treatment response. First aim of this study was to compare the expression of the *TMEM244* gene in the whole population of peripheral blood mononuclear cells (PBMC), sorted peripheral blood CD4+ T-cells, and cells isolated from skin biopsies, from SS, MF, and benign erythroderma (E) patients. Second aim was to assess *TMEM244* expression in different subpopulations of PBMC from healthy individuals (HI). The study is a combination of retrospective data as well as new samples and included a total of 16 SS, 6 MF, 8 E, and 44 HI. PBMCs were purified by density gradient centrifugation. CD4+ lymphocytes were separated by immunomagnetic-negative selection. Selected subpopulations of PBMCs were separated by phycoerythrin-conjugated antibody staining and positive selection on magnetic beads. Lymphocytes from the skin biopsies were digested with collagenase P and passed through nylon strainers. *TMEM244* expression was analyzed by RT-qPCR. Obtained results showed significantly higher expression of *TMEM244* in PBMC of SS patients (1,500E-06; n=13) compared to HI (29.4E-06; n=30; $p<0.00001$) as well as to MF/E patients (23.7E-06; n=9; $p<0.0001$). Similarly, median *TMEM244* expression was significantly higher in separated CD4+ T-cell population from SS (2,360E-06; n=6) than in CD4+ T cells from HIs (27.5E-06, n=14; $P<0.00084$) and those from MF/ erythroderma (70E-06, n=14; $P<0.002$). Presented study has also shown a difference between *TMEM244* expression in a single analyzed skin sample from SS patient (143E-06) compared to MF/E (14E-06; n=11). Performed analysis revealed higher *TMEM244* expression in T cells—both CD4+ (median=392E-06) and CD8+ (median= 557E-06) subpopulations than in CD19+ B cells (median=23E-06), CD56+ NK cells (median=106E-06), and CD14+ monocytes (median=51.4E-06). Moreover, the analysis of CD45RO+ memory T cells (median=189E-06), CD45RA+ naïve T cells (median=51E-06), and the youngest subset of CD31+ naïve T cells (median=75E-06) showed that the expression of *TMEM244* was associated with the post-activation state of T cells. In conclusion, obtained results indicate that the expression of *TMEM244* gene measured through RT-qPCR could be used as a new, easy and cheap blood diagnostic marker to distinguish SS from diseases with similar clinical presentation such as MF or erythroderma of non-malignant origin. What's more high *TMEM244* expression in cells with characteristic immunophenotype of Sézary cells (CD4+ and CD45RO+ cells), indicates its potential role in SS onset.