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HODGKIN (HL), FOLLICULAR (FL) AND DIFFUSE LARGE B CELL (DLBCL) LYMPHOMAS MICROENVIROMENT : CD26, CD38 AND CD39 ANALYSIS BY FLOW CYTOMETRY (FC)

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Introduction: Within the tumor microenvironment the adenosine, an immunosuppressive metabolite, is produced at high levels by CD38 and CD39 ectoenzymes and is accumulated due to the absence of the CD26 molecule. In a paper we have already showed how CD3+CD4+CD26-CD38+ lymphocytes characterize the immunosuppressed microenvironment of HL. We have analyzed CD26, CD38 and CD39 expression on CD4 T lymphocytes in order to verify whether they can characterize and distinguish the HL, FL and DLBCL microenvironment.

Materials and methods: Cell suspensions obtained by dissociating 21 non-neoplastic lymph nodes (N-N), 21 DLBCL, 23 FL and 15 HL were acquired by NAVIOS (BC) cytometer using the combination CD38Fitc/CD26Pe/CD3PC5.5/CD4PC7/CD39APC in order to analyze the positivity and intensity of antigen expression in CD4 T.

Results: CD38 was expressed on 28% of CD4 cells in N-N, 31% in DLBCL, 27% in FL and 52% in HL which significantly differs ($p<0,05$) from the other groups. All the subtypes significantly differed from N-N (11%) in the CD26-CD38+ subset and the high value (42 % of the CD4 cells) distinguishes HL from both FL (20%) and DLBCL (23%). This test resulted to have a high accuracy as obtained by the ROC curve analysis: the AUC was 0.9429 (95% CI: 0.876-1) with a cut off value of 21.6%. The percentage of CD39-positive CD4 cells is similarly significantly higher in all types of neoplastic samples (with mean values from 34 to 46%) than in N-N (19%) without differences between them. While maintaining the same significant differences with the N-N (32%) group, CD39 proportion in the CD26-CD38+ subset distinguishes the DLBCL (74%) from the other histotypes (FL 50% and HL 57%). DLBCL and HL express CD38 at a higher intensity on CD4 cell surface [value measured as the Mean Fluorescence Intensity (MFI)] with significant difference ($p<0.05$) between them and between FL and N-N. CD39 MFI is higher in DLBCL both in the all CD4 T and in the CD4+CD26-CD38+ subsets with significant differences ($p<0.05$) among all the other subtypes. CD39 MFI has a high capability to discriminate DLBCL from N-N, both in the CD4+ cells with AUC 0.8381 (95% CI: 0.7073-0.9689) and in CD4+CD26-CD38+ with AUC 0.781 (95% CI: 0.6339-0.928).

Conclusions: In the HL microenvironment a higher percentage of CD4+CD26-CD38+ is present, while CD38 MFI on all CD4 T defines the HL and the DLBCL neoplastic microenvironments and differentiates them from FL. In addition, a significant percentage of CD39 positivity characterizes CD4 T lymphocytes of the three neoplastic microenvironments but does not distinguish between them, while CD39 MFI distinguishes only DLBCL from the other lymphomas. The analysis of the percentage and intensity of CD38, CD26 and CD39 on CD4 T could be a quick diagnostic tool that

might contribute both to the characterization of the neoplastic microenvironment and the discrimination between lymphoma histotypes.