

Applicant's Name: Julie Michelle Wu, B.A.

Applicant's Division: Hematology

The Utility of CD71 Expression by Flow Cytometry in Differentiating Indolent From Aggressive CD10-Positive B Cell Lymphomas .

JM Wu, MJ Borowitz, EG Weir. The Johns Hopkins Hospital, Baltimore, Maryland.

Background:

Flow cytometry (FC) is an established methodology for identifying mature B cell lymphomas. The expression of CD10 raises a differential diagnosis that includes low-grade lymphomas (LGly) such as follicular lymphoma grades 1 or 2 (FL1, FL2), and high-grade lymphomas (HGly) such as FL3, Burkitt lymphoma (BL) and large cell lymphoma (LCL). Though forward light scatter (FSC) estimates malignant cell size, FC is limited in its capacity to distinguish CD10+ LGly from CD10+ HGly. Biologically aggressive tumors demonstrate high density of the transferrin receptor, CD71, due to large iron requirements for rapid cell growth. We hypothesize that CD71 fluorescence intensity (CD71i) is a useful marker for distinguishing indolent from aggressive CD10+ lymphomas by FC.

Design:

The Johns Hopkins Hospital FC files (1997-2004) were searched for cases of mature, CD10+ B cell lymphoma. In each case, FSC and CD71i of malignant B cells were measured and normalized by corresponding values for CD3+, DR- resting T cells. Nonparametric statistical analyses were used to determine significant differences between normalized values of LGly and HGly. Histologic diagnoses were confirmed in all cases.

Results:

A total of 44 LGly and 33 HGly were analyzed. Significant differences between LGly and HGly CD71i were observed by both the Mann-Whitney U test ($p < 0.01$) and ROC analysis after logistic regression (72% sensitivity, 71% specificity; $p < 0.01$). While FSC was significantly different between LGly and HGly ($p = 0.03$), the area under the curve (AUC) in ROC analysis was less than the AUC for CD71i. Neither FSC nor CD71i were significantly different between grades of FL. A comparison of all FL (FL1-3) and the remaining HGly (BL+LCL) showed significant differences in both CD71i ($p < 0.01$) and FSC ($p = 0.02$). Also, ROC analysis of LGly versus HGly showed an increased AUC for both CD71i and FSC when FL3 cases were excluded. Lastly, significant differences were observed in both CD71i and FSC when comparing FL and LCL ($p < 0.01$) but not when comparing FL and BL, regardless of FL3 exclusion.

Conclusion:

Both CD71i and FSC are generally useful in differentiating between CD10+ LGly and CD10+ HGly, though CD71i is superior to FSC based on a higher AUC in ROC analysis. While CD71i and FSC may also distinguish FL from BL and LCL, the ability to make this distinction improves when FL3 cases are excluded. The observation that FL3 has a CD71i and FSC intermediate between FL1-2 and HGly likely reflects the variable numbers of small cells in FL3.