To the editor:

Molecular classification of mature aggressive B-cell lymphoma using digital multiplexed gene expression on formalin-fixed paraffin-embedded biopsy specimens

The most frequent mature aggressive B-cell lymphomas are diffuse large B-cell lymphoma (DLBCL) and Burkitt lymphoma (BL). Patients suffering from molecularly defined BL (mBL) but treated with a regimen developed for DLBCL show an unfavorable outcome compared with mBL treated with chemotheraphy regimens for BL.1 Distinguishing BL from DLBCL by conventional histopathology is challenging in lymphomas that have features common to both diseases (aggressive B-cell lymphoma unclassifiable with features of DLBCL and BL [intermediates]).2 Moreover, DLBCLs are a heterogeneous group of lymphomas comprising distinct molecular subtypes: the activated B-cell–like (ABC), the germinal center B-cell–like (GCB), and the unclassifiable subtype as defined by gene expression profiling (GEP).3 Attempts to replace GEP with techniques applicable to formalin-fixed paraffin-embedded (FFPE) tissue led to algorithms for immunohistochemical staining (IHS).4 Disappointingly, the algorithms yielded conflicting results with respect to their prognostic potential, raising concerns about their validity.5 Furthermore, IHS algorithms did not provide a fully resolved classification: they did not identify mBL nor did they separate ABC from unclassified DLBCLs.4

We used digital multiplexed gene expression (DMGE) with FFPE-derived RNA to classify aggressive B-cell lymphomas. Our assay comprised only 30 genes (10 for the detection of mBL and 20 for the detection of ABC and GCB). We chose these genes by reanalysis of the microarray data reported in a previous study.6

CONFLICT OF INTEREST DISCLOSURE: The authors declare no competing financial interests.

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References

Figure 1. Digital multiplexed gene expression of mature aggressive B-cell lymphomas. (A) Molecular classification of mature aggressive B-cell lymphomas as mBL, non-mBL, and intermediates using FFPE-derived RNA. The expression of the genes is color coded such that high expression is shown in yellow and low expression in blue. The molecular labels assigned by the array using fresh-frozen RNA and DMGE (nCounter) assay using FFPE-derived RNA are indicated as colored labels in the top bars. (B) Molecular classification of non-mBL using FFPE-derived RNA. The classification according to IHS (Hans), the array using fresh-frozen RNA and the DMGE assay using FFPE-derived RNA are indicated as colored labels in the top bars.