DETECTION OF TERMINAL DEOXYNUCLEOTIDYL TRANSFERASE

To the Editor:

The recently published study of peripheral blood lymphocyte subpopulations in patients with acute immunodeficiency syndrome, by Murray et al.,1 may have contributed additional insight into normal T cell ontogenesis. However, the data on terminal transferase (TdT) must be interpreted with caution. It is stated that TdT levels are especially elevated in acute lymphocytic leukemia (ALL) of T cell origin. The concentration of TdT is actually lower in T cell than in null cell ALL.2,3 Furthermore, the enzyme is not detectable in mitogen-activated normal lymphocytes by biochemical assay4 or by Western blotting5; the report of putative TdT expression in such cells, as determined by indirect immunofluorescence (IF),6 may be a false-positive identification of TdT antigen.7

Murray et al purport to measure 'cytoplasmic TdT' with a kit supplied by Bethesda Research Laboratories (BRL). It should be noted that, at least in fresh human lymphocytes (whether normal8 or malignant9), TdT is predominantly a nuclear enzyme, as measured by immunobassay. Moreover, problems attendant on the use of the BRL kit have been described.10

Using the IF technique, Murray et al report the appearance of fluorescence in large lymphocytes with irregular nuclei. These were classified as 'null' cells and further described as having an increased nuclear-cytoplasmic ratio (presumably, in fact, a decreased nuclear-cytoplasmic ratio; typical of 'activated' lymphocytes). The likelihood of false-positive identification of TdT antigen in activated lymphocytes has been addressed.7 With the advent of monoclonal antibodies to human TdT11 it should be possible to determine with reasonable certainty whether cells, such as those studied by Murray et al, truly express this enzyme.

RONALD D. BARR
Department of Pediatrics
McMaster University
Hamilton, Ontario, Canada

RONALD P. McCAFFREY
Division of Medical Oncology
Boston University Medical Center
Boston, MA

REFERENCES

To the Editor

We agree with Drs Barr and McCaffrey that a higher incidence of false–terminal transferase (TdT)-positive cells has been observed in peripheral blood and other human tissues with the indirect immunofluorescence (IF) technique. The case of a single normal individual with 97% TdT-positive lymphocytes along with evidence of viral infection is interesting,1 particularly since the majority of acquired immunodeficiency syndrome (AIDS) patients in our study were subsequently human T cell leukemia virus-III antibody-positive and/or had other viral infections at the time of study. We used the IF technique not only because of its simplicity, but also because it was difficult to obtain and culture large numbers of lymphocytes (10⁷-10⁸ cells) from AIDS patients for biochemical or Western blotting analysis.2 It must be noted that the sensitivity of the Bethesda Research Laboratories kit is actually less than that of other IF methods tested in acute lymphocytic leukemia.3 Hence, the likelihood of false-positives may actually be lower. Nevertheless, it remains to be proven whether the lack of measureable TdT enzyme in normal phytohemagglutinin-activated lymphocytes can be reproduced in lymphocytes from AIDS patients.

A study by Bradstock et al. demonstrated coexpression of common lymphoblastic leukemia antigen and HLADR, but not T-lineage antigens on peripheral blood lymphocytes that were TdT-positive by IF. Since AIDS patients had more HLADR and Tα positive cells, this also suggests a possible bone marrow or even B cell origin4 for the TdT positive-cells seen. Despite the fact that the IF technique may sacrifice specificity for sensitivity, it remains a challenge to determine whether rabbit anti-TdT antibody is detecting cross-reactive antigens which might be virally induced or related
Detection of terminal deoxynucleotidyl transferase [letter]
RD Barr and RP McCaffrey

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