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Letter

Comments on: Cyclopentenyl cytosine inhibits cytidine triphosphate synthetase in paediatric acute non-lymphocytic leukaemia: a promising target for chemotherapy. A.C. Verschuur *et al. Eur J Cancer* 2000, **36**, 627–635

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I read with interest the article by Verschuur and colleagues entitled "Cyclopentenyl cytosine inhibits cytidine triphosphate synthetase in paediatric acute non-lymphocytic leukemia". *Eur J Cancer* 2000, **36**, 627–635. The authors report a significant increase in the activity of the enzyme cytidine triphosphate synthetase in the bone marrow cells of paediatric patients with acute non-lymphocytic leukaemia (ANLL) compared with the level in granulocytes from healthy volunteers, but not significantly different from the level in CD34+ non-malignant marrow cells. They base their paper on the former finding, ignoring the latter. I have proposed the opposite view and suggested, entirely on theoretical grounds, that an impairment of this enzyme in paediatric acute leukaemia could be mutagenic leading to G→A and C→T transitions in the DNA molecule [1,2].

The biochemical counterpart of cell differentiation is the replacement of cytoplasmic RNA by protein [3]. The enzyme cytidine triphosphate synthetase converts uridine triphosphate to cytidine triphosphate, an essential step not only for the synthesis of cytidine triphosphate required for RNA synthesis, including the synthesis of mRNA required for myeloid, erythroid megakaryocytic differentiation, but also for the synthesis of deoxycytidine triphosphate and deoxythymidine triphosphate required for DNA synthesis [4,5]. The demand for the enzyme in an active proliferating and differentiating marrow is clearly greater than in mature white cells of the peripheral blood. The chemistry of a leukaemic marrow should, on physiological grounds therefore, be compared with that of a normal marrow and not with that of mature granulocytes. May I, with respect, suggest that the comparison of the enzyme activity in ANLL marrow cells with that in the normal CD34+ marrow is the relevant one. This showed no significant difference, the mean is marginally higher in the normal marrow, but the numbers are too small for statistical analysis. The difference in enzyme activity between the ANLL marrow cells and the mature granulocytes is of the same order as the difference between the normal CD34+ marrow and the granulocytes, the latter reflecting again the physiological difference in enzyme activity between the normal marrow and normal granulocytes.

A raised cytidine triphosphate synthetase activity in the ANLL marrow cells is also at variance with their finding that the concentration of uracil ribonucleotides (8.7±2.8 pmol/μg protein) is more than 3-fold the concentration of the cytidine ribonucleotides (2.4±1.3 pmol/μg protein) in the same cells. If the enzyme activity is raised the opposite would be expected.

References

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