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# This Week's Citation Classic®

Catovsky D, Pettit J E, Galetto J, Okos A & Galton D A G. The B-lymphocyte nature of the hairy cell of leukaemic reticuloendotheliosis. *Brit. J. Haematol.* **26**:29-37, 1974.
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This study compared the properties of the neoplastic cells of "hairy cell" leukaemia with those of lymphocytes and monocytes. Evidence for a B-lymphocytic nature was provided by the demonstration of immunoglobulins on the cell surface and the absence of receptors characteristic of T lymphocytes and monocytes. [The *SCI*® indicates that this paper has been cited in over 225 publications.]

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When Bouroncle and colleagues[1] described hairy cell leukaemia as a distinct type of human leukaemia, the methodology for characterising the membrane phenotype of lymphocytes was not yet available. The peculiar morphology of the hairy cell with its long cytoplasmic villi, well demonstrated by phase contrast microscopy, had some resemblance with that of histiocytes as seen in tissue sections. For that reason and because of the ideas prevalent at the time that most haemopoietic cells were derived from the "reticuloendothelial system" (RES), the disease was considered a neoplasia of RES cells.[1]

In the 1970s the concept of RES was replaced by the better-defined mononuclear phagocyte system, and techniques became available to identify B and T lymphocytes. These were shown to have immunoglobulin molecules on the cell membrane (B cells) or specific receptors for sheep erythrocytes (T cells). It was at that time, whilst on a fellowship working under D.A.G. Galton, that I identified several patients with a disease similar to that described by Bouroncle and colleagues.[1] The next step was to set up the methods available at the time to study lymphocytes and mononuclear phagocytes (monocytes). For comparison, we used cells from other leukaemias that were known to be lymphocytic or monocytic. Although the answer obtained was not completely convincing by current standards, the evidence of the study suggested to us that hairy cells were closer to B cells than to monocytes, although showing some phagocytic properties.

Our publication was the first to suggest a B-cell nature for hairy cells and for that reason all the subsequent studies whether confirming or criticising our observations were bound to refer to it. Furthermore, as the methods and reagents used in the 1970s for membrane marker studies were still imperfect, the unequivocal demonstration of a B-cell origin for these cells was not achieved until recently.

The development of the hybridoma technology and the methods for molecular genetics[2] have now been used to show that hairy cells share membrane antigens with B lymphocytes, not with monocytes,[3] and express features of activated B cells[2,4] that are close to the late stages of the B-cell maturation pathway.[5] The demonstration of rearrangement of the genes for heavy and light chains of immunoglobulins (by Korsmeyer and colleagues[2]) proved conclusively that hairy cell leukaemia results from the monoclonal expansion of B cells.

In recent years, our group has used the knowledge of the antigenic profile of hairy cells to search for a possible counterpart of this cell in normal blood. Recent studies,[6] using a combination of monoclonal antibodies with the immunogold method at the ultrastructural level, have shown that a cell with similar morphology and membrane phenotype can be found as a minority population in the blood of normal individuals. By analogy with findings in other leukaemias, we have suggested that hairy cell leukaemia results from the neoplastic transformation of that cell, which of course may also be present in other haemopoietic tissues. The curious features of hairy cells have attracted the attention of investigators in the field of haematopathology and immunology. The remarkable results in the treatment of this disease with alpha interferon will guarantee that papers about hairy cell leukaemia and its cell of origin will continue to appear.

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