

This Week's Citation Classic™

Lewis M G, Ikonopisov R L, Nairn R C, Phillips T M, Hamilton Fairley G, Bodenham D C & Alexander P. Tumour-specific antibodies in human malignant melanoma and their relationship to the extent of the disease. *Brit. Med. J.* 3:547-52, 1969.

[Chester Beatty Res. Inst., Sutton, Surrey, Royal Marsden Hosp. and St. Bartholomew's Hosp., London, and Frenchay Hosp., Bristol, England; Dermatol. Dept., Oncol. Res. Inst., Sofia, Bulgaria; and Dept. Pathol., Monash Univ., Melbourne, Australia]

In a study of 103 melanoma patients, autoantibodies were found directed against either cell surface membranes or cytoplasmic contents. The antibodies were most often seen in the early stages of disease, but also reappeared in two individuals with metastases following autoimmunization with tumor-cell preparations. [The SCI® indicates that this paper has been cited in over 420 publications since 1969.]

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March 5, 1985

The idea for this paper was initially conceived as the result of studies carried out in Uganda, East Africa, between 1965 and 1968. These earlier investigations identified cytotoxic factors in the sera of Africans with malignant melanoma.^{1,2} This came to the attention of Peter Alexander and Gordon Hamilton Fairley, who invited me to join the staff of the Chester Beatty Research Institute to continue the work.

It was decided that a number of different assays should be used on the same serum samples to demonstrate the presence of antibodies and that freshly prepared melanoma cells obtained from the same patient should be used as the substrate. This posed a number of logistical problems. In the first place, how were we to obtain a sufficient supply of serum from melanoma patients and, more importantly, also get freshly removed tumor tissue? Second, who would provide the detailed clinical information on those patients, particularly the precise staging of the disease? And third, who would be available to develop the additional assays apart from those I had already developed? The first two obstacles were overcome by re-

cruiting to our team one of the most experienced surgeons in the field of melanoma research anywhere, the late Dennis Bodenham of Frenchay Hospital, Bristol, by the cooperation of numerous colleagues in the London area, and by the great efforts of members of Mulago Hospital, Kampala, who arranged to send regular shipments of tumor biopsies and serum from patients in Uganda. This meant that members of the group had to meet planes arriving from Entebbe and trains from Bristol at all hours of the day and night. Since we were not certain of the effect of storage on the specimens at that stage, the assays were performed immediately on their arrival, often resulting in the laboratory personnel and the investigators working somewhat irregular and unusual hours! The final problem of the variety of assays was solved by the composition of the research team. We were particularly fortunate to have two visiting professors, Rufus Ikonopisov from Bulgaria, and Richie Nairn from Melbourne, who, working with Terry Phillips and me, developed some unique approaches to the identification of tumor-specific and tumor-associated antimelanoma antibodies.

I believe the frequency with which this publication has been cited over the ensuing years is largely due to this close collaboration of individuals, each of whom brought to the project his own special skills and enthusiasm. The work resulted in one of the first detailed studies of humoral immunity in a human tumor system and introduced the feasibility of sequential investigations using relatively simple methods. This has resulted in a large number of similar^{3,4} and, in some cases, more sophisticated studies, not only in melanoma but many other human tumors.^{5,6}

Since this publication, three of my co-workers have died, Bodenham, Ikonopisov, and Hamilton Fairley, the latter killed in London by a terrorist bomb meant for someone else. I would like to dedicate this Citation Classic to their memories.

1. Lewis M G. Possible immunological factors in human malignant melanoma in Uganda. *Lancet* 2:921-2, 1967. (Cited 95 times.)
2. Lewis M G & Kiryabwire J W M. Aspects of behavior and natural history of malignant melanoma in Uganda. *Cancer* 21:876-87, 1968.
3. Morton D L, Malmgren R A, Holmes E C & Ketcham A S. Demonstration of antibodies against human malignant melanoma by immunofluorescence. *Surgery* 64:233-40, 1968. (Cited 400 times.)
4. Hellström I, Sjögren H O, Warner G & Hellström K E. Blocking of cell-mediated tumor immunity by sera from patients with growing neoplasms. *Int. J. Cancer* 7:226-37, 1971. (Cited 515 times.)
5. Lewis M G, Phillips T M, Rowden G & Jerry L M. Humoral immune reactions in cancer patients. (Waters H, ed.) *The handbook of cancer immunology. Volume 3. Immune status in cancer treatment and prognosis—part A.* New York: Garland STPM Press, 1978. p. 159-261.
6. Reisfeld R A & Ferrone S, eds. *Melanoma antigens and antibodies.* New York: Plenum, 1982. 445 p.