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Barnstable C J, Bodmer W F, Brown G, Galfre G, Milstein C, Williams A F & Ziegler A. Production of monoclonal antibodies to group A erythrocytes, HLA and other human cell surface antigens—new tools for genetic analysis. *Cell* 14:9-20, 1978. [Genetics Laboratory, University of Oxford; MRC Immunochemistry Unit, Department of Biochemistry, University of Oxford; and MRC Laboratory of Molecular Biology, Cambridge, England]

Monoclonal antibodies were used to identify a number of human cell surface antigens and to identify the chromosomal location of their respective genes. Among the antibodies was one (W6/32) recognizing HLA-A,B,C (class 1) antigens coded for by chromosome 6, three (W6-34, W6-42, W6-44) detecting antigens coded for by the short arm of chromosome 11, and one (W6/1) recognizing human blood group A erythrocytes. [The *SCI*® indicates that this paper has been cited in more than 1,140 publications.]

Monoclonal Antibodies to Human Cell Surface Antigens

Colin J. Barnstable

**Department of Ophthalmology and Visual Science
Yale University School of Medicine
New Haven, CT 06510**

In the mid-1970s, monoclonal antibodies (MAbs) were novel, and it was not at all clear how easy they would be to prepare or whether the assays available would be satisfactory for their use. The analysis of MAbs against cell surface molecules of nucleated cells had been started in a collaboration between the laboratories of Alan F. Williams and Cesar Milstein, and, in a fusion called W3, mouse MAbs against rat T-cell differentiation antigens were described.[1] Immunizations with human leukocyte membranes were begun in an attempt to find human T-cell differentiation antigens, but instead, MAbs against antigens of broad distribution resulted from the W6 fusion. At the time, I was undertaking my D.Phil, studies with Walter F. Bodmer on HLA antigens, and we joined the collaboration to analyze the W6 antibodies.

One of the antibodies (W6/32) was shown to recognize the 43 kilodalton, or heavy chain, of HLA Class 1 antigens by using mutant cell lines, by genetic mapping with human-mouse somatic cell hybrids, and by molecular analysis.

Two other antigens expressed on a wide variety of tissues were mapped to the short arm of chromosome 11. The antigens appear to be glycolipids and the genes on chromosome 11 probably represent glycosyl transferases. Via serendipity, it was discovered that one antibody, W6/1, recognized human blood group A. At the time, it was surprising to find an antibody that could be so easily raised against a polymorphic determinant in an immunization across the species barrier, but this was soon further substantiated by the production of MAbs against polymorphic determinants of HLA Class 1 and Class 2 antigens.[2]

There are probably two reasons why this paper has been cited frequently. One is that it was the first example of MAbs being raised against human cells; the second was that W6/32 has probably been the most useful antibody for the immunochemical analysis of HLA Class 1 antigens. It has also become a benchmark for the serological definition of HLA Class 1 antigens.

The approach of raising MAbs from xenogeneic immunizations has been a powerful one in defining surface molecules of eukaryotic cells, including leukocytes,[3] neuronal cells,[4] molecules of the immunoglobin superfamily,[5] and malignant cells,[6] to name but four examples. Furthermore, genetic manipulation of MAbs against cell surface moiecules for clinical use is a subject of major contemporary interest.[7]

Of a number of awards to the authors since 1978, perhaps the most important, and most deserved, is the Nobel Prize in physiology or medicine awarded to Milstein (with Georges Köhler and Niels Jerne) in 1984.

1. **Williams A F, Galfre G & Milstein C.** Analysis of cell surfaces by xenogeneic myeloma-hybrid antibodies: differentiation antibodies of the lymphocyte surface. *Cell* 12:663-73, 1977. (Cited 630 times.)
2. **Brodsky F M, Parham P, Barnstable C J, Crumpton M J & Bodmer W F**. Monoclonal antibodies for analysis of the HLA system. *Immunol. Rev.* 47:3-61, 1979. (Cited 560 times.) [See also: **Brodsky F M.** Citation Classic. *Current Contents/Life Sciences* 30(2): 16, 12 January 1987.]
3. **Knapp W et al.,** eds. *Leukocyte typing IV—white cell differentiation antigens.* Oxford, England: Oxford University Press, 1989.
4. **Barnstable C J.** Monoclonal antibodies which recognise different cell types in the rat retina. *Nature* 286:231-5, 1980. (Cited 180 times.)
5. **Williams A F & Barclay A N**. The immunoglobulin superfamily—domains for cell surface recognition. *Annu. Rev. Immunol.* 6:381-405, 1988. (Cited 400 times.).
6. **Smith M E F, Marsh S G E**, **Bodmer J G. Gelsthorpe K & Bodmer W F.** Loss of HLA-A,B,C allele products and lymphocyte function associated antigen 3 in colorectal neoplasia. *Proc. Nat. Acad. Sci. USA* 86:5557-61, 1989.
7. **Winter G & Milstein** C. Man-made antibodies. *Nature* 349:293-9, 1991.

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