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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.
[Genetics Lab., Dept. Biochemistry, Univ. Oxford, England; Biological Labs., Harvard Univ. and Sidney Farber Cancer Inst., Charles A. Dana Cancer Ctr., Boston; Dept. Neurobiology, Harvard Medical Sch., Boston, MA; and Natl. Inst. Medical Research, London, England]

This paper is a review of techniques and strategies used for the production, characterization, and experimental application of monoclonal antibodies reacting with human histocompatibility (HLA) antigens. Characteristics of antibodies recognizing both Class I and Class II antigens are described. Their use in protein purification and analysis of antigenic structure and evolution and as probes for the cellular function and expression of HLA is demonstrated by representative experiments. [The *SCI*® indicates that this paper has been cited in over 405 publications.]

Frances M. Brodsky
Becton Dickinson Immunocytometry Systems
2375 Garcia Avenue
Mountain View, CA 94039

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Soon after C. Milstein (MRC, Cambridge) demonstrated the potential of monoclonal antibodies for recognition of cell surface antigens,[1] anti-HLA monoclonal production was initiated in W.F. Bodmer's laboratory (Genetics Laboratory, Oxford). C.J. Barnstable, a third-year DPhil student, introduced the technique through his collaboration with A. Williams and Milstein, characterizing the HLA-specific monoclonal W6/32.[2] P. Parham, a visiting Harvard Junior Fellow, catalyzed the Bodmer lab effort by importing purified HLA from J. Strominger's lab for immunization, eventually producing the anti-HLA-A2 monoclonal antibody PA2.1.[3] I joined the HLA monoclonal project during my second year as a Marshall Scholar, when, trying to make anti-T-cell monoclonal antibodies, I produced the lab's first HLA-specific monoclonal (BBM.1).[4] Our collaborative efforts peaked with the "Genox" fusion (Genetics-Oxford) produced from mice, immunized at Mill Hill, and sent to us on the train by M.J. Crumpton. We passaged about 100 clones, finally isolating 1 stable one (Genox 3.53).

In Autumn 1978 Barnstable began his career at Harvard in neurobiology, and Parham returned to Strominger's lab where he continued our collaboration, transatlantic. Combining resources from the Bodmer and Strominger laboratories, we were able to expand the panel of anti-HLA antibodies and to carry out the biochemical and evolutionary studies described in this paper. As a prelude to organizing my own DPhil thesis, I wrote this review, which was almost not published due to a secretarial error in sending it to the wrong editorial office.

Recalling our work in Oxford reminds me of the Monty Python sketch of the four successful Yorkshiremen who try to impress each other with the hardships they suffered before achieving their present comfort. Their experiences were "luxury" compared to making monoclonals in the Genetics Laboratory. Tissue culture conditions were such that our incubator alternately housed "Yankee yeast" and "Frances's fungus" (nomenclature courtesy of A.S. Whitehead). Economic conditions were such that during the 18 months of work described in this paper, we endured a Firemen's strike during which tissue culture was allowed only from 10 a.m. to noon, a nitrogen delivery strike that necessitated keeping the cell freezers in the cold room, and a manufacturer's strike that prevented us from getting tissue culture plates until L. Herzenberg generously sent a case from California. Many of the reliable but convoluted techniques we describe in this paper ensured that our cells would survive these varying circumstances. Fortunately, subsequent developments in many laboratories have made monoclonal production much more straightforward. They have also made interpretation of data more straightforward, rendering this paper's speculative discussion on the genetic organization of the HLA region historically interesting but incorrect.

The frequent citation of this paper is probably due to several factors. Originally, it was a useful source of methods for monoclonal antibody production and characterization. It also contains a comprehensive list of the Bodmer lab cell lines and the anti-HLA antibodies produced during that period. As these are all available from the National Institute of General Medical Sciences and American Type Culture Collection cell banks, this paper provides a useful reference for these reagents, which are still in international use by many HLA laboratories.

1. Köhler G & Milstein C. Continuous cultures of fused cells secreting antibody of predefined specificity. *Nature* 256:495-7, 1975. (Cited 4,435 times.)
2. Barnstable C J, Bodmer W F, Brown G, Galfrè 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. (Cited 555 times.)
3. Parham P & Bodmer W F. Monoclonal antibody to a human histocompatibility alloantigen, HLA-A2. *Nature* 276:397-9, 1978. (Cited 145 times.)
4. Brodsky F M, Bodmer W F & Parham P. Characterization of a monoclonal anti-β_2-microglobulin antibody and its use in the genetic and biochemical analysis of major histocompatibility antigens. *Eur. J. Immunol.* 9:536-45, 1979. (Cited 115 times.)