# T Cell Hybridomas

Editor

Michael J. Taussig, Ph.D.

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After reading natural sciences at Trinity College, Cambridge, Dr. Taussig was a research student in immunology under Dr. Peter Lachmann in the Department of Pathology, Cambridge, receiving his Ph.D. in 1970 for a dissertation on the subject of antigenic competition. He was elected a Research Fellow of Trinity College, Cambridge in 1970 and was College Lecturer in Pathology from 1974 to 1979. While most of his research career has been spent in Cambridge, he has also worked at the Weizmann Institute of Science in Israel and the Basel Institute of Immunology in Switzerland. He joined the staff of the Agricultural Research Council's Institute of Animal Physiology in 1977.

Most of Dr. Taussig's research has been spent in the area of immunoregulation by T cells. In 1974 he discovered the molecules known as antigen-specific helper factors and demonstrated their relationship to the major histocompatibility complex and immune response genes. His recent work has been concerned with the characterization of helper and suppressor factors from T cells and T cell hybridomas. He has published over 60 papers in immunology and is author of a student textbook entitled *Processes in Pathology and Microbiology* (Blackwell Scientific Publications, Oxford).

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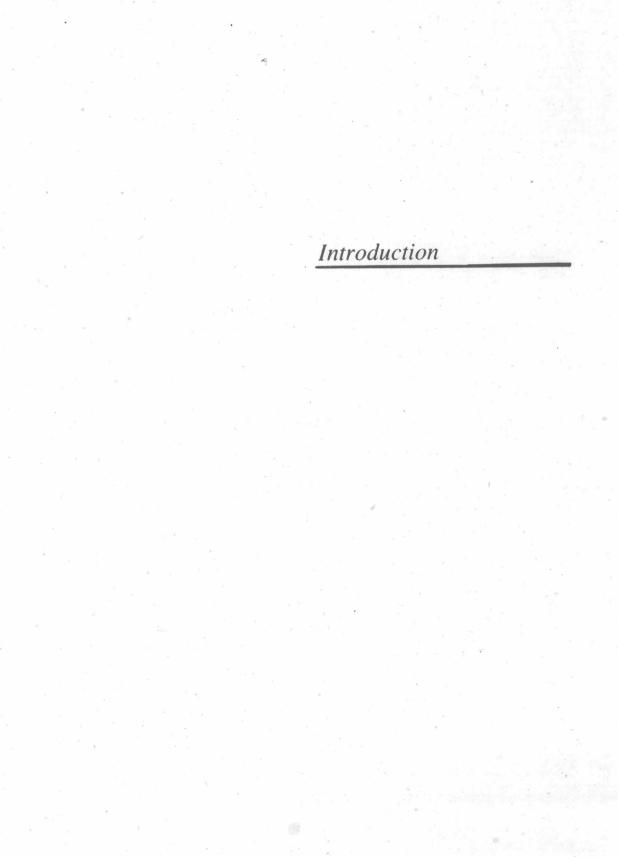
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T Cell Hybridoma

## WHY T CELL HYBRIDOMAS?

#### Michael J. Taussig

The purpose of this book is to bring together original papers and review articles on cloning and immortalization of T lymphocytes by hybridization and give some idea of the current scope and future potential of this method. It is by no means the first volume in this area and, given the rate at which work on T cell hybridomas is progressing, it is unlikely to be the last word; but I hope it will represent the "state of the art" as well as provide a comprehensive guide to the literature.

The development of T cell hybridomas was a natural offshoot of the Köhler/Milstein method for making monoclonal antibodies, but in comparison was rather slow starting. Following the first use of the thymoma BW5147 to immortalize mouse T cells by fusion, there were doubts about whether functional hybrids could be obtained. These soon disappeared, however, and in the last 3 to 4 years there has been a remarkable surge of activity in this area, with dozens of functional T hybridomas described in the fast-growing literature. It seems that all important T cell functions can probably be successfully immortalized by fusion with BW5147, including, with some expedients, cytotoxicity.

At this point, it is worth remembering that fusion is not the only means of preparing monoclonal T cell lines. T cells can also be transformed by radiation leukemia virus, 12.13 or cloned in the presence of interleukin-2.4 T cell hybridomas have some advantages as well as a few drawbacks. Among the former are the ease with which they can be prepared and cloned, and their rapid growth to any desired number in the absence of accessory cells or growth factors.14 The problem of stability has been much discussed and there is no doubt that, in general, T cell hybridomas are less stable than B cell hybridomas, i.e., their function is more likely to disappear in a relatively short time unless rescued by regular recloning. Chromosome loss over the first few weeks after fusion is probably partly responsible, and thereafter many lines of interest have proved to be as stable as antibody-producing hybrids. Another problem concerns the extent to which the parent thymoma cell determines the properties of its hybrids. For B cells, use of the NSO line can ensure that a monoclonal antibody is always homogeneous and possesses only the immunoglobulin chains of the normal B cell partner. BW5147, however, is not a T cell equivalent of NSO, and there are by now several instances where receptor or functional properties of a T cell hybridoma have been determined, at least in part, by the thymoma genome. The production of an idiotype-positive, arsonate-binding protein, 15 the expression of receptors for red cells, 16 and the MHC-restriction specificity of hybrids and their helper products<sup>17</sup> are all examples and there are probably others. Moreover, BW5147 will fuse with cells other than T cells (e.g., B cells) and may, impose a T cell phenotype on them, 18,19 This may explain why surface markers of murine T cell hybridomas are sometimes at odds with the functions of these cells, based on expectations from normal T cell populations.

The sought-after properties which make T cell hybridomas potentially so useful to immunology are, of course, their monoclonality and ability to grow rapidly and permanently. One area in which this is immediately exploitable is in disentangling the web of nonantigen-specific lymphokines and defining their biochemistry; T cell hybridomas should eventually bring order to this field which, through different assays and nomenclatures, has threatened to become impossibly complex. 20.21 The development of human-human hybridomas producing lymphokines is an important advance which may in the future be clinically useful in transplantation or allergy. T cell hybridomas have also become a principal source of

antigen-specific soluble factors and it will surely not be very long before the structure of these molecules is established and their relation to the T cell receptor understood.

Perhaps most impressive is the use of T cell hybridomas in elucidating the molecular nature and genetic origin of the T cell receptor itself. Three main approaches have been followed so far:

- 1. Isolation of the receptor from antigen-specific, MHC restricted hybridomas by means of monoclonal antireceptor antibodies. <sup>22</sup> The purified receptor is, apparently, a disulfide-bridged dimer of 80,000 to 90,000 mol wt, with component chains of 40,000 to 44,000 mol wt, a result which compares very closely with the receptor similarly isolated from human T cell clones. <sup>23</sup> It seems that the structure of the T cell receptor is finally at hand. It is interesting that the chain composition of the receptor bears little obvious resemblance to that of the antigen-specific T cell factors from T cell hybridomas <sup>24</sup> or clones. <sup>25</sup>
- 2. The use of DNA probes against B cell V<sub>H</sub> genes to ask whether antigen-recognition by T cell depends on the expression of these genes. The nearly universal finding is that, in antigen-specific T cell hybridomas, antibody V<sub>H</sub> genes are not rearranged or transcribed. For example, the experiments of Hood and colleagues leave little doubt that T and B cells use separate V gene families. It has also become clear that the sharing of a serological determinant, detected by anti-idiotypic or anti-V<sub>H</sub> antibodies, does not imply the expression of the same V gene in T cells and B cells. 26.28
- The application of somatic cell genetics to identify the chromosome(s) coding for the T cell receptor, 30 and to settle the debate over single and dual receptor models for associated recognition of antigen/MHC by T cells. 17,31,32 As regards the former, Marrack and Kappler<sup>30</sup> used the segregation of metacentric (Robertsonian) chromosomes in T cell hybridomas to show that chromosomes 4, 6, 16, and 17 were unlikely to contribute to the coding for the receptors, ruling out a role for light chain genes (chromosomes 6 and 16) and the MHC (chromosome 17). The question of whether genes on chromosome 12 are required for antigen recognition by T cells has not yet been resolved. The single receptor/dual receptor problem can be approached by genetic complementation in hybridomas, i.e., can the product of an antigen-specific locus functionally recombine with that of an independent, MHC-restricting locus in the same T-hybridoma cell? The results of different groups are, however, contradictory. According to Lonai et al., 17,31 complementation occurs both in the T cell receptor and in an antigen-specific helper factor, thus supporting the dual recognition (two loci) model. On the other hand, Kappler et al. 32 found no evidence for complementation in hybridomas constructed with dual antigen and dual MHC specificities, arguing against the independent recognition of antigen and MHC determinants.

The articles which follow further illustrate the important contribution being made by T cell hybridomas to formerly impenetrable areas of immunology. I would like to thank-all the authors for providing their contributions on time and for making the editorial task relatively painless.

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- 1. Hämmerling, G. J., Hämmerling, V., and Kearney, J. F., Eds., Monoclonal antibodies and T cell hybridomas, Research Monographs in Immunology, Vol. 3. Elsevier, Amsterdam, 1982.
- von Boehmer, H., Haas, W., Köhler, G., Melchers, F., and Zeuthen, J., Eds., T cell hybridomas, Curr. Top. Microbiol. Immunol., 100, 1982.
- 3. Feldmann, M. and Schreier, M., Eds., Monoclonal T cells and their products, Lymphokines, 5, 1982.
  - 4. Fathman, C. G. and Fitch, F. W., Eds., Isolation. Characterisation and Utilisation of T Lymphocyte Clones, Academic Press, New York, 1982,
  - Köhler, G. and Milstein, C., Continuous cultures of fused cells secreting antibody of predefined specificity, Nature (London), 256, 495, 1975.
  - 6. Goldsby, R. A., Osbourne, B. A., Simpson, E., and Herzenberg, L. A., Hybrid cell lines with T-cell characteristics. *Nature (London)*, 267, 707, 1977.
  - Hämmerling, G. J., T lymphocyte tissue culture lines produced by cell hybridisation, Eur. J. Immunol., 7, 743, 1977.
  - 8. Köhler, G. Lefkovits, I., Elliott, B., and Coutinho, A., Derivation of hybrids between a thymoma line and spleen cells activated in a mixed leukocyte reaction, Eur. J. Immunol., 7, 758, 1977.
  - 9. Melchers, F., T cell hybrids: short cut or dead end?, Nature (London), 271, 9, 1978.
  - Nabholz, M., Cianfriglia, M., Acuto, O., Conzelmann, A., Haas, W., von Boehmer, H., MacDonald, H. R. and Johnson, J. P., Cytolytically active murine T cell hybridomas, *Nature (London)*, 287, 437, 1980.
  - Kaufmann, Y., Berke, G., and Eshhar, Z., Cytotoxic T lymphocyte hybridomas which mediate specific tumor cell lysis in vitro, *Proc. Natl. Acad. Sci. U.S.A.*, 78, 2502, 1981.
- Ricciardi-Castagnoli, P., Doria, G., and Adorini, L., Production of antigen-specific suppressive T cell factor by radiation leukaemia virus-transformed suppressor T cells., Proc. Natl. Acad. Sci. U.S.A., 78, 3804, 1981.
- Adorini, L., Doria, G., and Ricciardi-Castagnoli, P., Fine antigenic specificity and genetic restriction of lysozyme-specific suppressor T cell factor produced by radiation leukaemia virus-transformed suppressor T cells., Eur. J. Immunol., 12, 719, 1982.
- Beezley, B. B. and Ruddle, N. H., A critical evaluation of the T cell hybrid technique., J. Immunol. Methods, 52, 269, 1982.
- Clark, A. and Capra, J. D., Ubiquitous nonimmunoglobulin p-azobenzene-arsonate-binding molecules from lymphoid cells., J. Exp. Med., 155, 611, 1982.
- Taussig, M. J. and Binns, R. M., Binding of red cells by T cell hybridomas, in T Cell Hybridomas, Taussig, M. J., Ed., CRC Press, Boca Raton, Fla., 1984, chap. 3.
- Lonai, P., Bitton, S., Hubb, F. J. S., Puri, J., and Hämmerling, G. J., Two separate genes regulate self-la and carrier recognition in H-2-restricted helper factors secreted by hybridoma cells, J. Exp. Med., 154, 1910, 1981.
- Taussig, M. J., Holliman, A. and Wright, L. J., Hybridisation between T and B lymphoma cell lines, Immunology, 39, 57, 1980.
- Iverson, G. M., Goldsby, R. A., and Herzenberg, L. A., Expression of Thy-1.2 antigen on hybrids of B cells and a T lymphoma, Curr. Top. Microbiol. Immunol., 81, 191, 1978.
- 20. **Ruddle**, N. H. and Conta, B. S., Lymphotoxin and immune (γ) interferon production by T cell lines and hybrids, *Curr. Top. Microbiol. Immunol.*, 100, 239, 1982.
- 21. Schrader, J. W. et al., T cell hybridomas and the analysis of T cell lymphokines, in T Cell Hybridomas, Taussig, M. J., Ed., CRC Press, Boca Raton, Fla., 1984, chap. 5.
- Haskins, K., Kubo, R., White, J., Pigeon, M., Kappler, J., and Marrack, P., The major histocompatibility complex-restricted antigen receptor on T cells. I. Isolation with a monoclonal antibody, J. Exp. Med., 157, 1149, 1983.
- Meuer, S. C., Acuto, O., Hussey, R. E., Hodgdon, J. C., Fitzgerald, K. A., Schlessman, S. F., and Reinherz, E. L., Evidence for the T3-associated 90K heterodimer as the T-cell antigen receptor., *Nature* (*London*), 303, 808, 1983.
- Taussig, M. J. and Holliman, A., Structure of an antigen-specific suppressor factor produced by a Thybrid line., Nature (London), 277, 308, 1979.
- Fresno, M., McVay-Boudreau, L., and Cantor, H., Antigen-specific T lymphocyte clones. III. Papain splits purified T suppressor molecules into two functional domains, J. Exp. Med., 155, 981, 1982.
- Kraig, E., Kronenberg, M., Kapp, J. A., Pierce, C. W., Abruzzini, A. F., Sorensen, C. M., Samelson, L. E., Schwartz, R. H., and Hood, L. E., T and B cells that recognise the same antigen do not transcribe similar heavy chain variable region gene segments., J. Exp. Med., 158, 192, 1983.