of conglutinin and immunoconglutinins are provided by the late D. G. Ingram. Characterization of these serum factors (conglutinins of normal bovine serum and immunoconglutinin antibodies produced in many mammalian species following antigen stimulation) that interact with adsorbed complement components, their role in immune reactions and their use as serological tools are competently dealt with. L. N. Ruben comprehensively reviews the variety of *in vivo* and *in vitro* immunological studies being performed on amphibians and clearly illustrates the value of this vertebrate class, particularly the tailless anurans, in the study of basic characteristics of immune responses.

This putative overview of animal models contains no chapter on avian immunology – surprisingly, since the chicken and the quail have offered invaluable and unique insight into the origins and differentiation of T and B lymphocytes. The invertebrates are ignored altogether, although several backboneless phyla are helpful in exploring the evolution of the cells and molecules involved in vertebrate immunity. These are disappointing omissions in a book that otherwise will have interest and considerable value for many immunobiologists.

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HLA in Endocrine and Metabolic Disorders

edited by N. R. Farid, Academic Press, 1981. £25.80/$39.00 (xiii + 357 pages) ISBN 0 12 247780 4

This is the first book entirely devoted to reviewing the connections between endocrine and metabolic diseases, and the histocompatibility genes. A gallant attempt was made to describe clinical, metabolic and immunological features to HLA serologists and geneticists. Conversely, several chapters are designed to explain problems of tissue typing and genetics to clinicians interested in autoimmune or metabolic endocrinology. All the credit for this welcome interdisciplinary approach must go to the editor, N. R. Farid, who also wrote two erudite chapters on autoimmune thyroid diseases. The contributors were selected among well-known researchers in different areas of expertise so that they are very familiar with their own subject and fairly ignorant of other viewpoints. This makes the book all the more valuable if one wishes to approach one's own research with new eyes to formulate working hypotheses. Much of the data on susceptibility to disease in relation to HLA is still incomplete and results are liable to prejudiced interpretations. Reading this book might help to correct any mental astigmatism introduced in specialized fields such as endocrine autoimmunity. Autoimmunologists tend to see the HLA region as mostly concerned with immunocyte networks and are liable to forget that enzymes concerned with steroid synthesis or iron absorption are coded in the same haplotypes. There are two excellent chapters on congenital adrenal hyperplasia syndromes which are due to absence of various enzymes required in steroid synthesis and on idiopathic haemochromatosis where the patients absorb too much iron. These two sets of diseases are linked to loci near the region of chromosome 6 which controls immune responsiveness yet they are totally unconnected to autoimmunity or infections. Another chapter deals with metabolic bone disorders, and one of these, Paget's disease, is now thought to be due to viral invasion of the osteoclasts which are related to the macrophage series. It is known that macrophage activities are programmed within the HLA region, so genes controlling antigen processing are probably involved in this disease.

There is still controversy about the nature of '*Ir* genes'. Initially it was envisaged that each epitope had a corresponding gene determining response. This implied possible hiatuses in the immunological repertoire. The advent of monoclonal probes for actual gene products on immunocytes suggests that all immune responses depend upon many immunoregulatory steps, each with its positive and negative feedback, and it is no longer necessary to envisage 'high' or 'low' response genes as initially formulated. Especially since low responders can be turned into high responders by simple manipulations such as giving a few doses of cyclophosphamide.

A basic tenet in classical genetics was to classify inheritance as dominant or recessive. When this principle is applied to diseases that depend on the interactions of several genes as in the autoimmune endocrine disorders, these old-fashioned attempts at classification lead to involved and sterile arguments. Another important stumbling block is that many of the endocrine syndromes are heterogeneous, with some variants showing HLA linkage and others no connections at all. This is well illustrated in diabetes mellitus, where only the Type I insulin-dependent syndromes are linked to HLA haplotypes, whereas the bulk of diabetic patients in the world belong to a large group of genetically determined disorders at present lumped together as Type II or non-insulin-dependent DM which bear no relationship to HLA genes and have little connections with autoimmunity. In general the autoimmune aspects of the endocrine diseases dealt with are well analysed and the book is fairly up to date with a good literature survey up to 1980. It will prove of great benefit to workers in many fields and is highly recommended to endocrinologists, geneticists, autoimmunologists and tissue typing scientists.

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Monoclonal Antibodies to Neural Antigens

edited by Ronald McKay, Martin C. Raff and Louis F. Reichardt, Cold Spring Harbor Laboratory, 1981. (xv + 282 pages) ISBN 0 87969 138 7

Neurobiology is a field that has profited enormously from the application of new technology in recent years. Patch clamping, the development of new flourescent dyes for cell labeling, molecular biological approaches to the study of the nervous system and a host of new immunological approaches involving monoclonal antibody technology have all contributed to knowledge of the organization, function and development of the nervous system.

Monoclonal Antibodies to Neural Antigens edited by McKay, Raff and Reichardt is the result of a meeting at Cold Spring Harbor on the application of this new immunological approach to a variety of problems in neurobiology.

The monoclonal antibody technique itself involves the generation of highly specific and pure populations of antibodies by fusing isolated spleen

cells of immunized animals (usually mice) with myeloma cells. Cloning of the resulting antibody-producing hybrids after growth in selective medium results in the generation of a 'monoclone' all the cells of which make antibody of the desired specificity. The technique and its applications in neurobiology are nicely outlined in a preliminary chapter written by the three editors.

One of the advantages of a book of this kind is that the information resulting from a new technological application reaches its interested audience more quickly than the usual symposium volume. One of the disadvantages is that the quality of the chapters is very mixed. Some are well organized comprehensive presentations of extremely interesting material that are obviously taken from author-submitted material. Others are sketchy presentations hastily produced and edited by scribes present at the meeting; some do not contain sufficient information or illustrative material by which to judge the work. Some of the chapters dealing with the production of polyclonal (conventional) antibodies to nervous system components are hardly representative of the most exciting work in the field. In many chapters, abbreviations are used that are not explained. However, in general, the book is well conceived and readable.

The chapters are divided among five areas: defining neuronal cell types and cell lines; defined antigens; the synapse; the retina; and the neuromuscular junction. The initial series of chapters deals with attempts to identify subpopulations of neuronal cell types with these highly specific monoclonal reagents. In general, this work shows that unique labels have not yet been generated. For example, none of the antibodies discussed is sufficiently specific to label only very well defined subpopulations such as dorsal root ganglion neurones or spinal cord subpopulations such as motoneurones. The majority of monoclonal antibodies label more than one kind of neurone.

The most interesting and specific distinctions made by monoclonal antibodies reported here are those of Cohen *et al.* that distinguish central from periphal neurones in mammals. The immunogens used included rat cerebellum and rat dorsal root ganglion cells respectively.

Ciment and Weston have isolated antibodies that are specific for subpopulations of sensory neurons of chick and quail, one of which also stains a subpopulation of quail neural crest cells. Such studies are of obvious importance to developmental neurobiologists interested in cell lineages since the neural crest provides the stem cells for both sensory and sympathetic ganglion neurones.

Functionally defined neuronal subsets with known electrophysiological properties have been labeled in the leech with a number of monoclonal antibodies produced by Zipser and McKay. They believe these antigens to reflect different neuronal functions, and are attempting to relate the molecular heterogeneity to the known behaviours regulated by the neurones. This may be possible in an animal such as the leech that has a relatively simple nervous system since a great deal is already known about the specific neurones involved in the physiological correlates of certain behaviours.

Ross *et al.* report production of antibodies to rat tyrosine hydroxylase (TH) and to bovine dopamine beta hydroxylase. The antibodies have been used both to identify cells containing the enzymes and to purify the enzymes themselves. Cuello and Milstein have generated antibodies to substance P and to serotonin. They have used internally labelled ^{3}H-containing antibodies in high resolution autoradiographic immunocytochemistry in the brain.

Lemke and Brockes have prepared monoclonal antibodies to glial growth factor; they are using the antibodies for affinity purification of the factor.

Matthew *et al.* have used synaptic membranes as an immunogen: some of their antibodies show localized binding to synaptic regions of rat brain. DeBlas *et al.* have produced some monoclonal antibodies that affected synaptic transmission presynaptically by increasing $^{45}Ca^{2+}$ uptake and acetylcholine release at synapses.

Barnstaple has applied monoclonal antibodies made to adult rat retina to developmental studies of the retina. He has generated antibodies that recognize specific subpopulations of retinal cells. He has demonstrated that of the three antigens localized specifically to the photoreceptor layer, each appears at a different developmental stage.

Trisler *et al.* have produced one of the most intriguing of monoclonal antibodies yet reported. One antibody, called TOP recognized a cell surface antigen that localized preferentially to dorsoposterior retina where the antigen concentration was highest. A 35-fold gradient of antigen was detected aligned with the dorsoposterior–ventroanterior axis of the eye. The monoclonal antibody will obviously be valuable to those interested in positional information in the retina.

Burden has reported a number of monoclonal antibodies that specifically stain synaptic regions and are either associated with synaptic basal lamina or located intracellularly. Bayne *et al.* have produced an antibody that binds a basal lamina antigen or chick muscle that co-distributes with the acetylcholine receptor. The appearance of the antigen preceded that of the receptor clusters and it is possible that it plays a role in acetylcholine receptor localization.

From the number of different approaches to the study of the nervous system made possible by specific monoclonal antibody labels for cells, subcellular components and individual molecules, phenomena that interest developmental neurobiologists, physiologists and neurochemists are made more accessible. *Monoclonal Antibodies to Neural Antigens* represents the product of an unique kind of meeting – informal presentations by investigators exploring the uses of a new technology. With all the complexities of technique and application, certain common findings related to the technique are emerging. The results presented here allow some generalizations about the applications: an antibody that stains a given neuronal subpopulation uniquely is more difficult to isolate than we had first supposed; functional blockers are also difficult to find among monoclonal antibodies. The technique involves some immensely tedious labour and some unique rewards (Trisler *et al.*, Zipser and McKay); it provides a means of looking at neuronal development that has not heretofore been possible. The next meeting and set of reports on this subject should be even more rewarding, since this volume illustrates what good progress has been made in a relatively short time.

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