sion of Fuel Impurities, Marchwood, England (1963), p. 383; G. Mason and W. C. Clark, *Chem. Eng. Sci.* **20**, 854 (1965); T. Gillespie and G. D. Rose, *J. Colloid Interface Sci.* **24**, 246 (1967).
24. The exact expression for the capillary force per unit length between two contacting parallel cylinders is $F_T = 2T\sin\theta/(1 - \cos\theta)$, which for small values of θ can be reduced to $F_T = 4T/\theta$. The relationship between the deforming force per unit length, F_E, and the elastic deformation of two contacting parallel cylinders is given, for example, in R. J. Roark, *Formulas for Stress and Strain* (McGraw-Hill, New York, ed. 4, 1965), chap. 13, table XIV. It may be written $b = 2.15(PD/2E)^{1/2}$ for identical cylinders of diameter D and Poisson's ratio 0.3, where b is the width of the contact zone. The angle θ may be written as $\theta = b/D$, which leads to $F_E = DE\theta^2/2$ approximately, as in the text.
25. S. L. Phoenix and J. Skelton [*Text. Res. J.* **44**, 934 (1974)] summarize the available data and present new measurements for fibers of textile dimensions.
26. Values of 2.4×10^8 and 4.0×10^8 newton/m^2 were found by Phoenix and Skelton (*25*) for polyester and nylon fibers, respectively. A value of 3.0×10^8 newton/m^2 is reasonable for the approximate calculations presented here.
27. The flexural rigidity of a filament is proportional to d^4, where d is the diameter of the filament. Thus a yarn composed of n independent filaments has a total flexural rigidity proportional to nd^4. If the filaments are consolidated, the yarn behaves as a cylinder of diameter D, where $D^2 \sim nd^2$. Thus the ratio, k, of the yarn stiffness with and without consolidation is $k \sim D^4/nd^4 = n^2d^4/nd^4 = n$.
28. A. E. Stearn, *J. Text. Inst.* **62**, T353 (1971).
29. Y. Litav *et al.*, *ibid.* **63**, T 224 (1972).
30. Typical examples of the magnitudes of the changes in fabric bending behavior brought about by finishing treatments are given in J. D. Owen, *ibid.* **59**, T313 (1968).
31. V. Köpke and H. A. Nordby, *ibid.* **71**, T458 (1970); E. Nielsen and H. M. Elder, *ibid.* **65**, T488 (1974).
32. M. S. Nassar, M. Chaikin, A. Datyner, *ibid.* **65**, T464 (1974); *ibid.* **64**, T718 (1973).
33. The fibers in paper made from wood pulp commonly take the form of flattened ribbons. These ribbons are typically 20 to 40 mm long, 30 to 40 μm wide, and a few micrometers thick. Paper differs from the textile assemblies that we have been considering in that the flattened cross section permits the establishment of large areas of molecularly close contact on drying.
34. See, for example, A. M. Nissan, in *The Formation and Structure of Paper*, F. Bolam, Ed. (British Paper and Board Makers Association, London, 1962), p. 119.

Lymphocyte Surface Immunoglobulins

Molecular properties and function as receptors for antigen are discussed.

John J. Marchalonis

Recognition of nonself antigenic configurations on infectious agents, tumors, and assorted macromolecules is mediated by specific receptors that occur on the surface of lymphocytes. Knowledge of the nature of these recognition molecules is critical to an understanding of the mechanisms of immune function. Although immunologists have pondered the problem of antigen recognition for over 70 years (*1*), studies that provide definite information on the molecular properties of lymphocyte receptors for antigen were performed only within the past few years. It is now possible to draw general conclusions regarding antigen-specific receptors on bone marrow–derived lymphocytes (B cells) and on thymus-derived lymphocytes (T cells). The viewpoint I develop in this article is that membrane-associated immunoglobulin related to the immune macroglobulin antibodies (that is, the immunoglobulin M, or IgM, class) serves a recognition role in many immunologically specific reactions of both B and T lymphocytes.

Basic properties of lymphocyte populations. Members of lymphocyte populations within an individual animal are phenotypically restricted in their capacity to respond to antigens. In accordance with the clonal selection hypothesis of Burnet (*2*), sometime during the ontogenetic development of lymphocytes, the individual cells become committed to the extent that each lymphocyte can respond to only one antigen. It is thought that each cell expresses on its surface one type of receptor for antigen. Combination of the proper antigen with this receptor initiates the chain of immune differentiation that results in the production of antibodies to the antigen. The most obvious molecular candidate for the role of cell surface receptor for antigen is the antibody itself; a conjecture that was stated as early as 1900 by Ehrlich (*1*). However, direct proof of this "minimal hypothesis" has been difficult to attain for two reasons. First, clonal restriction of the response made precise studies arduous because few cells in a normal population—for example, usually at most only one cell in a thousand (*3*)—respond to a given antigen. This problem necessitated the development of methods capable of analyzing binding of antigen by individual cells and hindered quantitative biochemical approaches that measure bulk or average properties of a cell population. The second problem arises from recent discoveries that functionally distinct classes of lymphocytes exist and play specialized roles in the generation of an immune response.

Lymphocytes in the mouse and in various other mammals and birds can be divided into two broad categories on the basis of surface markers and functional properties (*4*). Such cells develop in ontogeny from cells of the hemopoietic system. Hemopoietic stem cells arise in the yolk sac of the embryo and localize in the bone marrow of the adult mammal. The stem cells ancestral to lymphocytes are generated in the bone marrow, but migrate to primary lymphoid organs such as the thymus and the bursa of Fabricius in birds or the bursal equivalent in mammals where they differentiate, respectively, into T cells and B cells. Both types of cells possess specific receptors for antigen. The B cells are the precursors of antibody-forming cells, whereas T cells are responsible for cell-mediated immune reactions such as rejection of allografts, elimination of tumors, and delayed hypersensitivity reactions and, moreover, can act as "helper cells" that collaborate with B cells in the generation of antibodies to certain antigens. Largely because of the ease with which surface immunoglobulin is demonstrable on B cells, the present consensus is that the receptor for antigen on these cells must be immunoglobulin. The situation has not been so clear with T lymphocytes. In the first place, it has been considerably more difficult to detect surface immunoglobulin on T cells than on B cells, and varied results have been reported. As is cited below, surface immunoglobulin of T cells has now been shown by a number of techniques. Another aspect of the problem clouding the nature of the T lymphocyte receptor for antigen stems from the fact that all functions carried out by T lymphocytes are not necessarily immunological (*5, 6*), and it is inaccurate to speak of "the" T cell receptor. In general, it might be more apt to restrict comments to T cells carrying out a particular function.

Some of the heterogeneity of surface recognition processes of lymphocytes are shown in Fig. 1, by presenting a hypothetical scheme depicting the evolutionary ori-

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gins of lymphocyte functions. The primordial cell-surface recognition capacities probably were present on the most primitive lymphocyte precursor and have been retained by the highly differentiated lymphocytes of mammals and birds (*7*). Processes that might be termed "quasi-immune," involving recognition and DNA synthesis in response to interaction with certain allogeneic cells, occur in a number of invertebrates—including coelenterates, echinoderms, and protochordates (*5*)—along the evolutionary line leading to vertebrates. These reactions are suggestive of certain T cell–mediated reactions of mammals such as the graft-versus-host reaction (GVHR) and the mixed lymphocyte reaction (MLR). In these reactions, responses are strongest with allogeneic cell combinations; blast transformation rather than differentiation into immune effector cells results, and a memory component is lacking (*5*). A number of workers (*5, 6*) believe it is necessary to distinguish such reactions from specific immune functions of mammalian T cells, such as delayed type hypersensitivity and specific "helper" activity. The capacity of T type lymphocytes to carry out specific functions in the recognition of foreign antigens probably is not present below the phylogenetic level of vertebrates. Within this subphylum of the chordates, however, evidence of antigen-specific T cell reactivity is widespread. All vertebrates reject allografts (*8*), and specific helper function has been reported to occur in teleosts (*9*), amphibians (*10*), birds (*11*), and mammals (*4*). Putative B cell function is also present in all vertebrates. Representatives of each vertebrate class can synthesize antibodies, at least of the IgM class, in response to challenge with foreign antigen (*7, 12*). It might prove significant in this context that neither antibodies nor antigen-specific T cell function have been observed in species more primitive than cyclostomes. Thus, evolutionary and functional considerations suggest that the problem of antigen recognition by lymphocytes is a complex one and that at least three types of T lymphocytes express recognition molecules and one type of B lymphocyte receptor might exist. The T cell receptors considered here do not include receptors for hormones, such as insulin (*13*), which also occur on the plasma membrane of these cells.

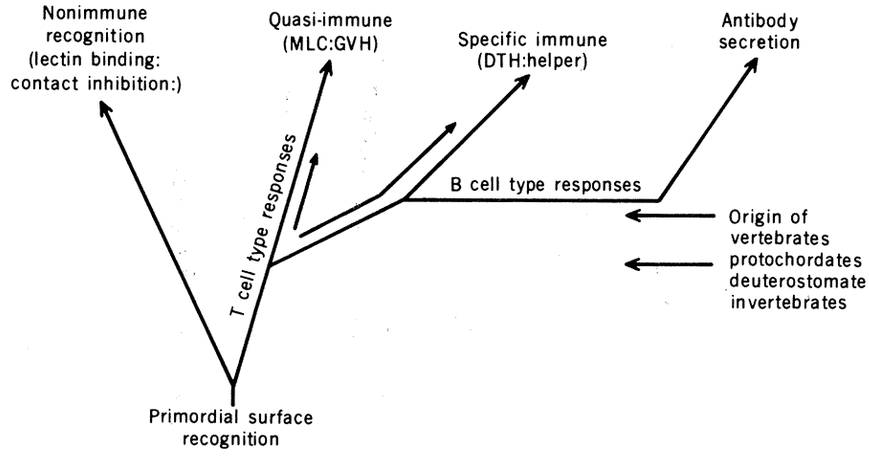

Fig. 1. Hypothetical scheme for the evolutionary emergence of cells performing immune and nonimmune recognition and effector function. This model implies that all lymphocytes had a common evolutionary precursor.

Criteria for Membrane Receptor Function

It is necessary to consider the properties of the lymphocyte membrane receptor for antigen in a rigorous fashion consistent with criteria that have been applied in other systems, particularly recognition and activation of cells by various hormones. If immunoglobulin is the lymphocyte surface receptor for antigen, three properties must be met. (i) It should be possible to detect immunoglobulin on the plasma membranes of specifically reactive lymphocytes. This observation per se cannot establish that immunoglobulin is the receptor for antigen. However, definite proof of its absence would suggest that another molecule must carry out the recognition role. (ii) Surface immunoglobulin must be demonstrated to possess specific binding capacity for antigens. This is difficult to do because of clonal selection, but several techniques offer indirect and direct evidence supporting combination of antigen and surface immunoglobulin. (iii) The combination of antigen with surface antibody should initiate specific processes of immune differentiation. The evidence for this criterion is not yet definitive, but a number of studies now show that binding of antibody against immunoglobulins can trigger division on some systems (*14*) and that complexes of T cell surface immunoglobulin and antigen play an important role in collaboration with B cells (*15*). My discussion is limited to the present evidence that immunoglobulin of B cells and T cells satisfies these criteria; certain physicochemical characteristics of membrane immunoglobulins are also described.

Evidence for the existence of lymphocyte membrane immunoglobulin. Various techniques, both direct and indirect, have recently established the presence of surface immunoglobulins on B cells and on at least some T cells. Direct binding of antibody against immunoglobulins to lymphocyte surfaces (Table 1) generally detects immunoglobulin on B cells quite readily, but is less suitable for disclosing surface immunoglobulins on thymus lymphocytes or T cells. Either fluorescent or radioactively

Table 1. Direct evidence for immunoglobulin on lymphocyte surfaces. The species investigated here are man, mouse, rabbit, sheep, pig, and chicken. Abbreviation: Ig, immunoglobulin.

Method	Present on	
	B cells	T cells
Binding of fluorescein-labeled antibodies to Ig	+++ (*97*)	± or + (*17, 18*)
Binding of radioactively labeled antibodies to Ig	+++ (*44*)	± or + (*16, 45*)
Binding of virus-labeled antibodies to Ig (electron microscope)	+ (*15a*)	+ (*15a*)
Cytotoxicity produced by antibodies to globulin plus complement	+ (*19*)	+ (*19*)
Direct isolation		
(a) Complexes of antibody to globulin and surface Ig	+ (*98*)	+ (*68, 69*)
(b) Freeze-thaw lysis (human Burkitt lymphomas and chronic lymphocytic leukemia cells)	+ (*99*)	
(c) Use of lactoperoxidase catalyzed–radioiodination of surface proteins	+ (*37, 38, 42, 54*)	+ (*21, 37, 49, 57, 73*)
(d) Isolation of plasma membrane followed by extraction of Ig	+ (*21*)	+ (*20, 21, 40*)

Table 2. Indirect evidence for immunoglobulin on lymphocyte surfaces: inhibition of lymphocyte function by antisera to immunoglobulins. NA, not applicable.

Function	Inhibition by antiserums	
	B cells	T cells
Antigen binding	Yes (*3, 23, 25–30*)	Yes (*25–30*)
Antigen-specific "hot-antigen suicide"	Yes (*31*)	Yes (*31*)
Antibody production	Yes (*100*)	See helper function
Antigen-specific helper function	NA	Yes (*101*)
Production of macrophage inhibition factor	NA	Yes (*102*)
Delayed type hypersensitivity	NA	Yes (*103*)
Graft-versus-host reaction (GVHR)	NA	Yes (*33, 34*)
Mixed lymphocyte reaction (MLR)	NA	Yes (*104*)
		No (*104*)

labeled antiserums under relatively insensitive conditions have been used for distinguishing T cells from B cells. Hammerling and Rajewsky (*15a*) observed comparable amounts of IgM on B and T lymphocytes from peripheral blood using electron microscopy of labeled antibody to immunoglobulins, the label in this case being turnip yellow virus. Some workers found that both thymus and peripheral T lymphocytes expressed surface immunoglobulin when rigorous studies involving iodine-labeled antibody to immunoglobulins were performed (*16*). A number of investigators have reported immunoglobulin localization on thymus lymphocytes (*17*) and antigen-activated peripheral T cells (*18*) by immunofluorescence. Burckhardt *et al.* (*19*) have used the cytotoxicity assay to show the presence of immunoglobulins on B and T cells. They reached two conclusions that are important for understanding the relations between surface immunoglobulins of T and B cells; these will be considered later in this article. In the first place, antiserums made against the μ chain of the myeloma protein MOPC 104E were not cytotoxic for thymus lymphocytes; antiserums made against μ chains of highly purified IgM from normal serum were effective against both B and T cells. Second, cross absorptions of antiserums suggested that the IgM-like immunoglobulins of B and T cells were serologically distinguishable. Interesting results were obtained when isolated plasma membranes of pig (*20*) and rat (*21*) thymus lymphocytes were assayed for the presence of immunoglobulin. Although the intact cells lacked surface immunoglobulin, as measured by immunofluorescence, immunoglobulin accounted for 0.2 and 2 percent, respectively, of plasma membrane protein. Since these quantities were similar to those of spleen plasma membranes, the immunoglobulin of intact thymus cells appears somehow hidden with respect to binding of immunoglobulins.

Another means of establishing the presence of immunoglobulins on lymphocytes is to determine whether antiserums to immunoglobulins will inhibit binding of antigen and other functions of B and T lymphocytes (Table 2). Initially, it was hoped that the inhibition approach would provide direct information on the nature of the antigen receptor. However, the fact that antiserum to a particular cell membrane component blocks lymphocyte function does not necessarily show that the molecule in question is the antigen receptor. This point was demonstrated by Bluestein (*22*), who studied the mechanism by which antiserum to histocompatibility antigens blocked in vitro antigen-specific proliferation of guinea pig T lymphocytes. The Fab monomer bound to the cells but did not inhibit proliferation; hence this reagent was not combining directly with the receptor or even binding to a proximal molecule and causing steric hindrance. The Fab dimer of the antibody to H antigen blocked proliferation, thereby suggesting the need for aggregation in the inhibitory process. Moreover, the $F(ab)_2$ fragments of antibody to H antigen brought about complete inhibition of antigen-specific proliferation when the antiserum was added 3 hours after addition of antigen. The observed inhibition thus reflected some process by which the cell became refractory to proliferation, rather than reflecting the combination of antiserum with the receptor for antigen. In the absence of further information, inhibition of antigen-specific lymphocyte function is here interpreted only as evidence for the presence of immunoglobulin on the cells. Both B and T lymphocytes bind various antigens, including proteins, erythrocytes, and haptens. In the case of B cells, this binding is inhibited by antiserums to μ chains and κ light chains, while some antigen-binding cells are inhibited by antiserums to γ chains (*23, 24*). Antiserums to κ light chains are generally quite effective (*24–31*) in the inhibition of antigen binding by T cells. Antiserums to μ chains are the only antiserums to heavy chains that are effective inhibitors (*24*), and not all antiserums to chains show inhibition (*25*). Although it was once thought that T cells could not bind antigen in a manner demonstrable by standard techniques such as radioautography (*23*) or rosette formation with erythrocytes (*32*), numerous recent studies establish that T cells combine specifically with antigen, and such combination can be inhibited by antiserums to light chains and often to μ chains. Other T cell functions that were specific for foreign antigens were inhibited by antiserums to light chains. Some workers successfully blocked allogeneic reactions to weak determinants such as GVHR and MLR with antiserums to light chains (*33, 34*), thereby showing the involvement of immunoglobulin at some stage of these complex cellular responses.

Another means of demonstrating the presence of immunoglobulin on T cells has been through the use of "antireceptor" antibodies (that is, antibodies to receptors). McKearn *et al.* (*35*) have established that antiserums to T cell receptors involved in recognition of histocompatibility antigens will block allograft rejection in rats. Moreover, they have shown that their antiserums are directed against idiotypic determinants on immunoglobulins, thereby indicating a receptor role for immunoglobulin in T cell recognition of strong histocompatibility antigens. Studies by Binz *et al.* (*35a*) on mice also suggest that T cells mediating rejection of grafts across H-2 antigenic barriers (strong) possess immunoglobulins characterized by the same idiotypes expressed by circulating antibodies to these antigens. The results obtained with antibodies directed against receptors suggest that T and B cell recognition units express antigenically similar variable region conformations.

The preceding direct and indirect data show that B cells and T cells express surface immunoglobulin. Two further points warrant comment. First, it has been possible, with the use of any of the direct techniques cited above, to develop conditions where B cells clearly possessed immunoglobulin while T cells apparently lacked this membrane protein. B cells might therefore possess many more surface immunoglobulin molecules than do T cells. Some workers (*24, 36*) for example, believe that there might be a difference of two orders of magnitude in the number of surface immunoglobulins between the two cell types. Other explanations have been proposed, such as accessibility of immunoglobulin antigen determinants on T cells (*25, 37*); for example, some membrane component might surround the immunoglobulin constant region antigenic determinants and render them inaccessible to antibodies to immunoglobulins (see above). Hogg and Greaves (*25*) obtained evidence consistent with this alternative when they showed that antigen binding by T cells was

blocked by antiserum to μ chain which was specific for hinge region determinants but not by those directed against Fc region antigens alone.

Antigenic and iodine-labeling data generally suggest that the μ chain of B cell membrane IgM is completely exposed (*37, 38*), but a recent study by Fu and Kunkel (*39*) indicates that a substantial portion of the Fc region is "buried." Haustein *et al.* (*40*) have shown that immunoglobulin of the T lymphoma WEHI 22 is tightly associated with the isolated plasma membrane. This finding suggests that either the immunoglobulin is itself an integral membrane protein or it is tightly associated with one. Another possible explanation for the discrepancy in the ease of detectability of immunoglobulins of B cells and T cells is that complexes of antigen or antibody with T cell membrane immunoglobulin might be shed rapidly and thus be lost in the medium (*41*). Studies with monoclonal human B lymphocytes—chronic lymphocytic leukemia cells (*42*)—and monoclonal murine T cells—lymphoma cells bearing theta antigen (*43*)—indicate that the number of surface immunoglobulins on B cells averages about 8×10^4 molecules per cell (range 10^4 to 5×10^5), whereas that of the T lymphoma cells ranged from 10^4 to 4×10^4 per cell. Similar numbers have been obtained by other approaches (*44, 45*). Thus, there is a quantitative difference in immunoglobulin density between B and T cells, but other factors also are involved in immunoglobulin expression.

The second issue to be considered here is the source of lymphocyte membrane immunoglobulin. B cells have receptors that bind homologous or heterologous IgG immunoglobulins (*46*), but there is no question that they synthesize membrane-bound IgM (*47*). Some workers have obtained evidence suggesting that at least part of the immunoglobulin detected on T cells was produced by exogenous sources and did not originate in the T cell (*48*). The T cells clearly do not produce immunoglobulin at a rate anywhere comparable to that exhibited by B cells or plasma cells; however, various recent studies show that they synthesize significant membrane-associated immunoglobulin. This was elegantly demonstrated by Roelants *et al.* (*29*), who reported that immunoglobulin antigen receptors on T cells formed complexes with antigen, and that these complexes drifted to one pole of the cell, and were removed. The cells were capable then of regenerating their receptors in a metabolic process. Santana *et al.* (*17*) were able to visualize IgM on T lymphocytes by immunofluorescence and, likewise, showed that T cell membrane immunoglobulin is "capped-off" and resynthesized. Moroz and her co-workers (*49*) reported that theta-bearing thymus lymphocytes synthesize too much immunoglobulin for it to be accounted for quantitatively by contaminating plasma cells. Haustein *et al.* (*43*) found that four continuously cultured lines of monoclonal murine T lymphoma cells incorporated [^{3}H]leucine into immunoglobulin. Some of these T lymphoma lines possessed endogenous immunoglobulin and receptors for the Fc region of mouse IgG immunoglobulin and, therefore, paralleled B cells in their capacities to synthesize an IgM-like immunoglobulin and also to bind IgG cytophilically.

Other types of evidence militating against the B or plasma cell origin of T cell membrane immunoglobulin are also available. I am not giving an exhaustive listing of these but, rather, cite only a few of the more clear-cut examples: The specificity of T cells for a synthetic polypeptide antigen consisting of a copolymer of tyrosyl, glutamyl, alanyl, and lysyl residues differs from that shown by B cells (*30*). Hapten-binding B cells showed increased affinity after immunization, hapten-binding T cells do not (*50*). The same antigen-binding T cell does not express both κ and λ chains (*25*), which it could if passively adsorbed antibody were present. No double antigen-binding cells were found among antigen-binding peripheral T cells of animals immunized with two antigens (*25*).

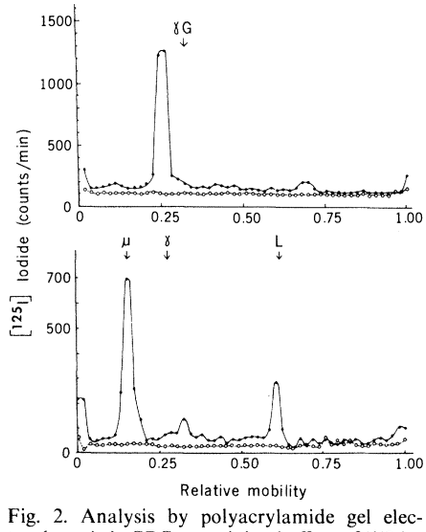

Fig. 2. Analysis by polyacrylamide gel electrophoresis in SDS-containing buffers of ^{125}I-labeled surface immunoglobulin of human chronic lymphocytic leukemia cells of patient Mat. (Top) Unreduced samples resolved on 5 percent polyacrylamide gel. • — •, Specifically precipitated immunoglobulin; ○, ^{125}I (count/min) associated with control precipitation system. γG, location of human γ-globulin marker (150,000 daltons). (Bottom) Samples reduced with 2-mercaptoethanol to cleave interchain disulfide bonds and analyzed on 10 percent gel under conditions which resolve light chains and heavy chains. • — •, Specifically precipitated immunoglobulin; ○—○, counts associated with control precipitate. μ, γ, and L indicate positions at which μ chain, γ chain, and light chain migrated in these gels. Iodine-labeled surface immunoglobulins were solubilized by the detergent Nonidet P-40. [Data from (*42*)]

Molecular properties of lymphocyte membrane immunoglobulin. The preceding data indicate that normal and neoplastic T and B lymphocytes express membrane immunoglobulin that consists predominantly of μ and light chains. The approaches used, however, do not establish the state of the surface molecules or even whether intact polypeptide chains are present. A variety of cell surface arrangements are possible because, although serum immunoglobulins usually occur as monomers or multiples of a four chain unit comprising two pairs of light chains and heavy chains, binding of antigen requires only that a variable region of the light chain acts in accord with the variable region of the heavy chain to form the antigen-combining site. Moreover, in recombination experiments carried out in solution it was found that interchain disulfide bonds were not required for antigen binding (*51*). Schematically, membrane IgM capable of combining with antigen might consist of $L\mu$, half-molecule; $(L\mu)_2$ monomer; or $(L\mu)_{2n}$ where five is the usual serum IgM multiple. These would not necessarily be linked via disulfide bonds.

Various adaptations of lactoperoxidase-catalyzed iodine labeling of tyrosines in proteins (*52*) for use with cells (*38, 53*) served as important tools in the partial characterization of surface immunoglobulins of lymphocytes of man (*37, 42, 54*), mouse (*37, 38, 55*), rat (*21*), and chicken (*56*). Immunoglobulin characterization has now been reported for normal (*21, 37, 38, 55*) and neoplastic (*42, 54*) B lymphocytes and various T cell populations, including thymus lymphocytes (*21, 27, 49, 55–57*), peripheral T lymphocytes (*58*), specifically activated T lymphocytes (*37, 58–62*), and monoclonal T lymphoma cells (*37, 40, 46, 57, 63*). The general mode of operation was to label the surface of living lymphocytes, extract iodine-labeled membrane proteins, and isolate immunoglobulin by specific serological precipitation or by immunoadsorbents.

Initial studies showed that the predominant immunoglobulin present on the membranes of murine (*37, 38*) and human (*37, 42, 54, 58*) B lymphocytes contained light chains and μ chains and had an apparent mass of approximately 200,000 daltons. Analyses by polyacrylamide gel electrophoresis in SDS-containing buffers are shown for intact (Fig. 2, top) and reduced (Fig. 2, bottom) surface immunoglobulins of monoclonal B lymphocytes (chronic lymphocytic leukemia cells of patient

Mat). The mobility of the intact immunoglobulin is clearly retarded relative to that of the human IgG marker (150,000 daltons). Upon reduction, performed to cleave interchain disulfide bonds, the molecule is resolved into polypeptide chains migrating like light chains and μ heavy chains. IgM of the form $(L\mu)_2$ is the major surface immunoglobulin on murine B cells. But half-molecules have been found in B lymphocyte surface immunoglobulins of mice (*64*) and rats (*21*) and free light chains have sometimes been reported (*65*). Polypeptide chains of reduced ^{125}I-labeled surface immunoglobulins of normal murine B lymphocytes obtained from the spleens of congenitally athymic "nude" mice are shown in Fig. 3. Antigenic evidence supports the polyacrylamide gel data that the heavy chain that migrates like μ chain is indeed μ chain. The slightly faster migrating heavy chain (apparent molecular weight, 65,000) is clearly distinct from μ and γ chains in mobility, and recent studies indicate that it is antigenically distinct from μ chain (*64, 66*). This chain most likely differs from μ in carbohydrate content also (*65, 66*). Although the identification is still tenuous, some workers have referred to the second type of murine B cell immunoglobulin as IgD (*64, 66*) by analogy with human B lymphocytes, which sometimes express both IgM and IgD on their surfaces (*67*). Because the extraction methods described give bulk values, it is not possible at this time to decide whether $(L\mu)_2$ and putative IgD occur on the same cells. Some workers have also isolated IgG from mouse (*37*) and rat (*21*) B lymphocytes, but this immunoglobulin occurs at low levels relative to surface IgM. Light chains and μ heavy chains have been isolated from the surfaces of bursal lymphocytes from the chicken, but the intact immunoglobulin was so aggregated that it was not possible to obtain an estimate of its size (*56*). The current data thus indicate that the major form of surface immunoglobulin on B lymphocytes resembles the monomer of IgM and that a second type (IgD?), which probably differs from IgM in antigenic properties and carbohydrate content, is also present on some B lymphocytes.

The problem of the nature of T lymphocyte surface immunoglobulin has been a challenging one because conditions routinely used to label and extract B cells are not suitable for normal (*49, 55*) or neoplastic (*43, 62*) T lymphocytes. Furthermore, it was of crucial importance to obtain T lymphocytes free of contaminating B cells or plasma cells, which might contribute immunoglobulin detectable in bulk analyses. The preceding indirect and direct observations establish that T lymphocytes bear membrane immunoglobulin. Two

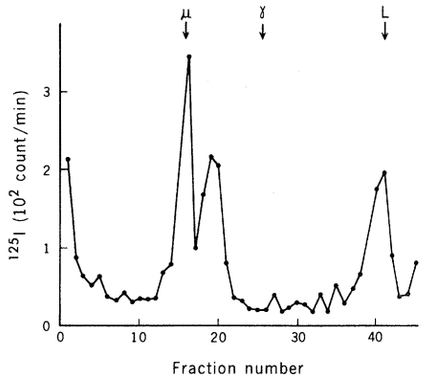

Fig. 3. Analysis by polyacrylamide gel electrophoresis in SDS-containing buffers of ^{125}I-labeled, reduced surface immunoglobulin of murine B cells obtained from the spleens of congenitally athymic mice homozygous for the mutation *nu* (nude). Immunoglobulin was isolated with the use of an immunoadsorbent specific for κ chains (*65*); similar results are obtained by serological precipitation (*73*). μ, γ, and L refer to migration positions of mouse μ, γ, and light chains in this gel. Surface immunoglobulins were solubilized by the nonionic detergent Nonidet P-40.

questions can now be proposed regarding this immunoglobulin. (i) Can immunoglobulin be isolated from T lymphocyte populations in quantities sufficient to permit chemical characterization? (ii) What is the source of this immunoglobulin? A number of investigators have reported the isolation and partial characterization of surface immunoglobulins from various T lymphocyte populations (Table 1). Thymus lymphocytes of man (*37*), mouse (*37, 49, 57*), chicken (*56*), and rat (*21*) were reported to have light chains and μ chains that were usually linked via disulfide bonds into the $(L\mu)_2$ structure. Moroz and her colleagues (*49*) reported two apparent exceptions: (i) the light and μ chains of human and C57Bl mouse thymus immunoglobulin lacked interchain disulfide bonds and (ii) the immunoglobulin associated with BALB/c thymus consisted mainly of IgA. Available evidence based on the lactoperoxidase catalyzed-labeling approach (cited above) as well as isolation of complexes of the Fab monomer fragment of the ^{125}I-labeled antibody to the immunoglobulin and thymus immunoglobulin (*68*) indicate that the major component of thymus surface immunoglobulin has a mass of about 200,000 daltons, contains typical light chains (usually κ chains in the mouse), and contains a heavy chain antigenically related to μ chain but not necessarily identical to it (*15, 19, 43, 49, 57, 68, 69*).

Since thymus lymphocytes consist chiefly of immunologically inactive cells fated to die within that organ while T lymphocytes destined for export make up a small proportion (*4*), it was necessary to study peripheral antigen-reactive T cells in order to obtain a reliable view of putative T cell receptors.

Detailed investigations were pursued with antigen-specific activated T cell populations and continuously cultured monoclonal T lymphoma cells. The first type of T lymphocytes can be activated to antigens by in vivo (*70*) or by in vitro (*71*) processes and are extremely useful for study of antigen-specific T cell effects such as helper function. Moreover, certain populations of activated T cells provide excellent material for biochemical studies because reactive T cell populations can be obtained virtually free of B lymphocytes (< 0.2 percent) (*46*). The polypeptide chain pattern shown in Fig. 4 was obtained for surface immunoglobulin of activated CBA T lymphocytes obtained from thoracic duct lymph of lethally irradiated (CBA × C57Bl)F_1 mice injected with CBA thymus cells. The major heavy chain peak is comparable to μ chain in mobility, and some γ chain (probably cytophilic) is also present. Lymphoma T cells have been shown to express (*37, 43, 45*) and synthesize (*43, 63*) membrane immunoglobulin. It is worth noting that these cells are clearly distinguishable from B cells when assessed for the presence of surface immunoglobulin by immunofluorescence. They are negative for immunoglobulin under conditions that readily detect this marker on B cells. There is no possibility of B cell or plasma cell contamination when cloned continuously cultured T lymphoma cells are used. Moreover, immunoglobulin of some T lymphoma lines has functional similarity to immunoglobulin from helper T cells (*72*). Figure 5 shows intact and reduced ^{125}I-labeled surface immunoglobulin of the T lymphoma line, WEHI 7. The intact immunoglobulin is larger than mouse IgG (150,000 daltons) and consists of light chains and heavy chains with a mobility similar to that of μ chains. The heavy chains of all T lymphoma lines studied (*40, 43*) migrate slightly, but significantly, faster than serum μ chains. It is noteworthy that their mobility is less than that of the putative δ chain of B lymphocytes (*73*). Thus, a pattern is developing that T lymphocytes possess one endogenous surface immunoglobulin which is most similar to the $(L\mu)_2$ monomer of IgM, but various structural and functional (*37, 43, 73, 74*) differences indicate that the T cell immunoglobulin is not identical to the B cell IgM or to serum molecules. It might prove to be an IgM subclass, or amino acid sequence differences might prove sufficiently distinctive to require its nomination as a new immunoglobulin class.

Evidence that lymphocyte surface immunoglobulin binds antigen. Two types of

approaches indicate that surface immunoglobulin possesses the capacity to bind antigen. The first method can be applied to individual antigen-binding lymphocytes which combine with fluorescent antigens. Initially the antigen is uniformly distributed over the surface of the cell; but, if the cells are maintained at 37°C, the antigen forms aggregates or "patches" and eventually accumulates in a large cap at one pole of the cell (*75*). This "capped" antigen, presumably complexed with its receptor, is then shed or taken into the cell. An analogous process occurs on the surfaces of B lymphocytes when fluorescent antibody (at least divalent) to immunoglobulin is added. If immunoglobulin is the lymphocyte receptor for antigen, then antigen and immunoglobulin should cap together. This result has been observed for protein (*29, 76*) and erythrocyte (*26*) antigens binding to B lymphocytes. It is more difficult to perform this sort of experiment directly with T lymphocytes because these usually do not bind detectable levels of antibodies to immunoglobulins. However, Ashman and Raff (*26*) have found that erythrocyte antigens binding to T cells form caps just as they do when binding to B cells. Roelants *et al.* (*29*) have made a strong case that IgM on T cells, which binds protein antigens, is capped along with the antigen. These data provide evidence consistent with immunoglobulin's functioning as the antigen receptor on B and T cells. It is not a conclusive proof, however. The same results would obtain if the true receptor for antigen were not immunoglobulin, but some molecule which was contiguous with the immunoglobulin in the fluid membrane of the cell.

A second approach to test the capacity of lymphocyte surface immunoglobulin to bind antigen is to isolate iodine-labeled membrane immunoglobulin and determine whether it combines with suitably chosen antigens. Rolley and Marchalonis (*77*) described experiments designed to isolate complexes of dinitrophenylated (DNP) hemoglobin (mouse) and cell surface immunoglobulin obtained from spleen lymphocytes of congenitally athymic *nu/nu* mice. This was feasible since B cells of unimmunized mice had a high level of lymphocytes (0.1 to 1.0 percent) capable of reacting with saturating concentrations (50 to 100 μg) of ^{125}I-labeled DNP hemoglobin. Similar high numbers of binding cells specific for the DNP hapten were found by others (*28*). Cytophilic antibodies apparently did not play a major role in the DNP binding by B cells because the number of antigen-binding cells was not increased by incubation with antiserums to DNP (*75*). Complexes of DNP hemoglobin and cell surface immunoglobulin were detected by

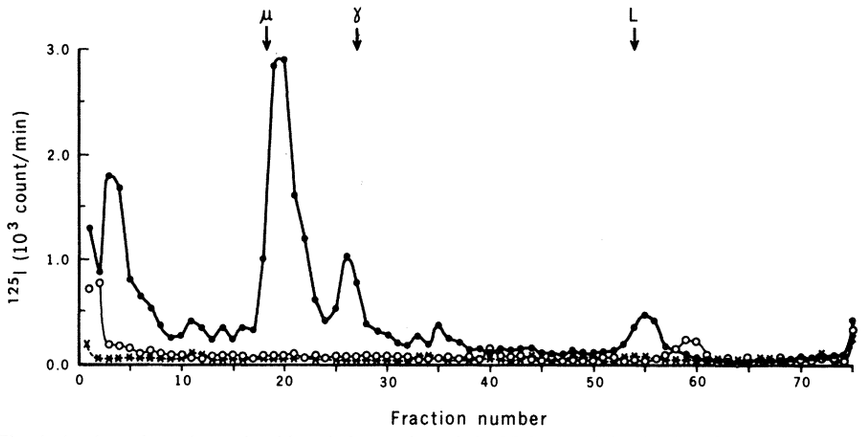

Fig. 4. Analyses by polyacrylamide gel electrophoresis in SDS-containing buffer of reduced surface immunoglobulin of peripheral lymphocytes of CBA strain mice activated in vivo to histocompatibility antigens of C57B1 mice by the method of Sprent and Miller (*70*). •, Counts from the surface of T lymphocytes specifically precipitated as immunoglobulin; ○, counts from the surface of T lymphocytes associated with the control precipitate (chicken IgG + rabbit antiserum to chicken IgG). *, A specificity control of which ^{125}I-labeled surface proteins of murine testis cells, which lack immunoglobulin, were reacted with the specific anti-mouse immunoglobulin system. μ, γ, and L indicate the positions at which μ, γ, and light chain migrated (*105*). Surface immunoglobulins were solubilized by metabolic release (turnover). Data for similar preparations can be found in (*58*).

specific coprecipitation, that is, with the use of systems specific for DNP and for mouse immunoglobulins (Fig. 6). Such complexes were isolated from the cell surface after metabolic release at 37°C and by limited proteolysis with trypsin. Moreover, the population of iodine-labeled cell surface immunoglobulin was found to mimic the heterogeneous population of antibodies normally found in serums inasmuch as removal of cell surface immunoglobulin specifically reactive to DNP by affinity chromatography did not remove the capacity of the immunoglobulin pool to combine with other antigens, such as horseshoe crab hemocyanin. Further studies with B cell populations highly enriched in cells of a given specificity are required to completely establish the structural properties of B cell receptor immunoglobulin. Our study, however, provided direct evidence in support of the hypothesis that B cell immunoglobulin functions as antigen receptor.

Since there are at present techniques that allow the biological enrichment of T lymphocytes to a variety of antigens (*70, 71*), it is possible to carry out investigations of the binding specificity of ^{125}I-labeled surface immunoglobulins of activated T cells. Up to now, studies have been carried out with murine T lymphocytes ac-

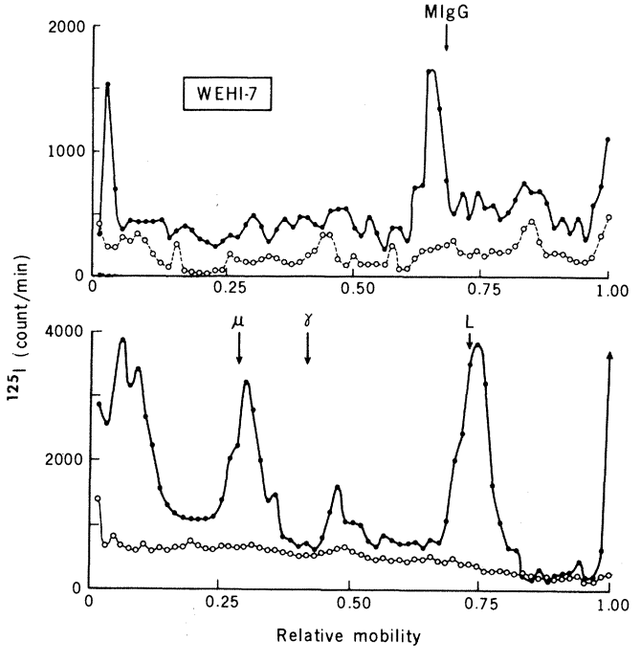

Fig. 5. Iodine-labeled surface immunoglobulin of cells of the monoclonal T lymphoma cultured line WEHI 7 analyzed by polyacrylamide gel electrophoresis in SDS-containing buffers. (Top) Unreduced sample; •, specifically precipitated immunoglobulin; ○, control precipitate; IgG, position at which mouse IgG migrates. (Bottom) Reduced sample; •, specifically precipitated immunoglobulin; ○, counts associated with control precipitate; μ, γ, and L indicate positions of μ, γ, and light chains. Surface immunoglobulins were solubilized by metabolic release (turnover). [Data from (*43*)]

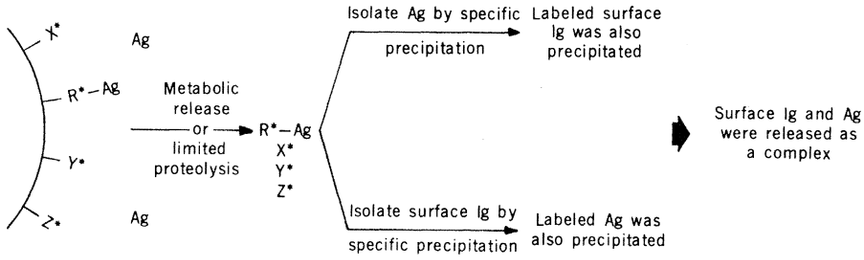

Fig. 6. Scheme illustrating the sequence of experiments used to show the surface immunoglobulin of B lymphocytes bound to dinitrophenylated antigen (*77*). *Ag* (DNP-hemoglobin), *R** (receptor immunoglobulin) *X** and *Z** (labeled lymphocyte membrane components which do not bind antigen). The asterisk indicates that these surface molecules have been iodine-labeled by the lactoperoxidase-catalyzed reaction.

tivated specifically to syngeneic tumor-associated transplantation antigens (*60*), histocompatibility antigens (*59*), foreign erythrocytes (*61*), and foreign proteins (*61*). In all cases, detectable amounts of surface immunoglobulin showing specific binding to the activating antigen were observed. For example, helper T cells activated to sheep erythrocytes (SRBC) were obtained by reconstituting lethally irradiated (850 rads) CBA mice with syngeneic thymus lymphocytes plus SRBC plus a synthetic polynucleotide adjuvant consisting of a complex of polyadenylic acid and polyuridylic acid (*61*). This complex stimulates T cells (*78*), and helper cells appear rapidly, preceding the appearance of antibody-secreting cells. Two days after injection of this mixture, spleens were removed and used as a source of helper T cells to SRBC in an assay in vitro consisting of spleens of congenitally athymic (*nu/nu*) mice and added test T cell populations. Specifically activated helper T cells to SRBC produced a hemolytic plaque-forming cell response more than ten times larger than that supported by normal CBA thymus lymphocytes or by CBA T cells activated (as above) to chicken γ-globulin. ^{125}I-Labeled surface proteins of activated T cells were obtained by metabolic release and divided into two portions (Fig. 7). Immunoglobulin was removed from one portion by specific precipitation; the other was treated with an indifferent immunological precipitation system. The latter portion thus contained ^{125}I-labeled surface immunoglobulin, but proteins which might adhere to antigen-antibody complexes had been removed. When tested for the presence of iodine-labeled proteins binding to SRBC or control erythrocytes, the immunoglobulin-containing sample had a large amount of labeled material bound to SRBC but very little bound to mouse or horse red blood cells. The immunoglobulin-depleted fraction showed no binding to any of the red cells tested, as would be expected if immunoglobulin were the binding agent. The specific precipitate (antibody to mouse immunoglobulin plus mouse immunoglobulin) was analyzed and found to contain IgM-like immunoglobulin (as above).

Further experiments showed that the ^{125}I-labeled surface immunoglobulin came from helper T lymphocytes because treatment with antiserum to the theta alloantigen in the presence of complement blocked helper activity and completely eliminated detection of immunoglobulin. These results were consistent with the low percentage of B cells in these activated populations (< 2 percent) and the virtual absence of cells forming antibodies to SRBC (less than five plaque-forming cells per 10^6 cells). It should be stressed that these results were obtained with activated T cell populations, but the above results of Roelants *et al.* (*29*) with lymph node T lymphocytes from nonimmunized mice suggest that the receptor on resting T lymphocytes is likewise IgM-like immunoglobulin. The direct isolation results cited here for B and T lymphocyte surface immunoglobulin demonstrate that membrane immunoglobulin can bind foreign antigens and certain tumor antigens and strong alloantigens. Other recognition systems might occur in weak allogeneic interactions such as MLR and GVHR as was discussed earlier. Moreover, the possibility remains that surface immunoglobulin acts in concert with other membrane proteins in the early events of lymphocyte differentiation (*24, 79*).

Roles of surface immunoglobulin in lymphocyte activation and differentiation. Binding of antibody to immunoglobulin with lymphocytes of certain species initiates DNA synthesis and blast transformation (*14, 80*). This event, however, does not suffice to demonstrate a unique physiological role for membrane immunoglobulin in murine differentiation because mitogens such as bacterial lipopolysaccharide (*47, 80*) and insoluble concanavalin A (*47*) will cause B lymphocytes to differentiate into cells actively secreting immunoglobulins. Moreover, combination of surface immunoglobulin with antiserum to immunoglobulin or with mitogens that bind to immunoglobulin—for example, binding of concanavalin A—is not sufficient to bring about activation of murine B cells. These considerations lead to the problem of the mechanisms by which binding of a ligand to a surface receptor can bring about the initial enzymatic events necessary for differentiation. It is beyond the scope of this article to include the analysis of possible models of antigen-directed lymphocyte differentiation. Various models have been proposed (*80*) but the exact mechanism by which the event of antigen binding is translated into cell differentiation remains a problem.

T cell surface immunoglobulin complexed with antigen has been shown to act as a specific collaborative factor in specific in vitro cooperation between T and B cells (*15, 61, 68, 69*). This type of cooperation requires macrophages as an obligatory accessory cell that concentrates the complexes for presentation to B cells. T cell surface immunoglobulin possesses the capacity to mediate helper activity, whereas B cell or serum immunoglobulins do not (*15, 80a*). Consistent with these functional activities, T cell surface immunoglobulin is cytophilic for macrophages while B cell surface IgM-type immunoglobulin is not (*74*). This functional property is thought to derive from the structure of the Fc portion of T cell immunoglobulin. This collaborative effect of T cell immunoglobulin suggests an important physiological role for receptor-antigen complexes but does not answer the basic question regarding the initial events of lymphocyte activation.

Alternative recognition systems on T lymphocytes. The data reviewed above constitute a strong case that immunoglobulin functions as a receptor for antigen on antigen-binding T cells and on T cells specifically reactive as helper cells. The nature of the receptor in the allogeneic reactions which I referred to as quasi-immune in Fig. 1 remains to be established. The success of Warner and his associates (*33*) and Riethmuller *et al.* (*34*) in blocking GVHR with antiserums to light chains shows the presence of immunoglobulin determinants on the reacting cells. For reasons described above, this inhibition per se does not demonstrate that immunoglobulin is the actual recognition molecule. The argument has been vigorously proposed that the receptor in the MLR cannot be immunoglobulin (*81*). This type of reaction is interesting from an evolutionary point of view because somewhat similar phenomena have been observed in species such as annelid worms and coelenterates, which apparently lack immunoglobulins (*5*). In addition, arguments based on the inheritance patterns of immune responsiveness in mice and guinea pigs have raised

the possibility that a set of recognition molecules, alternative to immunoglobulin, exists on T lymphocytes of mammals (*83*). McDevitt (*82*) has hypothesized that this recognition system which might function in the GVHR and MLR and in immune responses to certain synthetic polypeptide antigens (*82, 83*) represents a set of receptors more primitive than immunoglobulin. Two types of molecules, namely, histocompatibility antigens (*82*) and products of immune response genes linked to genes encoding histocompatibility antigens (*82, 83*), have been suggested as likely candidates for the T cell receptors in these reactions. It should also be remembered that T lymphocytes possess a number of surface molecules that initiate diverse physiological responses. Examples of such molecules are receptors for insulin (*13*) and surface glycoproteins which bind lectins. In the latter case, however, membrane IgM-like immunoglobulin is one of the glycoproteins which binds to certain lectins (*84*).

The case for the products of H-linked immune response genes serving as T cell receptors for antigen is not compelling for the following reasons: (i) T cells of nonresponder mice recognize antigen; it is their proliferation or differentiation capacity which is deficient (*85*); (ii) functional evidence suggests that Ir-1 genes are expressed in both B cells and T cells (*86*); (iii) proteins (for example, Ia antigens) encoded by genes lying within the I region (immune response region) occur predominantly on B cells (*87*); and (iv) T cells possess IgM-like immunoglobulin which can bind antigen (as mentioned above). Katz and Benacerraf (*88*) have proposed that I-region gene products might play a vital role in collaboration between T and B cells by serving as the B cell surface receptor for a distinctive molecule on specifically activated T cells. If such molecules are present on T cells, these Ir gene products might be sterically close to the immunoglobulin receptor and allow conjoint recognition of complex macromolecular determinants (*24*) or serve in the process in which T cells, having recognized antigen, proliferate and become effective helper or otherwise reactive cells (*79*). Propinquity between T cell antigen receptors and H antigens is suggested by experiments in which specific combination of T cells with antigen was blocked by antiserums to these antigens (*30*) as well as by antiserums to immunoglobulins. This interpretation is not conclusive because other phenomena such as that reported by Bluestein (*22*) might be implicated. Moreover, antiserums to the theta (Thy 1)-antigen will inhibit antigen-binding T cells in some cases (*30, 89*), and antiserum to H-2 antigens have been reported to inhibit the binding of antigen by B cells (*89*). The H antigens and Ia molecules represent two physically distinct (H antigen, 45,000 daltons; Ia antigen, 35,000 daltons) membrane glycoproteins (*87*), which are specified by closely linked genes. They also differ from surface immunoglobulin (light chain, 22,000 daltons; and heavy chain, approximately 70,000 daltons) physicochemically and antigenically. The H antigens and Ia antigens provide markers of biologic individuality and might be involved in the mediation of recognition and differentiation responses of certain sets of T lymphocytes. Since H antigens are not restricted to lymphocytes but are present on virtually all cells, it would be difficult to propose that they might perform some unique T lymphocyte recognition role. Munro *et al.* (*90*) have reported an antigen-specific collaborative T lymphocyte factor that apparently lacked immunoglobulin antigenic determinants but was blocked by antiserums to H-2 determinants. Since the factor functioned in the response to the synthetic polypeptide (Tyr, Glu)-Ala--Lys, which cross reacts antigenically with H-2 antigens (*91*), it is critical to ascertain whether similar factors occur for a variety of antigens. Moreover, because of the ubiquitous cellular distribution of H-2 antigens, this factor should not be localized only to T lymphocytes, but might exist on other cells such as macrophages. The exact nature of the factor remains to be determined. It might, for example, consist of the variable regions of immunoglobulin combined adventitiously with solubilized fragments of H-2 antigens in a noncovalently associated complex.

Conclusions and Further Problems

It is now evident from consideration of a wealth of indirect and direct data that B lymphocytes and at least some immunologically competent T lymphocytes express membrane immunoglobulin which has the capacity to bind antigens. The predominant B cell surface immunoglobulin resembles the $(L\mu)_2$ subunit of IgM, and an additional molecule tentatively identified as IgD has recently been isolated. The relative roles of these two molecules in lymphocyte activation remain to be determined. Surface immunoglobulin of T lymphocyte populations including peripheral T lymphocytes specifically activated to protein or cell antigens and monoclonal T lymphoma lines possess a single type of immunoglobulin. This immunoglobulin has a mass of approximately 200,000 daltons and consists of typical light chains and heavy chains that appear similar to μ chains but can be distinguished from classical μ chain by antigenic, electrophoretic, and functional criteria. At this time it is

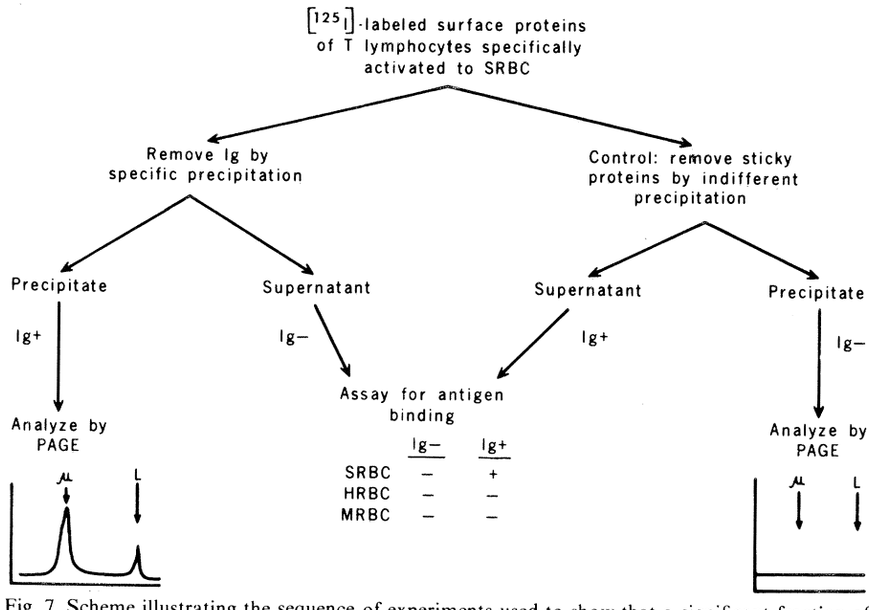

Fig. 7. Scheme illustrating the sequence of experiments used to show that a significant fraction of iodine-labeled surface immunoglobulin of helper T lymphocytes specially activated to sheep erythrocytes (SRBC) bound specifically to this antigen (*61*). The specific precipitation system consisted of mouse immunoglobulin plus rabbit antiserum to this protein (specific for light chains and γ chains); the control system consisted of chicken IgG and rabbit antiserum to this protein. Abbreviations: Ig, immunoglobulin; PAGE, polyacrylamide gel electrophoresis; HRBC, horse red blood cells; MRBC, mouse red blood cells. Actual data for ^{125}I-immunoglobulin bound to cells were as follows (count/min): Samples containing immunoglobulin: SRBC, 5500 ± 130; HRBC, 250 ± 120; MRBC, 600 ± 370. Samples depleted of immunoglobulin; SRBC, 250 ± 100; HRBC, 180 ± 50; MRBC, 490 ± 100.

reasonable to presume that the genes encoding μ^B, μ^T, and the putative δ chain arose by tandem duplications of an ancestral μ-type chain. The μ^B and δ are probably closely linked and lie within the heavy chain translocon, whereas the μ^T gene might occur elsewhere in the genome (*92*). Isolated surface IgM of B cells and IgM (T) of activated T lymphocytes have been shown to bind specifically to antigen. Although the roles that such surface immunoglobulins play in the biochemical mechanisms underlying immune activation remain to be elucidated, an antigen recognition role for these molecules is now clearly established.

In addition to the biochemical events of activation, other challenging problems of the biology of lymphocyte receptors remain open. One of these puzzles stems from the rapidly accumulating evidence that the surface membranes of B and T cells differ in a number of physicochemical (*21, 93*) properties that undoubtedly condition differential responses to mitogens and antigens. These membrane differences most probably are reflected in seeming paradoxes, such as the difficulty of demonstrating T cell immunoglobulin by surface immunofluorescence despite the fact that immunoglobulin receptors for antigen on T cells can be as numerous as on some B cells (*29*). Studies involving isolation and analysis of lymphocyte membranes have been initiated (*21, 40, 94*), and direct answers to the problems of the nature and arrangement of lymphocyte surface macromolecules should be forthcoming. Another area of contention arises because of heterogeneity within the T lymphocyte population. Are antigen-specific "suppressor T cells" (*95*) distinct from "helper" T cells to the same antigen? Would the receptor be the same in both cases? In this example, the minimal hypothesis would be to presume that the receptors are the same and the divergent functions represent different differentiation pathways of the cells after contact with antigen. Moreover, distinct sets of T cells (Fig. 1) probably exist where one set can react to classical foreign antigens or strong histocompatibility antigens and become effector cells, whereas another set responds to certain allogeneic cell configurations by blast transformation in MLR (*5, 6*). The nature of the recognition molecules remains an open question in the latter system. A crucial issue that requires extensive investigation is the mechanisms by which membrane immunoglobulins interact with other membrane molecules in triggering lymphocyte differentiation. In order for immune activation to occur there may be a specific requirement for membrane components—such as products of immune response genes, histocompatibility antigens, molecules binding to antigen-antibody complexes, or other—to interact with surface immunoglobulin which is bound to antigen. Although no data are available regarding the nature of possible receptor-transducer-effector complexes on the lymphocyte membrane, discrete complexes of at least three proteins have been characterized from erythrocyte membranes (*96*). Such supramolecular complexes might play a crucial role in the activation of lymphocytes.

Summary

Immunoglobulins have been isolated from the surface of B (bone marrow–derived) and T (thymus-derived) lymphocytes. Two types of membrane immunoglobulin occur on B lymphocytes; one type resembles the 200,000-dalton subunit of IgM, the second possesses a heavy chain electrophoretically distinct from μ chain and does not correspond to any of the known classes of mouse immunoglobulins. It might correspond to human δ chain. T lymphocytes possess only one type of surface immunoglobulin. This molecule has a mass of approximately 200,000 daltons and contains light chains and heavy chains similar to, but not identical to, μ chains. Evidence now exists that surface IgM-like immunoglobulins of B lymphocytes and T lymphocytes activated to certain antigens can bind specifically to antigen. These observations suggest that surface immunoglobulin functions as a receptor for antigen on B cells and at least on some T cells. The mechanisms by which combination of antigen with surface immunoglobulin initiate differentiation remain to be determined.

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