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Immunology

Human B-cell alloantigens DC1, MT1, and LB12 are identical to each other but distinct from the HLA-DR antigen

(major histocompatibility complex/two-dimensional gel electrophoresis/polymorphism)

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ABSTRACT **Some human B-lymphoblastoid cell lines are shown to express at least two types of Ia-like antigens. One antigen is defined by alloantisera to HLA-DR, and the other antigen is defined by alloantisera and a monoclonal antibody to the specificities DC1, MT1 (MB1), and LB12, which are in linkage disequilibrium with HLA-DR. The subunits of the DC1 molecule differ from those of the DR molecule. The light chains of both molecules are structurally polymorphic.**

The *HLA-D/DR* region of the human major histocompatibility complex (MHC) controls the expression of a noncovalent complex of two membrane glycoproteins of $M_r \approx 34{,}000$ and 29,000 (1). The complex, termed DR, is analogous to the Ia antigens, in particular the I-E/C antigen, encoded in the *I* region of the murine MHC (2). Both the *I* and the *HLA-D/DR* regions determine the specificity of interactions between cells of the immune system, perhaps via the cell surface proteins encoded in these regions. The E/C and the DR antigens display extensive serologically defined polymorphism that can be correlated with structural polymorphism of the lower molecular weight subunit (3–10). To date, HLA-DR 10 alleles (DR1–DRw10) have been well defined (11). The ability to respond to a particular antigen or susceptibility to a disease is often correlated with the expression of particular alleles of the DR and Ia antigens (12, 13). The *I* region of the mouse has been divided into at least five subregions and encodes at least two Ia antigens, each comprised of different large and small subunits. The *HLA-D/DR* region has not been subdivided and, as yet, only one DR molecule has been rigorously defined. However, recent genetic and serological data indicate that the human MHC encodes multiple DR-like antigens. Of particular interest are several series of serological specificities expressed on B cells found in linkage disequilibrium with various DR specificities. These have been termed DC (14), MB (15), MT (16), and LB (17) antigens by various investigators. At present, there is not a consensus as to whether these new specificities represent supertypic determinants on the DR molecule or determinants on a molecule distinct from HLA-DR. This report presents evidence to demonstrate that the DC1, MT1, MB1, and LB12 specificities describe the same molecule, which is distinct from the DR antigen characterized to date.

MATERIALS AND METHODS

Immunoprecipitation. The two B-lymphoblastoid cell lines used were derived from offspring of consanguineous marriages and were homozygous at the *HLA* loci (WT46: *HLA-A32,-B13,* and *-DRw6*; and PGF: *HLA-A3, -B7,-D2,* and *-DR2*). Cell lines were obtained from the Genetics Laboratory of Oxford University (Oxford, England). Human alloantisera were obtained from multiparous women or by planned immunization (18) (Table 1). The rabbit anti-p27,33 serum was prepared against the DR antigen purified from the cell line LB (*DRw6,6*) as described (19). The purified IgG fraction of the monoclonal antibody Genox 3.53 (20) was the gift of Frances Brodsky (Stanford University).

Table 1. Serological reagents

Antiserum	Laboratory of origin	HLA-DR specificity associations	Other local specificity
Ia715	Mann	DR1,2,w6	MT1(MB1)
DR16213.3 (anti-LB12)	van Rood	DR1,2,w6	LB12
Fe131/6	Ferrara (14)	DR1,2,w6	DC1
Fe77/43	Ferrara (14)	DR1,2,w6	DC1
Genox 3.53	Bodmer (28)	DR1,2,w6	—
JongBles 12505 (anti-LB13)	van Rood	DR4,5,w8	LB13
Fe73/30	Ferrara (14)	DR2	—
Fe75/28	Ferrara (14)	DR3,w6	(DC2?)
Ia350	Mann	DR3,5,w6,w8	(MT2?)
Ia172	Mann	DR3,5,w6,w6	MT2
anti-p27,33	Strominger	All	—

Cell lines were labeled for ≈16 hr at 1×10^6 cells per ml in methionine-free RPMI 1640 medium containing [^{35}S]methionine (0.25 mCi/ml; (1 Ci = 3.7×10^{10} becquerels; New England Nuclear) as described (4). After labeling, the cells were washed twice with medium and resuspended to 2×10^6/ml in medium. Aliquots (0.2 ml) containing 4×10^5 intact cells were incubated on ice for 2 hr with 25–150 μl of alloantiserum, 10 μl of xenoanti-p27,33 serum, or 10 μl of normal rabbit serum (NRS). Cells were washed four times with medium to remove unbound antibody and then lysed with 0.5 ml of a lysate containing a 5-fold excess of unlabeled cells that had been prepared by incubating 2×10^6 cells per ml in 0.5% Nonidet P-40/0.01 M Tris·HCl, pH 7.6/1 mM $MgCl_2$/0.1 mM phenylmethylsulfonyl fluoride. The labeled cell lysate was incubated on ice for 30 min and centrifuged at 10,000 × *g* for 30 min. The supernatant was incubated for 30 min with 100 μl of 10% formalin-fixed, heat-killed *Staphylococcus aureus* Cowan I strain (SaCI) bacteria (21). The monoclonal antibody Genox 3.53 was an IgG1

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Abbreviations: MHC, major histocompatibility complex; NRS, normal rabbit serum; SaCI, *Staphylococcus aureus* Cowan I strain; RαMIg, rabbit anti-mouse immunoglobulin; 2-D, two-dimensional; IEF, isoelectric focusing.

and did not bind well to the SaCI protein A. Therefore, the SaCI was coated with rabbit anti-mouse IgG antiserum (RαMIgG; Miles) as described (22) before use as the immunoadsorbent. The immunoadsorbents with the bound antibody-antigen complexes were washed as described (22). The immunoprecipitated proteins were eluted from the SaCI by boiling in Laemmli gel (23) sample buffer containing 2% $NaDodSO_4$.

One- and Two-Dimensional Gel Electrophoresis. The one- and two-dimensional gel electrophoresis was performed as described (4, 22, 24) with some modifications. The discontinuous $NaDodSO_4$/polyacrylamide gel electrophoresis was performed as described by Laemmli (23). The resolving gel (140 × 220 × 1 mm) contained a 7–15% linear gradient of acrylamide.

The samples analyzed by two-dimensional (2-D) gel electrophoresis were separated by $NaDodSO_4$/polyacrylamide gel electrophoresis in the first dimension and by isoelectric focusing (IEF) in the second dimension. Generally, the M_r range 37,000–27,000 was excised from each lane of the $NaDodSO_4$/polyacrylamide gel containing an immunoprecipitate. Alternatively, a strip including a more limited M_r range—e.g., 35,000–31,000 or 31,000–28,000—was cut out across all lanes of the $NaDodSO_4$/polyacrylamide gel. The $NaDodSO_4$ gel pieces were equilibrated in ≈10 vol of 8 M deionized urea/2% NP-40/0.2% pH 9–11 Ampholines for 1 hr at room temperature with one change of solution. The $NaDodSO_4$ gel pieces were then polymerized in the IEF gel. After the IEF gel was polymerized, it was placed on a LKB Multiphor 2117 flat bed gel apparatus with the $NaDodSO_4$ gel pieces at the anode. When polymerization of the IEF gel around the $NaDodSO_4$ gel pieces was not complete, the pieces were pushed into contact with the IEF gel and a glass strip was laid over the junction. The wick at the anode was laid on the IEF gel slightly overlapping the $NaDodSO_4$ gel pieces. The IEF gel contained 8 M urea/2% Nonidet P-40/7% acrylamide/0.19% *N,N'*-methylenebisacrylamide/2% (wt/vol) LKB Ampholine carrier ampholytes. The Ampholines used were pH 3.5–10/pH 4–6/pH 6–8 (1:0.25:0.25). The IEF gel was subjected to electrophoresis for 8 hr at 1000 V with the circulating cooling bath at 7°C. All gels were fluorographed (25).

RESULTS

Comparison of the DC1, MT1, LB12, and DRw6 Antigens. Three alloantisera investigated in this study react with a determinant whose expression is closely associated with the expression of DR1, DR2, and DRw6. These alloantisera are Fe131/6, Ia715, and DR 16213.3 (anti-LB12), which define the local specificities called DC1, MT1 or MB1, and LB12, respectively. The reactions of these sera were compared with those of two alloantisera, Fe75/28 and Ia350, that presumably recognize a determinant on the DR molecule. A rabbit xenoantiserum, anti-p27,33, made by using the purified DR antigen as the immunogen, recognizes all DR specificities and was used as a control. The antisera were incubated with metabolically labeled intact cells, which were then washed to remove unbound antibody and lysed with detergent; the immune complexes were precipitated with SaCI. This procedure eliminated several proteins that coprecipitate with DR antigens when whole cell lysates are treated with xeno- or allo-anti-DR sera. In particular, two invariant proteins, M1 and p35, that are associated with all DR specificities and migrate near the DR heavy chain in $NaDodSO_4$/polyacrylamide gels were eliminated (4, 22).

The results of the immunoprecipitations from the cell line WT46, which is homozygous, for DRw6, are shown in Fig. 1. The alloantiserum Fe75/28 reacts with DR3- or DRw6-positive B cells, and serum Ia350 reacts with cells bearing specificities DR3, DR5, DRw6, or DRw8. Both alloantisera and the xenoanti-DR serum (anti-p27,33) precipitated proteins of apparent M_r 34,000 (H1) and 30,000 (L1) from WT46. Fe75/28 and Ia350 also precipitated the DR molecule from a B-cell line homozygous for DR3 but were negative on the DR2 homozygous cell line PGF (see Fig. 4, lane 9). In contrast, the three sera, Ia715, Fe131/6, and anti-LB12, precipitated proteins of apparent M_r 32,000 (H2) and 29,000 (L2) from WT46. Thus, the MT1 (MB1), DC1, and LB12 determinant(s) appears to be expressed on a molecule different from the DR molecule. As the three alloantisera appear to have the same specificity, the molecule they recognize will just be referred to as DC1. The alloantiserum against LB13 recognizes a determinant associated with specificities DR4, DR5, and DRw8 (17). It did not specifically immunoprecipitate any proteins from WT46.

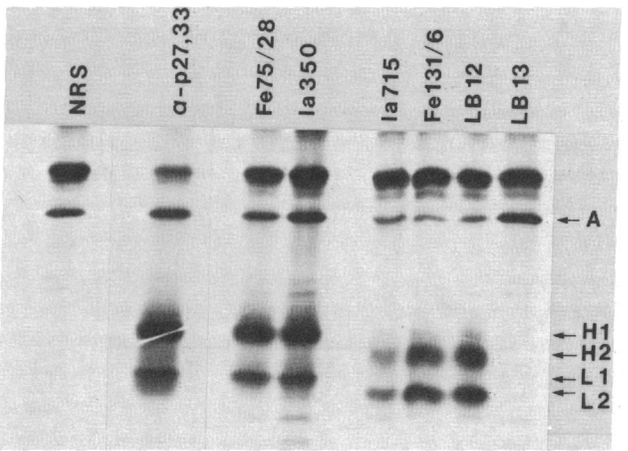

FIG. 1. $NaDodSO_4$/polyacrylamide gel analysis of HLA-DR and MT1, DC1, and LB12 antigens from the cell line WT46 (*DRw6*). The antigens were isolated by immunoprecipitation with the antisera indicated. The heavy and light chains of the DRw6 molecule are designated H1 and L1, respectively, and the subunits of the DC1 (MT1, LB12) molecule are designated H2 and L2. A, actin.

An aliquot of the immunoprecipitates shown in Fig. 1 were subjected to 2-D gel electrophoresis to compare the DC1, LB12, MT1, and DRw6 molecules. The immunoprecipitates were subjected to electrophoresis on $NaDodSO_4$/polyacryla-

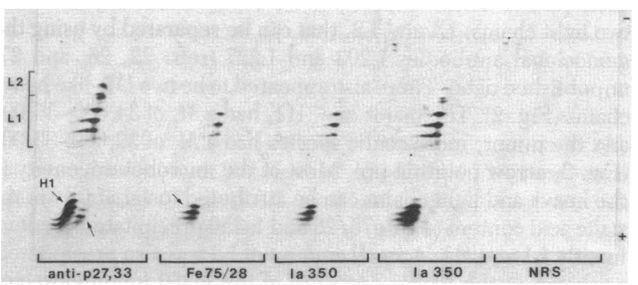

FIG. 2. 2-D gel analysis of the HLA-DR antigen from WT46 (see Fig. 1). The M_r range 37,000–27,000 was excised from each lane of the first-dimension $NaDodSO_4$/polyacrylamide gel, and the pieces were polymerized in the second-dimension IEF gel along the anode (+). Brackets at the bottom of the figure indicate the positions of the $NaDodSO_4$ gel pieces, each of which was oriented with M_r decreasing from left to right. The direction of IEF was perpendicular to that of $NaDodSO_4$ electrophoresis gel. Brackets at the left indicate the pH range over which the light chains L1 and L2 focused. Fe75/28 and Ia350 precipitated predominantly H1 (arrow pointing down) and L1. The two Ia350 immunoprecipitates shown are the same sample, except that the one on the right was exposed to film 2.5 × longer than the one on the left to show that some L2 was also precipitated. Arrow pointing up shows presumptive H2 in the anti-p27,33 immunoprecipitate.

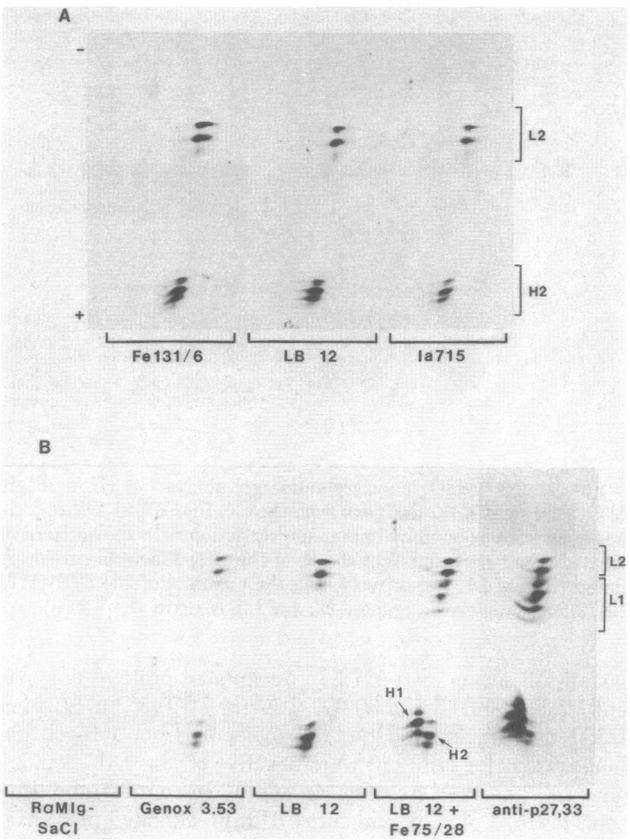

FIG. 3. 2-D gel analysis of the DC1, LB12, and MT1 antigens from WT46. (*A*) The Fe131/6, LB12, and Ia715 immunoprecipitates shown in Fig. 1 were analyzed. (*B*) An LB12 immunoprecipitate was compared on the same 2-D gel with a mixture of an LB12 and an Fe75/28 immunoprecipitate, with the immunoprecipitate with the monoclonal antibody Genox 3.53, and with the immunoprecipitate with the immunoadsorbent without antibody. The $NaDodSO_4$ gel analysis of the other half of the immunoprecipitates with RαMIg/SaCI alone and with Genox 3.53 are shown in Fig. 4, lanes 1 and 2, respectively.

mide gels in the first dimension and IEF in the second dimension. As shown in Figs. 2 and 3*B*, anti-p27,33 precipitated a DR light chain consisting of at least six bands, as observed previously (4, 22). This complex pattern is due to the expression of two light chains, L1 and L2, that can be separated by using the monoclonal antibodies L203 and L227 (refs. 22, 26, and 27; unpublished data). There also appeared to be two DR-like heavy chains (Fig. 2). The major one, H1, had a M_r of 34,000–35,000 and the minor, more acidic species had a M_r of 32,000–33,000 (Fig. 2, arrow pointing up). Most of the microheterogeneity in the heavy and light chains can be attributed to variability in the sialic acid content (4). Fe75/28 and Ia350 precipitated predominantly L1 and H1. A small amount of L2 was also precipitated, as shown in the longer exposure of the Ia350 immunoprecipitate. The immunoprecipitates with both alloantisera gave the same 2-D gel pattern. In contrast, Fe131/6, anti-LB12, and Ia715 precipitated one light chain, which appeared to be identical to L2 (Fig. 3). The heavy chain, H2, of the DC1 (LB12, MT1) molecule had a lower M_r than H1, as shown in Fig. 1, and overall had a more acidic pI range than H1 (Fig. 3*B*). The DC1 heavy chain appeared to be the same as the minor species of heavy chain precipitated by the xenoantiserum. As shown in Fig. 3*A*, Fe131/6, anti-LB12, and Ia715 all recognized the same molecular species. In Fig. 3*B*, an LB12 and an Fe75/28 immunoprecipitate were mixed and analyzed by 2-D gel electrophoresis to demonstrate unambiguously the differences between the heavy and light chains of DRw6 and DC1.

In addition to screening alloantisera, the monoclonal antibody Genox 3.53 (20) was tested on the cell line WT46. Genox 3.53 binds to B cells that type as DR1, DR2, or DRw6 and thus was a candidate for an anti-DC1 antibody. Immunoprecipitations using Genox 3.53 were performed as described for the alloantisera except that the immunoadsorbent used was RαMIg/SaCI. Analysis of the Genox 3.53 immunoprecipitates by $NaDodSO_4$/polyacrylamide gel electrophoresis showed a high background and little specific precipitation when compared with the precipitation with immunoadsorbent in the absence of antibody (Fig. 4, lanes 1 and 2). Altering the amount of Genox 3.53 antibody used did not improve the precipitation. However, the bands specifically immunoprecipitated by Genox 3.53 were resolved from the background precipitation by 2-D gel electrophoresis as shown in Fig. 3*B* in which it is compared with the immunoprecipitate of LB12. By this type of analysis, we concluded that Genox 3.53 recognized the DC1 molecule on the cell line WT46.

Detection of Polymorphism Among DC1 Molecules. The DC1, LB12, and MT1 determinants are expressed on most B cells bearing specificity DR1, DR2, or DRw6. To determine whether the different DR types are associated with the same DC1 molecule, the immunoprecipitated DR and DC1 antigens from the DR2 homozygous cell line PGF were compared with those from the DRw6 homozygous cell line WT46. Fig. 4 shows that the xenoanti-DR serum and the alloanti-DR2 serum, Fe73/30, both precipitated a heavy and a light chain of $M_r \approx 34,000$ and 29,000, respectively, from the cell line PGF. The serum Fe73/30 was negative on the cell line WT46. As reported previously (4), the $NaDodSO_4$ gel electrophoretic mobility of the DR light chain varies with the DR specificity. The anti-LB12 serum recognized a heavy chain on PGF different from the DR2 large subunit but similar to the LB12 heavy chain from WT46. The LB12 and DR2 light chains from PGF were not readily distinguishable by gel mobility.

Analysis by 2-D gel electrophoresis (Fig. 5) confirmed that the LB12 heavy chains from PGF and WT46 were similar. The immunoprecipitates from PGF using an alloantiserum to MT1 (Ia715) or DC1 (Fe77/43) resulted in a 2-D pattern similar to that observed with anti-LB12. The three sera also precipitated a small and variable amount of H1 from PGF. It is not known whether this is due to contaminating anti-DR2 antibodies or to crossreaction. In contrast to the heavy chains, the LB12 light chains from PGF and WT46 differed in their isoelectric points. The 2-D gel analysis also showed that the patterns of the LB12

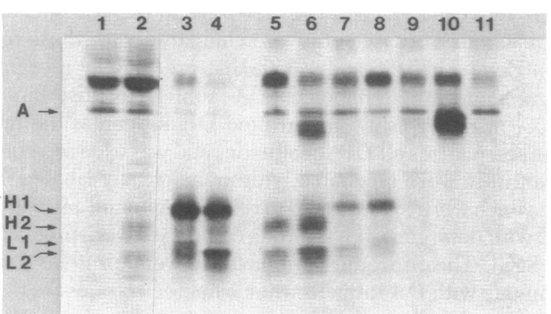

FIG. 4. $NaDodSO_4$/polyacrylamide gel analysis of DR and DC1 antigens isolated by immunoprecipitation from WT46 and PGF (DR2). The cell line and antibody used for each are as follows: lane 1, WT46, RαMIg/SaCI without antibody; lane 2, WT46, 25 μg of Genox 3.53; lane 3, WT46, anti-p27,33 serum; lane 4, PGF, anti-p27,33 serum; lane 5, WT46, LB12; lane 6, PGF, LB12; lane 7, PGF, Fe73/30; lane 8, WT46, Fe75/28; lane 9, PGF, Ia350; lane 10, WT46, Fe73/30; and lane 11, PGF, NRS. The heavy band below actin in lanes 6 and 10 is the HLA-A or -B heavy chain.

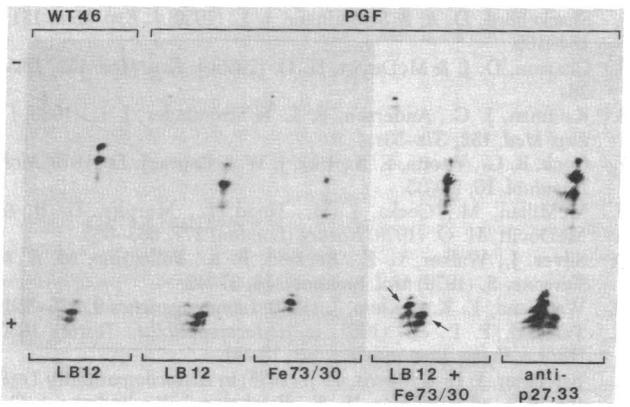

FIG. 5. 2-D gel analysis of DR and DC1 antigens from PGF and WT46 (see Fig. 4). The cell line used is indicated at the top of the figure, and the antiserum used is indicated at the bottom. An LB12 and an Fe73/30 immunoprecipitate were mixed to demonstrate the differences in the DC1 and DR subunits. Arrow pointing up, DC1 heavy chain (H2); arrow pointing down, DR heavy chain (H1).

and DR2 light chains were not identical. The DR2 alloantiserum Fe73/30 precipitated what appeared to be two light chains. The two major spots in the light chain 2-D gel pattern are separated by ≈2 charge units and probably represent the major sialic acid-containing species of the two chains. Fainter bands are detectable ≈+1 and −1 charge unit on either side of each major spot. The LB12 light chain from PGF differed in pI from either of the two DR2 light chains. An LB12 and an Fe73/30 immunoprecipitate from PGF were also subjected to electrophoresis together to demonstrate the differences between the DR2 and the LB12 subunits. The xenoanti-p27,33 serum appears to precipitate both DR- and DC1-like subunits (compare ref. 4).

The heavy and light chains of the DR and DC1 (LB12) antigens from PGF and WT46 are compared directly in Fig. 6. For this experiment, strips containing the light chains (M_r 31,000–28,000) and the heavy chains (M_r 31,000–36,000) were excised across the lanes of the $NaDodSO_4$/polyacrylamide gel and then polymerized in the IEF gel and focused. The results again emphasize the differences between the light chains and between the heavy chains of the DR and DC1 molecules isolated from a given cell line. However, only the DR and DC1 light chains, and not the heavy chains, display structural variability when homologous products from different cell lines are compared.

DISCUSSION

The DC1, MT1, MB1, and LB12 B-cell determinants are closely associated with the expression of specificities DR1, DR2, and DRw6. It has been debated whether the human alloantisera used to define these and other MT, MB, and LB determinants (*i*) are multispecific, (*ii*) recognize public or supertypic determinants, or (*iii*) detect a molecule distinct from the DR antigen in linkage disequilibrium with HLA-DR. This report demonstrates that alloantisera against DC1, MT1, MB1, or LB12 and the monoclonal antibody Genox 3.53 recognize the same two-chain molecule, which is distinct from the DR antigen.

The DC1 specificity was first described by Tosi *et al.* (14) By testing a battery of human alloantisera for binding to a membrane glycoprotein preparation of "HLA-DR" from the cell line Daudi (*DRw6,blank*), they were able to define three populations of molecules carrying the specificities DRw6, DC1, and DC2. They showed that both the DRw6 and DC1 molecules had a two-chain structure but were not able to resolve a difference in the molecular weights of the DC1 and DRw6 heavy chains.

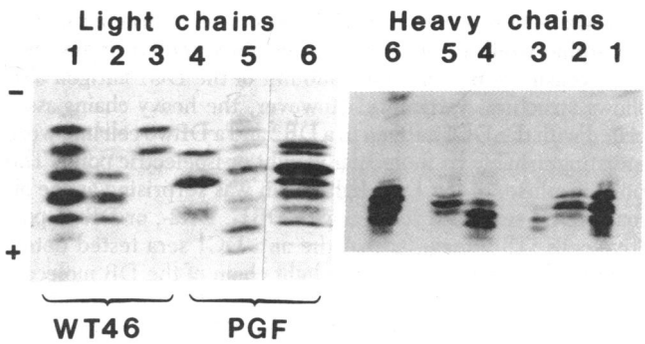

FIG. 6. Comparison of the heavy and light chain subunits of the DR and DC1 antigens from WT46 (lanes 1–3) and PGF (lanes 4–6). The antigens were immunoprecipitated with anti-p27,33 serum (lanes 1 and 6), LB12 (lanes 3 and 4), Fe 75/28 (lane 2), or Fe 73/30 (lane 5) and subjected to electrophoresis on a $NaDodSO_4$/polyacrylamide gel. The strip containing the light chains (M_r 31,000–28,000) was cut out across all lanes of the gel, as was the adjacent strip containing the heavy chains (M_r 35,000–31,000). Both gel strips were polymerized in the IEF gel along the anode such that the direction of IEF was the same as that of the $NaDodSO_4$ gel electrophoresis.

This study confirms that the DC1 molecule is composed of a large and a small subunit, as is the DR molecule. However, the DC1 heavy chain, H2, has an M_r ≈2000 less than that of the DR heavy chain, H1, and a more acidic isoelectric point range. The difference in molecular weight could be due to glycosylation differences. The DR heavy chain contains two oligosaccharide moieties and removal of one would reduce the M_r by 2000–3000 (unpublished data). This would not account for the shift of H2 to a more acidic pI unless one also postulates an increase in sialic acid content.

The data presented in this paper show that both DRw6-positive and DR2-positive B-cell lines express at least two heavy chains and two or three light chains that can combine to form three Ia-like molecules. In the cell line WT46, the complex composed of H2 and L2 is DC1. The DRw6 specificity appears to be predominantly on the molecule composed of H1 and L1. A complex of H1 and L2 can also be isolated by using the monoclonal antibodies L203 and L227 (refs. 22, 26, and 27; unpublished data). The alloanti-DRw6 sera Fe75/28 and Ia350 also precipitated a small amount of L2. This could be due to the presence of other antibodies such as anti-DC1 or anti-DC2 or to crossreaction. One possibility is that the molecule composed of H1 and L2 carries the *MT2* determinant, which is associated with DR specificities 3,5,w6, and w8. The alloantisera Ia350 and Ia172 have this reaction pattern and thus are considered to have anti-MT2 antibodies. Like Ia350, Ia172 precipitated L1 and H1 from WT46. However, Ia172 precipitated more L2 from WT46 than did Ia350 (unpublished observation). Both Ia172 and Ia350 were negative on the cell line PGF suggesting they do not contain anti-DC1 antibodies. Therefore, the variable amount of L2 precipitated may be due to the difference in the amount of anti-MT2 antibodies in the two alloantisera. The rabbit xenoanti-p27,33 serum appears to recognize all four DR and DC1 subunits although it has not been confirmed by sequential immunoprecipitations that the anti-p27,33 serum contains both anti-DR and anti-DC1 antibodies.

Other B-cell determinants have been characterized that are closely associated with different groups of DR specificities but probably distinct from DR. Markert and Cresswell (28) have analyzed two of these, MB2 (associated with DR3 and DR7) and MT2, on a cell line that is also homozygous for DR3. Analysis by 2-D gel electrophoresis indicated that the cell line studied expresses at least two light chains and two or three heavy chains.

It has been shown that the DR light chain is structurally polymorphic while the heavy chain exhibits limited, if any, polymorphism (3–6). The small subunit of the DC1 antigen also shows structural variability. However, the heavy chains associated with the DC1 antigen in a DR2 and a DRw6 cell line were indistinguishable by molecular weight or isoelectric point. The polymorphism of the DC1 light chain was surprising as the alloanti-DC1 sera used reacted with DR1-, DR2-, or DRw6-positive cells. This suggests that the anti-DC1 sera tested detect a "public" determinant(s). The light chain of the DR molecule is probably encoded by a locus in the *HLA-D/DR* region. It has not been conclusively shown that the DR heavy chain is also MHC encoded. As expression of the DC1, LB12, and MT1 determinant(s) is in linkage disequilibrium with DR1, DR2, and DRw6, it is likely that at least one of the DC1 subunits is also MHC encoded. Van Rood *et al.* (17, 29) have identified *LB13* as a possible allele of *LB12*. Studies of families that have a recombination event between *HLA-DR* and *HLA-B* or between *HLA-A* and *-B* have tentatively mapped *LB13* between the *HLA-DR* and *HLA-B* loci.

Preliminary reports suggest that the DR and DC, MT, MB, LB antigen series may be distinguished functionally as well as structurally. One study concluded that matching donor and recipient for MB antigens led to more successful kidney transplants than matching for HLA-A -B or -DR antigens (30). Many studies have shown that susceptibility to some diseases and HLA-DR type are correlated (12). It appears that the presence of DC1 may also be correlated with increased risk for some diseases. The number of individuals positive with alloantiserum Ia715 is increased in certain disease populations, such as those with primary sicca syndrome (31, 32) and systemic lupus erythematosus (33), when compared with normal populations. Preincubation of human monocytes with rabbit xeno-anti-DR (anti-p23,30) antiserum or with human alloantiserum to B-cell antigens can induce a population of T cells that can suppress a polyclonally activated B-cell response (34). The alloantisera Ia172 and Ia715 induce this type of suppression, whereas Ia350 does not (ref. 35; unpublished data). The mechanism of this regulatory response is not known, but it indicates a functional difference between DR and DC1 antigens. Further structural, functional, and genetic studies should determine the number of Ia-like antigens encoded in the human MHC and their role in the immune system.

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