POLYMORPHISM OF Fc RECEPTOR ON MURINE B CELLS
IS IgH-LINKED

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Fc receptors occur on several hematopoietic cell lineages, and can mediate crucial effector functions in each of the cell types. The Fc receptors on mast cells, macrophages (1–5), granulocytes (6–9), and lymphocytes (10–21) have been shown to exhibit different binding specificities. Moreover, in some cases distinct Fc receptor–binding specificities are found on a single cell (8, 9, 13, 21–29). Murine macrophages, which have been studied extensively, appear to possess three distinct Fc receptors for IgG, one binding IgG1 and IgG2b, a second binding IgG2a, and a third binding IgG3 (22–29). The IgG2a receptor is sensitive to trypsin proteolysis and fails to bind IgG2a at 4°C or in the presence of cytochalasin. In contrast, the IgG1/IgG2b and IgG3 receptors are unaffected by these treatments (22–24, 27, 28). In addition, mutant cell lines lacking certain receptor activities have been isolated and the receptors can be independently modulated (22–24, 29). In contrast, Fc receptors isolated by affinity chromatography on IgG2a- or IgG2b-Sepharose or by immunoprecipitation bind equally well to IgG1, IgG2a, and IgG2b (26, 30). However, affinity-isolated Fc receptors can, under certain circumstances, distinguish between IgG1/IgG2b and IgG2a (31). In contrast to our understanding of macrophage and mast cell Fc receptors, little is known about Fc receptors on lymphocytes (20).

Immunoglobulin binding to cell surfaces via Fc receptors mediates immunological effector functions. The opsonization of immune complexes and particulate antigens (32–34), as well as the release of molecules that regulate immune responsiveness (35, 36), are facilitated by IgG binding to Fc receptors on macrophages. Mast cell release of histamine is mediated by antigen-IgE complexes bound to the IgE Fc receptor (37–39). Further, T cell binding of immunoglobulin via Fc receptors appears to result in modulation of immune responses (40–43). For example, Fc binding of IgE by T cells elicits release of IgE-binding factors which act to regulate the IgE response (40, 41). Similar results have been found with T cells that bind IgG and IgA by means of their Fc receptors (42, 43). Indeed, in the majority of systems where the cellular basis of

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Fc-mediated immune modulation has been examined. T cells or macrophages appear to be involved (40–46). There is one system however, where the B cell is apparently directly affected by Fc binding of IgG (47). B cells treated with whole rabbit anti-mouse IgM do not induce B cells to proliferate, although F(ab')2 fragments do. Recent results (48) indicate that whole anti-Ig does lead to B cell depolarization, enlargement, and enhanced Ia antigen expression. Thus, although B cells become activated by whole anti-Ig, Fc-mediated binding of the anti-Ig seems to inhibit DNA synthesis. The crosslinking of surface Ig (sIg)1 to Fc receptors appears to act as a regulatory signal acting directly on the B cell.

To better understand this potentially important B cell receptor(s), we have begun to characterize those capable of binding IgG. Our results indicate that a single Fc receptor binds both rat and mouse IgGs of the IgG1, IgG2a, and IgG2b subclasses. Furthermore, we find that B cells of A/J, AL/N, and NZB/J mice bind 3.5–7-fold less rat IgG than B cells of other strains, reflecting a difference in the specificity of the IgG Fc receptor rather than a difference in the number of Fc receptors expressed by A/J B lymphocytes. An examination of backcross mice and IgH recombinant mouse strains indicates that Fc receptor polymorphism is loosely linked to the IgH locus of chromosome 12 and maps telomeric to the prealbumin locus.

Materials and Methods

**Mouse Strains.** Adult BALB/cJ, C57BL/6J, C57BL/10J, SJL/J, DBA/2J, AKR/J, A/J, A/HeJ, NZB/BLJ, C3H/HeJ, C3H/FeJ, and PL/J mice were obtained from The Jackson Laboratory (Bar Harbor, ME) and breeding facilities at Washington University. AL/N, C.AL9, and C.AL20 mice were obtained from Dr. Michael Potter (NIH, Bethesda, MD).

*Igh* recombinant mouse strains, AXC and CXAXCB were constructed by crossing mice with different allotypes and selecting for recombination between the *Igh-V* marker locus (*Igh-Dex*) and the *Igh-C* marker allotype, or for recombinations between *Igh-C* and *Pre-1*, the serum prealbumin locus (49–51).

**Cells and Culture Conditions.** Normal lymphoid cell populations were separated into T and B cells by panning. Polystyrene dishes (16 × 100 mm, No. 1001; Falcon Labware, Oxnard, CA) were coated with affinity-purified goat anti-mouse IgM or mouse anti-rat Ig according to the method of Wysocki and Sato (52). Briefly, 5–10 ml of purified antibody (10 μg/ml in 0.05 M Tris, 0.15 M NaCl, pH 9.5) was added to polystyrene dishes for 1 h at room temperature. Dishes were then washed in phosphate-buffered saline (PBS)/1% fetal calf serum (FCS) and further incubated in PBS/1% FCS to block remaining protein-binding sites. For indirect panning, plates coated with mouse anti-rat Ig were incubated with appropriate amounts of monoclonal antibody 14.8, directed to the B cell marker B220 (53) or monoclonal anti-Thy-1.2 (Jlj) (54) for 1 h at room temperature. Plates were thoroughly washed and spleen cells (2 × 10⁷) were gently layered onto the plates in Dulbecco’s modified Eagle’s medium (DME), 5% FCS and incubated at 4°C for 60 min. Nonadherent cells were removed in eight washes after which adherent cells were harvested by vigorous pipeting.

T and B cell blasts were induced by mitogen stimulation and purified on Percoll density gradients in some experiments. Briefly, spleen cells were treated with either concanavalin A (Con A) (2 μg/ml) or lipopolysaccharide (LPS) (50 μg/ml). Cells were cultured in DME supplemented with glucose, sodium bicarbonate, nonessential amino acids, glutamine, 1**Abbreviations used in this paper:** AV, avidin; BSA, bovine serum albumin; Con A, concanavalin A; DME, Dulbecco’s modified Eagle’s medium; DNP, dinitrophenyl; FACS, fluorescence-activated cell sorter; FITC, fluorescein isothiocyanate; FCS, fetal calf serum; LPS, lipopolysaccharide; PBS, phosphate-buffered saline; PE, phycoerythrin; sIg, surface immunoglobulin.
penicillin, streptomycin, 10% FCS, and 5 × 10⁻³ M 2-mercaptoethanol. Cultures were maintained in a humidified incubator at 37°C with 5% CO₂, 7% O₂, 88% N₂. Con A-treated cells were harvested on day 2 after stimulation and LPS blasts were collected on day 3. The blasts were then isolated and analyzed by fluorescence-activated cell sorter (FACS).

Fluorescent Antibody-binding Assay. 4 × 10⁵ cells in DME/0.5% bovine serum albumin (BSA)/0.02 M NaN₃ were placed in individual wells of V-bottom 96-well microtiter dishes (Dynatech Laboratories, Alexandria, VA), and optimal amounts of antibodies in a volume of 30 μl were added to each well. Cells were incubated on ice for 30 min. Each sample was underlaid with 10% BSA in DME containing 0.02 M NaN₃ and centrifuged at 250 × g for 10 min. This step was repeated after aspiration of the supernatant and resuspension of the cells. After the second wash, cells were resuspended in 25 μl of fluorescin isothiocyanate (FITC)-mouse anti-rat Ig or FITC–goat anti-mouse IgG (Southern Biological Associates, Birmingham, AL) for 30 min on ice. FITC–mouse anti-rat Ig and FITC–goat anti-mouse IgG were spun at 120,000 g for 30 min to remove aggregated antibody. Samples were underlaid with BSA and centrifuged as before. Cells were resuspended in 50 μl DME/0.5% BSA/0.02 M NaN₃ containing 10 μg/ml propidium iodide (Sigma Chemical Co., St. Louis, MO). Propidium iodide (red fluorescence) was used to exclude dead cells from analysis. Biotin-conjugated antibodies were also used in combination with FITC–avidin (AV) or phycoerythrin (PE)-AV to detect cells. PE was obtained from Molecular Probes, Junction City, OR. In dual-fluorescence studies, the procedure outlined above was duplicated except that a rat anti-mouse kappa (hybridoma 187.1) (57) conjugated to PE was used to identify B cells.

Monoclonal anti-B220 (14.8) (53), anti-κ (187.1) (57), anti-IgM (331.12) (58), and anti-I-A<sup>+</sup> (25-9-17) (59) were obtained from the Cell Distribution Center at the Salk Institute, La Jolla, CA. Anti-Thy-1.2 (Jll) (54) and anti-I<sup>+</sup> (AF4-73.3) (60) were kindly provided by Drs. T. McKearn (Cytogen, Inc., Philadelphia, PA) and A. Stall (Becton, Dickinson & Co., Mountain View, CA), respectively. Anti-FcR monoclonal (2.4G2) was kindly provided by Dr. J. C. Unkeless (25) (The Rockefeller University, New York).

Cells were analyzed on a FACS IV equipped with an argon ion laser tuned to 488 nm and operating at 200 mW of power. Photomultiplier tube voltage and gain setting were constant throughout all experiments. Fluorescence histograms were generated with logarithmic amplification (log base 10) of fluorescence emitted by single viable cells.

Inhibition Assays. Titrations of the biotin-conjugated or FITC-labeled IgG were performed to determine at which point slightly less than maximal staining was observed, so that labeled IgG was limiting. The fluorescence assay used to detect optimal Ig binding to B lymphocyte Fc receptors requires approximately 10–100 times the concentration of purified antibodies that provides optimal staining for immunofluorescence when using antibodies specific for cell surface determinants. Under conditions where labeled IgG is limiting, inhibition by unlabeled IgGs can be quantitated. Aggregated myeloma or hybridoma isotype standards were titrated into a constant number of cells (3 × 10⁵) and allowed to incubate for 5 min. A constant amount (~50 μg/ml) of labeled IgG is then added at 4°C for 25–30 min. The cells are washed and analyzed for fluorescence, as described above. Inhibition was measured as the decrease in relative fluorescence intensity caused by the competing IgG.

Myeloma and Hybridoma Antibody Standards. Murine myeloma proteins were obtained by injecting MOPC-21 (IgG1), MPC-11 (IgG2b), LPC-1, UPC-10 (IgG2a), or J606 (IgG3) cells into the peritoneal cavity of pristane-primed BALB/c mice (61). The ascites fluid was precipitated with 50% saturated ammonium sulfate. The proteins were isolated by DEAE chromatography and preparative isoelectric focusing. Affinity-purified murine hybridomas 52-1A (IgG2a, anti-dinitrophenyl [DNP]), 29-13 (IgG2b, anti-DNP), and HDP-1 (IgG1, anti-DNP) (kindly provided by Dr. M. Scott, Mallinckrodt, Inc., St. Louis, MO) were also used as isotype standards.

Rat hybridoma antibodies of IgG1, IgG2a, and IgG2c isotypes were produced in our laboratory using standard methods. The affinity-purified antibodies used in these studies were: IgG1 (49C2D3, anti-DNP), IgG2a (50C1C1, anti-DNP), IgG2b (148d4-1,
anti-N-acetylglucosamine), and IgG2c (120 a3-5, antiphosphorylcholine). EA4.1 (IgG2b, unknown specificity) was also used in these studies as an isotype standard. Rat myeloma proteins IR595 (IgG1) and IR418 (IgG2a) were kindly provided by Dr. H. Bazin (University of Louvain, Belgium) (62). Aggregated immunoglobulins were produced using bis-diazotized benzidine (63) or by heat aggregation.

Results

IgG Binding to Mouse B Lymphocyte Fc Receptors. In the studies reported here, we used a fluorescence assay to quantitate Fc binding of immunoglobulins to mouse B lymphocytes. The advantage of a fluorescence assay using flow microfluorometry techniques is that individual cells are analyzed for Fc receptor expression. Further, the fluorescence assay provides a strong signal that is highly reproducible between assays and is stable for several hours at 4°C. In data not shown, we found that isolated B lymphocytes (slgM +) and LPS blasts bound IgG strongly; however, we did not detect significant IgG binding to isolated T (Thy-1.2+) cells or Con A blasts.

In most of the experiments, we used LPS blasts as our test population because they provide a population of pure B cells (>95%), as determined by expression of slg and B220. Each of the mouse IgG subclasses, IgG1, IgG2a, and IgG2b (Fig. 1 a) and each of the rat IgG subclasses, IgG1, IgG2a, and IgG2b (Fig. 1 b) bind to mouse B cell blasts in similar amounts.

To determine whether one or more Fc receptors was responsible for the binding of rat and mouse IgG subclasses to B cells, a series of inhibition assays were performed. The assays are based on the inhibition of a standard labeled IgG by known quantities of purified representatives of the IgG subclasses. Histograms demonstrating the inhibition of biotin-conjugated mouse IgG2a (LPC-1, UPC-10) and IgG2b (MPC-11, 29-13), as well as rat IgG2b (EA4.1), are shown in Fig. 2, a–c, respectively. Fc-mediated binding of mouse IgG2a (LPC-1, UPC-10) is inhibited by both aggregated IgG2a (LPC-1, UPC-10) and aggregated IgG2b (MOPC-195, MPC-11) (Fig. 2 a, Table I). Similarly, the binding of the IgG2b (MPC-11, 29-13) standard is inhibited by immunoglobulins of the IgG2a (LPC-1) and IgG2b (MOPC-195, MPC-11) subclasses (Fig. 2 b, Table I). The binding of IgG1 (HDP-1) to the Fc receptor is inhibited by IgG1, IgG2a, and IgG2b (data not shown). Thus, we conclude that the IgG1, IgG2a, and IgG2b all bind to the same Fc receptor. Further, the concentration of competing antibody that provides maximal inhibition of the IgG1, IgG2a, or IgG2b standard proteins is the same in all cases (~750 µg/ml of LPC-1, MPC-11, MOPC-21, or MOPC-195). Fig. 2 c illustrates that rat IgG2b (EA4.1, 148d4-1) is specifically inhibited by mouse IgG1 (MOPC-21), IgG2a (LPC-1), and IgG2b (MPC-11). The rat IgG2b appears to bind the mouse B cell IgG1/IgG2a/IgG2b Fc receptor, because it is inhibited by each of these subclasses. Table I summarizes the data from several inhibition experiments. The results show that representatives of IgG1, IgG2a, and IgG2b subclasses can each inhibit Fc binding of IgG1, IgG2a, or IgG2b. These data support the existence of one Fc receptor that binds each of the three IgG subclasses, IgG1, IgG2a, and IgG2b. Elsewhere, we will show evidence for a second Fc receptor on B cells that binds mouse IgG3 and the related rat IgG2c. Our findings on the B cell Fc receptor stand in contrast to

2 Baum, C. B., J. P. McKearn, and J. M. Davie. Manuscript in preparation.
the Fc-binding activities expressed by mouse macrophages, where one Fc receptor appears to bind the IgG1 and IgG2b subclasses and another receptor binds IgG2a (2, 6-8, 38, 40, 41, 47).

**Polymorphism in the B Cell Fc Receptor.** An examination of rat IgG Fc binding to the B lymphocytes of various mouse strains indicates that most strains exhibit relatively high levels of rat IgG binding. The strain survey was initially performed using rat IgG2b proteins (EA4.1, 148d4-1) and, subsequently, strains were tested for IgG1 and IgG2a binding. Lymphocytes from A/J, AL/N, and NZB/J strains expressed significantly lower levels of rat IgG binding (3.5-7-fold). Fig. 3a shows a comparison of the Fc binding exhibited by the B cell blasts of BALB/c mice, a high Fc-binding strain, to the B cell blasts of A/J mice. It should also be noted that the difference in binding of rat IgG occurred in unstimulated splenic lymphocytes as well as in B cell blasts (Fig. 3b). The strain survey of rat IgG Fc binding is summarized in Table II. Mouse IgG1, IgG2a, and IgG2b subclasses each bound equally well to both high (BALB/c) and low (A/J) rat IgG-binding
strains, as illustrated in Fig. 4. Further, B cell blasts of the BALB/c and A/J mouse strains exhibit equivalent binding of a monoclonal antibody (2.4G2) specific for the IgG1/IgG2b Fc receptor previously described by Unkeless et al. (25). Therefore, we conclude that the variation in binding of rat IgG subclasses is the result of a difference in specificity rather than a difference in the number of Fc receptors on mouse B lymphocytes.

An examination of the strain survey indicates a possible correlation between low Fc binding and IgH haplotype. All conventional strains of the IgH-C*, IgH-C*, and IgH-C* haplotypes are low binders of rat IgG. These haplotypes are similar: the NZB/J strain matches the A/J IgH-C haplotype in the IgH-3 (IgG2b), IgH-1 (IgG2a), and IgH-2 (IgA) loci, and the AL/N strain matches A/J at the IgH-4 (IgG1), IgH-5 (IgD), and IgH-6 (IgM) loci (64). The allotype-congenic strains C.AL9 and C.AL20 express the IgCH haplotype of AL/N mice but carry the prealbumin and Lm-1 alleles of the BALB/c strain, which expresses high rat IgG binding (51). B cells of the C.AL9 and C.AL20 mice bind high levels of rat IgG in contrast to AL/N mice, thereby suggesting that the FcR locus might be in the neighborhood of the prealbumin locus.

Although suggestive, the strain survey does not prove linkage to IgH. We therefore undertook an examination of backcross mice in order to further clarify
TABLE 1

Specificity of Binding to Fc Receptors on BALB/c B Cells*

| Stain            | Inhibitor     | FACS channel shift | Percent inhibition |
|------------------|---------------|--------------------|--------------------|
| FITC-Mouse IgG1  | No inhibitor  | 30                 | 0                  |
|                  | Mouse IgG2a   | 3                  | 79                 |
|                  | IgG2b         | 5                  | 69                 |
|                  | IgG1          | 9                  | 50                 |
| FITC-Mouse IgG2a | No inhibitor  | 47                 | 0                  |
|                  | Mouse IgG2a   | 7                  | 71                 |
|                  | IgG2b         | 9                  | 63                 |
|                  | IgG1          | 12                 | 55                 |
| FITC-Mouse IgG2b | No inhibitor  | 59                 | 0                  |
|                  | Mouse IgG2a   | 6                  | 79                 |
|                  | IgG2b         | 6                  | 79                 |
|                  | IgG1          | 16                 | 54                 |
| FITC-Rat IgG2b   | No inhibitor  | 67                 | 0                  |
|                  | Mouse IgG1    | 16                 | 58                 |
|                  | IgG2a         | 8                  | 76                 |
|                  | IgG2b         | 6                  | 81                 |

* See Fig. 2.

FACS channel shifts represent the difference in relative fluorescence intensity between control and experimental groups on a logarithmic scale (60 channels represent 10-fold).

† Percent inhibition is determined by the formula: log(1 - (channel shift with inhibitor)/channel shift with no inhibitor)) x 10. The percent inhibition represents the mean of two or more experimental determinations.

this relationship. Backcross [(C57BL/6 x A/J)F1 x A/J] mice were analyzed for Igh haplotype as well as for Fc binding of rat immunoglobulins. Igh haplotype was determined by typing of IgM and IgD allotypes with allotype-specific monoclonal antibodies (58, 60). The Fc-binding characteristics of heterozygotes were similar to those of homozygous high binders and were clearly distinguishable from low Fc-binding mice. The results of the backcross analysis (Table III) indicate that there is loose, but significant, linkage of the Fc receptor polymorphism to the heavy chain locus. The recombination frequency is ~32% with a P value <0.005. We find no evidence for linkage to the H-2 locus as shown by H-2 congenics (Table II) or by analysis of backcross mice (Table III); in addition, no linkage was found to the x chromosome. As a further control we examined Igh linkage to H-2: no linkage was found. The backcross experiments provide additional evidence for a linkage of the Fc receptor polymorphism to the Igh locus.

To further define the genetic linkage of the Fc receptor polymorphism to the Igh locus, we undertook an examination of Igh recombinant mouse lines (51). Several mice of each line were tested individually for Fc binding of rat IgG2b and for Igh-6 (IgM) and Igh-5 (IgD) allotypes (58, 60). These results are shown in Table IV. The Igh recombinant strain analysis is consistent with moderate
linkage of the FcR polymorphism to the \textit{Igh} locus on chromosome 12. This analysis indicates a higher degree of linkage with the \textit{Pre-1} and \textit{Lm-1} loci that map 10 and 15 map units telomeric to \textit{Igh-C}, and places the FcR locus \~20 map units distal to \textit{Lm-1}, at the end of chromosome 12 near the \textit{Ly-7} locus (51). A genetic map of chromosome 12 showing the apparent location of the gene(s) responsible for the Fc receptor polymorphism is shown in Fig. 5.

\section*{Discussion}

There has been relatively little work reported on the IgG subclass specificity of mouse B lymphocyte Fc receptors. Lane et al. (20) showed that a non-immunoglobulin-producing B lymphocyte cell line expressed an Fc receptor activity specific for the IgG1/IgG2a/IgG2b subclasses (20). In this report, we extend these results to normal B lymphocytes that express a single Fc receptor which binds the IgG1, IgG2a, and IgG2b subclasses. In results reported elsewhere,\textsuperscript{2} we show that there is an additional Fc receptor specific for IgG3. We also find that rat IgG1, IgG2a, and IgG2b bind to the same receptor that binds mouse IgG1, IgG2a, and IgG2b. We conclude that the B cell IgG1/IgG2a/IgG2b receptor is probably distinct from macrophage Fc receptors, because mouse macrophages apparently possess one receptor for IgG1/IgG2b and an-
other for IgG2a. In addition, clear biochemical differences occur between the IgG Fc receptors of B cell and macrophage cell lineages in mice as well as humans, although the nature of these differences remains undetermined (20, 24, 26, 65).

The other interesting observation made in this report is that a polymorphism occurs in the mouse B lymphocyte IgG Fc receptor. A strain survey shows that A/J, AL/N, and NZB/J mice bound low levels of rat IgG compared with other strains. Backcross analysis and examination of Igh recombinant strains indicate that the Fc receptor polymorphism maps telomeric to the Igh region at or near the end of chromosome 12.

Biochemical studies are currently under way to determine whether the polymorphism arises from a difference in primary structure or from differences in posttranslational modification. Recently (66), a polymorphism in an IgE-binding factor was described which is apparently the result of differences in oligosaccharide processing. The B cell Fc receptor polymorphism is expressed as a difference in the specificity of the receptor for its ligand. This polymorphism may therefore

### Table II

| Strain          | Igh-C allotype | Fc binding of rat IgG |
|-----------------|----------------|-----------------------|
| BALB/cJ         | a              | High                  |
| C58/J           |                |                       |
| C57BL/6J        | b              | High                  |
| C57BL/10J       |                |                       |
| SJL/J           |                |                       |
| B10.A           |                |                       |
| B10.S           |                |                       |
| DBA/2J          | c              | High                  |
| DBA/212Ha       |                |                       |
| AKR/J           | d              | High                  |
| CE/J            | f              | High                  |
| P/J             | h              | High                  |
| CBA/J           | J              | High                  |
| PL/J            |                |                       |
| A/J             | e              | Low                   |
| A/HeJ           |                |                       |
| A.BY            |                |                       |
| A.SW            |                |                       |
| NZB/J           | n              | Low                   |
| AL/N            | o              | Low                   |
| C.AL-9          | o              | High                  |
| C.AL-20         | o              | High                  |
Comparison of mouse IgG binding by B cell blasts from A/J and BALB/c mice. B cell blasts were exposed to normal mouse serum (NMS) or ~300 μg/ml of purified mouse IgG1, IgG2a, and IgG2b. Binding was assessed by indirect immunofluorescence and flow microfluorometry.

**Table III**

*Segregation Analysis of FcR, Igh-C, and I-A in Backcross Mice*

| Fc binding | Probability of linkage |
|------------|------------------------|
| High       | Low                    |
| IgM allotype b  
(+(b/e))  | 26* | 11 | $P < 0.005$
| (+(c/e))  | 14 | 27 |

| Fc binding | Probability of linkage |
|------------|------------------------|
| High       | Low                    |
| 1-A b      | 12 | 11 | $P = 0.5$
| 9 | 15 |

Comparison of inheritance of 1-A b and IgM allotype b

| 1-A b | Probability of linkage |
|-------|------------------------|
| +     | 12 | 11 | $0.25 < P < 0.5$
| -     | 8 | 16 | * Number of individual backcross mice.

shed some light on the nature of the IgG Fc receptor's binding site and those factors that affect the receptor's specificity. A polymorphism in the human monocyte IgG Fc receptor has recently been described (67, 68), although no chromosomal assignment has yet been made. Furthermore, the linkage of the murine monocyte/macrophage IgG Fc receptor is unknown. Since the B cell and macrophage IgG Fc receptors differ from one another biochemically and in their specificity (26, 65, and this report), it would be interesting to compare the linkage

![Diagram of IgG binding](image-url)
TABLE IV

B Cell Fc Receptor Typing of Igh Recombinant Strains

| Strain | Igh-V | Igh-C | Tind | Tsu  | Tpre | Pre-I | Lm-1 | B cell FcR |
|--------|-------|-------|------|------|------|-------|------|------------|
| BALB/c | a     | a     | a    | a    | a    | a     | a    | + (High)   |
| A/He   | e     | e     | e    | e    | e    | 0     | b    | - (Low)    |

Strain

AXC-1*  a X e e e e 0  -
-2  a X e e e e 0  -
-3  a X e e e e 0 X  +
-4  a X e e e e 0  -
-5  a X e e e e 0 b  -
-6  a X e e e e 0  -
-7  e X a a a a a a +
-8  e X a a a a a X 0 b  -
-9  e X a a a a a a +
-10 e X a a a a X 0 b  -
-11 e X a X e e e 0 X a X  -
-12 e X a X e e e 0 b  -

CXAXCB-1† e e e e e X a a +
-2  a a a a a X 0 X a  +
-3  e e X a a a a a a +
-4  e e X a a a a a a +
-5  e e X a a a a a a +
-6  e a X e e e 0 b X  +
-7  a a a a a X e 0 b X  +

* AXC strains are recombinant between Igh-V and Igh-C (49-51).
† CXAXCB strains are recombinant between Igh-C and Pre-1 (51). BALB/c, A/He, and C.B-17 are the parental strains.

Figure 5. Genetic map of chromosome 12. Modified from reference 51.

of the B cell and macrophage Fc receptor loci to determine if they map to the same location and form a cluster of related genes.

Fc receptors may play a critical physiologic role in B cell development, differentiation, or function. We are currently attempting to exploit the B cell Fc receptor polymorphism to further elucidate the functional role of Fc receptors in B lymphocyte biology.

Summary

Analysis of mouse IgG binding to Fc receptors on mouse B cells indicates that the IgG1, IgG2a, and IgGb subclasses bind to the same receptor. No differences in affinity were detected among subclass or between mouse strains. This same
receptor bound rat IgG with an affinity that differed between mouse strains. This polymorphism in affinity for rat IgG maps to chromosome 12 distal to the IgH locus.

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Note added in proof. Since submission of this manuscript, Teillaud et al. (J. Immunol. 134:1774) have reported that a single receptor activity accounts for the binding of IgG1, IgG2a, and IgG2b antibodies to murine myeloma and hybridoma cell lines, consistent with our findings.

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