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Expression of IgG Fc Receptor Antigens in Placenta and on Endothelial Cells in Humans

An Immunohistochemical Study

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Expression of leukocyte IgG Fc receptor (FcγR) antigens by placenta, endothelial cells (EC) of normal tissues, and ECs of kidney and skin from subjects with immune complex diseases was studied immunohistochemically using anti-FcγR monoclonal antibodies (MAb). Monoclonal antibodies against all three leukocyte FcγR classes stained placental villous macrophages. Placental villous trophoblasts were stained intensely by anti-FcγRIII MAb 3G8, while both anti-FcγRI (MAb 32) and anti-FcγRII (MAbs IV3, KU79, CIKM5, 2E1, KB61, and 41H16) antibodies did not react with these cells. Anti-FcγRII MAbs IV3, KU79, CIKM5, 2E1, KB61, and 41H16 immunostained placental villous capillary EC, in contrast to anti-FcγRI MAb 32 and anti-FcγRIII MAb 3G8, CLB-Granl, and B73.1, which did not bind. Anti-FcγRI MAb 32, anti-FcγRII MAb IV3 and CIKM5, and anti-FcγRIII MAb 3G8 did not react with the ECs of tonsil, liver, kidney, spleen, intestine, lung, or uterus. Similarly no EC staining was seen with these four MAbs in 14 skin and 14 kidney biopsies from subjects with immune-complex diseases. FcγR antigens are expressed constitutively only by placental villous ECs and are not induced on nonplacental ECs by immune-complex–mediated diseases. (Am J Pathol 1991, 138:175–181)

Receptors for the Fc region of IgG, FcγR, are an important bridge between antibodies and cellular effector systems. A heterogeneous but homologous group of FcγR, integral membrane glycoproteins that are members of the immunoglobulin gene superfamily, is expressed on the surfaces of human leukocytes. Three classes of leukocyte FcγR—FcγRI, FcγRII, and FcγRIII—have been defined by cell-specific expression, molecular weight, affinity and specificity for ligand, differences in cDNAs, and reactivity with monoclonal antibodies (MAb). FcγRI (CD64), a 72-kd high-affinity receptor for monomeric IgG, is present on monocytes and macrophages and can be induced on neutrophils. FcγRII (CD32), a low-affinity 40-kd receptor that only binds complexed IgG, is present on monocytes, macrophages, neutrophils, eosinophils, basophils, B cells, Langerhans cells, and platelets. FcγRIII (CD16), a 50- to 80-kd low-affinity receptor for multimeric IgG, is present on NK cells, macrophages, and neutrophils (reviewed in Ravetch and Anderson[1] and in Huizinga et al[2]). Although the expression of all three FcγR classes on inflammatory cells is well characterized, little is known about their expression on other cell types.

The human placenta exhibits at least two properties that may depend on the presence of FcγR.[3,4] It is a functional and physical barrier between fetus and mother that may serve as a sink for immune complexes of infectious or alloimmune origin. Furthermore the placenta transfers IgG from the maternal circulation to the fetus. Experiments using binding of fluorescein-conjugated heat-aggregated IgG[5] or hemadsorption of IgG-sensitized erythrocytes[6,7] to placental tissue sections revealed indirectly the presence of FcγR on villous endothelial cells, mononuclear phagocytes (Hofbauer cells), and trophoblastic cells. Studies with anti-FcγR MAbs confirmed the presence of FcγR on these structures.[8–12] The heterogeneity of placental FcγR, as well as their similarity to leukocyte FcγR, has not been evaluated immunohistochemically in a systematic fashion. Herein we detail the presence of antigens within the placenta reactive with MAbs to all three FcγR classes. FcγRII antigens were found to be specifically expressed on placental villous capillary endothelium but not on the endothelium of a panel of normal tissues. To

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Table 1. *Description of anti-FcγR Monoclonal Antibody Used in this Study*

MAb	CD	FcγR	Isotype	Expression							Source	Form	Reference
				Ma	Mo	N	E	P	B	NK			
32	64	FcγRI	IgG1	+	+	i	−	−	−	−	Medarex, West Lebanon	IgG	14
IV3	32	FcγRII	IgG2b	+	+	+	+	+	−	−	Medarex, West Lebanon	IgG	15
KU79	32	FcγRII	IgG2b	u	+	+	u	−	+	−	T. Mohanakumar, St. Louis	Sup	16
CIKM5	32	FcγRII	IgG1	u	+	+	−	u	u	−	G. Pilkington, Melbourne	Asc	17
2E1	32	FcγRII	IgG2a	u	+	+	−	u	u	−	F. Farace, Villejuif	Sup	18
KB61	32	FcγRII	IgG1	+	u	+	−	u	+	−	D. Mason, Oxford	Sup	19
41H16	32	FcγRII	IgG2a	+	+	+	−	u	+	−	T. Zipf, Houston	IgG	20
3G8	16	FcγRIII	IgG1	+	i	+	+	−	−	+	Medarex, West Lebanon	IgG	21
CLB-Gran1	16	FcγRIII	IgG2a	+	+	+	−	−	−	+	T. Huizinga, Amsterdam	Asc	22
B73.1	16	FcγRIII	IgG1	+	u	+	−	−	−	+	B. Perussia, Philadelphia	Asc	23

MAb, monoclonal antibody; CD, cluster of differentiation; Sup, supernatant fluid of hybridoma culture; Asc, hybridoma ascites fluid; Ma, macrophage; MO, monocyte; N, neutrophil; E, eosinophil; P, platelet; B, B lymphocyte; NK, natural killer cell; +, present; −, not present; u, expression unclear; i, inducible.

test the hypothesis that FcγR may be induced on vascular endothelium by immune complexes or immune-complex–induced inflammation, renal and skin biopsies from subjects with immune-complex–mediated diseases were included in this study.

Materials and Methods

Tissue

Four normal third-trimester placentas and umbilical cords were obtained from patients with uncomplicated pregnancies. Control tissues used in this study were obtained from surgical specimens and were normal according to histologic examination. These tissues were obtained through The Ohio State University Tissue Procurement Service. In addition to normal skin and kidney specimens, 14 skin biopsies and 14 kidney biopsies from individuals with immune-complex disease were examined. Tissues were snap frozen in isopentane precooled in liquid nitrogen and stored at −70°C for no longer than 12 months.

Immunohistochemistry

A description of all anti-FcγR MAbs, their expression,[13] class, and source, is given in Table 1.

Tissues were immunohistochemically stained using the labeled avidin D technique.[24] Four-micron–thick sections were cut using a cryostat, air dried onto glass slides, and fixed in 4°C acetone for 10 minutes. Primary antibodies were used at a dilution that in preliminary experiments gave optimal staining of placental tissue. Following incubation for 45 minutes, slides were washed in TRIS-buffered saline (TBS) and incubated with biotinylated, affinity-purified, horse anti-mouse IgG (Vector Laboratories, Burlingame, CA). Slides were washed, incubated with horseradish peroxidase avidin D (Vector), washed, and developed with 3-amino-9-ethylcarbazole (AEC) (Sigma Chemical Co., St. Louis, MO) in 3% hydrogen peroxide in 0.02 mol/l (molar) acetate buffer. Tissues were counterstained with Gill-III hematoxylin. Negative controls consisted of substitution of the primary MAb with irrelevant MAb of the same mouse immunoglobulin isotype (Anti-Leukocyte Common Antigen [LCA], IgG1, Dako, Carpinteria, CA; Anti-Cytomegalovirus Early Nuclear Protein, IgG2a, Dupont, Doraville, GA; Leu-M5, IgG2b, Becton-Dickinson, Mountain View, CA).

Results

Placental Reactivity

Anti-FcγR MAbs exhibited several distinct patterns of immunoreactivity with human placental tissue (Table 2).

Table 2. *Immunoreactivity of anti-FcγR Monoclonal Antibodies with Placenta and Umbilical Cord*

Antibody	Placental villi			Umbilical cord		
	EC	TROPH	IF	VEC	AEC	IF
FcγRI						
32	−	−	+	−	−	+ (r)
FcγRII						
IV3	+	−	+	−	−	+
KU79	+	−	+	−	−	+
CIKM5	+	−	+	−	−	+
2E1	+	−	+	−	−	+
KB61	+	−	−	−	−	+ (r)
41H16	+	−	+	−	−	+
FcγRIII						
3G8	−	+ (s)	+	−	−	+
CLB-Gran1	−	−	+	−	−	+
B73.1	−	−	+	−	−	−

EC, endothelial cells; TROPH, trophoblasts; IF, inflammatory cells; VEC, venous endothelial cells; AEC, arterial endothelial cells; +, staining present; −, no staining; s, strong; r, rare.

There were no differences in staining patterns between the tissues of four different donors.

Placental Reactivity with Anti-FcγRI MAb

Monoclonal antibody 32 reacted with Hofbauer cells of the placental villi and mononuclear cells of the umbilical cord. It did not react with villous endothelial cells or trophoblasts (Figure 1A).

Placental Reactivity with Anti-FcγRII MAbs

Anti-FcγRII MAbs reacted intensely with the endothelium of placental vessels, particularly of villous capillaries and venules (Figure 1B and C). Staining was present throughout the cryostat-sectioned endothelial cells and it was not possible to distinguish accurately cytoplasmic staining from a combination of both cytoplasmic and surface staining. Immunohistochemical staining of representative placental sections with a polyclonal antibody to von Willebrand factor resulted in an identical pattern of positivity, supporting the interpretation that the vascular endothelium was a focus of positivity (not shown). The endothelium of the umbilical vein and arteries was negative.

Anti-FcγRII MAbs, with the exception of MAb KB61, immunostained Hofbauer cells (Figure 1B and C). Mononuclear cells scattered throughout the cord were positive with all antibodies. In contrast, trophoblasts did not stain with any of the anti-FcγRII MAbs tested. Furthermore trophoblast staining was absent in unfixed (air dried) as well as acetone-fixed placental tissues.

Placental Reactivity with Anti-FcγRIII MAbs

Anti-FcγRIII MAbs did not react with placental endothelial cells nor with umbilical vein or artery endothelium. Monoclonal antibodies 3G8, CLB-GranI, and B73.1 uniformly immunostained Hofbauer cells, but only MAbs 3G8 and

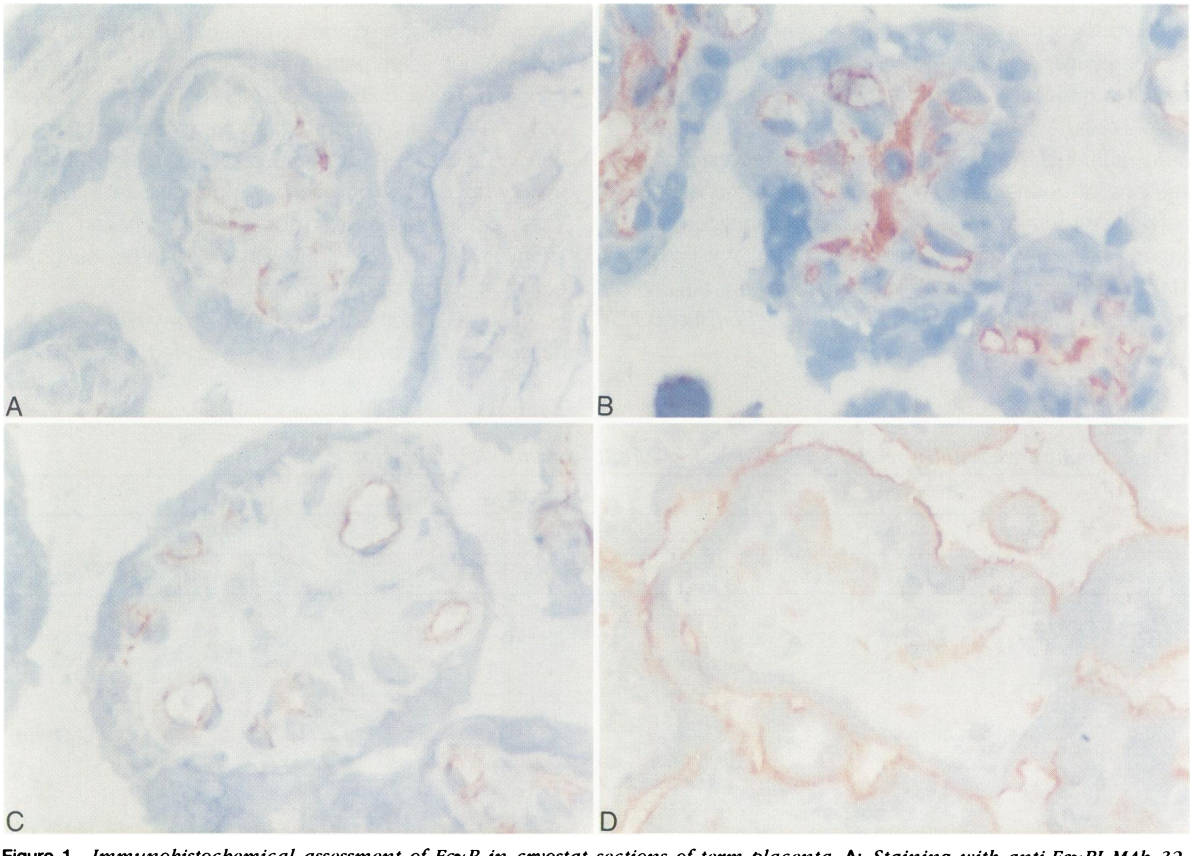

Figure 1. *Immunohistochemical assessment of FcγR in cryostat sections of term placenta.* **A:** *Staining with anti-FcγRI MAb 32. Hofbauer cells are positive (red-brown color); endothelial cells and trophoblasts are negative (×160).* **B:** *Staining with anti-FcγRII MAb IV3. Endothelial cells and Hofbauer cells are positive; trophoblasts are negative (×160).* **C:** *Staining with anti-FcγRII MAb KB61. Only endothelial cells are positive (×160).* **D:** *Staining with anti-FcγRIII MAb 3G8. Hofbauer cells are positive and there is intense staining of the maternal surface of trophoblasts (×100; aminoethylcarbazole with hematoxylin counterstain).*

CLB-Gran1 immunostained the mononuclear cells of the cord.

Monoclonal antibody 3G8 intensely immunostained the maternal surface of the villous trophoblasts, the majority of which appeared to be syncytiotrophoblasts by histologic criteria (Figure 1D). Staining clearly was confined to the membrane region of villous trophoblasts that was in direct contact with maternal blood. This pattern of staining also was seen with $F(ab')_2$ fragments of MAb 3G8.

Normal Tissue Endothelial Reactivity

Because the endothelium of placental villi strikingly expressed FcγR antigen, the presence of FcγR antigens on endothelium of other normal tissues was examined with representative antibodies to each FcγR class (Table 3).

No anti-FcγRI, II, or III MAb exhibited immunoreactivity with normal tissue endothelium, including the endothelium of arteries, arterioles, capillaries, venules, veins, high endothelial venules of the tonsil, or glomeruli.

Within these normal tissues, anti-FcγRI, II, and III MAbs exhibited variable reactivity with inflammatory cells. For the purpose of this study, inflammatory cells were defined as isolated mononuclear and polynuclear nonparenchymal cells. No distinction was made between resident inflammatory cells, ie, dendritic cells, and infiltrating inflammatory cells. Immunohistochemical staining of representative sections of normal skin and kidney with a monoclonal antibody mixture to the leukocyte common antigen confirmed the validity of this definition (not shown). Anti-FcγRIII MAb 3G8 intensely stained alveolar macrophages in contrast to the weaker staining seen with anti-FcγRI and II MAbs.

Monoclonal antibody IV3 and 3G8 exhibited staining of sinusoidal lining cells of the liver. Whether this staining was confined to kupffer cells or also was present on endothelial cells could not be determined accurately. Monoclonal antibody 2E1 reacted with few scattered individual cells in the sinusoids, a pattern that was most suggestive of kupffer cell reactivity. Monoclonal antibody 3G8 stained intensely the epithelium of sebaceous glands of the skin.

Skin and Renal Tissues Containing Immune Complexes

Because there was no constitutive expression of FcγR antigens on the endothelium of normal tissues, the hypothesis that FcγR are induced on vascular endothelial cells *in vivo* by immune complexes or immune-complex–mediated inflammatory reactions was tested. Skin biopsies from 14 patients with a variety of immune-complex–mediated disorders were immunostained with anti-FcγRI MAb 32, anti-FcγRII MAbs IV3 and ClKM5, and anti-FcγRIII MAb 3G8. The diagnoses included vasculitis (n = 3), dermatitis herpetiformis (n = 5), and systemic lupus erythematosus (n = 6). Diagnoses were based on clinical histories, histology of the biopsies, and the presence of a characteristic immunofluorescent pattern for IgG, IgA, IgM, C3, and fibrinogen. The endothelial cells of all dermal vessels were negative in every patient biopsy, regardless of the underlying disease. All biopsies contained positive inflammatory cells, many of which were perivascular in nature. These cells were classified as inflammatory based on histology and immunoreactivity with a MAb to the leukocyte common antigen (not shown).

Vascular endothelium within 14 kidney biopsies from patients with immune-complex–mediated glomerulone-

Table 3. *Immunoreactivity of anti-FcγR Monoclonal Antibody with Normal Tissue*

	Normal tissue						
	Tonsil	Skin	Lung	Uterus	Kidney	Intestine	Liver
Antibody	(n = 3)	(n = 1)	(n = 1)	(n = 1)	(n = 3)	(n = 1)	(n = 1)
FcγRI							
32	IF+	negative	IF+ (r) (alveolar macrophages)	IF+ (r)	IF+ (r)	IF+	SLC+ (f)
FcγRII							
IV3	IF+	dermal IF+	IF+ (alveolar macrophages)	IF+	IF+	IF+ Colon mucosa+	SLC+ (d)
FcγRIII							
3G8	IF+	sebaceous epithelium+	IF+ (alveolar macrophages)	IF+ (r) glands+	IF+	IF+ Colon mucosa+ Small intestine mucosa+	SLC+ (d)

IF, inflammatory cells; EC, endothelial cells; SLC, sinusoidal lining cells; r, rare; f, focal; d, diffuse.

phritis was negative with anti-FcγR MAbs. The underlying pathology in these biopsies was membraneous glomerulopathy (n = 5), systemic lupus erythematosus (n = 4), and IgA glomerulonephritis (n = 5). Diagnoses were based on clinical histories, histology of biopsies, electron microscopic examination, and the presence of a characteristic immunofluorescent pattern for IgG, IgA, IgM, C3, and fibrinogen. Tissue sections for anti-FcγR staining were taken from the frozen-section kidney and skin blocks that exhibited positive immunofluorescence.

Discussion

This investigation demonstrates that monoclonal antibodies identifying the three known leukocyte FcγR classes react with the major cellular constituents of the placental villous, ie, trophoblasts, Hofbauer cells, and endothelial cells. These results support and expand those studies that have functionally and phenotypically located FcγR on these cell types.[5-12]

Anti-FcγRII MAbs uniquely stained the placental endothelium. Receptors for human FcγR have been described on human placental endothelial cells using fluorescein-conjugated heat-aggregated IgG, fluorescein-conjugated immune complexes, hemadsorption of IgG-sensitized erythrocytes, and immunostaining with anti-FcγRII MAbs IV3, 2E1, CIKM5, KB61, and 41H16.[5,6,8,11,12] The functions of FcγR on ECs are ill defined. FcγR on placental villous ECs may protect the fetus by binding immune complexes of alloimmune or infectious origin and may facilitate transport of IgG from the maternal circulation to the fetal circulation.[3] The findings of our study suggest that these functions may be mediated by FcγR antigenically similar to leukocyte FcγRII.

Only anti-FcγRIII MAb 3G8 stained the placental villous trophoblasts, specifically at the maternal surface. This staining was independent of the MAb Fc portion as demonstrated by immunostaining with $F(ab')_2$ fragments of MAb 3G8. Studies using hemadsorption of IgG-sensitized erythrocytes previously showed the presence of FcγR on trophoblasts.[6,7] Furthermore quantitative studies of IgG FcR using purified trophoblast plasma membranes support the distinctive plasma membrane-staining pattern noted herein.[3]

The role that FcγRIII might play in placental transfer of IgG is unclear. Leukocyte FcγRIII have very low affinity for monomeric IgG, the species that is transferred across the placenta. However reactivity of only one of the three tested anti-FcγRIII MAbs (MAb 3G8, but not MAbs CLB-GranI or B73.1) with villous trophoblasts could represent identification of a novel FcγRIII-like receptor unique to the placenta and involved in IgG transport. Alternatively MAb 3G8 positivity may indicate the presence of an FcγRIII-like variant that manifests a more conventional function, that of binding immune complexes specifically of alloimmune origin. Future studies with cultured syncytiotrophoblasts evaluating *in situ* hybridization and IgG binding may provide answers to some of these questions.

Others have studied placental-derived tissue. Stuart et al[10] reported the presence of FcγRII mRNA, and FcγRII antigen as detected by immunoreactivity with MAb IV3, within syncytiotrophoblasts. These findings seem contradictory to the lack of MAb IV3 staining of syncytiotrophoblasts seen in our study and in a recent study by Micklem et al.[11] Two reasons for the differences seem possible. These conflictual findings might be explained by the use of human hydatidiform mole by Stuart et al,[10] while we and Micklem et al[11] studied normal human placenta. In addition, the methods of tissue fixation were different. Whereas Stuart et al[10] used formalin-fixed paraffin-embedded tissue, which is known to result in marked antigen alteration and loss,[25] we used acetone-fixed and, in some cases, nonfixed (air dried), frozen tissue. Furthermore our findings of intense EC, Hofbauer cell, and trophoblast positivity with anti-FcγR MAbs suggest that antigenicity of cell types in our study was well preserved in all tissues evaluated (Table 2).

All three classes of FcγR were represented on placental mononuclear phagocytes (Hofbauer cells). Previous studies using enzymatically isolated placental cells showed that placental phagocytic cells express FcγR.[26] Similarly studies with anti-FcγRII MAbs CIKM5, IV3, 2E1, KB61, 41H16, and anti-FcγRIII MAbs 3G8 and Leu11b showed staining of Hofbauer cells.[9,11,12] Hofbauer cells are phenotypically related to other tissue macrophages, expressing a number of monocyte/macrophage-specific antigens.[9] Thus it is not surprising that these cells, like macrophages of the lung and peritoneal cavity,[27] express all three classes of FcγR.

We evaluated the EC of multiple tissues for staining with anti-FcγR MAbs but found reactivity only with the ECs of the placental villi. The ECs of the umbilical vessels and of the vasculature of a panel of normal tissues were negative. Evidence for the expression of FcγR by nonplacental ECs is controversial and may be related to technique. For example, bovine pulmonary ECs cultured *in vitro* fail to bind IgG-sensitized erythrocytes unless infected with virus or damaged by leukocyte lysate.[28] Similarly noninfected human umbilical vein ECs do not bind IgG-sensitized erythrocytes, heat-aggregated IgG, or thyroglobulin-antithyroglobulin IgG immune complexes.[29,30] However incubation of heat-aggregated IgG with human umbilical vein endothelial cells has been shown to induce tissue factor activity, possibly through FcγR-mediated binding.[31] Micklem et al[11] recently reported that anti-FcγRII MAbs immunostained hepatic endothelium based on observation of a sinusoidal pattern. We also report herein a

sinusoidal pattern of staining, particularly with anti-FcγRII MAb IV3 and anti-FcγRIII MAb 3G8, but additional studies are required to establish definitively the endothelial nature of this staining.

In response to a variety of inflammatory mediators, ECs express a number of membrane antigens that facilitate the inflammatory response.[32] To test the hypothesis that FcγR expression on ECs may occur *in vivo* in response to immune complexes or to the cytokines present locally in immune complex-induced inflammation, skin and kidney biopsies from subjects with specific immune-complex–mediated disorders were studied with representative anti-FcγR MAbs. The distinct lack of EC staining in these tissues might be secondary to a number of different phenomena: 1) leukocyte anti-FcγR MAbs may not recognize nonplacental EC FcγR, 2) ECs may not express FcγR, or 3) immunoreactive sites on EC FcγR may be blocked by immune complexes. The latter possibility is unlikely given the strong EC staining seen within the placenta. Furthermore two of the MAbs used in this study recognize epitopes outside the ligand-binding site on FcγR and would not be affected by bound immune complexes, eg, MAbs 32[14] and ClKM5.[33]

Although the results of this study revealed distinct FcγR class-specific placental immunostaining patterns, there are several intraclass exceptions and inconsistencies. Anti-FcγRIII MAb 3G8, for instance, was the only CD16 MAb that reacted with villous trophoblasts. This phenomenon may relate to the existence of several isoforms within each class. Currently seven isoforms have been described for FcγRII[10,34,35] and three for FcγRIII.[36,37] These isoforms, and perhaps others that are not described, may have sufficient epitopic diversity to account for the variability of antibody reactivity seen with anti-FcγRII and III MAbs. A similar phenomenon may be responsible for the description of FcγRIII on eosinophils.[38,39] Although Hartnell et al[38] found no staining of human eosinophils with anti-FcγRIII MAb Leu-11b, Looney et al[39] reported positivity with MAb 3G8.

References

1. Ravetch JV, Anderson CL: Fcγ receptor family: Proteins, transcripts, and genes. *In* Metzger H, ed. Fc Receptors and the Action of Antibodies. American Society of Microbiology, Washington, D.C., 1990, 211–238
2. Huizinga TWJ, Roos D, Von dem Borne AEGKr: Neutrophil Fc-γ receptors: A two-way bridge in the immune system. Blood 1990, 75:1211–1214
3. Johnson PM, Brown PJ: Fcγ receptors in the human placenta. Placenta 1981, 2:355–370
4. Simister NE: Transport of monomeric antibodies across epithelia. *In* Metzger H, ed. Fc Receptors and the Action of Antibodies. American Society for Microbiology, Washington, D.C., 1990, 57–73
5. Johnson PM, Trenchev P, Faulk WP: Immunological studies of human placentae: Binding of complexed immunoglobulin by stromal endothelial cells. Clin Exp Immunol 1975, 22: 133–138
6. Matre R: Similarities of Fcγ receptors on trophoblasts and placental endothelial cells. Scand J Immunol 1977, 6:953–958
7. Matre R, Tonder O, Endresen C: Fcγ receptors in human placenta. Scand J Immunol 1975, 4:741–745
8. Matre R, Haaheim LR, Tonder O: A monoclonal antibody inhibiting human placental Fcγ-receptor activity. Int Arch Allergy Appl Immunol 1984, 75:227–229
9. Goldstein J, Braverman M, Salafia C, Buckley P: The phenotype of human placental macrophages and its variation with gestational age. Am J Pathol 1988, 133:648–659
10. Stuart SG, Simister NE, Clarkson SB, Kacinski BM, Shapiro M, Mellman I: Human IgG Fc receptor (hFcRII; CD 32) exists as multiple isoforms in macrophages, lymphocytes, and IgG-transporting placental epithelium. EMBO J 1989, 8:3657–3666
11. Micklem KJ, Stross WP, Willis AC, Cordell JL, Jones M, Mason DY: Different isoforms of human FcRII distinguished by CDw32 antibodies. J Immunol 1990 144:2295–2303
12. Schmidt RE: N4 cluster report: CDw32. *In* Knapp W, Dorken B, Gilks WR, Reiber P, Schmidt RE, Stein H, von dem Borne AEGKr, eds. Leukocyte Typing IV. White Cell Differentiation Antigens. New York, Oxford UP, 1989, pp 599–602
13. Knapp W, Dorken B, Gilks WR, Reiber P, Schmidt RE, Stein H, von dem Borne AEGKr, eds. Leukocyte Typing IV, White Cell Differentiation Antigens. New York, Oxford UP, 1989
14. Anderson CL, Guyre PM, Whitin JC, Ryan DH, Looney RJ, Fanger MW: Monoclonal antibodies to Fc receptors for IgG on human mononuclear phagocytes. Antibody characterization and induction of superoxide production in a monocyte cell line. J Biol Chem 1986, 261:12856–12864
15. Looney RJ, Abraham GN, Anderson CL: Human monocytes and U937 cells bear two distinct Fc receptors for IgG. J Immunol 1986, 136:1641–1647
16. Vaughn M, Taylor M, Mohanakumar T: Characterization of human IgG Fc receptors. J Immunol 1985, 135:4059–4065
17. Pilkington GR, Kraft N, Murdolo V, Lee GTH, Hunter SV, Atkins RC, Jose DG: Serological typing of acute leukemia using the monoclonal antibodies PHM 1, 2, 3, 6, ClKM5, and the rabbit antisera RARC2a (Ad) and RAALLP50. *In* Bernard A, Boumsell L, Dausset J, Milstein C, Schlossman SF, eds. Leucocyte Typing. Human Leucocyte Differentiation Antigens. Berlin, Springer-Verlag, 1984, pp 588–595
18. Farace F, Mitjavila M-T, Betaieb A, Dokhelar MC, Wiels J, Finale Y, Kieffer N, Breton-Gorius J, Vainchenker W, Tursz T: New hematopoietic differentiation antigens detected by anti-K562 monoclonal antibodies. Cancer Res 1988, 48: 5759–5765
19. Pulford K, Ralfkiaer E, MacDonald SM, Erber WN, Falini B, Gatter KC, Mason DY: A new monoclonal antibody (KB61) recognizing a novel antigen which is selectively expressed on a subpopulation of human B lymphocytes. Immunology 1986, 57:71–76
20. Zipf TF, Lauzon GJ, Longenecker BM: A monoclonal antibody detecting a 39,000 m.w. molecule that is present on B lym-

phocytes and chronic lymphocytic leukemia cells but is rare on acute lymphocytic leukemia blasts. J Immunol 1983, 131: 3064–3072
21. Fleit HB, Wright SD, Unkeless JC: Human neutrophil Fcγ receptor distribution and structure. Proc Natl Acad Sci USA 1982, 79:3275–3279
22. Werner G, Von dem Borne AEGKr, Bos MJE, Tromp JF, van der Plas-van Dalen CM, Visser FJ, Engelfriet CP, Tetteroo PAT: Localization of the human NA1 alloantigen on neutrophil Fc-γ receptors. *In* Reinhert EL, Haynes BF, Nodler LM, Bernstein ID, eds. Leucocyte Typing III. Vol 3; Human Myeloid and Hematopoietic Cells. New York, Springer-Verlag, 1988, pp 198–121
23. Perussia B, Starr S, Abraham S, Fanning V, Trinchieri G: Human natural killer cells analyzed by B73.1, a monoclonal antibody blocking Fc receptor function. I. Characterization of the lymphocyte subset reactive with B73.1. J Immunol 1983, 130:2133–2141
24. Sharma HM, Kauffman EM, Conrad CM: An improved immunoperoxidase technique using horseradish peroxidase Avidin D. Lab Med 1989, 20:109–112
25. Taylor CR: Immunomicroscopy: A Diagnostic Tool for the Surgical Pathologist. Philadelphia, WB Saunders, 1986, pp 20–22
26. Moskalewski S, Czarnik Z, Ptak W: Demonstration of cells with IgG receptor in human placenta. Biol Neonate 1975, 26:268–273
27. Anderson CL, Looney RJ, Culp DJ, Ryan DH, Fleit HB, Utell MJ, Frampton MW, Manganiello PD, Guyre PM: Alveolar and peritoneal macrophages bear three distinct classes of Fc receptors for IgG. J Immunol 1990, 145:196–201
28. Ryan US, Schultz DR, Ryan JW: Fc and C3b receptors on pulmonary endothelial cells: Induction by injury. Science 1981, 214:557–558
29. Cines DB, Lyss AP, Bina M, Corkey R, Kefalides NA, Friedman HM: Fc and C3 receptors induced by herpes simplex virus on cultured human endothelial cells. J Clin Invest 1982, 69:123–128
30. Daha MR, Miltenburg AM, Hiemstra PS, Klar-Mohamad N, Van Es LA, Van Hinsbergh VW: The complement subcomponent Clq mediates binding of immune complexes and aggregates to endothelial cells in vitro. Eur J Immunol 1988, 18:783–787
31. Tannenbaum SH, Finko R, Cines DB: Antibody and immune complexes induce tissue factor production by human endothelial cells. J Immunol 1986, 137:1532–1537
32. Pober JS: Cytokine-mediated activation of vascular endothelium: Physiology and pathology. Am J Pathol 1988, 133: 426–433
33. Van de Winkel JGJ, Tax WJM, Jacobs CWM, Huizinga TWJ, Willems PHGM: Cross-linking of both types of IgG Fc receptors, FcγRI and FcγRII, enhances intracellular free Ca^{2+} in the monocytic cell line U937. Scand J Immunol 1990, 31: 315–325
34. Brooks DG, Qiu WQ, Luster AD, Ravetch JV: Structure and expression of human IgG Fc RII(CD32). J Exp Med 1989, 170:1369–1385
35. Warmerdam PAM, Van de Winkel JGJ, Gosselin EJ, Capel PJA: Molecular basis for a polymorphism of human Fcγ receptor II (CD32). J Exp Med 1990, 172:19–25
36. Scallon BJ, Scigliano E, Freedman VH, Miedel MC, Pan Y-CE, Unkeless JC, Kochan JP: A human immunoglobulin G receptor exists in both polypeptide-anchored and phosphatidylinositol-glycan-anchored forms. Proc Natl Acad Sci USA 1989, 86:5079–5083
37. Ravetch JV, Perussia B: Alternative membrane forms of FcγRIII (CD16) on human natural killer cells and neutrophils. J Exp Med 1989, 170:481–497
38. Hartnell A, Moqbel R, Walsh GM, Bradley B, Kay AB: Fcγ and CD11 CD18 receptor expression on normal density and low density human eosinophils. Immunology 1990, 69:264–270
39. Looney RJ, Ryan DH, Takahashi K, Fleit HB, Cohen HJ, Abraham GN, Anderson CL: Identification of a second class of IgG Fc receptors on human neutrophils. J Exp Med 1986, 163:826–836

Note Added in Proof

Additional immunostaining of five immature placentas ranging from 25 to 33 weeks of gestational age has shown the same pattern of FcγR MAb reactivity reported herein with mature placentas.