Two Mechanisms for IgG Uptake in Cultured Human Trophoblast: Evidence for a Novel High Affinity Fc Receptor

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ABSTRACT

The mechanism of IgG transport by the placental trophoblast was examined by studying IgG uptake by purified trophoblast maintained in culture. This model retains the ability to bind and endocytose human IgG from human serum. Comparison of the relative IgG uptake by the trophoblast among the four subclasses of both human and mouse IgG indicates that the trophoblast IgG receptor has different affinities from those described for the three known human Fcγ receptors, FcRγI, FcRγII, and FcRγIII. These results suggest the presence of a novel trophoblast Fcγ receptor. Although FcγRIII has been reported to be present on trophoblasts, immunocytochemical studies failed to detect binding to the cell surface of antibody-specific for FcγRIII, 3G8 MAb. In addition, blocking studies with MAb 3G8 did not interfere with IgG uptake. Scatchard analysis of human IgG uptake revealed a biphasic curve consistent with two distinct mechanisms for the transport of IgG by the trophoblast. The first is a higher affinity system (K_a = 1.7 × 10^7 M^{-1}, 1.7 × 10^4 binding sites/cell) which exhibits IgG subclass and species specificity, and the second is a low affinity system (K_a = 6.9 × 10^3 M^{-1}, 7.5 × 10^7 binding sites/cell). (*Pediatr Res* **38:** 1–6, 1995)

Abbreviations

hIgG, human immunoglobulin G
mIgG, mouse immunoglobulin G
FBS, fetal bovine serum
FcR, antibody binding receptor on the cell membrane

The human fetus acquires antibody as a result of transport of maternal Ig across the placenta (1). This process is selective for the transfer of IgG—the transfer of IgM and IgA is much less efficient (2). It is generally believed that the transcytosis of IgG is mediated by FcR and that IgG transfer proceeds by a mechanism resembling the transcytosis of IgG in other, better characterized epithelia, such as the neonatal intestine and fetal yolk sac (3–5).

Three classes of Fcγ receptors (FcγRI, FcγRII, and FcγRIII) have been identified in human leukocytes (6, 7). These differ in their affinities for IgG and in their specificity for binding to hIgG and mIgG subclasses. The three types of Fcγ receptors have been demonstrated in placental tissues by immunocytochemical techniques (8–10). It has not been established whether any of these Fcγ receptor subtypes mediate the transfer of circulating maternal IgG across the trophoblast.

A trophoblast isolated from the human placenta and maintained in monolayer culture will orient with the microvillous surface facing upward, permitting the investigation of the binding and uptake of IgG (11). This model retains many transport functions characteristic of syncytiotrophoblast *in vivo* as demonstrated in our laboratory and others (12–14). We have used this preparation to study IgG receptor function in differentiated human trophoblasts. The IgG receptors expressed by trophoblasts were characterized functionally by: 1) investigating the specificity of uptake of subclasses of human and mouse IgG and comparing these results with the reported specificities of the Fcγ receptors, 2) demonstrating the internalization of IgG by immunocytochemistry, and 3) studying the kinetics of human IgG uptake. We have identified two mechanisms of IgG uptake—a higher affinity system with clear specificity for the IgG subclasses and a less specific low affinity system.

METHODS

Materials. The sources of the materials were as follows: Medium 199, antibiotics, HEPES, γ-globulin-free FBS and general tissue culture biologicals were from Life Technologies, Inc. (Grand Island, NY); Percoll from Pharmacia (Piscataway, NJ); keratinocyte medium from Clonetics (San Diego, CA); FBS from Gemini Bioproducts (Calabasas, CA); PlastekC culture plates from Mattek (Ashland, MA); hIgG, hIgG subclasses, bovine IgG, mIgG, lactoperoxidase, Sephadex G-25, trypsin, pancreatin and general laboratory chemicals from

Sigma (St. Louis, MO); protein A- and protein G-agarose from Boehringer Mannheim (Indianapolis, IN). The mIgG subclasses were obtained from Organon Teknika Corp. (Durham, NC); [^{125}I]NaI and [^{131}I]NaI from Amersham Corp. (Arlington Heights, IL); Dynabeads coated with goat anti-mIgG from Dynal (Lake Success, NY); antibody to CD45 from Becton Dickinson (San Jose, CA). Antibody to cytokeratin was a gift of Dr. T.-T. Sun (NYU Medical Center) and MAb (Fab$_2$ fragment) directed against FcγRIII (*3G8*) was a gift of Dr. J. Unkeless (Mt. Sinai School of Medicine, New York, NY). Affinity-purified rhodamine-conjugated secondary antibodies were purchased from Jackson Immunoresearch (West Grove, PA). Freshly prepared, purified human neutrophils were provided by Dr. M. Philips (NYU Medical Center).

Trophoblast isolation. Human placentas were obtained from noncomplicated full-term pregnancies by either vaginal or cesarean section delivery. The trophoblast was isolated by enzymatic digestion of dissected tissue using a modification of the procedure of Bax et al (15). Briefly, villi were teased apart from connective tissue before digestion in PBS containing 5.5 mM glucose, 0.33 mM sodium pyruvate, 2 mg/ml pancreatin, and 2 mg/ml trypsin. After a first digestion of 35–40 min at 37°C with gentle shaking, the tissue was collected by centrifugation, and fresh digestion buffer was added. After incubation for an additional 20–25 min, the trophoblast was released into the supernatant by vigorous shaking, and then passed sequentially through one, two, and three layers of sterile surgical gauze. The cells were pelleted and centrifuged through a discontinuous Percoll gradient as described by Kliman *et al.* (12). The recovered trophoblast was passed sequentially through 250- and 100-μm nylon mesh. In some experiments (as indicated in the text), the isolated cells were incubated with mouse-anti CD45 antibody, and the macrophage cells were removed by magnetic microspheres coated with goat-anti-mIgG as described by Douglas and King (16). The resulting purified trophoblast was >99% cytokeratin positive, whereas <0.4% of the cells were positive for CD45 as demonstrated by immunofluorescence. The trophoblast was plated in Medium 199 containing 15% FBS and antibiotics at a density of 4 × 10^5 cells/cm^2 on Mattek C culture dishes. Fungizone (2 μg/ml) was included when placentas were obtained from vaginal deliveries. After attachment overnight, the cultures were washed with PBS and fed with keratinocyte medium containing 10% γ-globulin-free FBS and antibiotics (KBM) as described by Douglas and King (17). IgG uptake assays were done after 48–72 h of culture.

Binding and uptake of IgG by trophoblast. Ig was iodinated by the lactoperoxidase method with [^{125}I]NaI or [^{131}I]NaI as described by Kadner *et al.* (18). The radiolabeled IgG was separated from free iodine by passage through a Sephadex G25 column. Before each experiment the radiolabeled IgG was determined to be >98% intact protein by spin filtration using the Centrifree Micropartition System (Amicon, Beverly, MA). Protein integrity was also checked by SDS-polyacrylamide gel electrophoresis and by binding to protein A- or protein G-agarose.

The trophoblast was incubated with KBM containing 25 mM HEPES and 5 × 10^5 to 1.5 × 10^6 cpm/ml labeled IgG (sp act 1–2 × 10^6 cpm/μg) at either 37 or 4°C. The cultures were washed five times with cold PBS, and the cells lysed with 1% SDS, 10 mM Tris, 1 mM EDTA. Lysates were collected, and the radioactivity was measured using a Packard Cobra Auto-Gamma counter. For kinetic studies increasing amounts of unlabeled hIgG were added to the incubation medium. For studies of IgG subclass discrimination by the low affinity system, 10 mg/ml hIgG was added to the incubation medium.

Immunofluorescence microscopy. Cells were grown for 3–4 days on 12-mm glass coverslips coated with 1 μg/cm^2 fibronectin (Sigma). For detection of cytoskeletal proteins (*e.g.* cytokeratin) or the macrophage marker CD45, cells were fixed for 5–7 min in ice-cold methanol. For detection of alkaline phosphatase and *3G8*, the cells were fixed in 4% paraformaldehyde in PBS for 30 min as previously described (19). The fixed coverslips were incubated with or without 0.1% Triton-100 for 5 min and then for 1–3 h with antibodies at a 1:50 to 1:100 dilution followed by rhodamine-conjugated goat anti-rabbit or mouse IgG (Jackson Immunoresearch, West Grove, PA), as appropriate. The detergent treatment did not affect the overall staining patterns. When the uptake of IgG was measured, specimens were fixed in paraformaldehyde after the incubation period and then permeabilized with 0.2% Triton X-100. A rhodamine-conjugated goat anti-hIgG was then used in a single labeling step. Preparations were viewed and photographed on a Zeiss Axiophot microscope.

RESULTS

Uptake of IgG by cultured trophoblast. The uptake of IgG was studied using an isolated trophoblast prepared by standard procedures (see "Methods"). As determined by immunofluorescence staining with antibodies to cytokeratin and placental alkaline phosphatase, the trophoblast population was >97% pure. The cells were cultured for 72 h in keratinocyte medium to permit them to differentiate into large multinucleate cells which exhibit a syncytiotrophoblast phenotype. At this time, large amounts of human chorionic gonadotropin and progesterone are produced by the cells as reported by Kliman *et al.* (12) and confirmed by our laboratory (14). Electron microscopic examination of the cells revealed microvilli on the free surface with enlarged endoplasmic reticulum and numerous mitochondria (data not shown).

To confirm the appropriateness of the experimental model, the cells were incubated with human serum at 4 or 37°C, and the IgG was visualized by immunofluorescence microscopy (Fig. 1). At 4°C, IgG binding to the cell membrane was detected as uniform surface staining with some areas having a more punctate appearance. At 37°C, all of the cells were brightly stained with IgG on both the cell surface and in large vesicles, taken to be endosomes, indicating that internalization of IgG is a property that is maintained by the trophoblast in culture.

The species specificity of IgG uptake was investigated using radioiodinated IgG to provide additional evidence that the cultured trophoblast model maintained the properties of syncytiotrophoblast in native tissue. hIgG was taken up by the cells in a time-dependent manner (Fig. 2). Incubation in the
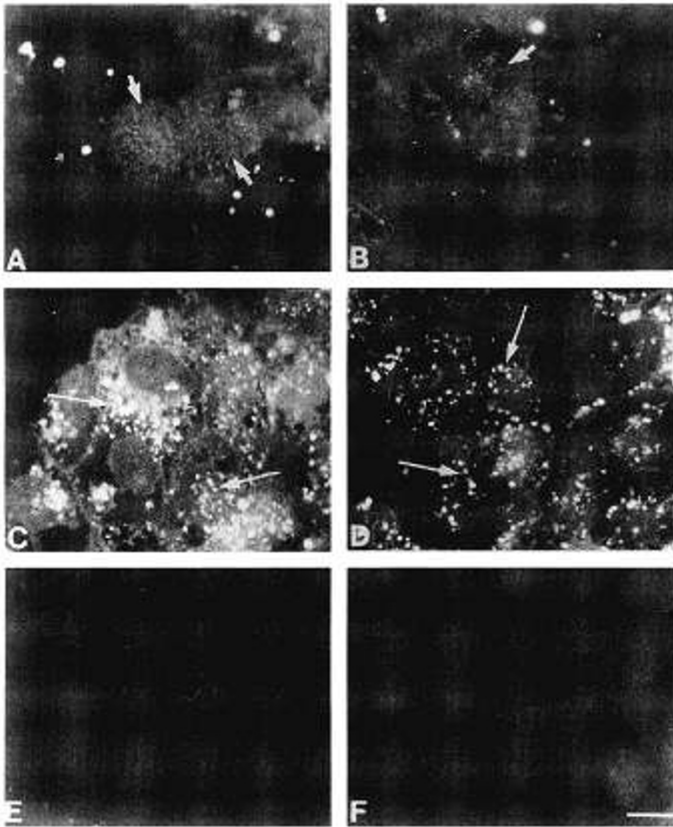
Figure 1. Internalization of hIgG by a cultured trophoblast. An isolated trophoblast free of Hofbauer cells was cultured on fibronectin-coated glass coverslips for 72 h and then incubated for 2 h in the presence (A–D) or absence (E and F) of human serum at either 37 or 4°C. The cells were fixed and reacted with rhodamine-conjugated goat anti-hIgG antibody as described in "Methods." hIgG binding to the cell membrane at 4°C (*panels A* and *B*) is visualized as uniform surface staining with some areas having a more punctate appearance (*arrows*). At 37°C (*panels C* and *D*) the cells are brightly stained with IgG present both on the cell surface and in large vesicles (*arrows*). Control cultures incubated in the absence of human serum at 4°C (*panel E*) or 37°C (*panel F*) showed only a low level diffuse staining of the nuclei. Bar = 8 μM.

presence of excess hIgG (10 mg/ml) reduced, by ~60%, the uptake of hIgG by trophoblast. By comparison, bovine IgG uptake was 30% that of hIgG and was not reduced in the presence of excess hIgG. These results are consistent with qualitative immunohistochemical observations made on cryostat sections of human placental villous tissue where the binding of hIgG to the trophoblast was not blocked with bovine IgG (20) and perfusion studies where hIgG was transferred across the placenta approximately 3-fold more rapidly than bovine IgG (21). The uptake of mIgG was also measured and found to be similar in magnitude to the uptake of hIgG (Fig. 2). Addition of excess unlabeled hIgG during the 120-min uptake period reduced the amount of ^{125}I-labeled mIgG associated with the cells to the same extent as it did the uptake of hIgG (data not shown).

Uptake of IgG subclasses. IgG receptors can be classified by the relative rates of uptake of the four subclasses of hIgG. hIgG subclasses were incubated with the trophoblast cells for up to 2 h using our standard assay conditions. As can be seen in Figure 3, IgG1 and IgG3 were taken up well, at a rate comparable to complete human IgG. IgG2 and IgG4 are taken up
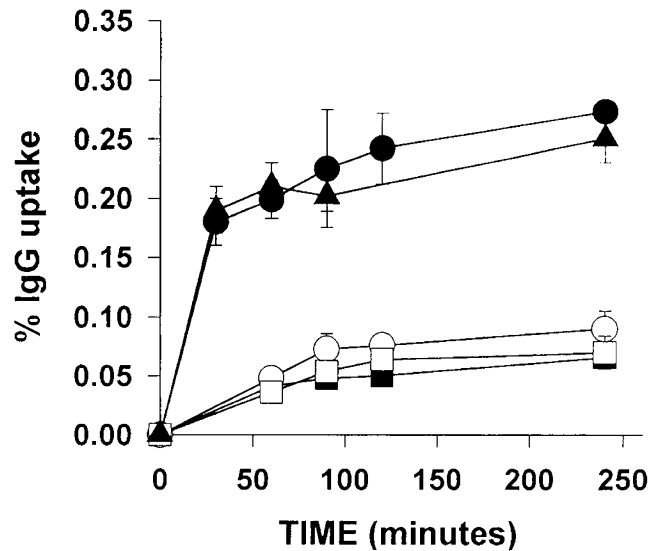
Figure 2. Human, mouse, and bovine IgG uptake by the human trophoblast. An isolated trophoblast was cultured for 72 h. Uptake studies were performed in triplicate with either ^{125}I-labeled human and ^{131}I-labeled bovine IgG ± 10 mg/ml hIgG or ^{125}I-labeled mIgG alone for the indicated times as described in "Methods." The data shown are the results obtained from trophoblast isolated from one placenta and are representative of three different trophoblast preparations from three placentas. ●, ^{125}I-labeled hIgG; ○, ^{125}I-labeled hIgG + 10 mg/ml hIgG; ▲, ^{125}I-labeled mIgG; ■, ^{131}I-labeled bovine IgG; □, ^{131}I-labeled bovine IgG + 10 mg/ml hIgG.
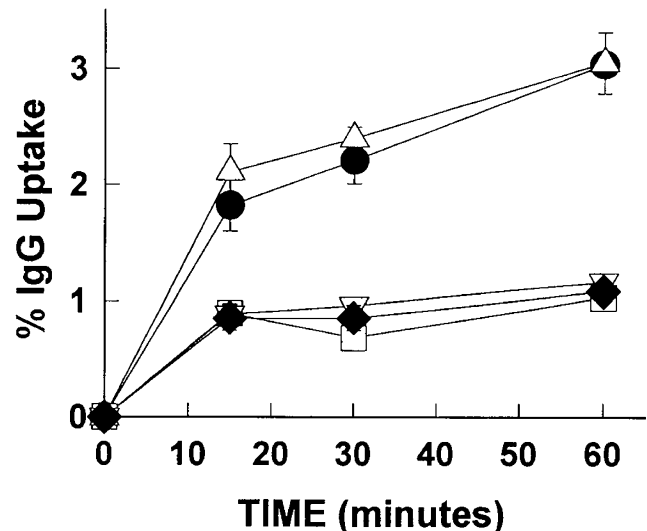
Figure 3. Uptake of hIgG subclasses. A trophoblast isolated free from Hofbauer cells and cultured as described in "Methods" was incubated with ^{131}I-labeled bovine IgG and ^{125}I-labeled hIgG1, hIgG2, hIgG3, or hIgG4 for the times indicated. The data shown are the results obtained from trophoblast isolated from one placenta and are representative of three trophoblast preparations from three placentas. The *error bars* are derived from the values obtained from triplicate wells. ●, IgG1; □, IgG2; △, IgG3; ∇, IgG4; ◆, bovine IgG.
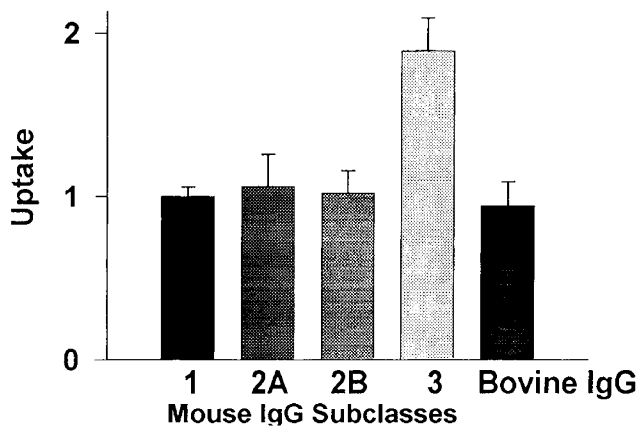
poorly, similar in magnitude to bovine IgG. In these experiments, Hofbauer cell-free trophoblast cultures were used (see "Methods"). However, removal of Hofbauer cells did not affect the relative rates of uptake of the four subclasses of hIgG (data not shown). The relative avidities for the subclasses (hIgG3, hIgG1 >> hIgG2, hIgG4 = bovine IgG) are the same as the reported specificities of the FcγRIIaHR (22) and FcγRIII (6)

receptors but are different from that of FcγRIIaLR (hIgG3>hIgG1, hIgG2 >> hIgG4) (22) and FcγRI (hIgG1 > hIgG3 > hIgG4 >> hIgG2) (23).
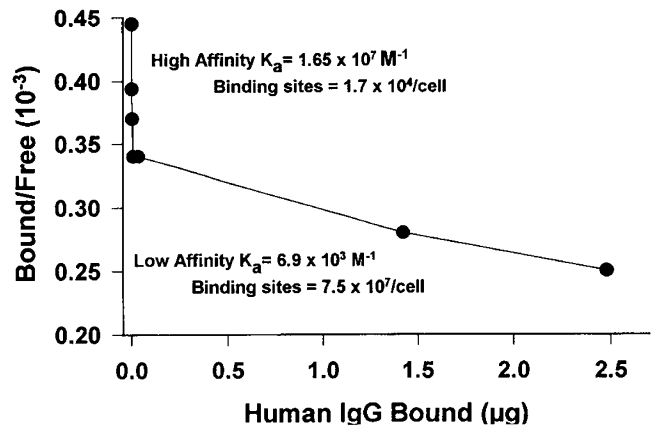
Human FcγRII and FcγRIII can be differentiated by their avidities for mIgG subclasses: hFcγRII-mIgG1, mIgG2b >> mIgG2a, mIgG3 and hFcγRIII-mIgG3 > mIgG2a > mIgG2b >> mIgG1 (24). Shown in Figure 4 is a comparison of the uptake of the mouse IgG subclasses by the cultured human trophoblast. The relative uptake specificity for the subclasses was mIgG3 >> mIgG1, mIgG2a, and mIgG2b = bovine IgG. The observed hierarchy of mouse IgG subclass specificity suggests that the IgG receptor expressed by trophoblast is a novel receptor, differing functionally from all of the known FcγR receptors.

FcγRIII receptors have been reported on the human trophoblast in the placenta using immunologic techniques (see "Discussion"). We investigated the possible presence of FcγRIII on cultured trophoblast using a MAb *3G8*, which is specific for FcγRIII and blocks IgG binding to neutrophils which express FcγIII (25, 26). After incubation of isolated neutrophils with *3G8* antibody and fluorescent-conjugated secondary antibodies, bright staining was observed over the entire cell surface, confirming the reactivity of this antibody with FcγRIII receptors (data not shown). By contrast, there was no specific staining with trophoblast. In blocking studies with *3G8* antibody, trophoblast was incubated with Fab2 fragments in high concentrations before and during incubation with ^{125}I-labeled hIgG. No significant decrease in uptake of human IgG by trophoblast was observed (data not shown).

Kinetics of IgG uptake. To further characterize the trophoblast IgG receptors, we determined the association constant (K_a) and number of binding sites on trophoblast. The cells were incubated with increasing concentrations of hIgG, and the data were then subjected to Scatchard analysis. For these studies only purified cells, Hofbauer-free, were used. A biphasic curve is evident indicating the existence of two IgG receptors (Fig. 5). The first is a higher affinity, low capacity system with a K_a of 1.7×10^7 M^{-1} and 1.7×10^4 binding sites per cell. The
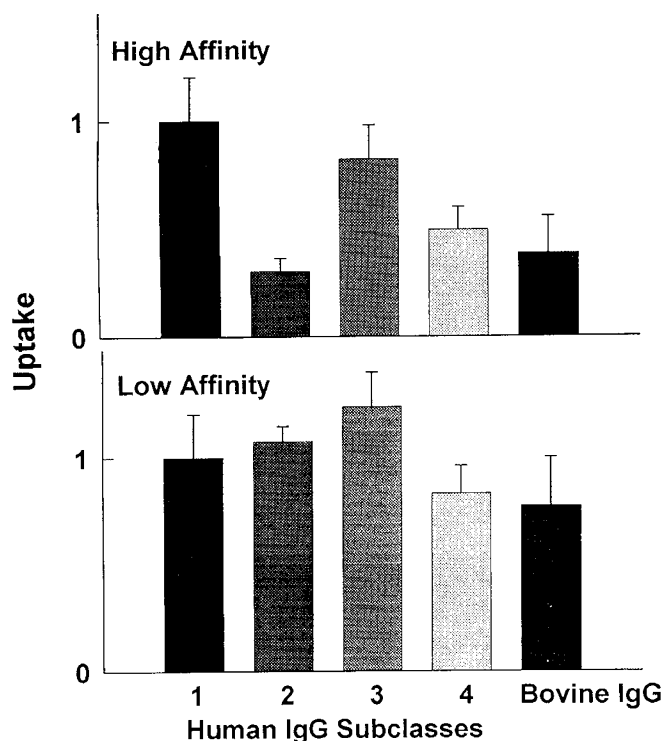

Figure 5. Kinetic analysis of hIgG uptake. An isolated trophoblast free of macrophage (Hofbauer cell) contamination was cultured for 72 h and then for 2 h in the presence of ^{125}I-labeled hIgG with increasing concentrations of unlabeled hIgG. The radioactivity associated with the cells was determined as described in "Methods." The amount of IgG bound to the cells was calculated for each concentration and depicted as a Scatchard plot (bound/free *vs* bound IgG). A biphasic curve was evident and the corresponding association constants (K_a) and the number of binding sites were calculated from the plot for both the high and low affinity systems. The data shown are the results obtained from a trophoblast isolated from one placenta and are representative of three different placentas.

second is a low affinity, high capacity system with a measurable K_a of 6.9×10^3 M^{-1} and 7.5×10^7 binding sites per cell.

The ability of the two transport mechanisms to discriminate between the four subclasses of hIgG was also compared (Fig. 6). The higher affinity mechanism was investigated by incubating the trophoblast cells with 3 µg/ml human radioiodinated IgG subclasses for 2 h. The low affinity system was assayed by measuring uptake of the subclasses in the presence of 10 mg/ml hIgG. The higher affinity receptor clearly is able to differentiate between the four hIgG subclasses and bovine IgG as was observed in Figure 3, whereas the low affinity system is not.

DISCUSSION

MAb directed against the three classical FcγR have been used to attempt to identify placental IgG receptors. These studies clearly demonstrated that FcγRI is absent from the trophoblast but is associated with the stromal cells, including Hofbauer cells (8–10). FcγRII is expressed by the endothelium and on stromal cells. In one study FcγRII was also localized to the trophoblast layer in hydatidiform mole and its mRNA was detected in cultures of enriched trophoblast (27). It is possible that the Northern blotting technique used in this study was sufficiently sensitive to detect FcγRII receptors on contaminating Hofbauer cells. FcγRII receptors have not been identified on purified trophoblast. The presence of FcγRIII on trophoblast has been controversial. FcγRIII has been reported to be present on trophoblast by flow cytometry on isolated cytotrophoblast (28) and by immunocytochemistry on placental sections (8, 9). However, in agreement with our immunolocalization results, Wainwright and Holmes (29) reported that antibodies to FcγRIII which react with Hofbauer cells from term placenta failed to show any reactivity with placental term trophoblasts.

Figure 4. Uptake of mIgG subclasses. Trophoblast was incubated with ^{131}I-labeled bovine IgG and ^{125}I-labeled mIgG1, mIgG2A, mIgG2B, or mIgG3 for 2 h as described in "Methods." The data are expressed as the relative amount of mouse subclass IgG uptake compared with the uptake of mIgG1. IgG1 has been given a value of 1. The results presented are the mean ± SD from data obtained from trophoblast preparations from four placentas.

Figure 6. Discrimination of the hIgG subclasses by the high affinity and low affinity mechanisms. To measure the high affinity mechanism, isolated trophoblast was cultured for 72 h and incubated with 3 μg/ml ^{125}I-labeled hIgG1, hIgG2, hIgG3, or hIgG4 and ^{131}I-labeled bovine IgG for 2 h. To assay the low affinity system, cultured trophoblast was incubated as above with the addition of 10 mg/ml hIgG. The relative uptake for each subclass was determined by comparing the uptake of each subclass to the uptake of IgG1, which was given a value of 1. The results presented are the mean ± SD from data obtained from a trophoblast isolated from four different placentas.

Despite the reports of the presence of receptors on trophoblasts that react with MAb against FcγRII and FcγRIII, the involvement of these receptors in the transport of IgG has not been established. In the present study, we have characterized the receptors by their transport function as expressed by the relative affinities for the subclasses of hIgG and mIgG. By using highly purified trophoblast preparations we were able to measure the properties of the receptors of the syncytiotrophoblast itself. The cultured trophoblast preparation retains the ability to bind and endocytose IgG from human serum (Fig. 1). The relative affinities of the trophoblast higher affinity receptor for the four subclasses of human and mouse IgG exclude functional identity with any of the known human FcγR.

Because of the reports in the literature of the presence of FcγRIII receptors on trophoblast (8, 9, 30) we investigated the possible involvement of FcγRIII using a MAb specific for FcγRIII, 3G8. Preincubation of trophoblast with 3G8 did not inhibit the uptake of IgG, although it is known to effectively block the uptake of IgG by neutrophils (25, 26). Furthermore, as assessed by immunofluorescence microscopy, the antibody failed to bind to cultured trophoblast. These results exclude the functional involvement of the FcγRIII receptors in the uptake of IgG, and support the conclusion that the trophoblast receptor is novel. Our results do not completely rule out the possibility that novel, alternatively spliced forms of FcγRII or FcγRIII

could be responsible for the observed higher affinity uptake of IgG. However, for FcγRII, all of the known allotypic forms have identical or nearly identical extracellular domains that are not distinguishable by MAb (6, 22). Similarly, the two FcγRIII allotypic forms differ only in their mode of membrane association, with FcγRIIIB being glycosyl phosphatidyl inositol linked. Neither form binds monomeric IgG with high affinity. FcγRIIIA forms multimeric complexes with FcεRI γ and/or CD3/TcR ζ chains (6). It is not known if other forms of these accessory subunits exist in the trophoblast that may alter the specificity and affinity of FcγRIIIA. However, the lack of binding of mAb 3G8 tends to rule out this possibility as well.

Scatchard analysis of IgG transport yielded biphasic kinetics, indicating that the trophoblast has two receptors for IgG uptake. The first corresponds to a single higher affinity receptor ($K_a \sim 1.7 \times 10^7$ M^{-1}) that discriminates between the four subclasses of human and mouse IgG. The second represents a low affinity mechanism ($K_a \sim 7 \times 10^4$ M^{-1}) that does not discriminate among any of the different IgG used in this study. Kinetic studies have also been conducted by other investigators using isolated placental membranes with reported K_a values of 8.6×10^6 (30), 4×10^7 (31), and 4×10^6 M^{-1} (32). Studies of Rees and Wallace (33) and Lubega (34) both presented evidence of biphasic kinetics of IgG uptake, suggesting that low and high affinity IgG receptors were present. However, all of the previous studies were performed on membrane preparations from placenta, which contains many cell types including the Hofbauer cells which express FcR. In the kinetic studies that we have performed, the trophoblast was >99% pure with Hofbauer cells removed, permitting the conclusion that trophoblast has both a high and low affinity mechanism for IgG uptake.

Two additional proteins have been suggested as the placental IgG receptors. Matre et al. (35), using affinity chromatography, isolated a 40-kD protein, which was present on the microvillous membrane of the syncytiotrophoblast. Binding studies showed the human subclass specificity of this receptor to be hIgG1, hIgG3 >> hIgG2, hIgG4. The affinities for the mouse subclasses of IgG have not been determined, leaving open the question as to whether the receptor is the same as the one that we have studied. Makiya and Stigbrand (36) have provided evidence that alkaline phosphatase, which is abundant on the apical membrane of syncytiotrophoblast, can serve as an IgG receptor. However, the reported K_a of alkaline phosphatase for human IgG was 3.7×10^6 M^{-1}, far lower than that we have observed for the high affinity system (1.7×10^7 M^{-1}).

The placenta in vivo is exposed to maternal concentrations of IgG (10 g/L) that would allow both transport systems to function in the initial binding of IgG and its uptake into the syncytiotrophoblast. If both systems contribute to the transcytosis of IgG, the present studies would suggest that the four subclasses would be transferred to the fetus with a selective advantage for IgG1 and IgG3. Analyses of cord serum (37) have shown IgG1 in higher concentration than in maternal serum (10.89 g/L versus 6.65 g/L) and IgG2 in lower concentration (2.65 versus 1.58), consistent with their relative rates of uptake by trophoblast. However, the reported concentrations of IgG3 (0.56 g/L versus 0.45 g/L) and IgG4 (0.43 g/L versus

0.35 g/L) are not significantly different in the fetal and maternal circulations despite the apparent differences in their uptake by the cultured trophoblast. The efficiency of uptake may not accurately reflect the efficiency of maternal-fetal transfer across the placenta, and additional factors such as the half-life of transferred proteins in the fetal circulation may play a role in determining the circulating concentrations.

IgG is the only circulating maternal protein known to be specifically and preferentially transferred across the placenta. It is important to note, however, that several other maternal blood proteins, for which specific transport mechanisms have not been identified, including albumin, IgM, and ceruloplasmin, are transferred into the fetal circulation and are present at levels that, although not nearly equal to those in maternal blood, are nonetheless substantial (38). The low affinity IgG uptake system that is described in this study appears to have high capacity and lacks the ability to discriminate among IgG subclasses. We suggest that this system may not be specific for IgG but may also function for the uptake of other proteins as well. Some of this "nonspecific" uptake may result in the transfer of maternal proteins across the trophoblast to the fetal circulation, although this process is probably not very efficient. In this way, the trophoblast would to some degree resemble endothelial cells, which are responsible for the transfer of proteins from the blood to the interstitial fluid.

Note Added in Proof. C.M. Story, J.E. Mikulska, and N.E. Simister (*Journal of Experimental Medicine* (1994) 180:2377–81) have recently reported a receptor cloned from a cDNA library of human term placenta that is homologous to mouse and rat intestinal Fc receptors. Transfected cells bound human Fc effectively at pH 6.0 and very modestly at pH 7.5.

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