Glycoprotein gE of Herpes Simplex Virus Type 1: Effects of Anti-gE on Virion Infectivity and on Virus-Induced Fc-Binding Receptors

MICHAEL F. PARA,† ROBERT B. BAUCKE, AND PATRICIA G. SPEAR*
Department of Microbiology, University of Chicago, Chicago, Illinois 60637

Received 18 June 1981/Accepted 3 September 1981

An Fc-binding glycoprotein, designated gE, was detected previously in cells infected with herpes simplex virus type 1 (HSV-1) and in virion preparations isolated from infected cells. For the studies reported here, we purified gE from HSV-1 strain HFEM(syn) by affinity chromatography and preparative electrophoresis and then immunized a rabbit to produce an antiserum to glycoprotein gE. We found that this antiserum selectively precipitated gE and its precursors from detergent-solubilized extracts of HSV-1 strain HFEM(syn)-infected HEp-2 cells, from extracts of other cell lines infected with the same virus, and from extracts of HEp-2 cells infected with several other HSV-1 strains. The antiserum did not precipitate any proteins from uninfected cells. The several forms of gE detected by immunoprecipitation accumulated in variable quantities in different cells infected with the different virus strains and also varied slightly with respect to electrophoretic mobility, suggesting some differences in the gE's from different HSV-1 strains and some effects of the host cell on the nature and extent of post-translational processing. One of the electrophoretic forms of gE previously detected in purified preparations of virions could be precipitated by anti-gE from extracts of purified HSV-1 strain HFEM(syn) virions. Moreover, anti-gE neutralized HSV-1 infectivity, but only in the presence of complement. Finally, F(ab')2 fragments of the anti-gE immunoglobulin partially inhibited the binding of 125I-labeled immunoglobulin G to the Fc receptors on HSV-1-infected cells.

Infection of cultured cells with herpes simplex virus (HSV) results in the expression of receptors for the Fc region of immunoglobulin G (IgG) (27, 29, 30). These receptors, whose physiological significance is not yet understood, have been detected after infection of a variety of different cell types, including cells of fibroblastic, epithelial, and hematopoietic origin (7, 8, 12, 18, 19, 29). In addition, other human herpesviruses (specifically, cytomegalovirus [15, 23, 28] and varicella-zoster virus [21]) have also been reported to induce the expression of Fc-binding receptors.

Recently, we reported the use of affinity chromatography to identify three electrophoretically distinguishable Fc-binding polypeptides, some or all of which were glycosylated, in extracts of HSV type 1 (HSV-1)-infected cells (2). The results of pulse-chase experiments and comparisons of proteolytic digestion products indicated that the three polypeptides were derived from the same gene product (designated gE) and that they probably differed in the extent of glycosylation or other post-translational processing. The Fc-binding activity of gE, coupled with the appearance of gE on the cell surface concomitant with the expression of Fc-binding receptors on intact cells, suggested that gE might in fact be the receptor.

To characterize gE further and to investigate the relationship of gE to Fc-binding activity on cell surfaces and virions, we purified this glycoprotein and prepared an antiserum against it. In this paper we report that the antiserum selectively precipitated gE and its precursors from a variety of cell types infected with several different HSV-1 strains, that it neutralized HSV-1 infectivity in the presence of complement, and that F(ab')2 fragments of immunoglobulins from the anti-gE serum interfered with the Fc-binding activity of intact HSV-1-infected cells.

MATERIALS AND METHODS

Cells and viruses. The cell lines used in this study were African green monkey kidney (Vero) cells, HEp-2 cells, BHK-21 clone 13 cells, and human embryonic lung (HEL) cells; all of these cell lines were obtained from Flow Laboratories, Rockville, Md. The cells were grown in Dulbecco modified Eagle minimal essential medium supplemented with 10% heat-inactivated fetal bovine serum. Infected cells were maintained...
in medium 199 supplemented with 1% heat-inactivated calf serum (medium 199V). For viral titrations, Vero cells were used, and the overlay medium (medium 199V) contained 0.1% pooled human gamma globulin (24). The viruses used in this study were HSV-1 strains F (11), M2 (14), MP (14), 14-012 (9) (obtained from F. Rapp, Pennsylvania State University, Hershey), HFEM (17) (obtained from A. Buchan, University of Birmingham, Birmingham, England), and HFEM-(syn), a syncytial plaque variant of strain HFEM (2). These strains were propagated by infecting HEp-2 cells at low input multiplicities (0.01 PFU/cell) and maintaining the infected cells in medium 199V at 34°C; cell lysates were prepared when cytopathic effects were complete. From its initial isolation, strain F has been passaged only a few times at low multiplicities of infection in HEp-2 cells. Virions were isolated from cytoplasmic extracts of HEp-2 cells as previously described (5, 26).

Reagents and radioactive compounds. The media and serum used were purchased from K. C. Biologicals, Kirkland, Wash.; 100% Fetal Bovine Serum, Bio-Rad, to 50 ml; and sodium deoxycholate, Sigma Chemical Co., St. Louis, Mo. Bovine serum albumin, ovalbumin, and guinea pig complement were from Miles Laboratories, Inc., Elkhart, Ind. DEAE-Bio-Gel and all electrophoresis reagents were from Bio-Rad Laboratories, Richmond, Calif.; Freund adjuvants were from Difco Laboratories, Detroit, Mich. The radiochemicals Na$_{125}$I (carrier-free; 17 Ci/mg) and [${}^{35}$S]methionine (500 to 600 Ci/mmole) were from New England Nuclear Corp., Boston, Mass. Staphylococcus aureus Cowan strain was obtained from the American Type Culture Collection, Rockville, Md.; this bacterium was grown and prepared for use in immunoprecipitation experiments by the method of Kessler (16).

Infection and labeling of the cells. Monolayer cultures were infected by exposing the cells for 2 h at 37°C with shaking to a minimal volume of medium 199V containing 10 PFU of virus per cell; after adsorption the inoculum was replaced with medium 199V, and incubation was continued at 37°C. For long-term labeling of cultures, the medium was replaced at the times indicated with medium 199V containing 10% the usual concentration of methionine and 3 μCi of [${}^{35}$S]methionine per ml; these cultures were harvested 24 to 26 h after infection. For pulse-labeling, the cultures were washed with medium 199V lacking methionine and then incubated for 5 to 7 min with medium 199V containing 10 μCi of [${}^{35}$S]methionine per ml; then the cultures were harvested immediately or after an additional incubation in nonradioactive complete medium 199V.

Preparation of antiserum. We used affinity chromatography and preparative SDS-acrylamide gel electrophoresis, as described by Baucke and Spear (2) and below, to isolate gE from extracts of HSV-1 strain HFEM(syn)-infected HEp-2 cells. Briefly, for each immunization 2.4 × 10$^8$ unlabeled infected cells were solubilized in approximately 5 ml of phosphate-buffered saline (PBS; 0.14 M NaCl, 3 mM KCl, 10 mM Na$_2$HPO$_4$, 1.5 mM KH$_2$PO$_4$, 0.5 mM MgCl$_2$, 1 mM CaCl$_2$) containing 1% Nonidet P-40, the lysates were centrifuged at 25,000 rpm in an SW27.1 rotor for 2 h, and the resulting supernatant was divided for application to three or four 1-ml IgG-bovine serum albumin-Sepharose columns. After the columns were washed, the bound proteins were eluted with 3 M potassium thiocyanate in PBS containing 0.5% Nonidet P-40, pooled, and precipitated with 5% trichloroacetic acid; the precipitates were washed sequentially with ethanol and acetone and then solubilized for SDS-acrylamide gel electrophoresis. The dimensions of the gel slab were approximately 0.15 by 10 by 14 cm, and the entire sample was loaded in one well about 4 cm wide. After electrophoresis, the gE in the uncloned polyacrylamide gel was located by its known migration compared with a bovine serum albumin marker lane (stained) at the border of the slab gel. A 5-mm polyacrylamide strip containing gE was cut from the gel, minced, and mixed with 1 ml of PBS. The preparation was then emulsified with 1 ml of Freund adjuvant. The initial immunization was with Freund complete adjuvant, and subsequent immunizations were with Freund incomplete adjuvant. A New Zealand white rabbit was immunized by subcutaneous injections at several sites on the back, neck, and flanks with portions of the inoculum. A total of three immunizations were given at 2-week intervals, and 1 week after the third immunization approximately 50 ml of blood was obtained from an ear artery. The blood was allowed to clot at 37°C for 30 min and incubated overnight at 4°C, and the serum was collected for storage at −70°C. Subsequent bleedings were performed 1 week after a booster immunization. Premune serum was obtained from the same rabbit several weeks before the immunization protocol was started.

Immunoprecipitation. Proteins were solubilized from infected or uninfected cells or from purified virions for immunoprecipitation experiments. The cells from 25-cm$^2$ monolayer cultures were washed with PBS lacking MgCl$_2$ and CaCl$_2$, lysed in 1 ml of extraction buffer (Ca$^{2+}$- and Mg$^{2+}$-free PBS containing 0.1% SDS, 0.5% sodium deoxycholate, and 1% Nonidet P-40), and then frozen at −20°C until they were used. Similarly, purified virions were collected by centrifugation and lysed in extraction buffer (1 ml of purified virions [approximately 3 × 10$^9$ PFU] from 10$^9$ cells). Before immunoprecipitation the lysates were thawed, and insoluble material was removed by centrifugation at 25,000 rpm in an SW27.1 rotor for 2 h; 0.1 to 1 ml of extract was mixed with 10 μl of serum and placed on ice for 1 h. To separate the immune complexes from the unreacted material, 100 μl of Formalin-fixed S. aureus (10% [vol/vol] in extraction buffer containing 0.1% ovalbumin) was added, and the mixtures were left for an additional 1 h on ice. The S. aureus cells with bound immune complexes were collected by centrifugation in a microfuge. To remove non-specifically adsorbed proteins, the pellets were washed by two suspensions in extraction buffer and recentrifugation. Then a third wash was performed with 50 mM Tris-hydrochloride (pH 7.5) containing 100 mM NaCl. The precipitated proteins and antibodies were solubilized from the cells for analysis by SDS-
polyacrylamide electrophoresis (13). The gels were fixed and stained, and the radioactive bands were located by fluorography (3).

Neutralization. We tested antibody-mediated neutralization of viral infectivity in the presence and absence of complement by using a plaque reduction assay. We prepared mixtures which contained approximately 500 PFU of HSV-1 strain HFEM(syn) per ml, 20 μl of serum (either immune or preimmune and either untreated or heated to 56°C for 30 min) per ml, and different concentrations of guinea pig complement. These mixtures were incubated at 37°C for 1 h, and 1-ml samples were added to Vero cell monolayers for 2 h at 37°C with shaking to assay for residual infectious virus, as described above for viral titration.

F(ab')2 inhibition of 125I-labeled IgG binding. F(ab')2 fragments were prepared from Na2SO4-precipitated immunoglobulins obtained from anti-gE serum and normal rabbit serum. The precipitated proteins were collected by centrifugation at 7,500 × g for 20 min at room temperature. The precipitate was reconstituted in water and dialyzed against 0.0175 M phosphate buffer (pH 6.9). The IgG fraction was isolated by chromatography on DEAE–Bio-Gel, as described previously (22). The F(ab')2 fragments were prepared by a modification (2, 22) of the pepsin digestion method of Nisonoff (20). The IgG used in the binding assay was labeled with 125I by the chloramine T method of Byrt and Ada (4), as modified by Baucke and Spear (2). The 125I-labeled IgG obtained had a specific activity of 10⁶ cpm/mg.

To determine the effects of the F(ab')2 fragments on the binding of 125I-labeled IgG to infected cells, we performed the following experiment. Replicate cultures of HEp-2 cells in 25-cm² flasks were infected with HSV-1 strain HFEM(syn) at a multiplicity of 10 PFU/cell. The inoculum was removed after 2 h, and the cells were incubated in medium 199 without serum. At 18 h after infection, the medium was removed, and the cells were rinsed with PBS and then incubated at 37°C with different concentrations of F(ab')2 fragments in 1 ml of borate-buffered saline (experiment 1) or PBS (experiment 2). After 1 h, 0.5 ml of buffer (borate-buffered saline or PBS) containing 25 μg of 125I-labeled IgG was added to each culture. After another 1 h of incubation at 37°C on a shaker, the cells were washed five times with PBS to remove unbound 125I-labeled IgG, detached from the flask with Versene, and assayed for radioactivity with a gamma counter.

RESULTS

Preparation of antiserum. For immunization of the rabbit, glycoprotein gE was isolated from unlabeled extracts of HSV-1-infected cells by affinity chromatography and preparative polyacrylamide gel electrophoresis, as described above. However, we performed pilot experiments with [35S]methionine-labeled extracts to monitor the polypeptide compositions of fractions obtained during the isolation of gE. Although the eluate obtained from the IgG-bovine serum albumin-Sepharose column was greatly enriched for gE, as previously described (2), significant amounts of other proteins were present. These proteins were separated from gE by preparative SDS-acrylamide gel electrophoresis, and only the band of gel containing gE was cut from the slab, mixed with Freund adjuvant, and used for immunizing rabbits as described above. A small segment of the gel was subjected to electrophoresis a second time in order to verify that it contained only material with the electrophoretic mobility of gE.

Specific immunoprecipitation of gE and its precursors. The antiserum raised by the immunization procedure was evaluated by reactions with extracts from infected and uninfected labeled HEp-2 cells and electrophoretic analyses of immune complexes that were capable of binding to Formalin-fixed protein A-containing S. aureus. As Fig. 1B shows, the immune serum precipitated a single [35S]methionine-labeled polypeptide.
from extracts of continuously labeled HSV-1-infected cells and did not precipitate any labeled proteins from mock-infected HEp-2 cells, nor did the pre-immunization serum react with any proteins from the continuously labeled infected cells. The polypeptide precipitated from infected cells had the same apparent molecular weight as the major form of Fc-binding gE eluted from affinity columns (2) and also incorporated radiolabel from [14C]glucosamine (data not shown), as does gE.

Because newly synthesized forms of Fc-binding gE exhibit greater electrophoretic mobility than the stable form resulting from post-translational processing (2), we tested the antiserum for its ability to precipitate polypeptides from extracts of pulse-labeled infected cells. These cells were harvested either immediately after a 5-min pulse with [35S]methionine or after varying times of incubation in nonradioactive medium in order to compare the electrophoretic mobilities of transient and stable forms of immunoprecipitable polypeptides. As Fig. 1A shows, only one polypeptide was precipitated from extracts of cells harvested immediately after the pulse, and its apparent molecular weight was about 65,000, compared with a molecular weight of 80,000 for the stable immunoprecipitable forms. Increasing the time of incubation in nonradioactive medium resulted in the disappearance of the 65,000-molecular-weight species and apparent sequential modifications of the immunoreactive pulse-labeled polypeptide to yield multiple diffuse bands of protein with apparent molecular weights of 80,000 to 85,000. The 6-h chase yielded a stable immunoprecipitable polypeptide with an apparent molecular weight of 80,000, which corresponded to the species found in continuously labeled cells and in virions (see below). The stable and transient forms of the polypeptide detected by immunoprecipitation had the same electrophoretic mobilities as similarly stable and transient polypeptides previously identified by their Fc-binding activity; the Fc-binding polypeptides were also shown previously to share amino acid sequences in common and were collectively designated gE (2).

Immunoprecipitation of gE from various cell types. To determine whether HSV-1 induced the synthesis of gE in various species and types of cells, we infected BHK-21, HEL, Vero, and HEp-2 cells with HSV-1 strain HFEM(syn), and the proteins solubilized from each preparation were mixed with anti-gE serum for immunoprecipitation. Figure 2 shows the electropherogram of the extracts and immunoprecipitates obtained from these cells. Although the conditions of infection and labeling were uniform, the amounts of [35S]methionine incorporated into the cells and the amounts of radiolabel in precipitated gE varied among the cell types. Precipitation of extracts from Vero cells consistently yielded the most weakly labeled band of gE. Whether this was due to the presence of smaller amounts of labeled gE in the Vero cells, to a lower specific activity of the gE, or to fewer shared antigenic determinants with the gE made in HEp-2 cells could not be determined by this analysis. A comparison of the electrophoretic mobilities of the stable forms of gE showed that the glycoprotein made in Vero cells migrated slightly faster and the glycoprotein made in BHK-21 cells migrated slightly slower than the gE's from the two human cell types (HEp-2 and HEL cells). Thus, polypeptides antigenically related to gE were synthesized in several kinds of cells from different species and showed similar but not identical electrophoretic mobilities.

Immunoprecipitation of gE induced by various HSV-1 strains. To investigate the possibility of strain variability of gE and to test the specificity of the anti-gE serum further, we performed immunoprecipitation experiments with solubilized proteins from cells infected with five different HSV-1 strains. HEp-2 cells were infected with HSV-1 strains F, HFEM, mP, MP, and 14-012 under uniform conditions of infection, continuous labeling from 4 to 22 h after infection, and preparation of extracts for the reaction with anti-gE. As Fig. 3 shows, polypeptides that were
antigenically related to the gE of HSV-1 strain HFEM(syn) were produced by all strains and exhibited approximately the same electrophoretic mobility. Multiple forms of gE were precipitated from all of the extracts except the extract from HSV-1 strain MP-infected cells, in contrast to the results shown in Fig. 1 and 2. This could be explained by the fact that HSV-1 strains F, HFEM, and MP continue to synthesize viral proteins later in the infectious cycle than strains HFEM(syn) and MP (unpublished data). Consequently, at the time of cell harvest there would have been a greater abundance of newly synthesized forms of gE that had not been processed yet to the most slowly migrating form. Alternatively, HSV-1 strains may differ in the efficiency with which gE is processed.

**Detection of gE in the virion and neutralization of viral infectivity by anti-gE.** We performed two types of experiments to investigate the presence of immunoreactive gE in virions; these were immunoprecipitation experiments and neutralization-of-infectivity experiments. Detergent-solubilized proteins from HSV-1 strain HFEM(syn) virions were mixed with anti-gE or the preimmune serum, and the precipitates obtained were analyzed by electrophoresis along with samples of the virion extract. Figure 4 shows that anti-gE specifically precipitated a single polypeptide whose apparent molecular weight was about 80,000. This polypeptide was a minor component of the virion extract and was not readily detectable unless the gel was overloaded with respect to the other proteins in the extract.

The volume of unfractionated virion extract analyzed in the gel shown in Fig. 4 was only a small proportion of the volume used to obtain the immunoprecipitate (Fig. 4, lane a). Prolonged exposure of the gel (Fig. 4, lanes d and e) did not reveal any polypeptides precipitated by the preimmune serum but did reveal minor additional polypeptides in the anti-gE precipitate. The presence of these polypeptides could reflect the presence of antibodies other than anti-gE in the serum or some proteolytic digestion products of gE or, more likely, the nonspecific entrapment of material in immune complexes.

The anti-gE serum was tested for neutralizing activity. As Fig. 5 shows, the unheated antiserum was capable of neutralizing infectious HSV-1 strain HFEM(syn). However, this activity was entirely complement dependent in that it was heat labile (56°C, 30 min) and could be reconstituted by the addition of guinea pig complement. The complement dependence of this viral neutralization by the serum from the immunized rabbit persisted for several months after multiple immunizations and thus apparently was not solely due to the early or transient complement-
134 PARA, BAUCKE, AND SPEAR

FIG. 5. Effects of untreated and heated (56°C, 30 min) anti-gE and preimmune sera on the infectivity of HSV-1 strain HFEM(syn) virions in the presence and absence of guinea pig complement. The abscissa shows the volume of complement present per milliliter of reaction mixture. Other details of the plaque reduction assay are described in the text.

requiring antibodies elicited shortly after the primary immunization. In addition, when the isolated IgG fraction of the serum was supplemented with complement, it contained a significant amount of the neutralizing activity, if not all of it (data not shown). Finally, the neutralizing activity was not due to anticellular antibodies because adsorption of anti-gE with uninfected cells failed to reduce its activity.

Inhibition of 125I-labeled IgG binding by F(ab')2 fragments from anti-gE. Preincubation of F(ab')2 fragments from anti-HSV serum (but not normal serum) with HSV-infected cells reportedly inhibits subsequent 125I-labeled IgG binding to these cells (1, 18). This is presumably due to the presence in the anti-HSV serum of antibodies which are directed against the virally induced Fc receptor or otherwise sterically hinder the binding of the Fc portion of 125I-labeled IgG to the Fc receptor.

To help define the relationship between gE and Fc receptors on intact cells, we prepared F(ab')2 fragments from anti-gE immunoglobulins and normal rabbit IgG by pepsin digestion and then tested them for the capacity to inhibit 125I-labeled IgG binding. HSV-1 strain HFEM(syn)-infected HEp-2 cells were incubated for 1 h with varying amounts of F(ab')2 fragments before the addition of 125I-labeled IgG for the usual binding assay. Figure 6 shows the results of two independent experiments in which we used F(ab')2 preparations from two separate bleedings of the control and gE-immunized rabbits. Although 125I-labeled IgG binding was not blocked completely by the anti-gE F(ab')2 fragments in either experiment, both preparations of immune globulin fragments inhibited IgG binding to a much greater extent than normal serum globulin fragments. The apparent difference in inhibitory effect observed in the two experiments could have been due to differences in the preparations of F(ab')2 fragments used or to the fact that different buffers were used to incubate the cells with the fragments and 125I-labeled IgG. It is perhaps significant that 125I-labeled IgG binds to infected cells more efficiently at pH 8.0 than at pH 7.2 (unpublished data) and that experiment 1 (Fig. 6A) was performed with borate-buffered saline (pH 8.0), whereas experiment 2 (Fig. 6B) was done with PBS (pH 7.2).

DISCUSSION

In this report we describe the production of an antiserum to HSV-1 strain HFEM(syn) gE and the use of this antiserum (i) to identify antigenically related but electrophoretically distinct precursor forms of gE in infected HEp-2 cells; (ii) to identify antigenically related gE's in four different cell lines infected with HSV-1 strain HFEM(syn) and in HEp-2 cells infected with five other HSV-1 strains; (iii) to demonstrate the presence of gE in extracts from HSV-1 strain HFEM(syn) virions and complement-dependent neutralization of virion infectivity; and (iv) to demonstrate the inhibitory effect of F(ab')2 fragments of anti-gE antibodies on the binding of normal IgG to Fc receptors on infected cells.

The precursor-product relationship among electrophoretically distinct forms of Fc-binding polypeptides was established previously on the basis of similarities in their proteolytic digestion products and their kinetics of appearance after pulse-labeling (2). We confirmed and extended these findings by demonstrating the antigenic relatedness of the electrophoretically distinct forms of gE. Thus, functionally and antigenically related forms of gE exhibit changes in electrophoretic mobilities that accompany post-translational modifications, as has been reported previously for other HSV-1 glycoproteins (6, 10, 25).

The results of immunoprecipitations performed with extracts from infected cells of different species and from HEp-2 cells infected with different HSV-1 strains suggest that expression of gE is a common feature of HSV-1 infections and that gE itself is probably a viral
gene product. Whether any significance should be attached to the apparent differences in the amounts and electrophoretic mobilities of the labeled gE's precipitated from the different cell types is questionable for the reasons indicated above.

Immunoprecipitation of gE from extracts of purified virions and the neutralization of viral infectivity by anti-gE serum indicate that gE is present in virions and has some antigenic determinants exposed on the surface, even though we cannot be absolutely certain that anti-gE antibodies are entirely responsible for the neutralization. The finding that neutralization depends on the presence of complement is interesting and provides one explanation for the common observation that complement enhances the neutralization of polyspecific sera. It remains to be determined whether it is possible to raise complement-independent neutralizing antibodies specific for gE. Although antibodies capable of precipitating gE have been detected in humans with primary and recurrent HSV infections (M. Hilty, Ohio State University, personal communication), the role of the anti-gE antibodies in host defense remains to be elucidated.

The possibility that gE and the Fc receptor of HSV-infected cells are the same protein has been suggested previously; this suggestion has been based on their common affinity for the Fc region of IgG and their coincident time of appearance after infection (2). More recent studies demonstrating Fc-binding activity on the surfaces of intact virions (22) and our work showing that anti-gE serum can neutralize virion infectivity are consistent with this hypothesis. Most important, the inhibition of the Fc receptor function by the F(ab')2 fragments of anti-gE antibodies further implies that gE and the Fc receptor are the same protein. Other explanations for the results obtained must be considered, however. In particular, the juxtaposition of gE and the Fc receptor (if it were different from gE) on the cell surface could produce results similar to those shown in Fig 6. Definitive proof equating gE and the Fc receptor will require other approaches, such as the demonstration of Fc receptor activity on liposomes containing isolated gE or the simultaneous expression of gE and Fc receptors on cells transformed by incorporation of the isolated gE gene.

ACKNOWLEDGMENTS
Various aspects of this work were supported by grant MV13 from the American Cancer Society and by Public Health Service grants CA 19264 and CA 21776 from the National Institutes of Health. M.F.P. is a Fellow in Cancer Research supported by grant DRG-333 from the Damon Runyon-Walter Winchell Cancer Fund.

LITERATURE CITED


22. Para, M. F., R. B. Baucke, and P. G. Spear. 1980. Immunoglobulin G (Fc)-binding receptors on virions of herpes simplex virus type 1 and transfer of these receptors to the cell surface by infection. J. Virol. 34:512–520.


