

An anti-fusion regulatory protein-1 monoclonal antibody suppresses human parainfluenza virus type 2-induced cell fusion

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Fusion regulatory protein-1 (FRP-1) regulates virus-mediated cell fusion and induces polykaryocyte formation of monocytes without any fusogen. We have recently reported that FRP-1 and the 4F2/CD98 heavy chain are identical molecules. Cell fusion in Newcastle disease virus (NDV)-infected HeLa cells was enhanced when cells were incubated with anti-FRP-1 MAb. Anti-FRP-1 MAbs also induced human immunodeficiency virus gp160-mediated cell fusion. However, HBJ127, an anti-FRP-1/4F2/CD98 MAb that enhanced cell fusion in NDV-infected cells, delayed human parainfluenza virus type 2 (HPIV-2)-induced cell fusion in HeLa cells, although these viruses belong to the same genus *Rubulavirus*. No anti-FRP-1 MAbs enhanced cell

fusion in HPIV-2-infected HeLa cells. Anti-FRP-1 MAbs including HBJ127 showed no effect on virus growth and expression levels of virus-specific polypeptides in HPIV-2-infected HeLa cells, indicating that the delay in cell fusion by an anti-FRP-1 MAb is not due to suppression of virus replication. When HeLa cells were transfected with an expression vector harbouring HPIV-2 HN and F genes, cell fusion was also suppressed by HBJ127, but the effect was weak in comparison with virus-infected cells. These data indicate anti-FRP-1 antibodies not only induce/enhance, but also inhibit/delay virus-induced cell fusion and therefore FRP-1 molecules are multifunctional.

Introduction

Many enveloped viruses including paramyxoviruses and human immunodeficiency virus (HIV) induce syncytia. Syncytium formation is one of the major cytopathic effects of virus-infected cells, and virus infection from cell-to-cell occurs without the production of infectious virus particles. In paramyxoviruses, two kinds of virus glycoproteins, haemagglutinin–neuraminidase (HN) and fusion (F), participate in cell fusion in virus-infected cells. However, cell fusion regulatory mechanisms in host cells are not well understood. We previously reported that anti-L₉₂₉ cell antiserum enhanced syncytium formation in Newcastle disease virus (NDV)-infected L₉₂₉ cells and suggested that factor(s) are present on the cell surface of host cells capable of regulating virus-mediated cell fusion (Ito *et al.*, 1987). We have isolated

monoclonal antibodies (MAbs) which enhance cell fusion in NDV-infected HeLa cells (Ito *et al.*, 1992). These MAbs recognized gp80 and gp135 on the surface of HeLa cells. These molecules were considered to have the capability of regulating NDV-induced cell fusion and thus were designated fusion regulatory protein (FRP)-1 (gp80) and FRP-2 (gp135). The U2ME-7 cell line is a CD4⁺ U937 cell line transfected with the HIV *gp160* gene; the expression of gp160 is induced by cadmium chloride. Even after induction of HIV gp160, U2ME-7 cells did not form syncytia (Koga *et al.*, 1990). Anti-FRP-1 MAb or anti-FRP-2 MAb induced polykaryocyte formation in Cd⁺U2ME-7 cells (U2ME-7 cells treated with cadmium chloride) (Ohta *et al.*, 1994). FRP-1 was expressed selectively on monocytes. Anti-FRP-1 MAbs induced cell aggregation and multinucleated giant cell formation in monocytes (Tabata *et al.*, 1994). Moreover, induction of HIV-mediated cell fusion or cell aggregation and polykaryocyte formation of monocytes by anti-FRP-1 MAb was found to be related to the integrin system (Ohta *et al.*, 1994; Tabata *et al.*, 1994). FRP-1 and FRP-

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2 were identified as the 4F2/CD98 heavy chain and the $\alpha 3$ subunit of integrin, respectively, by immunological, amino acid sequencing and gene cloning methods (Ohta *et al.*, 1994; Ohgimoto *et al.*, 1995).

Anti-FRP-1 MAbs enhanced virus-mediated cell fusion and induced fusion of monocytes, but no anti-FRP-1 MAb was found to show inhibition/delay of cell fusion. In this study, we investigated whether anti-FRP-1 MAbs could enhance cell fusion in human parainfluenza virus type 2 (HPIV-2)-infected HeLa cells, as they do in NDV-infected HeLa cells. However, cell fusion in HPIV-2-infected HeLa cells was delayed when cells were incubated with HBJ127, an anti-FRP-1 MAb that enhanced cell fusion in NDV-infected HeLa cells. There were no anti-FRP-1 MAbs that enhanced cell fusion in HPIV-2-infected HeLa cells. We showed that inhibition of cell fusion by the anti-FRP-1 MAb was not due to low replication of HPIV-2. These results indicate that FRP-1 molecules have multiple functions in the cell fusion process.

Methods

■ **Cells and viruses.** HeLa and Vero cells were used in this study. The cells were cultured in Eagle's MEM supplemented with 5% foetal calf serum. The viruses used in this study were the HPIV-2 Toshiba strain and the NDV Sato strain.

■ **MAbs.** Seven anti-FRP-1/CD98/4F2 MAbs were used. Anti-FRP-1 MAbs [4-5-1 (IgG1) and 6-1-13 (IgG1)] were previously described (Ito *et al.*, 1992). Anti-CD98/4F2 MAbs HBJ127 (IgG1), 4F2 (IgG1) and H227 (IgG1) were kindly supplied by Y. Hashimoto (Tohoku University, Sendai, Japan), B. F. Haynes (Duke University, Durham, N.C., USA) and M. Nakao (Kurume University, Kurume, Japan), respectively. Anti-FRP-1 MAbs 38-2-2 (IgG2a) and 18-1-2 were newly made in our laboratory. Anti-HPIV-4a NP MAb (IgG1) was used as control antibody.

■ **Plaque assay.** HeLa cells infected with HPIV-2 were incubated at 37 °C with or without each anti-FRP-1 MAb and culture fluid was harvested at 12 h to 24 h post-infection (p.i.). The 10-fold diluted culture fluids were added to Vero cells on 12-well plates, incubated for 1 h at 37 °C and overlaid with MEM containing 0.6% SEA KEM agarose. Plaques were visualized after 3 days of incubation at 37 °C by staining with neutral red.

■ **ELISA.** HeLa cells, cultured in 96-well plates, were fixed with 3% paraformaldehyde for 20 min. They were permeabilized with PBS and Tween-20 for 20 min to detect the cytoplasmic virus NP protein. Then they were incubated with various mouse IgG2a MAbs against HPIV-2 (HN, F or NP) for 1 h and reacted with peroxidase-conjugated anti-mouse IgG2a rat serum.

■ **Flow cytometry.** HeLa cells were incubated with anti-HPIV-2 HN (108S1, IgG2a) or F (119-1A, IgG2a) MAbs (Tsurudome *et al.*, 1989) at 4 °C for 1 h and washed twice with PBS. Subsequently, the cells were reacted with fluorescein isothiocyanate (FITC)-conjugated anti-mouse IgG2a rat MAb (Serotec) at 4 °C for 30 min and washed twice. Immunofluorescence-stained cells were analysed on a FACScan (Becton Dickinson).

■ **Induction of cell fusion in HeLa cells by transfection with recombinant plasmids containing HN and F genes.** The expression vector pcDL-SR α 296 containing HPIV-2 HN and F gene cDNAs (pSR-HN, pSR-F) was used as described previously (Yuasa *et al.*, 1995).

pcDL-SR α 296 is a plasmid vector developed for expressing proteins in eukaryotic cells. It contains a poly(A) signal and two promoters, the SV40 early promoter and the R-U5 sequence of the HTLV-1 LTR (Takebe *et al.*, 1988). The pSR-HN and pSR-F vectors were transfected into HeLa cells by the calcium phosphate method using a kit (CellPfect; Pharmacia) and cell fusion was induced 24 h post-transfection as reported previously (Yuasa *et al.*, 1995; Tsurudome *et al.*, 1995).

Results

Inhibition of HPIV-2-induced cell fusion and enhancement of NDV-induced cell fusion by MAb HBJ127

HeLa cells (approximately 10^5 cells per well in a 96-multiwell dish) were infected with NDV at an m.o.i. of 1. The cells were incubated with MEM supplemented with 5% foetal calf serum and each anti-FRP-1/CD98/4F2 MAb (total seven MAbs, 5 μ g/ml) was added to the culture fluid at the same time. At 15 h p.i., the cells were stained with Giemsa and observed by microscopy. The addition of anti-FRP-1/CD98 MAbs 4-5-1, 6-1-13 and HBJ127 to the culture fluids of NDV-infected HeLa cells gave rise to giant polykaryocytes, while only slight cell fusion was observed in the presence of the other three MAbs (Table 1). On the other hand, no cell fusion was found in NDV-infected HeLa cells at 15 h p.i. in the presence of control MAb or anti-FRP-1/CD98 MAb 18-1-2, although at 24 h p.i. cell fusion could be seen.

Subsequently, the effects of anti-FRP-1/CD98 MAbs on HPIV-2-induced cell fusion were investigated. HeLa cells were infected with HPIV-2 at an m.o.i. of 1 and then incubated with each anti-FRP-1/CD98/4F2 MAb. At 18 h p.i., almost all HPIV-2-infected HeLa cells formed multinucleated giant cells with control antibody. Surprisingly, cell fusion of HPIV-2-

Table 1. Biological activities of anti-FRP-1 MAbs on cell fusion in virus-infected HeLa cells

MAb	Fusion index*	
	NDV-infected HeLa cells†	HPIV-2-infected HeLa cells‡
Control antibody	—	++++
4-5-1	++++	++++
6-1-13	++++	++++
4F2	+	++++
HBJ127	++++	+
H227	+	++++
38-2-2	+	++++
18-1-2	—	++++

* Polykaryocytosis: —, < 3%; +, 3–25%; ++, 25–50%; + + +, 50–75%; + + + +, 75–100%.

† Giemsa-stained at 15 h p.i.

‡ Giemsa-stained at 18 h p.i.

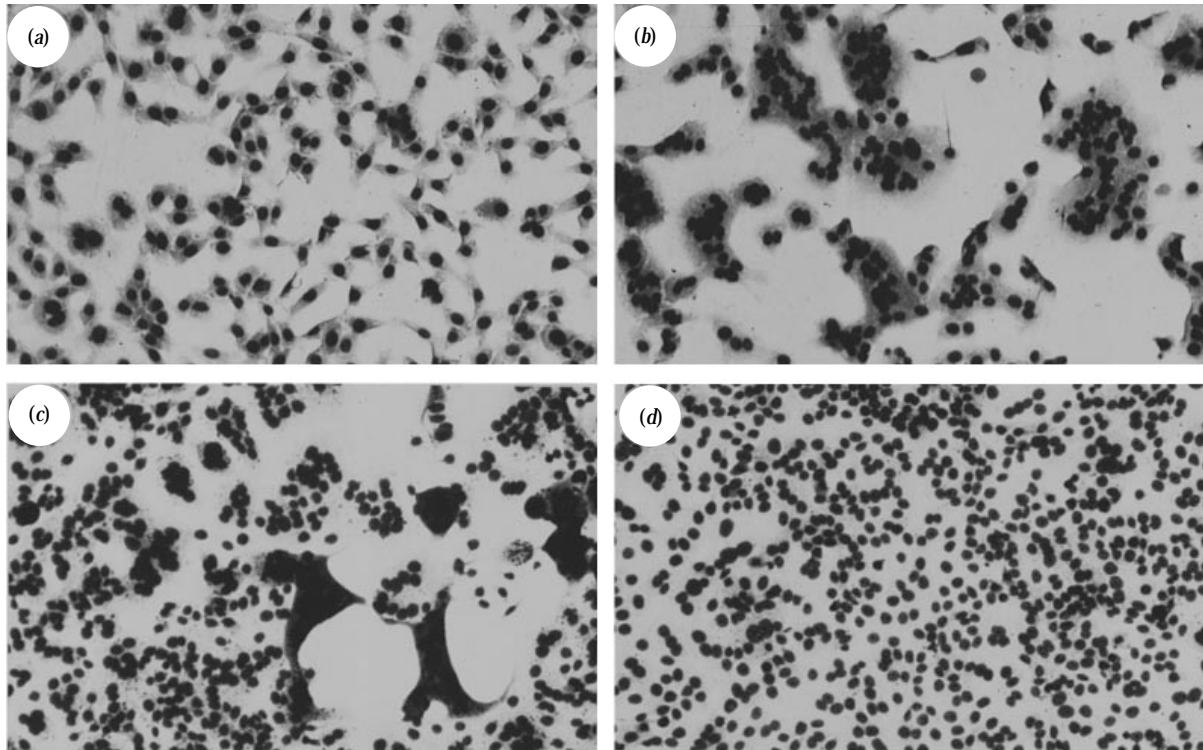


Fig. 1. Effect of HBJ127, an anti-FRP-1/4F2/CD98 MAb on cell fusion in NDV- or HPIV-2-infected HeLa cells. HeLa cells infected with NDV (a, b) or HPIV-2 (c, d) were cultured in the presence of control antibody (a, c) or HBJ127 (b, d). (a, b) NDV-infected HeLa cells were stained with Giemsa staining solution at 15 h p.i. (c, d) HPIV-2-infected HeLa cells were stained at 18 h p.i.

infected HeLa cells was suppressed by MAb HBJ127, which enhanced polykaryocyte formation in NDV-infected HeLa cells (Table 1; Fig. 1). Another six anti-FRP-1 MAbs showed neither enhancing nor suppressing effects on cell fusion in HPIV-2-infected HeLa cells.

Kinetics of polykaryocyte formation in HPIV-2-infected HeLa cells in the presence of anti-FRP-1 MAbs

A kinetic study of polykaryocyte formation in HPIV-2-infected HeLa cells was carried out (Fig. 2). HeLa cells were infected with HPIV-2 and incubated in MEM containing 5% foetal calf serum with MAb 4-5-1, HBJ127, 38-2-2 or control antibody. At appropriate times, the cells were stained with Giemsa and examined for morphological alterations including cell fusion. At 12 h p.i., multinucleated giant cells were observed in the presence of control antibody, MAb 38-2-2 and 4-5-1, but never in the presence of HBJ127. Almost all cells formed syncytia in the presence of control antibody at 18 h p.i. On the other hand, in the presence of HBJ127, little fusion was seen until 18 h p.i.; almost all cells formed polykaryocytes by 24 h p.i. In short, polykaryocyte formation in HPIV-2-infected HeLa cells was delayed by the addition of the anti-FRP-1/CD98 MAb HBJ127. Anti-FRP-1 MAbs 38-2-2 and 4-5-1 showed no effect on cell fusion of HPIV-2-infected HeLa cells.

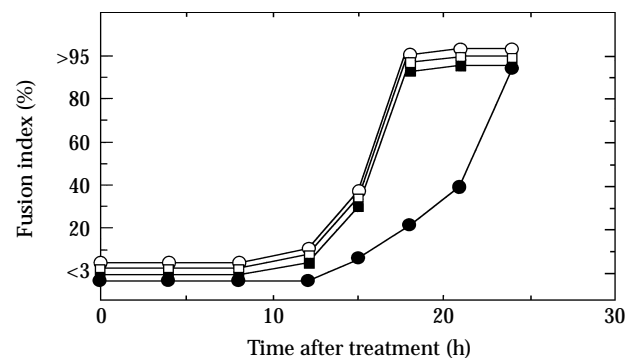


Fig. 2. Kinetic study of cell fusion. HPIV-2-infected HeLa cells were incubated with anti-FRP-1/4F2/CD98 MAb HBJ127 (●), 4-5-1 (■), 38-2-2 (○), or control antibody (□). At the times indicated, the cells were stained with Giemsa staining solution and observed under a microscope. To estimate the degree of cell fusion, nuclei or cells within multinucleated giant cells (> 3 nuclei/cell) were counted. The fusion index was calculated using the formula: fusion index (%) = (total number of nuclei within giant cells)/(total number of nuclei counted) × 100.

Virus growth in HPIV-2-infected HeLa cells in the presence of anti-FRP-1 MAbs

Subsequently, we examined virus growth and virus-specific polypeptide expression in HPIV-2-infected HeLa cells when the cells were incubated with each anti-FRP-1 MAb including

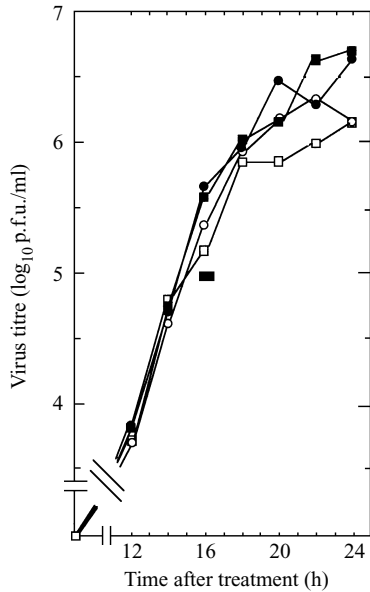


Fig. 3. Kinetic study of HPIV-2 growth. HPIV-2-infected HeLa cells in 6-well plates were incubated with or without anti-FRP-1/4F2/CD98 MAb in MEM plus 5% foetal calf serum. Culture fluids were harvested from 12 h p.i. to 24 h p.i. The plaque assay was performed as indicated (see Methods); ●, HBJ127; ■, 4-5-1; ○, 38-2-2; □, control antibody.

HBJ127, in order to investigate the mechanism by which the MAbs delayed HPIV-2-induced cell fusion. HeLa cells were infected with HPIV-2 at an m.o.i. of 1 and then incubated with

5% foetal calf serum together with MAb 4-5-1, HBJ127, 38-2-2 or control antibody. Culture fluids were harvested from 12 h p.i. to 24 h p.i. As shown in Fig. 3, there was little difference in virus yields between the cells treated with control antibody and anti-FRP-1 MAbs. Intriguingly, HBJ127 did not suppress virus growth in HPIV-2-infected HeLa cells, indicating that the delay of cell fusion by anti-FRP-1 MAb was not due to suppression of virus growth.

HPIV-2-specific polypeptide expression in the presence of anti-FRP-1 MAb

HeLa cells infected with HPIV-2 at an m.o.i. of 1 in 96-well plates were incubated with each anti-FRP-1 MAb or control antibody. At appropriate times, the cultures were examined for the expression of HPIV-2-specific polypeptides by ELISA. The expression levels of the viral glycoproteins HN and F correlated with that of polykaryocyte formation in control antibody-treated HPIV-2-infected HeLa cells (Figs 2 and 4). There was not much difference in expression levels of both HN and F between the cultures treated with control antibody or each anti-FRP-1 MAb. Anti-FRP-1 MAbs including HBJ127 had little effect on the expression of viral glycoproteins in HPIV-2-infected HeLa cells. Also, the expression of the viral cytoplasmic protein, NP, was not affected by anti-FRP-1 MAbs. The results indicated that delay of cell fusion in HPIV-2-infected cells by HBJ127 was not due to a direct effect of

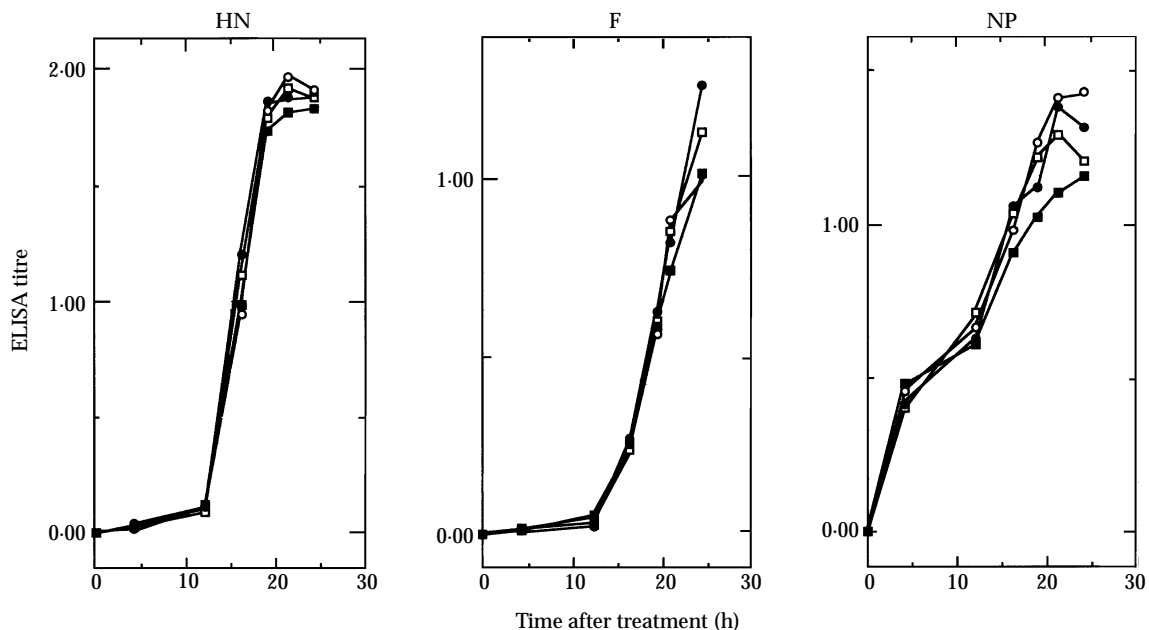


Fig. 4. Kinetic study of the expression levels of HN, F and NP proteins in HPIV-2-infected HeLa cells in the absence or presence of anti-FRP-1 MAbs. HPIV-2-infected HeLa cells were incubated in the presence of HBJ127 (●), 4-5-1 (■), 6-1-13 (○) or control antibody (□) [mouse IgG1 (all)]. At appropriate times, the cultures were fixed with 3% paraformaldehyde for 20 min. In case of detection of cytoplasmic protein (NP), cells were permeabilized with PBS-Tween-20 for 20 min. Subsequently, they were incubated with anti-HPIV-2 HN (108S1), F (119-1A) or NP (366-1) MAb (mouse IgG2a) for 1 h and washed three times. They were then reacted with peroxidase-conjugated anti-mouse IgG2a rat serum for 1 h, washed three times and the cultures were examined by ELISA.

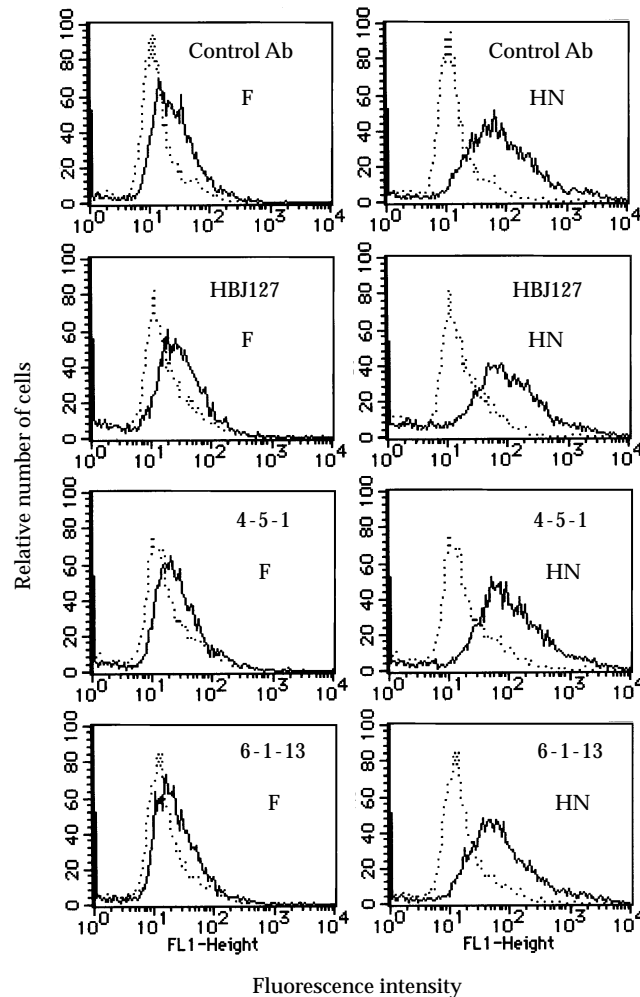


Fig. 5. The expression of HN and F proteins on the cell surface of HPIV-2-infected HeLa cells in the absence or presence of anti-FRP-1 MAbs. HPIV-2-infected HeLa cells were incubated in the presence of HBJ127, 4-5-1, 6-1-13 or control antibody (mouse IgG1). At 18 h p.i., cells were incubated with anti-HPIV-2 HN (MAb 108S1, mouse IgG2a) or F (MAb 119-1A, mouse IgG2a) at 4 °C for 1 h and washed twice with PBS. The cells were then reacted with FITC-conjugated anti-mouse IgG2a rat MAb (Serotec) at 4 °C for 30 min and washed twice. Immunofluorescence-stained cells were analysed on a FACScan.

HBJ127 on virus-specific polypeptide expression, but to a secondary effect via cellular factor(s) modified by stimulation of the FRP-1 molecule.

Expression of HN and F proteins on the cell surface of HPIV-2-infected HeLa cells in the presence of anti-FRP-1 MAbs

Virus-induced cell fusion is mediated by interaction between virus glycoproteins and host proteins on the cell surface. One of the possible mechanisms by which cell fusion of HPIV-2-infected HeLa cells was suppressed by anti-FRP-1 MAb is suppression of HN and/or F protein expression on the cell surface. Thus, the effect of anti-FRP-1 MAbs on expression of HN and F proteins was investigated. HeLa cells were infected with HPIV-2 and then incubated with MAb 4-5-1, HBJ127, 6-1-13 or control antibody at 37 °C. At 18 h p.i., the cells were suspended in PBS and incubated with anti-HPIV-2 HN or F MAb. The cells were reacted with FITC-conjugated anti-mouse IgG2a rat MAb and immunofluorescence-stained cells were analysed on a FACScan. As shown in Fig. 5, there

was little difference between the effect of anti-FRP-1 MAbs and control antibody on the expression of HN and F proteins at the cell surface. Therefore, the inhibition of cell fusion of HPIV-2-infected cells by HBJ127 is not due to low expression of HN and/or F proteins on the cell surface. Also, there was little difference in the expression of NP protein between HPIV-2-infected HeLa cells treated with anti-FRP-1 MAbs and control antibody (data not shown).

Effects of anti-FRP-1 MAbs on cell fusion in HeLa cells co-expressing HN and F proteins

HPIV-2 HN and F proteins were expressed in HeLa cells using the expression vector pcDL-SR α 296 containing cDNAs encoding each protein (pSR-HN or pSR-F), which was constructed from cDNA fragments previously prepared for nucleotide sequencing of the glycoprotein genes (Kawano *et al.*, 1990a, b). When HeLa cells were transfected with either pSR-HN or pSR-F, cell fusion was not observed. Cell fusion similar to that in virus-infected cells was seen when HeLa cells were cotransfected with pSR-HN and pSR-F (Yuasa *et al.*,

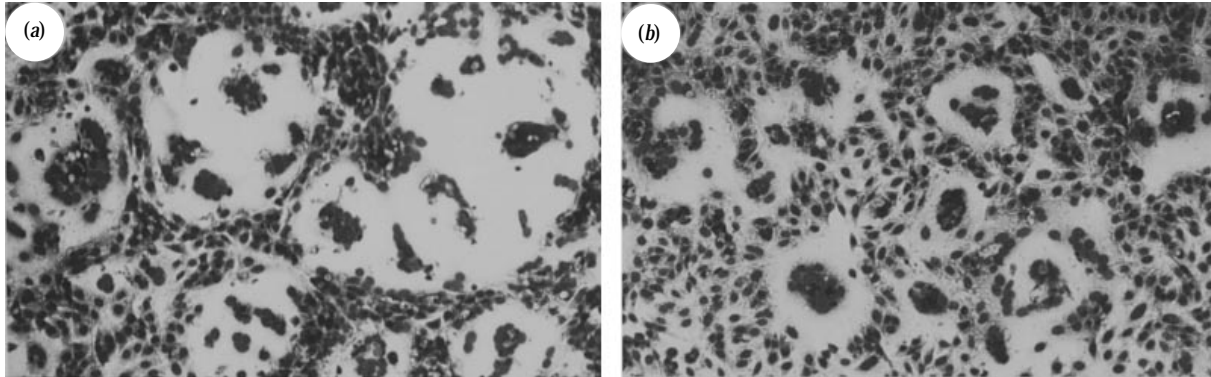


Fig. 6. Effect of HBJ127 on cell fusion in HeLa cells co-expressing HPIV-2 HN and F proteins after transfection with recombinant plasmids. HeLa cells on 24-well plates were incubated with MEM plus 10% foetal calf serum. Then 0.2 µg of HPIV-2 pSR-HN and -F were added to HeLa cells by the calcium phosphate method. After 4 h of incubation at 37 °C, cells were treated with 15% glycerol in HEPES-buffered saline (50 mM HEPES, 0.75 mM sodium phosphate, 140 mM NaCl) at room temperature for 3 min, and incubated in MEM plus 10% foetal calf serum at 37 °C with control antibody (a) or an anti-FRP-1 MAb HBJ127 (b). After 20 h incubation, the cells were stained with Giemsa staining solution and observed under a microscope.

1995). Consequently, the effects of MAb HBJ127, 4-5-1 and 6-1-13 on cell fusion in both HN and F protein-expressing HeLa cells were investigated. A decrease in fused cells was observed in the presence of HBJ127 (Fig. 6), while there was no difference in polykaryocyte formation in the presence of MAb 4-5-1, 6-1-13 and control antibody (data not shown). This result is consistent with that of HPIV-2-infected HeLa cells. However, the level of suppression of cell fusion by HBJ127 was lower with the expression system than with virus infection. Indeed, a fivefold higher concentration of HBJ127 was required to show a suppressive effect on cell fusion in the HN and F expressing cells compared with virus-infected cells.

Discussion

FRP-1/4F2/CD98 is a cell surface protein, which is expressed in all established cells derived from humans and monkeys (Teixeira *et al.*, 1987; Tabata *et al.*, 1994). We have recently reported that FRP-1 and the 4F2/CD98 heavy chain are identical molecules (Ohgimoto *et al.*, 1995). However, the function of the 4F2/CD98 molecule is not well understood. Our previous reports showed that (i) anti-FRP-1 MAbs enhanced cell fusion in NDV-infected cells (Ito *et al.*, 1992; Ohgimoto *et al.*, 1995); (ii) anti-FRP-1 MAbs induced HIV gp160-mediated cell fusion (Ohta *et al.*, 1994; Ohgimoto *et al.*, 1995); and (iii) anti-FRP-1 MAbs induced homotypic cell aggregation and cell fusion of peripheral blood monocytes (Tabata *et al.*, 1994). In this work, we reported that an anti-FRP-1 MAb, HBJ127, delayed cell fusion in HPIV-2-infected HeLa cells. HBJ127 is one of the anti-FRP-1/4F2/CD98 MAbs that enhanced cell fusion in NDV-infected HeLa cells and induced HIV gp160-mediated cell fusion. However, another six anti-FRP-1 MAbs showed neither enhancing nor suppressing effects on cell fusion in HPIV-2-infected HeLa cells. Thus, FRP-1 molecules showed opposite reactions in cell fusion between

HPIV-2-infected cells and NDV-infected cells, although both viruses belong to the same genus *Rubulavirus*.

We examined the effects of anti-FRP-1 MAbs including HBJ127 on virus growth and expression levels of virus-specific polypeptides in HPIV-2-infected HeLa cells, in order to determine the mechanism by which HBJ127 delayed HPIV-2-induced cell fusion. HBJ127 and other anti-FRP-1 MAbs had little effect on virus growth in HPIV-2-infected HeLa cells or the expression levels of virus glycoproteins and NP protein in these cells. These results indicate that the delay in cell fusion in HPIV-2-infected cells by HBJ127 is not due to a direct effect of HBJ127 on HPIV-2 replication, but to a secondary effect via cellular factor(s) modified by the stimulated FRP-1 molecule.

Both HN and F glycoproteins on the cell surface are required for cell fusion of paramyxoviruses (Ebata *et al.*, 1991; Morrison *et al.*, 1991; Hu *et al.*, 1992). Neither HBJ127, 4-5-1 nor 6-1-13 had any influence on the expression of the virus glycoproteins HN and F in HPIV-2-infected HeLa cells. HBJ127 also suppressed cell fusion in HeLa cells that transiently coexpressed HPIV-2 HN and F glycoproteins. These results indicate that FRP-1 interferes little with the virus life cycle in HPIV-2-infected HeLa cells. The time-course of virus growth and expression of virus-specific polypeptides, and expression of HN and F proteins on the cell surface, were not influenced by HBJ127, as found with the other anti-FRP-1 MAbs.

As previously reported (Ohgimoto *et al.*, 1995), L929 cells constitutively expressing human FRP-1/CD98 (L929/CD98H cells) were established. When L929/CD98H cells were infected with NDV, cell fusion was not induced in the absence of anti-FRP-1 MAb. When NDV-infected L929/CD98H cells were incubated in the presence of anti-FRP-1 MAbs 4-5-1 or HBJ127, multinucleated giant cells were induced (Ohgimoto *et al.*, 1995; unpublished data). Thus, it was concluded that anti-FRP-1 MAbs activate the FRP-1 molecule, which can transduce the cell fusion-enhancing signal into NDV-infected cells.

Expression of human FRP-1/4F2/CD98 cDNA in murine L₉₂₉ cells made the cells susceptible to the cell fusion-activating activity of anti-FRP-1 MAb on infection with NDV. There was no anti-FRP-1 MAb that showed suppression/inhibition of cell fusion. Hence, it was not clear whether FRP-1 had only inducing/enhancing activity on membrane fusion. The present work indicates that FRP-1 molecules transduce a cell fusion-suppressing signal into HPIV-2-infected cells, indicating that stimulation of FRP-1 molecules transduces not only a cell fusion-enhancing signal but also a suppressing signal. However, it is not clear at present why FRP-1 molecules have opposite effects on membrane fusion in HPIV-2-infected cells and NDV-infected cells, though they belong to the same genus.

In a HPIV-2 glycoprotein expression system the effect of anti-FRP-1 MAbs was the same as in HPIV-2-infected cells; that is, cell fusion of HeLa cells transiently co-expressing HPIV-2 HN and F proteins was suppressed by HBJ127. However, the effect on the glycoprotein expression system was weaker than that on the virus infection system. We constructed recombinant pcDL-SR α 296 plasmids encoding either the HN protein or the F protein of NDV. When the HN and F proteins were co-expressed in HeLa cells, cell fusion was observed (unpublished data). In this NDV expression system, however, there was no difference in cell fusion without or with the anti-FRP-1 MAbs HBJ127, 4-5-1 or 6-1-13 that had markedly enhanced cell fusion in NDV-infected HeLa cells. One possibility is that another virus-specific protein(s) (for example, the M protein) might participate in the fusion regulatory system via the FRP-1 molecule in paramyxovirus-infected cells.

In conclusion, one (HBJ127) of the anti-FRP-1 MAbs delayed cell fusion induced by HPIV-2. Virus growth, synthesis of virus-specific polypeptides and expression of virus glycoproteins on the cell surface were not suppressed by anti-FRP MAb. HBJ127 had an opposite effect on cell fusion in HPIV-2-infected cells compared to NDV-infected cells, although they belonged to the same genus *Rubulavirus*. The present data indicate that FRP-1 regulates virus-induced cell fusion and may enhance/induce or suppress/inhibit cell fusion depending on the virus-cell system.

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