Recently, we have demonstrated that human (h) glioma cell lines express large number of receptors (R) for interleukin 13 (IL13) (Debinski, W., Obiri, N. I., Powers, S. K., Pastan, I., and Puri, R. K. (1995) Clin. Cancer Res. 1, 1253–1258). These cells are extremely sensitive to a chimeric protein composed of hIL13 and a derivative of Pseudomonas exotoxin (PE), PE38QQR. We have found that the cytotoxicity of hIL13-PE38QQR was blocked by hIL4 but not by hIL4 on the U-251 MG and U-373 MG cells, contrary to what was observed on several adenocarcinoma cell lines. In the present study, we further explored interactions between receptor for IL13 and IL4 on glioma cells. Established human glioma cell lines, such as DBTRG MG, Hs 683, U-87 MG, SNB-19, and A-172, are very susceptible to hIL13-PE38QQR, and the action of the chimeric toxin is not blocked by hIL4 on all these cells either. Also, hIL4 is not a competitor for 125I-hIL4 binding sites on glioma cells. Of interest, a corresponding hIL13-based chimeric toxin, hIL4-PE38QQR, is poorly active or not active on all the tested glioma cell lines. When active, however, hIL4 toxin action was blocked by hIL13. hIL13 is a competitor for 125I-hIL4 binding in a competitive binding assay on glioma cells. hIL13 and hIL4 did not affect the growth of the tested glioma cell lines. Human glioblastoma multiforme explant cells exhibited similar responses to the chimeric toxins and interleukins when compared with that found in established glioma cultures. Our results suggest that the hIL13R on glioma cells is expressed in one predominant form, the form that does not interact with IL4. Thus, this type of hIL13R is apparently different from the one demonstrated previously on several adenocarcinoma cell lines.

Chimeric toxic fusion proteins composed of targeting ligands and bacterial toxins, such as Pseudomonas exotoxin (PE), are rationally designed promising compounds to be used in cancer treatment (1). Such chimeric toxins are in the initial steps of preclinical and clinical evaluation, and prominent antitumor activities were observed (2–4). The patients with relapsed brain tumors in particular appear to be very responsive to chimeric toxins (3). PE is a multidomain/multifunctional globular protein of Mr 66,000 (5, 6). Domain Ia of PE is the α2-macroglobulin receptor binding domain (7). Domain II must be cleaved by furin (8) in order to activate the toxin and enable the active portion of the toxin to translocate into the cytosol (9). Domain III of PE contains the ADP-ribosylation activity (10). This domain inactivates elongation factor 2 that leads to cell death.

Cancer cells of solid tumor origins express receptors for interleukins, such as interleukin 4 (IL4), a hemopoietic growth factor, and these receptors constitute an attractive target for anticancer therapy using chimeric toxins (4, 11–13). We have recently shown the presence of a common internalized receptor for hIL4 and hIL13 on a series of human adenocarcinoma cell lines (14). These cell lines are killed potently by chimeric toxins composed of hIL13 or hIL4 and a derivative of PE, PE38QQR. hIL13 and hIL4 blocked reciprocally the cytotoxicities of their respective chimeric toxins. We hypothesized that the common receptor for the two cytokines on the studied adenocarcinoma cells is composed of the main 140-kDa subunit of the hIL4R (15, 16) and a 70-kDa hIL13-binding subunit (17). This is because (i) a chimeric toxin must be internalized in a process of receptor-mediated endocytosis in order to allow a proper toxin processing and intracellular routing that results in cell death (1), and (ii) the 140-kDa hIL4R has been shown to be the subunit of hIL4R that internalizes in response to hIL4 binding (16). More recently, we have found a significant overexpression of hIL13R on human glioma cells, and the glioma cells are extremely sensitive to hIL13-PE38QQR (18). Of interest, hIL4 did not block the action of hIL13-PE38QQR on the first two tested glioma cell lines unlike on solid tumor cell lines of peripheral origins (14, 18). These findings raised a possibility of the presence of hIL13R that does not interact with IL4 and is overexpressed on some glioma cells. On the other hand, several recent reports suggested a pattern for IL13- and IL4R commonality in which cells that do bind IL13 should bind IL4, and IL13 binding is always fully competed for by IL4 (19–21).

In this study, we have further examined interactions between hIL13R and hIL4R in human glioma cells. We used five more established human glioma cell lines and, for the first time, cells of a human glioblastoma multiforme explant, and tested the cytotoxicities of chimeric toxins and responses to hIL13 and hIL4. Our results indicate that one predominant form of hIL13R is overexpressed on glioma cells. These results should be helpful in understanding the biology of the interleukin receptors and may be important in designing therapeutic strategies that target them.
and finally resuspended in RPMI-1640/25 mM HEPES with L-glutamine for 10 min. The pellet was washed one more time with the same solution. Cell lines were excised, and the remaining tissue was minced using a scalpel. The cytotoxic activities of chimeric toxins and antiproliferative activity of ILs were tested on several brain tumor cell lines, such as U-373 MG, DBTTRG MG, A-172, HS 683, U-251 MG, and SW-1088. The activity of cell lines were obtained from the ATCC, and they were maintained under conditions recommended by the ATCC. The SW-1088 cell line was a gift of Dr. J. Connor (Pennsylvania State University College of Medicine).

Glioma Explant Cells Preparation—Pathology-proven surgical specimen of glioblastoma multiforme was collected and transferred to the laboratory under sterile conditions. Peripheral and necrotic tissues were excised, and the remaining tissue was minced using a scalpel. Tumor tissue was incubated in a mixture composed of collagen types II and IV, Dispase, and NuSerum/Dulbecco’s modified Eagle’s medium, at 37°C with constant shaking for 45 min. Cell suspension was then passed through gauze and washed first with Hanks’ balanced salt solution and then with phosphate-buffered saline (Ca²⁺, Mg²⁺-free). Cells were then layered on the Ficoll-Paque and centrifuged at 400 g at 18–20°C for 35 min. The isolated cells were resuspended in 3 ml of media. Various concentrations of the chimeric toxins. The cytotoxic activities of hIL13-PE38QQR was specific as it acted on glioma cell lines and human glioma (G2) explant cells and failed to inhibit this cytotoxicity by hIL4. hIL13-PE38QQR was added at a concentration of 1.0 µg/ml. Three different batches of rhIL4 showed the same effect. The dashed line shows 50% of the difference between the background and control MTS conversion that was recorded at A₅₇₀ nm. hIL13-PE38QQR, ○, hIL4.

To evaluate the effect of interleukins on cell proliferation, the assays were performed as follows. 1 x 10⁶ cells per well were plated in a 96-well tissue culture plate in 200 µl of 0.5% fetal bovine serum-containing media, and the interleukins were added 20 h following cell plating. For 7- or 5-day incubation with the interleukins, MTS/PMS was added to the cells for 6 h, and the assay was performed as described above for the chimeric toxins. Competitive Binding Assay—rhIL3 and rhL were both produced in-house were labeled with 125I (Amersham Corp.) by using the IODogen reagent (Pierce) according to the manufacturer’s instructions. The specific activities of radiolabeled cytokines were estimated to be between 20 and 100 µCi/µg protein for 125I-hIL13 and 179 µCi/µg protein for 125I-hL14. Binding experiments were performed as described previously (17). Typically, 1 x 10⁶ to 1.5 x 10⁶ tumor cells were incubated at 4°C for 2 h with 125I-hIL13 (100–500 pM) or 125I-hL14 (100–500 pM) with or without increasing concentrations (up to 1000 nM) of unlabeled interleukins. The data were analyzed with the LIGAND program (17, 26) to determine receptor number and binding affinity.

RESULTS
To construct the chimeric toxin, the coding region of the IL13 gene was fused to a gene encoding a mutated form of PE, PE38QQR (14). PE38QQR has domain Ia and amino acids 365–380 in Lh deleted, plus the three lysine residues in domain III at positions 590, 606, and 613 are changed to two glutamines and arginine (QQR) (24). The chimeric gene is in the bacterial vector under the control of a bacteriophage T7 late promoter; the protein was expressed in E. coli BL21 (DE3) as described previously (14). hIL4-PE38QQR (4), hIL4-PE4E (12), hIL4, and hIL13 were subcloned into the same expression plasmid and produced as was the hIL13-PE38QQR. hIL13-PE38QQR Is Extremely Cytotoxic to Both Established Glioma Cell Lines and Glioblastoma Multiforme Explant Cells.—We tested the A-172, DBTTRG MG, and HS-683 established human glioma cell lines and, for the first time, glioma explant cells (G2) to determine and/or confirm if hIL13-PE38QQR is cytotoxic to them. All the established glioma cell lines were very responsive with an IC₅₀ (50% inhibitory concentration) of 0.1–5 mg/ml (Fig. 1). Of interest, human glioma explant cells were also extremely sensitive to the action of hIL13 toxin; the IC₅₀ for hIL13-PE38QQR was 0.2 ng/ml (Fig. 1).

The cytotoxic action of hIL13-PE38QQR was specific as it
was blocked by an excess of hIL13 on all cells (18). These data demonstrate that both established glioma cell lines and a primary culture of glioma cells possess hIL13 binding sites and such cells are extremely sensitive to hIL13-PE38QQR chimeric toxin.

hIL4 Does Not Block the Cytotoxicity of hIL13-PE38QQR on Glioma Cell Lines and Glioma Explant Cells—Because hIL13R has been shown to be related to IL4R (14, 17, 25), we explored further the specificity of hIL13-PE38QQR action on the glioma cell lines and G2 explant cells. The cells were treated with hIL13-PE38QQR with or without rhIL4 at a concentration of 1.0 μg/ml. The rhIL4 did not have any blocking action against hIL13-PE38QQR on either the established cultured cells (A-172, Hs 683, and DBTRG MG) or freshly explanted cultured glioma cells, even at a 1000-fold molar excess over the chimeric toxin (Fig. 1). These results indicate that the cell killing by the hIL13 toxin on these cells is independent of the presence of hIL4. The same results were obtained with the U-251 MG, U-373 MG (18), U-87 MG and SNB-192 cell lines.2 Since these data are in contrast to observations made on several adenocarcinoma cells (14), we repeated the cytotoxicity experiments, for example, on Colo 201 human colon adenocarcinoma cell employing a colorimetric assay used in the present study (instead of tritium incorporation in Refs. 12, 14, and 18) and reproduced exactly the same results.2

hIL13 Blocks the Action of hIL4 Toxins on the U-251 MG, DBTRG MG, and A-172 Glioma Cells, and Glioma G2 Explant Cells—To investigate the possibility that hIL13 and IL4 may nevertheless compete, although not reciprocally, for the same binding site on glioma cells, we also treated the cells with hIL4-based recombinant toxin, hIL4-PE38QQR (4) (Fig. 2). It has previously been demonstrated that all tested glioma cell lines express specific 140-kDa hIL4R, as determined by an immunoreactivity of an antibody raised against the protein (13). We found, again unexpectedly, that hIL4-PE38QQR was without any significant specific cytotoxicity to most of these cells (Fig. 2) including the Hs-683 and U-373 MG cells.2 Only the U-251 MG glioma cell line responded relatively well to hIL4-PE38QQR with an IC50 of 10 ng/ml. This cytotoxicity was blocked efficiently by an excess of hIL13 (Fig. 2). Thus, the cytotoxicity of hIL4-PE38QQR is blocked by an excess of hIL13; however, the cytotoxic action of hIL4-PE38QQR is absent on the majority of glioma cell lines and human glioma explant cells.

Since interleukins coupled to PE4E form of the toxin exhibit better cytotoxic activities on cancer cells (e.g. Ref. 12), we treated glioma cells also with hIL4-PE4E. Indeed, we have found higher cytotoxic potency of this chimeric protein when compared with hIL4-PE38QQR on several glioma cells as well as on G2 explant cells (Fig. 3). The IC50 ranged from 10 to 200 ng/ml on U-251 MG, DBTRG MG, A-172, G2 explant (Fig. 3), and U-87 MG2 cells. The cytotoxic action of hIL4-PE4E was blocked by an excess of hIL13 (Fig. 3) in a similar fashion to blocking this cytotoxicity by hIL4.2 The blocking on G2 cells was less than on other cell lines (Fig. 3), and a similar response was seen on SNB-19 cells.2 These results demonstrate that hIL4 and hIL13 have common binding sites on the glioma cell lines and are reminiscent of our previous findings on a series of adenocarcinoma cells (14). However, there is also a profound difference between our current and previous findings, since the commonality is not reciprocal, i.e., only hIL13 is a competitor for the two receptors.

Antiproliferative Effects of hIL13 and hIL4 on Glioma

2 W. Debinski, R. Miner, and R. K. Puri, unpublished results.

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FIG. 2. The cytotoxicity of hIL4-PE38QQR on glioma cells and blocking this cytotoxicity by hIL13. hIL13 was added at a concentration of 1.0 μg/ml. The dashed line shows 50% of the difference between the background and control MTS conversion that was recorded at A490 nm. ●, hIL4-PE38QQR; ○, + hIL13.

FIG. 3. Blocking the cytotoxicity of hIL4-PE4E by hIL13 on glioma cells. hIL13 was added at a concentration of 1.0 μg/ml. The dashed line shows 50% of the difference between the background and control MTS conversion that was recorded at A490 nm. ●, hIL4-PE4E; ○, + hIL13.

FIG. 4. hIL13 and hIL4 do not inhibit proliferation of the U-373 MG and human glioma G2 explant cells. Data represent in most cases the average of quadruplicate experiments. The dashed line shows 50% of the difference between the background and control MTS conversion that was recorded at A490 nm. ●, hIL13; ○, hIL4.
Cells—Despite being competitors for the same binding site on some cancer cells, we have observed differences in hIL13- and hIL4-induced cellular effects (14). Namely protein synthesis was inhibited in A431 epidermoid carcinoma cells in a dose-dependent manner by hIL4, whereas hIL13 had no effect on these cells, even at concentrations as high as 10 μg/ml hIL13 for a 72-h incubation (14). Similarly, hIL13 had no effect on the growth of glioma cells. The U-251 MG, U-373 MG glioma cells (Fig. 4), and G2 explant cells (Fig. 4) were unaffected by the 5-day and/or 1-week treatment with IL13. On all these cells, hIL4 had no activity on their growth either (Fig. 4).  

hIL13 Binding Affinity to A-172 and G2 Explant Cells—It was important to determine whether the hIL13Rs on the established glioma cell line, such as A-172 glioma cells, have different or similar binding affinity for hIL13 compared with the hIL13R that is expressed on freshly isolated cells. To investigate this, we performed competitive binding assays. As shown in Fig. 5A, unlabeled hIL13 competed for the binding of 125I-hIL13 to A-172 cells efficiently (upper panel). The Scatchard plot analysis of displacement experiments (lower panel) revealed one single binding site for hIL13 of intermediate affinity, \( K_d = 1.6 \text{ nM} \). There are 22,600 binding sites for hIL13 on the A-172 cell line. The competition of unlabeled hIL13 for the binding of iodinated ligand (Fig. 5B, upper panel) and the Scatchard analysis performed on G2 explant cells (Fig. 5B, lower panel) have shown similar results to that obtained on A-172 cells. However, the number of binding sites on explant cells is 300,000 per cell with \( K_d \) of 2.4 nM. In another experiment, the estimate of hIL13 binding sites indicated more than 500,000 binding sites per cell.

Thus, there is no difference in affinity of hIL13 to its receptor whether or not cells are permanently cultured or are derived from the primary culture, although the explant cells seem to be considerably more enriched in hIL13 receptors than the established glioma cell cultures.

hIL4 Does Not Compete for Labeled hIL13 Binding Sites but hIL13 Is a Competitor for 125I-hIL4 Binding Sites on Glioma FIG. 6. Cross-competition between hIL13 and hIL4 for the binding sites of labeled interleukins on glioma cells. A-172 glioblastoma cells (1 × 10^6) were incubated with 200 pM 125I-hIL13 (A) or 125I-hIL4 (B) with or without increasing concentrations (up to 100 nM) of unlabeled hIL13 or hIL4. Bound radioactivity was determined as described under “Experimental Procedures.” Data are presented as a mean of % total binding of cells incubated with radiolabeled interleukins only. Total of 125I-hIL13 bound to A-172 cells was 8699 ± 11 (cpm ± S.D.), and total bound 125I-hIL4 was 5789 ± 185 (cpm ± S.D.). The experiments were performed in duplicate. Bars represent S.D. when larger than symbol. ●, IL-4; ■, IL-13.
Cells—The first step in a chimeric toxin action is the binding to a specific internalized receptor. Since hIL4 does not neutralize the cytotoxic activity of hIL13-PE38QQR on glioma cells, we performed standard competition experiments at 4 °C using radiolabeled ligands. As seen in Fig. 6A, hIL13 displaced labeled hIL13 very efficiently on A-172 glioma cells. However, hIL4 did not compete for the binding of 125I-hIL13 at all at up to 100 nM of the competitor. On the other hand, as shown above (Figs. 2 and 3), hIL13 blocked the cytotoxic actions of both hIL4-PE38QQR and hIL4-PE4E on glioma cells. Therefore, we performed a reverse competition assay and found that either interleukin was a competitor for 125I-hIL4 binding sites (Fig. 6B).

Thus, the results of binding experiments suggest that the nonreciprocal interference of interleukins with the cytotoxic activities of their respective chimeric toxins on glioma cells is due to the nonreciprocal interference with the binding to the interleukin receptors.

hIL13 Is Not a Competitor for 125I-hIL4 Binding Sites on Cells Transfected with the 140-kDa hIL4R Receptor—We have shown that hIL13 blocks the cytotoxicities of hIL4-based chimeric toxins and competes for the binding sites of 125I-hIL4 on glioma cells. The 140-kDa hIL4R chain is believed to be a principal hIL4 binding protein. Therefore, we used cells transfected with the hIL4R (CTLL-hIL4R, Ref. 15) and performed competition binding assays. We have found that hIL13, unlike hIL4, does not compete for the 125I-hIL4 binding sites on CTLL-hIL4R cells (Fig. 7). This result was not unexpected. In similar experiments with the hIL4R transgenes, hIL13 did not compete for labeled hIL4 binding sites (e.g. Ref. 25). On the other hand, hIL13 is a competitor for 125I-hIL4 cross-linking to the 140-kDa protein (17, 19, 20). These results and our results obtained on glioma cells using chimeric toxins suggest that the interaction of hIL13 with the hIL4R involves more elements besides the 140-kDa hIL4R chain.

**DISCUSSION**

We have found that glioma cells exhibit different responses to hIL13- and hIL4-based chimeric proteins containing PE38QQR as well as the two interleukins themselves when compared with adenocarcinoma cells (14). All of the studied glioma cell lines are killed potently by hIL13-PE38QQR, and these killing activities are blocked specifically by an excess of hIL13. On an array of established human glioma cell lines, and represented by the U-373, U-251, DBTRG MG, Ha-683, U-87 MG, SNB-19, and A-172 cell lines, hIL4 cannot block the action of hIL13-based chimeric protein (Table I). The same phenomenon is present on primary cultured human glioma cells. Thus, there is one major form of internalized receptor for hIL13 on glioma cells that does not interact with hIL4. Of interest, a corresponding hIL13-PE38QQR hIL4-based chimeric protein, hIL4-PE38QQR, is weakly active or not active through the specific binding to the hIL4 binding protein (Table I). This is seen on the same cell lines that do respond very well to hIL13-PE38QQR. Thus, the hIL13R in glioma cells is apparently different from the one described previously (Adenocarcinomas in Table I) (14). When hIL4-PE38QQR, or hIL4-PE4E, exerts cytotoxic activity, this activity can be nevertheless neutralized by an excess of hIL13, as seen on adenocarcinoma cell lines (14). These data provide a new insight into the possible mechanisms of interrelatedness between hIL13R and hIL4R in glioma cells.

Studies with a mutated IL4 first suggested interrelatedness between IL13 and IL4 receptors (25). Although the existence of a novel subunit that is shared between the two receptors was postulated, the same group of investigators has recently pointed to an already identified 140-kDa IL4R chain as the component of the hIL13R (19). This is in support of our previous studies (14, 17) and that of others (20). The model system used in our protocols allows us to employ wild-type interleukins and monitor the effects of hIL4 or hIL13 on the hIL4R- and hIL13R-mediated cellular events. In such a model, we were able to show reciprocal inhibition of the cytotoxic activities of hIL4- and hIL13-based chimeric toxins by the interleukins alone (14). We suggested that in order to explain this phenomenon, the common form of hIL13 and hIL4 receptor on the studied adenocarcinoma cells must be internalized and is composed of a 140-kDa principal subunit of the hIL14R (16) and a 70-kDa hIL13-binding protein (17), which is in agreement with emerging consensus.

Our current data on glioma cells implicate another type of hIL13R that may not involve the 140-kDa subunit of the hIL4R. Several observations speak in favor of such a possibility. First, hIL4-PE38QQR has a very weak activity on most of the glioma cells tested. This result is surprising, since hIL4-PE38QQR tended to be more active from the corresponding hIL13 toxin on several adenocarcinoma cell lines (14). Therefore, glioma cells should express relatively low levels of hIL4 binding sites (as compared with number of hIL13 sites) that, in fact, has already been documented (13). However, even at these levels of hIL4 expression we would expect better cytotoxic activity of hIL4-PE38QQR on these cells (Table I). Second, we

![Graph](https://example.com/graph.png)

**FIG. 7.** Competition of hIL13 for the binding sites of labeled hIL4 on CTLL-2 cells transfected with the human 140-kDa IL4 receptor (CTLL-2-hIL4R), CTLL-2-hIL4R were incubated with 200 pM of 125I-hIL4 with or without excess hIL13 or hIL4. The results are expressed as % of total binding. Total 125I-hIL4 bound to cells was 4412 ± 344 (cpm ± S.D.). The experiments were done in duplicate and bars represent S.D. when larger than symbols. For IL-4; For IL-13.

**TABLE I**

|                  | hIL13-PE38QQR, cytotoxicity | hIL4-PE38QQR, cytotoxicity |
|------------------|-----------------------------|-----------------------------|
|                  | without ILs | with hIL13 | with hIL4 | without ILs | with hIL13 | with hIL4 |
| Gliomas          | ++ ++ ++   | ++ ++ ++   | ++ ++ ++   | 0/++     | ++ ++ ++   | ++ ++ ++   |
| Adenocarcinomas  | ++ ++ ++   | ++ ++ ++   | ++ ++ ++   | 0/++     | ++ ++ ++   | ++ ++ ++   |

* Arbitrary estimate of the cytotoxic potency (+ to ++ +); cytotoxicity blocked (−).

* Based on data in Ref. 14.
have recently shown the lack of involvement of the 140-kDa chain in a hIL13-evoked growth-inhibitory effect on human renal cell carcinoma cells (28). Third, hIL4 is deprived of any ability to influence the action of hIL13-PE38QQR on glioma cells, including freshly cultured explant cells, at even 1000-fold molar excess over the chimeric toxin. This finding is supported by the data obtained in studies on some renal cell carcinoma cells (17, 27) and suggests altogether the presence of cancer-specific receptor for hIL13. Binding experiments using 125I-hIL13 also have shown the lack of hIL4 competition for the radiolabeled ligand binding sites. However, the hIL4R that is present on U-251 MG cells, for example, interacts with hIL13, since hIL13 blocks the cytotoxicity of hIL4-PE38QQR. hIL13 also have shown the lack of hIL4 competition for the radiolabeled ligand binding sites. However, the hIL4R that is present on U-251 MG cells, for example, interacts with hIL13, since hIL13 blocks the cytotoxicity of hIL4-PE38QQR. hIL13 appears to be a good competitor for 125I-hIL4 bindingsitesina
evidenced by the high effectiveness of hIL13-PE38QQR on glioma cells, including freshly cultured explant cells, at even 1000-fold molar excess over the chimeric toxin. This finding is supported by the data obtained in studies on some renal cell carcinoma cells (17, 27) and suggests altogether the presence of cancer-specific receptor for hIL13. Binding experiments using 125I-hIL13 also have shown the lack of hIL4 competition for the radiolabeled ligand binding sites. However, the hIL4R that is present on U-251 MG cells, for example, interacts with hIL13, since hIL13 blocks the cytotoxicity of hIL4-PE38QQR. hIL13 appears to be a good competitor for 125I-hIL4 bindingsitesina
veast for the interaction with hIL13. The specific molecular forms of this and other hIL13 receptor forms are currently being revealed.3 One common feature of all these forms is their ability to undergo internalization readily upon binding a ligand, as evidenced by the high effectiveness of hIL13 toxin on various cancer cell lines and explant cells (14, 18).3

Established human glioma cells express up to 30,000 binding sites for hIL13 per cell and the explant cells even 10 times more. These binding sites represent an new attractive target for the treatment of brain cancers (18). Since human glioma established cell lines and also human glioma explant cells express an IL4-independent hIL13R, it may be possible to take advantage of this phenomenon pharmacologically.

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Receptor for Interleukin (IL) 13 Does Not Interact with IL4 but Receptor for IL4 Interacts with IL13 on Human Glioma Cells

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