A TRANSFORMATION-ASSOCIATED 130-kD CELL SURFACE GLYCOPROTEIN IS GROWTH CONTROLLED IN NORMAL HUMAN CELLS

By C. EBERHARD KLEIN,* HARVEY L. OZER,‡ FRANK TRAGANOS,* JENS ATZPODIEN,* HERBERT F. OETTGEN,* AND LLOYD J. OLD*

*From the *Memorial Sloan-Kettering Cancer Center; and the ‡Department of Biological Sciences, Hunter College of the City University of New York, New York 10021*

The study of gene products that were initially found associated with cellular transformation (fos, myc, p53) has provided insight into the sequence of events accompanying initiation and maintenance of normal cell growth (1–4). In addition, the study of proteins that were originally found involved in growth regulation of normal cells has contributed to the understanding of malignant transformation (5–10). Transformation-induced overexpression and growth-controlled expression in normal cells, therefore, are two characteristic properties of molecules that are critically involved in promotion of cell proliferation. To identify cell surface molecules that might play an important role in cell growth, we have used these characteristics to test a large number of human cell surface antigens defined by mAbs. Emphasis was placed on antibodies that reacted preferentially with human tumors or tumor cell lines. Over 150 mAbs previously developed in our laboratory were examined (11–22, and unpublished observations), and one group of antibodies (11, 12) that detects a 130-kD cell surface glycoprotein (gp130) was selected for detailed study.

We have found that gp130 is overexpressed on the cell surface of both virally and chemically transformed fibroblasts, fibrosarcoma cell lines, a cell line derived from a squamous cell carcinoma of the skin, and T cell leukemia cell lines, in comparison to their normal counterparts. Furthermore, gp130 is growth regulated in human diploid fibroblasts and T cells. These properties indicate that gp130 fits the model of a molecule relevant to cell proliferation. Other cell surface glycoproteins that reveal a similar regulatory pattern in the normal and transformed state have been identified as the receptors for transferrin (gp92) and IL-2 (gp55) (23–25). Our results raise the possibility that gp130 is a cell surface receptor for an as yet unidentified growth-promoting agent.

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Materials and Methods

Cells and Culture Conditions. Human cell lines and short term cultures were grown in RPMI 1640 supplemented with 2mM glutamine, 1% nonessential amino acids, 100 U/ml penicillin and 100 U/ml streptomycin. Primary cultures of normal keratinocytes were established and maintained in MEM as previously described (26). Tissue culture medium contained 10% FCS. Cell lines SV/HF-4, SV/HF-5, SV/HF-5/39 and SV/HF-tsA were derived from the diploid bone marrow fibroblast cell line Hs74 after transformation with SV40 (27). The fibroblast cell line KD was established from a lip biopsy of an 18-year-old healthy male. This line (28) and its chemically transformed derivatives (HUT 12 and HUT 14, reference 28) were provided by J. Leavitt, Linus Pauling Institute (Palo Alto, CA). The fibrosarcoma cell line 8387 was provided by S. Aaronson, National Institutes of Health (Bethesda, MD). Adult fibroblast cultures ($n = 8$) were derived from fresh surgical specimens of lung, skin, or various other tissues. The fibrosarcoma cell line HT 1080 was obtained from the American Tissue Type Culture Collection (ATCC, Rockville, MD), and the fibrosarcoma cell line SW 684, and normal fibroblast lines from fetal skin, F135-60-86 and F135-60-18, were obtained from the cell bank at Memorial Sloan-Kettering Cancer Center. Cell line SCL1, derived from a facial squamous cell carcinoma, was provided by N. E. Fusenig, Deutsches Krebsforschungszentrum (Heidelberg, Federal Republic of Germany). Five cytolytic T cell clones (NBL 4, 11, 46, 56, 99) in long-term culture (>2 mo) were provided by N. Flomenberg, Memorial Sloan-Kettering Cancer Center.

Monoclonal Antibodies. The following mAbs were used: mAbs recognizing gp130: Q14, 846, N9, R23 (references 11, 12); control mAbs recognizing unrelated cell surface glycoproteins: AJ2 (14), T16 (13), CNT10 (M. Jennings, unpublished data); mAbs for T cell purification: B-1 and B-4 (B cells), MY-4 and MY-8 (monocytes, granulocytes), MO-1 (monocytes) provided by J. Griffin, Harvard Medical School (Boston, MA), and H-25 (NK cells, some monocytes) provided by R. Knowles, Memorial Sloan-Kettering Cancer Center; mAbs inducing T cell activation: OKT3 (CD3, Ortho Pharmaceutical, Raritan, NJ) and 9.1 (CD2), 9.6 (CD2), SP34 (CD3) provided by S. Yang, Memorial Sloan-Kettering Cancer Center; mAbs confirming T cell activation: OKT9 (Ortho Pharmaceutical) recognizing the transferrin receptor, L243 (ATCC) recognizing a monomorphic epitope of human class II glycoproteins.

Rosetting Assays. Rosetting assays for the detection of cell surface antigens on cultured cells were performed according to methods previously described (14, 29).

Immunofluorescence. Adherent cells were detached using 2 mM EDTA or 0.05% Trypsin/0.02% EDTA in PBS. Short term trypsin treatment (3–4 min) at room temperature did not affect gp130 expression. Cells were suspended in RPMI 1640 containing 10% FCS and incubated with saturating amounts of mAb for 45 min at 4°C. Control samples were incubated with purified mouse IgG (Coulter Immunology, Hialeah, FL) or with a mouse mAb detecting an unrelated cell surface antigen (T16, CNT10) that was not expressed on the cell types studied. After two washes with PBS, FITC-conjugated $F(ab)_2$ fragments of goat anti–mouse IgG (Cappel Laboratories, Cochranville, PA) were added for 45 min at 4°C. After three final washes in PBS, the cell preparation was analyzed using a fluorescence microscope or a FACS, or was further processed for bivariate analysis of DNA content vs. cell surface immunofluorescence.

Radioimmunoprecipitation. Cells were metabolically labeled with [^{35}S]methionine (60–200 μCi/ml; New England Nuclear, Boston, MA) for 12 h. A long labeling period was used to maximize the possibility that steady-state conditions were examined. Glycoproteins were isolated from NP-40–solubilized cell extracts by adsorption to Con A (Pharmacia Inc., Uppsala, Sweden) (30). Immunoprecipitation was carried out as previously described (14). Briefly, samples of the Con A–bound fraction (1.5×10^6 cpm) were incubated with 1–2 μl of serum or ascites containing mAb for 2 h at 4°C. Immune complexes were then precipitated with protein A–Sepharose CL-4B (Pharmacia, Inc.) preincubated with rabbit anti–mouse Ig (Dako Corp., Santa Barbara, CA). After 10 washes with buffer (0.5% NP-40, 0.1% SDS, 0.15 M sodium chloride, and 0.01 M Tris, pH 7.5),

precipitated glycoproteins were processed by SDS-PAGE on 7.5% or 9% polyacrylamide gels. For fluorography, gels were immersed in 0.5 M sodium salicylate for 20 min. To compare glycoprotein synthesis of different cell cultures, equal numbers of counts of the Con A–bound fractions were immunoprecipitated. The amounts of precipitated glycoproteins were determined by quantitative density scanning of the fluorographs.

DNA Fluorescence. Cells processed for immunofluorescence analysis of surface glycoproteins were stained with propidium iodide (PI)[1] (Sigma Chemical Co., St. Louis, MO) (31). Aliquots of a stock solution of 250 μg/ml PI and 5% (vol/vol) Triton-X-100 in H_2O were added to the cell suspension (10^6 cells/ml) to reach final PI and detergent concentrations of 50 μg/ml and 1%, respectively. In addition, cells were treated with 1,000 U of high specific activity RNase per milliliter of cell suspension (RASE; Worthington Biochemical Corp, Warrington, PA). After a 20-min incubation at room temperature, samples were analyzed in a flow cytometer.

Bivariate Analysis of DNA vs. Immunofluorescence. The integrated values of PI red fluorescence, FITC–green fluorescence, and the duration of the red fluorescence pulse were recorded in list mode for each cell using a System 50H flow cytometer (Ortho Diagnostic Systems, Inc., Westwood, MA) interfaced to an Ortho 2150 data analysis system. The duration of the red fluorescence pulse (pulse width) of each cell was used to eliminate doublets (32). Linear and log fluorescence values for cellular DNA and immunofluorescence, respectively, were recorded for 10^4 cells. Interactive data analysis provided the mean fluorescence values of cells as well as single parameter frequency distribution histograms and bivariate displays of cellular DNA vs. log FITC fluorescence.

Preparation of T Lymphocytes. Peripheral blood mononuclear cells were separated from heparinized whole blood of healthy volunteers by sedimentation on a Ficoll-Hypaque density cushion (density 1.077 gm/cm^3, Pharmacia Fine Chemicals, Piscataway, NJ). After removal of monocytes by adherence to plastic petri dishes (45 min, 37°C), T cells were purified by negative selection using an indirect panning technique (33). Lymphocytes were incubated simultaneously with saturating amounts of mAbs B-1, B-4, MY-4, MY-8, H-25, MO-1, and N901 for 30 min at 4°C, washed twice, and resuspended in RPMI + 10% FCS. 4 ml of the cell suspension (5×10^6 cells/ml) were then dispensed into one 100-mm plastic dish (No. 1005, Falcon Labware, Oxnard, CA) precoated with 5 ml of affinity-purified goat anti-mouse Ig (20 μg/ml PBS, overnight at 4°C) (Boehringer-Mannheim Biochemicals, Indianapolis, IN). Cells were incubated at 4°C for 90 min on the dishes. The nonattached T lymphocytes were collected by swirling the plates and decanting the supernatant, followed by four gentle washes of the plates with media. Collected cells were washed twice with medium before further testing.

Activation of T Lymphocytes. T lymphocytes (98% CD3$^+$ cells, 0.5×10^6 cells/ml) were incubated in MLC for 5 d, or with mAbs: (*a*) OKT3 (ATCC clone ascites 1:1,000 vol/vol) for 16 h or 3–4 d; (*b*) 9.1 and 9.6 combined (1 μg/ml each), detecting the internal and external domain of the CD2 molecule, respectively, for 8 h or 3 d (S. Yang et al., manuscript in preparation); (*c*) 9.1 and SP34 combined (20 g/ml each), detecting the CD2 and CD3 molecule, respectively, for 3 d (34). T cell activation was confirmed by [^{3}H]thymidine uptake or by induction of transferrin receptor (mAb OKT9) and HLA-DR (mAb L243) expression, using flow cytometry.

Results

Strong Cell Surface Expression of a 130-kD Glycoprotein (gp130) Is Induced in Human Fibroblasts after Viral and Chemical Transformation. To determine whether the expression of a given cell surface antigen changes after malignant transformation, we compared the two human fibroblast cell lines Hs 74 and KD and their virally (SV/HF-5, SV/HF-5/39) or chemically (HUT 12, HUT 14)

[1] *Abbreviations used in this paper:* HU, hydroxyurea; PI, propidium iodide; TR, transferrin receptor.

transformed counterparts. Cell line SV/HF-5, which gave rise to line SV/HF-5/39, was derived from a soft agar colony after Ca–phosphate-mediated transfection of origin-defective SV-40 DNA into Hs 74 cells (27, 35). The other two transformed cell lines (HUT 12, HUT 14) were isolated from separate foci of KD fibroblasts after treatment with 4-nitroquinoline oxide (28). Although screening with the panel of mAbs identified several cell surface antigens that showed increased expression on transformed fibroblasts, changes in gp130 expression were particularly striking. Four mAbs defining four distinct epitopes on gp130 were used, and these antibodies gave parallel results in rosetting, FACS, and immunoprecipitation analysis, indicating detection of a single gp130 species. In subsequent experiments mAbQ14 was used.

Fig. 1 shows a comparison of gp130 expression by the normal fibroblast line Hs 74 and its SV40-transformed derivative, SV/HF-5/39. Surface expression of gp130 was highly increased on SV/HF-5/39 cells under optimal conditions for cell growth of both lines, i.e., intermediate cell density in medium supplemented with 10% FCS. Synthesis of gp130, as determined by metabolic labeling, was similarly increased in the transformed line (Fig. 2). The level of radiolabeled gp130 was 15–20-fold higher in SV/HF-5/39 cells as compared with Hs 74 cells. The two chemically transformed lines, HUT 12 and HUT 14, also showed high levels of gp130; synthesis of gp130 was not detectable in the parent line under comparable conditions. These results indicate that induction of gp130 expression in transformed fibroblasts is not dependent on a particular transforming agent. Further studies showed that induction of gp130 expression was an early consequence of Hs 74 transformation. Three independent SV40-transformed derivatives of the Hs 74 line (SV/HF-4, SV/HF-5, and SV/HF-tsA) showed increased gp130 expression at an early passage (passage 2–10) after isolation, as shown in Fig. 3 for SV/HF-5 cells. These cell lines had been isolated under different selection conditions after transfection with diverse constructs of wild-type (27) and tsA 58 origin-defective (Radna, R., and H. Ozer, unpublished results) SV40 genomes. In addition, the three human fibrosarcoma cell lines (HT 1080,

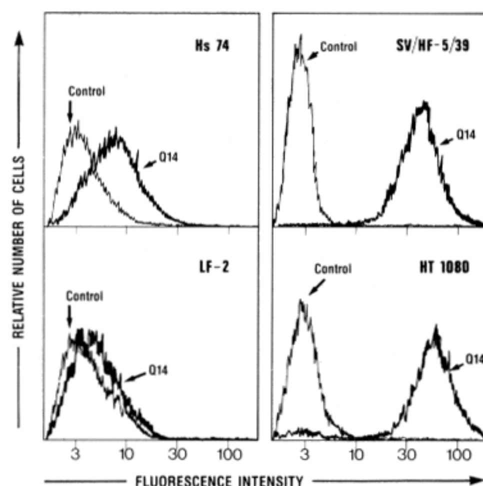

FIGURE 1. Surface expression of gp130 on normal and transformed human fibroblasts as analyzed by flow cytometry. Cells were incubated with mAbQ14 (gp130) or mAbT16 (control). Cell lines: Hs 74 (normal fetal fibroblast), LF-2 (normal adult fibroblast), SV/HF-5/39 (SV40-transformed Hs 74), HT 1080 (fibrosarcoma cell line).

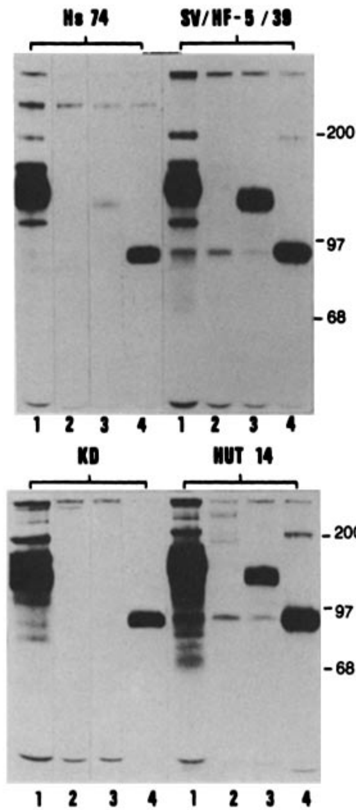

FIGURE 2. gp130 synthesis in normal and transformed fibroblasts. Con A–bound fractions of NP-40 cell lysates from [^{35}S]methionine-labeled parallel cultures (Hs 74 and SV/HF-5/39; KD and HUT 14, respectively) were analyzed by immunoprecipitation and SDS-PAGE. The fluorogram shows immunoprecipitates obtained with different mAbs: (lane *1*) AJ2 (gp210/170/140/30, constitutively expressed on all cell types, not transformation related); (lane *2*) T16 (gp40-50, not expressed on fibroblasts); (lane *3*) Q14 (gp130); (lane *4*) OKT9 (gp92, TR).

SW 684, 8387) expressed high levels of gp130 on the cell surface, indicating that in vivo transformation is also frequently associated with increased expression of gp130 (Fig. 1). The 14 normal fibroblast cell lines tested, including Hs 74 and KD, showed significantly lower cell surface expression of gp130 than transformed fibroblasts, with adult fibroblasts being consistently lower than fetal fibroblasts (Fig. 1).

Cell Surface Expression and Synthesis of gp130 Is Growth Regulated in Normal Fetal Fibroblasts. Normal fibroblast lines derived from fetal skin (F135-60-86, F135-60-18) were studied at an early passage under various growth conditions.

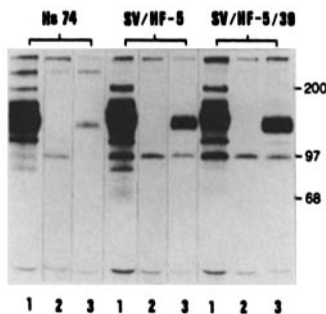

FIGURE 3. Increased gp130 synthesis after in vitro transformation. Normal Hs 74 fibroblasts were compared with SV40-transformed Hs 74 fibroblasts at an early stage after isolation (SV/HF-5), and at a later stage after immortalization (SV/HF-5/39). Con A–bound fractions of [^{35}S]methionine-labeled cultures were prepared as described. Immunoprecipitates were obtained with mAbAJ2 (lane *1*), mAbT16 (lane *2*), and mAbQ14 (lane *3*). See Fig. 2 for mAb characteristics.

Growing cultures were first incubated in medium containing a low concentration of serum (0.5% FCS). After 4 d of serum starvation, cultures were stimulated for 3 d with 20% FCS alone, or with 20% FCS and 1.5 mM hydroxurea (HU). Parallel cultures were maintained at low serum concentration. Immunoprecipitation of [^{35}S]methionine-labeled cultures showed that gp130 synthesis was very low in serum-starved cells and significantly higher in serum-stimulated cultures (Fig. 4). In cultures growing in 20% FCS and 1.5 mM HU, synthesis of gp130 was even higher than in cultures growing in 20% FCS alone. We then examined gp130 expression at different stages of the cell cycle. Bivariate analysis of DNA and cell surface immunofluorescence was performed on cultures maintained in the same way as those used for immunoprecipitation tests. In serum-stimulated cultures (20% FCS), the mean fluorescence intensity of gp130 was 3.5 times higher than in serum-starved cultures (Fig. 5 *C*). Comparison of the G_0–G_1 cell populations demonstrated similar differences; serum-stimulated G_0–G_1 cells revealed a 3.2 times higher expression of gp130 than G_0–G_1 cells of serum-starved cultures (Fig. 5 *B*). As G_0 and G_1 cells cannot be distinguished on the basis of DNA content per cell, we cannot tell whether expression of gp130 increased after serum stimulation in G_0 cells or in the transition of G_1 cells; it remained increased in cycling cells, as indicated by high gp130 levels in S and G_2M cells (Fig. 5 *B* [II]).

As expected, cultures stimulated with FCS for 3 d in the presence of HU also showed an increase in mean fluorescence intensity of gp130. The level of gp130 was 6.4 times higher than in serum-starved cultures (Fig. 5 *C*). Analysis for DNA content revealed that cells in such cultures were predominantly arrested in S-phase. Interestingly, S-phase cells of these cultures consistently showed higher gp130 expression than S-phase cells of cultures stimulated with FCS in the absence of HU.

gp130 Is Not Found on the Cell Surface of Normal Keratinocytes but Highly Expressed in a Squamous Cell Carcinoma. To determine whether transformation-induced expression of gp130 occurs in other cell types, we studied normal and transformed human keratinocytes (Fig. 6). gp130 was not detected on epidermal cells derived from fresh surgical skin specimens or on keratinocyte cultures (KC,

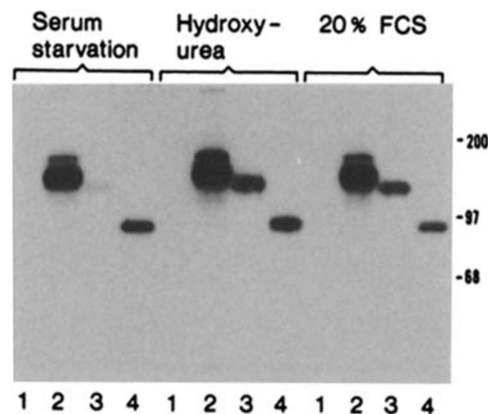

FIGURE 4. Growth control of gp130 synthesis in normal fetal fibroblasts. Cultures of fetal skin fibroblasts (F135-60-86, passage 6) were serum starved for 4 d (0.5% FCS). Parallel cultures were then serum stimulated with 20% FCS or with 20% FCS and 1.5 mM HU or maintained in medium containing 0.5% FCS. After 60 h the culture medium was changed to methionine-free medium containing 65 Ci/ml [^{35}S]methionine and corresponding amounts of dialyzed FCS (0.5%, 20% + HU or 20%) for 12 h. NP-40 cell lysates were then processed for immunoprecipitation. The fluorogram shows immunoprecipitates obtained with mAbT16 (control, lane *1*); mAbAJ2 (control, lane *2*); mAb Q14 (gp130, lane *3*) mAb OKT9 (TR, lane *4*).

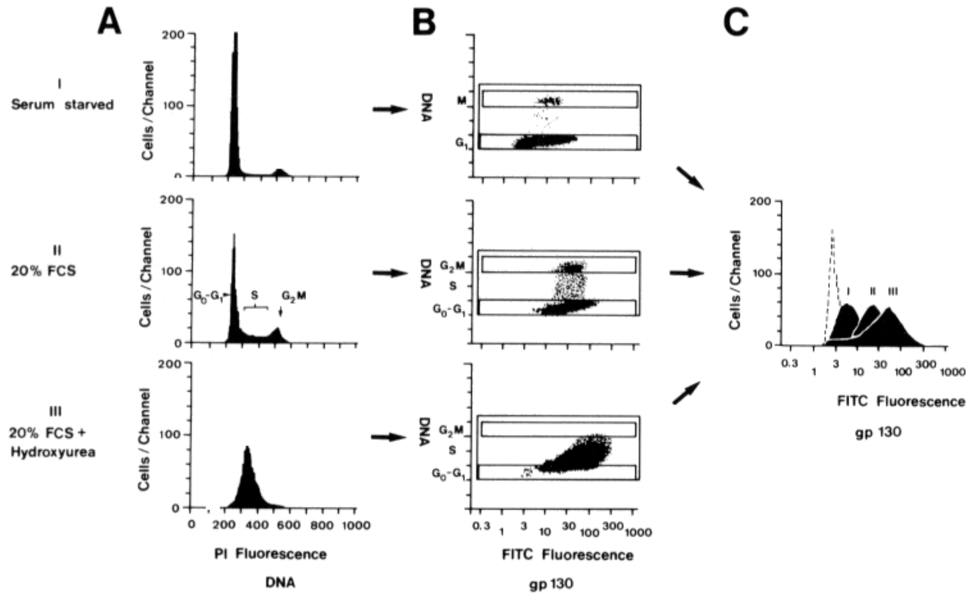

FIGURE 5. Cell surface expression of gp130 is increased on serum-stimulated G_0–G_1 cells and on S/G_2M cells. Parallel cultures of fetal skin fibroblasts (F135-60-86) were treated as described in Fig. 4 and processed for bivariate analysis of DNA content and cell surface immunofluorescence (gp130; mAbQ14). (*A*) DNA histograms. (*B*) Bivariate recording of DNA content and gp130 immunofluorescence. Note the shift of serum-stimulated G_0–G_1 cells (II) to higher gp130 fluorescence intensity as compared with the serum-starved G_0–G_1 cells (I). (*C*) Single-parameter histograms of gp130 immunofluorescence from whole cultures I, II, III; the histogram with the noncontinuous line represents the three superimposed controls (mAbT16).

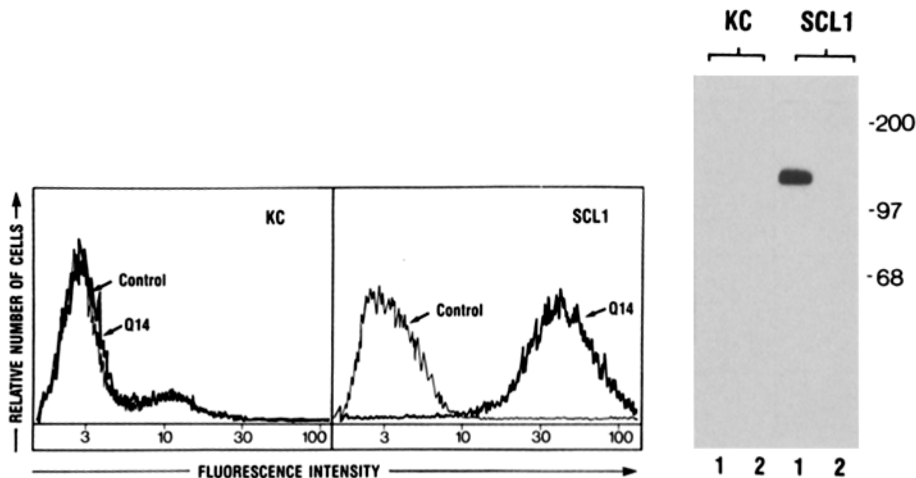

FIGURE 6. Synthesis and expression of gp130 in normal keratinocytes and in a squamous cell carcinoma line. Cultures of KC normal adult keratinocytes (14 d in culture) and the SCL1 squamous cell carcinoma line were processed for immunofluorescence by flow cytometry *(left)* and for immunoprecipitation *(right)*. *(Left)* mAbQ14 (gp130) and mAbCNT10 (control); *(Right)* lane *1*, mAbQ14, lane *2*, mAbCNT10.

n = 14). In contrast, a cell line derived from a facial squamous cell carcinoma (SCL-1) showed high expression of gp130, as measured by immunofluorescence tests (Fig. 6 *A*) and by immunoprecipitation after metabolic labeling (Fig. 6 *B*).

gp130 Is Induced in Activated T Cells and Overexpressed in a T Cell Leukemia Line. In indirect immunofluorescence tests using flow cytometry, gp130 was not detectable on PBMC, highly purified peripheral blood T cells, or cord blood cells. When T cells were stimulated in MLC or with mAbs reacting with the T cell receptor (CD3) or the sheep red blood cell receptor (CD2), gp130 expression was induced at low to moderate levels (Table I). Similar levels of gp130 were found on cloned IL-2-dependent T cell lines (Table I).

In tests on cultured T cell leukemias, gp130 was detected on 4/6 cell lines (Table I). 100% of HUT 102 and CRF-CEM cells expressed gp130 at high levels, whereas only a small percentage of MOLT-4 cells showed weak gp130 expression. Cell surface expression of gp130 on HUT 102 cells was at least five fold higher than on fresh normal activated T cells or T cell lines. These results indicate that transformation is associated with overexpression of gp130 in a subset of T cell leukemias.

Comparison of gp130 and Transferrin Receptor Expression. The transferrin receptor (TR) is a cell surface glycoprotein known to be involved in cell prolif-

TABLE I

Cell Surface Expression of gp130 on Human T Cells

T cells	gp130 expression*	
	Strength	Positive cells
		%
Resting T cells		
Peripheral blood, n = 10	−	0
Cord blood, n = 2	−	0
Activated T cells		
MLC, n = 2	+	6–8
mAb OKT3 (CD3), n = 3	++	8–70
mAb 9.1 (CD2), 9.6 (CD2), n = 3	++	15–60
mAb 9.1 (CD2), SP34 (CD3), n = 2	++	7–13
T cell clones		
NBL 4	++	15
NBL 11	+	13
NBL 46	+	8
NBL 56	++	53
NBL 99	+	70
T cell leukemias		
HUT 102	++++	100
CRF-CEM	+++	100
MT-1	++	50
MOLT-4	+	8
P12	−	0
Jurkat	−	0

* Cell surface expression of gp130 was assessed by flow cytometry after indirect immunofluorescence staining with mAbQ14. Expression ranged from weak (+) to very strong (++++).

eration (25). It has been shown that TR is growth controlled in human T lymphocytes and that its induction is required for cell division (24). High levels of TR have been found in tissues and cell lines derived from many different types of human cancer (23, 36). In comparing the patterns of TR and gp130 expression, we found significant differences. First, the increase of gp130 synthesis after in vitro transformation of fibroblasts was markedly higher (15–20-fold) than the increase observed for TR synthesis (<2-fold, Fig. 2). Second, synthesis of gp130 in normal fibroblasts was clearly modulated by the growth state of normal fibroblasts, whereas this could not be demonstrated for TR (see Fig. 4). Third, in contrast to the low levels of gp130 detected in activated T cells and in long-term cultures of cloned T cells, TR was synthesized at significantly higher levels in these cells. Finally, gp130 was not detectable in a number of human tumor cell lines expressing high levels of TR.

Discussion

Several oncogene products have been found overexpressed in transformed cells and growth controlled in normal cells (1–4, 37–39). In this study, we have found that gp130 shares these two characteristics. gp130 is a plasma membrane glycoprotein that can be detected with immunorosetting or immunofluorescence assays on the surface of cultured cells. Pulse chase experiments have demonstrated a 100-kD precursor protein (12). Furthermore, treatment of this precursor protein with endoglycosidase H resulted in an 80-kD polypeptide possibly representing the primary translational product (12). In our experiments, gp130 was not detectable in immunoprecipitates of spent medium after culture of [^{35}S]methionine-labeled high expressor cell lines, suggesting that the glycoprotein is not secreted. The gene encoding gp130 has been assigned to chromosome 11q13-qter by serological analysis of mouse–human somatic cell hybrids (40, 41).

Strong expression of gp130 was induced in fibroblasts by in vitro transformation with two transforming agents. In addition, high levels of gp130 were found in human cancer cells of diverse types: fibrosarcomas, a squamous cell carcinoma, and T cell leukemias. Normal cultured cells of the same lineage showed low or no detectable expression of gp130. Furthermore, gp130 is known to be highly expressed on the cell surface of tumor cell lines derived from many other tissues including neuroblastomas, melanomas, astrocytomas and lung carcinomas (11, 21, our unpublished data). In tests on tissue sections with immunoperoxidase and immunofluorescence, gp130 was found to have a restricted distribution in normal tissues (endothelial cells, sebacious glands, reference 21). In the case of malignant melanoma, 36/62 tumors were strongly positive for gp130 (21). gp130 was not detectable in skin melanocytes in tissue sections, but is expressed by cultured melanocytes growing in the presence of phorbol ester and cholera toxin.

In two distinct normal cell systems, human fibroblasts and T lymphocytes, gp130 expression was shown to be modulated by the growth state of normal cells. Our data indicate that gp130 expression increases significantly in serum-stimulated fetal fibroblasts in G_0 or G_1, possibly associated with the transition from G_0 to the G_1 phase of the cell cycle, and that it persists at these higher

levels during the S- and G_2 M-phase of the cycle. In HU-treated cultures, there was growth arrest of fibroblasts in S-phase (under our culture conditions of single exposure to HU over a 3-d period). Interestingly, expression of gp130 on the surface of these HU-treated cells was higher than expression in S-phase cells growing in the absence of the inhibitor, a finding that raises the possibility that altered S-phase characteristics after cell transformation might lead to the increase of gp130 expression in transformed cells. On the other hand, gp130 may be constitutively overexpressed and totally uncoupled from cell cycle control in the transformed state. It is not likely that the high level of gp130 in transformed cells is due simply to an increased proportion of replicating cells (42) because the parent line and the SV40-transformed fibroblasts show similar growth rates (27). Further studies are required to clarify the relationship between gp130 expression and cell kinetics in normal and transformed cells and to identify parallels between expression of gp130 and other cell cycle–regulated gene products (e.g., p53).

TR provide cells with iron, an essential nutrient, and cell surface expression of TR is a prerequisite for cell division. The expression pattern of this proliferation-associated glycoprotein initially seemed to be similar to that of gp130. Comparing conditions involved in the regulation of the two glycoproteins, we found significant differences between gp130 expression and TR expression, indicating that these glycoproteins are controlled by different mechanisms.

We conclude that gp130 has characteristics of a gene product that may be involved in the control of cell growth. Modulating gp130 expression by growth factors, anti-gp130 antibodies (24, 43–45), and transfection with gp130 expression vectors (37, 46–48) provide approaches to exploring the role of gp130 in normal and abnormal cell proliferation.

Summary

Two characteristics of cell surface molecules involved in the regulation of cell proliferation are altered expression in relation to growth phase in normal cells and overexpression in transformed cells. Here, we describe a similar pattern of expression for a 130-kD cell surface glycoprotein (gp130) in human cells. Synthesis and cell surface expression of gp130 were greatly increased in both virally and chemically transformed fibroblasts, fibrosarcomas, a squamous cell carcinoma of the skin, and T cell leukemia lines. Furthermore, gp130 expression was induced in serum-starved fetal fibroblasts by serum stimulation, and in fresh T cells by various activating agents. Expression in response to serum stimulation was associated primarily with the transition from a quiescent state (G_0) into the cell cycle (G_1).

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