Acta Dermatovener (Stockholm) 51: 413–422, 1971

PROLIFERATIVE CELLS IN THE HUMAN SEBACEOUS GLAND

Labelling Index and Regional Variations

Gerd Plewig, Enno Christophers and Otto Braun-Falco

From the Department of Dermatology, University of Munich, Munich, BRD

Abstract. The proliferative activity of human sebaceous glands was analysed by means of ^{3}H-thymidine autoradiography and planimetry. Labelling indices (L.I.) and planimetric values were determined separately for the two portions within each gland: the differentiating cell pool (DCP) with basement membrane-bound germinative cells and large lipid cells, and the undifferentiated cell pool (UCP) with multilayered cells, which in serial sections proved to form a sponge-like skeleton throughout the gland.

Three body sites (scalp, forehead, back) were investigated in a total of 77 specimens from 63 healthy men. Significant differences in L.I. were found between the undifferentiated cell pool (23.7%, forehead) and the differentiating cell pool within each gland and for all body sites under study. The L.I. of the forehead was 10.1% compared with 8.9% from the back and 8.6% from the scalp.

A constant correlation was found to exist between glandular cross sectional areas (planimetry) and the number of labelled cells ($r = 0.8298$, scalp). The largest sebaceous glands were found on the back. The observation of an inhomogeneous basal cell population is considered to be a major obstacle in determining the true germinative cell population.

Although there is an extensive body of information on the rate of sebum production in man (19, 24–27, 29), very little is known about the proliferative activity and movement of cells within the sebaceous glands. The current techniques of measuring new cell production and cellular movements within an organ by the use of colchicine or tritiated thymidine have raised a number of difficulties when applied to the sebaceous gland. Only a few investigators have tried to elaborate on the kinetic aspects of human sebaceous glands (8, 9, 30). One of the reasons for this lack of knowledge, as will be pointed out later, is the peculiar anatomy of the gland: it has a sac-like construction with lobules of various size and shape. Their contents are continuously emptied through a rather narrow central duct. Because of this structure, more complicated mechanisms of cell movement and sebum secretion through the duct can be expected than, for instance, in the epidermis. Furthermore, the two portions of the gland, fundus (acini or lobules) and the sebaceous duct, form a junction of entirely different types of tissue: those which produce lipid and finally disintegrate, and those which become horny cells.

The purpose of this study was to examine the proliferative activity of the sebaceous gland in a large number of normal individuals and to evaluate area-dependent differences.

MATERIAL AND METHODS

A total of 63 healthy men with uninvolved skin, age 21–52, were examined. Biopsies were taken as follows: from the mid-scalp, 26 biopsies in 26 men; from the forehead, 26 biopsies in 22 men; from the upper back, 25 biopsies in 16 men.

Multiple biopsies from the same individual were taken several days or weeks apart. 5–10 μCi of ^{3}H-thymidine (^{3}H-TdR), (spec. act. 2.6 Ci/mM or 6.0 Ci/mM; New England Nuclear Corporation), suspended in 0.1–0.2 ml of physiologic saline, were injected intradermally between 10 a.m. and 3 p.m. Excisional biopsies were taken 45 min after injection. Specimens were fixed in buffered neutral formalin, sectioned 5–6 μ thick and prepared for autoradiography by the dipping method (Kodak NTB II) and processed as previously described (17).

Two types of quantitative evaluation of the specimens were performed; cell counting and planimetry. Sebaceous glands of all sizes were used, with adequate labelling both of the epidermis and of the sebaceous glands. Evaluation started with planimetry of multiple, often serial sections, projecting them against a wall with a Leitz-Prado slide projector and a Leitz micrometer slide table

Fig. 1. Human sebaceous gland from the back (subject 9). The lower portion of sebaceous duct is to the upper right. Coral-reef-like extensions of the undifferentiated cell pool (UCP, shaded areas). Reconstruction from planimetry × 232 of 7 consecutive microtome sections of 6 μ thickness each. Black indicates superficial position: decreasing shades of grey indicate depth of position. The circumferences of the lobules show little size variation in contrast to the UCP, which is characterized by marked fluctuations.

at a constant magnification of 400 : 1 according to previously described techniques (3). No attempt was made to restrict the observations to sebaceous glands, which were associated with anagen hairs (8). This obviously would bias regional variations of hair-patterns and appeared nearly impossible without true serial sections.

After planimetry, the same areas within the specimens were identified under a light microscope and cell counts were performed under 400-fold magnification. Sebaceous gland cells were grouped according to anatomical position and cellular morphology. Counts were made for:

The Differentiating Cell Pool (DCP)

1. the number of germinative cells
2. the number of differentiating lipid cells
3. the number of ^{3}H-TdR-labelled cells.

Aside from this, a portion of the gland consisting of groups of undifferentiated multilayered cells, called the Undifferentiated Cell Pool (UCP), was evaluated separately. Counts were made for:

4. the number of basal cells
5. the number of suprabasal cells
6. the number of ^{3}H-TdR-labelled cells in this compartment.

The planimetric evaluation of the sebaceous gland consisted of two separate measurements according to the above-mentioned groupings:

7. the area of the germinative and lipid cells (DCP)
8. the area of the undifferentiated cell pool (UCP).

It should be pointed out that all quantitative determinations were restricted to true sebaceous gland cells. No

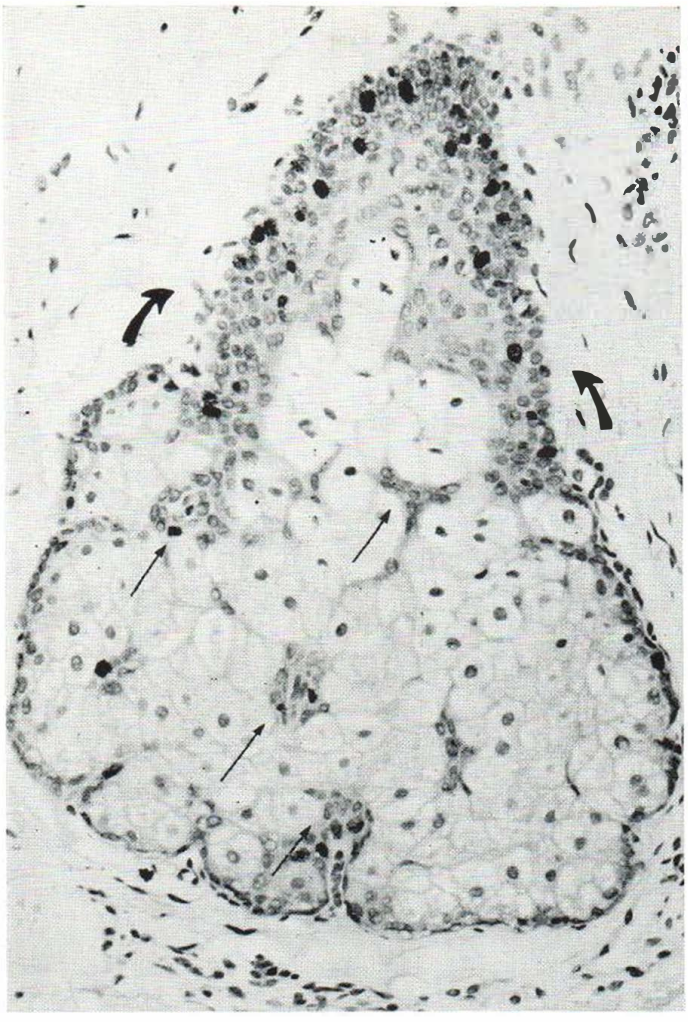

Fig. 2. Sebaceous gland. Forehead, 21-year-old man. ^{3}H-TdR labelling 45 min. Cranial is the sebaceous duct (bold arrows). Cell clusters (fine arrows) of the undifferentiated cell pool (UCP). Hematoxylin, × 157.

keratin-forming cells of the sebaceous duct, as judged by light-microscopy, were therefore included.

The data were statistically examined by Student's *t*-test, analysis of variance, and correlation analysis when indicated. A variance ratio F and correlation coefficients r were computed (23).

RESULTS

1. *Anatomical remarks*

During the course of this study it became obvious that marked differences in morphology and in ^{3}H-TdR uptake occurred within the glands. This made it necessary to separate two portions of cells within the acini. One portion, which will henceforth be called the differentiating cell pool (DCP), comprised (*a*) small basement membrane-bound, so-called germinative cells, and (*b*) large lipid cells.

The other portion, which will henceforth be called the undifferentiated cell pool (UCP), consisted of undifferentiated, multilayered cells with homogeneous cytoplasm and without light-microscopical evidence of lipid droplets. This portion was 2–8 cell layers in thickness. It could be found adjacent to the sebaceous duct or in the periphery of the acini. There, it might be located close to the connective tissue strands separating two lobules, or it might present itself as cell clusters within the periphery of an acinus. Reconstruction from planimetry of consecutive microtome sections revealed that this cell portion formed a coral-reef or sponge-like skeleton within the sebaceous gland (Figs. 1 and 2). Various terms have been used for these cells (7–12, 14, 15, 20, 21, 26–28, 30).

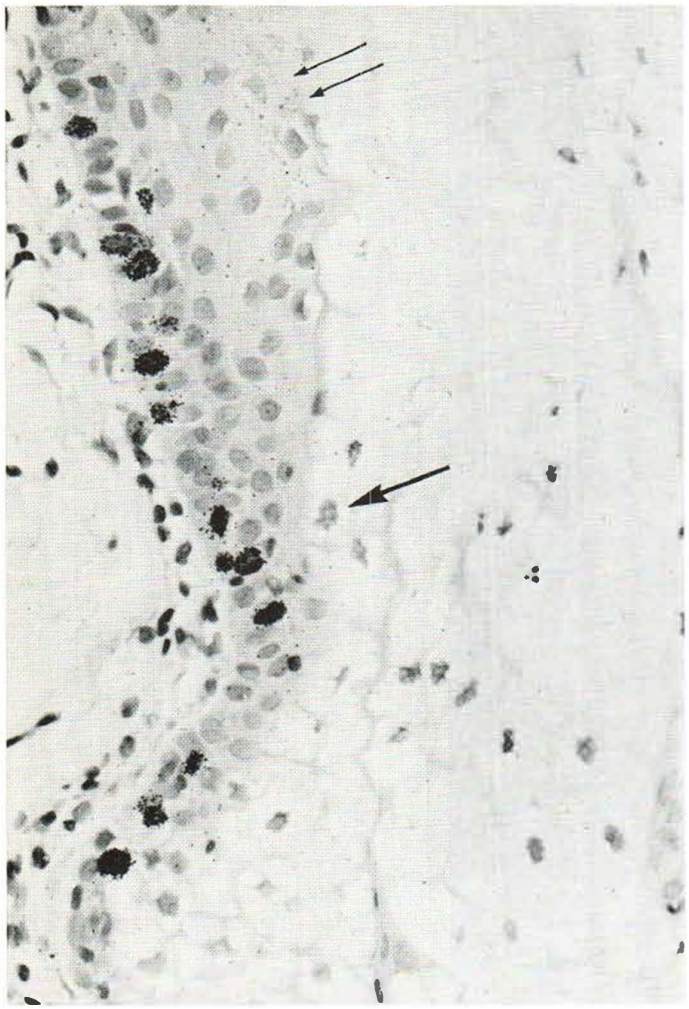

Fig. 3. Sebaceous duct with parts of a sebaceous acinus below. Forehead, 21-year-old man. ^{3}H-TdR labelling, 45 min. Pronounced labelling in the cranial, keratinizing portion of the sebaceous duct with keratohyalin granules (fine arrows). Pronounced labelling in the transitional zone towards the sebaceous acinus, with cells showing lipid production (bold arrow). Hematoxylin, × 325.

II. *Labelling index*

A. *Regional variations.* 45 min after injection of the tracer, ^{3}H-TdR-labelled cells were found in the basal layer of the acini (Fig. 3). On only 4 occasions out of 12 238 counted labelled cells, was a ^{3}H-TdR-labelled nucleus seen in the mid-portion of the gland (Fig. 4). These were truly luminal cells without connection to the basement membrane as judged by adjacent serial sections.

The highest labelling index (L.I.), namely 10.1%, was found on the forehead, whereas the back (8.9%) and the scalp (8.6%) showed considerably lower values (Tables I and II).

Statistical analysis of this experiment showed a significant difference at the 95% level for the three regions with a variance ratio of $F = 3.754$ with 2 and 74 degrees of freedom.

B. *Variations within the gland.* The L.I. for the two germinative portions of the sebaceous glands differed markedly (Tables I and II). For instance, on the forehead 23.7% of the basal cells in the UCP were labelled, whereas less than half as many were found among the single-layered germinative cells of the acini (10.1%). An almost identical relationship between the two proliferating portions was found in the two other regions, the scalp and the back. On the average, the labelled cells found in the undifferentiated cell pool (UCP) were approximately twice as numerous as in the differentiating cell pool. Correlation effects within the two groups (UCP and DCP) of a single body site showed statistically significant differences ($P < 0.001$) for all three regions. However, no significant differences in labelling indices

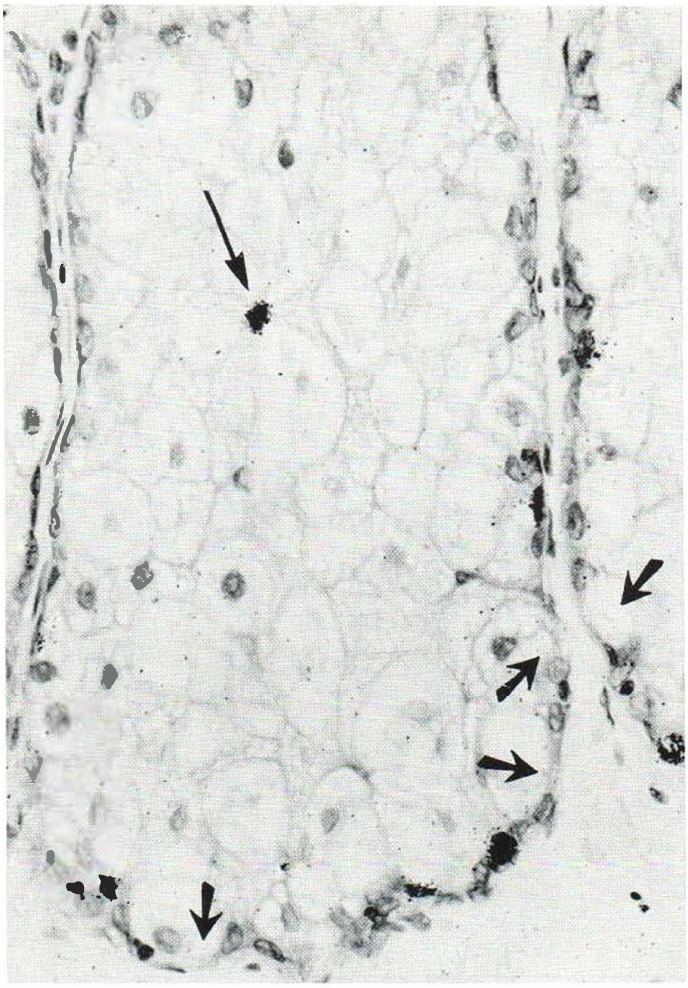

Fig. 4. Periphery of sebaceous gland. Forehead, 25-year-old man. ^{3}H-TdR labelling, 45 min. Labelled cells in basal layer. Inhomogeneous basal cell layer with lipid cells (bold arrows). Fine arrow indicates a labelled cell in the centre of the acinus, which had no connection with a basement membrane on serial sectioning. Hematoxylin, × 320.

of the UCP from forehead, scalp and back were found at the 95% level with a variance ratio $F = 3.019$ with 2 and 74 degrees of freedom.

III. *Planimetry*

After histological examination it was found that sebaceous glands of the back were much larger than expected. Cross-sectional surface areas, as measured by planimetry, which can be taken as representative of sebaceous gland volumes (3, 31), surpassed those of the scalp and forehead, sometimes by a factor of 2 or 3. For instance, the average of the ten largest cross-sectional areas of single sebaceous glands from the back was 0.2735 mm^2, compared with the largest cross-sections derived from the scalp of 0.1596 mm^2 or the forehead of 0.2175 mm^2 (Table III). These findings do not confirm Yamada's statements (32).

It should be noted that randomized planimetrical data of the sebaceous gland, as used in this study, do not give information on regional differences in glandular volume per unit skin surface. This is due to the fact that constant points of reference, as for instance epidermal surface length (3), cannot be used.

IV. *Correlation between cell counts and planimetry*

A good correlation between the number of cells and the respective cross-sectional area could be observed. All three cell types encountered previously (germinative, lipid, and labelled cells) can be related to the cross-sectional areas. For con-

Table I. *Cell counts, labelling indices in % and planimetric areas in cm² for the differentiating cell pool (DCP) and the undifferentiated cell pool (UCP) of the forehead*

n = negro, white = all other subjects ■ ▽ ▼ △ symbols indicate multiple biopsies from the same subject

	Differentiating Cell Pool				Undifferentiated Cell Pool				
No./age	Germinative cells	Lipid cells	Labelled germinative cells	Labelled germinative cells L.I. (%)	Basal cells	Supra-basal cells	Labelled cells L.I. (%)	Area (cm²) germinative & lipid cells DCP	Area (cm²) basal & supra-basal cells UCP
1/23	663	536	76	11.5	333	572	29.1	693	168
2/27 ■	1 161	961	131	11.3	199	336	22.6	1 366	245
3/27 ■	1 086	1 006	125	11.5	431	675	27.6	1 361	88
4/39 ▽	1 756	1 481	204	11.6	563	931	25.4	1 974	265
5/39 ▽	1 026	848	111	10.8	390	594	23.6	1 211	194
6/42 ▼	2 033	1 560	180	8.9	256	415	18.0	1 957	138
7/42 ▼	1 242	941	122	9.8	158	262	22.8	1 177	74
8/22	1 229	951	102	8.3	279	425	23.3	1 452	117
9/32	1 720	1 354	221	12.9	158	350	33.5	1 597	80
10/26	1 587	1 173	197	12.4	294	491	33.0	1 845	163
11/24	1 195	1 011	120	10.0	415	687	19.3	1 676	206
12/46	1 631	1 028	134	8.2	308	658	19.5	1 540	109
13/21	1 340	1 014	113	8.4	255	365	27.5	1 392	124
14/49	2 110	1 437	166	7.9	395	505	13.7	2 121	142
15/32	1 498	1 148	135	9.0	634	1 001	23.5	1 472	328
16/26	1 451	1 082	96	6.6	331	579	15.7	1 955	219
17/29*n*	1 896	1 372	160	8.4	341	560	24.6	1 951	174
18/30*n*	1 488	945	169	11.4	283	470	23.0	1 551	171
19/31*n*	1 540	1 129	150	9.7	448	655	20.1	1 766	192
20/42*n*	1 712	1 335	116	6.8	531	841	19.8	1 556	304
21/42*n*	1 431	919	151	10.6	250	403	26.8	1 576	147
22/25*n*	1 862	1 345	279	15.0	312	433	25.3	2 758	136
23/29*n*	1 775	969	143	8.1	199	373	28.1	1 679	169
24/29*n* △	1 325	983	156	11.8	242	390	20.5	1 857	110
25/29*n* △	1 474	1 013	157	10.7	312	573	15.7	2 257	178
26/34*n*	1 287	975	150	11.7	488	805	23.2	1 717	341
Sum	38 518	28 516	3 864		8 805	14 349			
Mean ± S.D.				10.1 ± 2.0			23.7 ± 5.1	1 671	176

venience we plotted the number of labelled germinative cells (DCP and UCP) against the respective planimetrical value for both the differentiating (DCP) and the undifferentiated cell pool (UCP). These correlations, e.g. for the back, are shown in Fig. 5. Plotted on a semilogarithmic scale the curve shows a linear function of the two factors. Although not recorded graphically the same constant relationship was found on the forehead and the scalp.

As pointed out earlier, particular attention was paid to portions of the gland which showed an accumulation of undifferentiated cells (UCP). Quantitative measurements of cell counts and area determinations were also applied here. As can be seen from Table V, the UCP accounted for about 10% of the total gland area. In terms of cell counts, however, the share of undifferentiated cells became even larger.

No statistically significant differences or correlations for the three regions in this experiment were found ($F = 1.028$ for the area ratios, $F = 0.442$ for cell ratios, both with 2 and 74 degrees of freedom).

V. *Correlation of basal cells : differentiating cells*

From the data given in Tables I and II, a correlation was established between basal (germinative) cells and differentiating (lipid) cells of the DCP. Statistical analysis of this experiment showed a good correlation (over 86%), and a difference among sites was established at the 95% level with a variance ratio of $F = 3.536$ with 2 and 74 degrees of freedom.

Table II. *Labelling indices in % for germinative cells of the differentiating cell pool (DCP) and the undifferentiated cell pool (UCP) of scalp and back*

n = negro, white = all other subjects ○ ● ✳ ▲ symbols indicate multiple biopsies from the same subject

No.	Age Back	Age Scalp	Labelled germinative cells (back) %	Labelled cells UCP (back)	% Labelled germinative cells (scalp) (%)	Labelled cells UCP (scalp) (%)
1	25	26	10.2	12.6	7.9	10.9
2	24 ●	27	4.9	21.3	8.8	21.3
3	24 ●	44	7.1	17.9	11.1	13.2
4	25 ✳	35	6.8	15.5	11.4	42.3
5	25 ✳	52	8.3	19.5	11.1	16.5
6	25 ✳	42	8.2	16.4	4.0	11.0
7	25 ✳	34	7.5	26.5	6.6	9.4
8	25 ✳	28	6.0	11.1	7.4	15.6
9	25 ✳	42	7.5	18.0	8.2	18.1
10	21	23	13.2	20.9	11.1	29.4
11	28	29	8.8	19.3	8.0	23.1
12	29 □	24	10.0	19.2	10.3	25.8
13	29 □	25	13.9	28.4	9.4	34.8
14	39	23	13.0	32.5	9.3	23.5
15	46	26	6.7	6.9	9.8	19.3
16	25	36	12.9	13.9	10.6	17.0
17	25	31	11.0	36.5	6.1	12.6
18	30 ▲	33	9.9	20.9	9.4	18.3
19	30 ▲	22 *n*	10.3	20.8	7.5	20.1
20	30 ▲	24 *n*	9.3	21.0	7.7	19.5
21	31 ○	31 *n*	7.7	7.3	5.4	15.8
22	31 ○	42 *n*	8.1	14.1	10.0	37.5
23	37	39 *n*	7.7	13.5	8.0	17.5
24	29 *n*	26 *n*	8.3	23.3	7.9	17.7
25	22 *n*	25 *n*	7.3	22.8	8.8	17.7
26	32 *n*		7.2	18.6		
Mean ± S.D.			8.9 ± 2.3	19.2 ± 6.9	8.6 ± 1.9	20.3 ± 8.2

DISCUSSION

The anatomical features of the sebaceous gland as well as chemical and quantitative characteristics of the glandular end product—sebum (7, 10–12, 14, 15, 19, 21, 22, 24–31) are far better understood than the functional and kinetic aspects: namely, kinetics of cell proliferation (1, 4, 5, 8, 9, 20, 30), mechanisms of lipid formation, diurnal and seasonal variation (7, 10, 21, 22), and dependence upon stimuli or repressors (2, 6, 13, 24).

^{3}H-TdR labelling of the sebaceous gland in man (8, 9, 30) and mitotic indices in animals (1, 2, 4, 5, 20) have been reported before. Epstein et al. (8) reported a labelling index of 6.10%, while Sweeney et al. (30) found 7.14% labelled cells.

Table III. *The 10 largest cross-sectional areas of single sebaceous glands from various body sites, expressed in mm²*

	Scalp (mm²)	Forehead (mm²)	Back (mm²)
	0.1900	0.2112	0.2606
	0.1856	0.1775	0.2993
	0.1693	0.1875	0.2687
	0.1375	0.1787	0.2887
	0.1406	0.3575	0.2981
	0.1625	0.3043	0.2350
	0.1537	0.2143	0.2318
	0.1856	0.1731	0.2306
	0.1343	0.1812	0.2575
	0.1375	0.1900	0.3650
Mean	0.1596	0.2175	0.2735

Table IV. *Calculated ratio of areas (DCP : UCP) and ratio of cell counts (DCP : UCP) for the investigated body sites*

Site	Area ratio in cm² DCP : UCP	Cell ratio DCP : UCP
Back	9.31 : 1	2.78 : 1
Forehead	10.92 : 1	3.16 : 1
Scalp	8.96 : 1	2.98 : 1

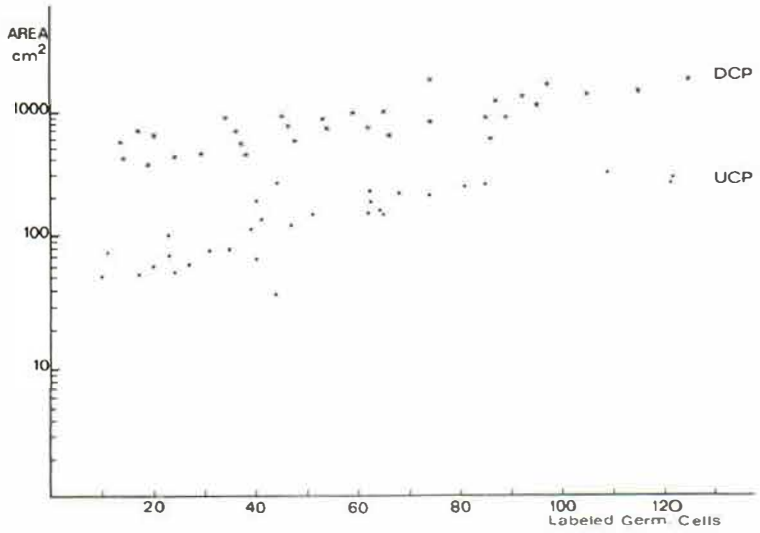

Fig. 5. Correlation between labelled germinative cells (DCP) or labelled basal cells of the undifferentiated cell pool (UCP) and planimetry of respective gland areas from the back. Linear function on a semilogarithmic scale.
DCP: $r = 0.8149$, slope 0.0584.
UCP: $r = 0.8196$, slope 0.2515.

Table V. *Correlation of basal cells to differentiating lipid cells*

The figures are the mean number of cells, calculated from among the means of all subjects within one region. Statistical analysis of this experiment showed a good correlation. There is a difference among the sites which is significant at the 95% level. (Variance ratio $F = 3.536$ with 2 and 74 degrees of freedom)

Site	Basal cells (DCP)	Differentiating cells (DCP)	Percentage basal cells of total cells	Sample correlation coefficient
Back	100	84	54.4	.8686
Forehead	100	75	58.1	.8789
Scalp	100	76	56.8	.8650

These figures compare with ours of 8.62% for the germinative cells (DCP) from the scalp, and 19.18% for the UCP. Similarly, when labelled cells were calculated per total gland (adapted data), these authors give figures of 3.91% (8) and 3.38% (30), which are lower than the figures reported here, namely 5.6% (Table VI).

The reasons why our data are higher than those reported previously are not clear. Certainly, variables such as number of probands, age, sex, body site, and environmental circumstances should be considered. It has become clear that significant differences in labelling indices of the DCP exist between the different body sites (Table VI). These variations are a typical sign of area-dependent

Table VI. *Labelling indices and labelled cells per 1 000 cells*

Data of other authors are adapted for comparison. Figures in parentheses relate to all gland cells except the undifferentiated cell pool. ⊣⊢ not given

References	Site	Number of subjects or specimens	Age and Sex	Labelling index in % basal cells	Labelled cells per 1000 cells
Epstein et al. (8)	Arm	2	22–83 ♂ & ♀	6.10	39.1
	Scalp	2			
Sweeney et al. (30)	Arm				
	Back	4	25–45 ♂	7.14	34.8
	Cheek				
Grana et al. (9)	Arm	⊣⊢	25–45 ♂	4.70	33.0
	Back			4.98	33.8
	Back	26		8.91	53.5 (48.9)
	Scalp	25	21–52 ♂	8.62	56.7 (49.0)
	Forehead	26		10.12	67.3 (58.6)

differences in the functional behaviour of skin. They compare with recent observations in human epidermis, where the number of ^{3}H-TdR-labelled cells in the forehead and scalp was nearly twice as high as on the back (17, 18).

The sebaceous gland represents an example of a regenerating tissue with a clear distinction between two compartments (proliferating and differentiating). It is complicated, however, by anatomical features. Like almost all tissues of this class, labelled cells (proliferating cells) are found in the basal layer and differentiate towards the sebaceous duct. Identification of the proliferating fraction of a cell population is usually based on the anatomical position of these cells at the basement membrane. There are indications, however, that this is an oversimplification and that some basal cells are in fact already in the process of differentiation (Fig. 4). In electronmicroscopical studies, several authors have shown that in the sebaceous gland some basal cells contained lipid droplets (7, 10, 21, 22) and thus have commenced differentiation. Some of the contradictory data on the proliferative activity are possibly due to the difficulty of determining the true proliferating cell pool.

It is interesting to note that in the sebaceous gland the relation of basal cells to differentiating cells is unusually high. For instance on the back, 54.4% of counted cells were basal cells (Table V). Yet in human forearm epidermis only about 33% of living cells are basal cells (16), and in the guinea pig ear their fraction amounts to 30% (3). The comparatively high number of basal cells in the sebaceous gland again supported the hypothesis that the basal cell population throughout the entire sebaceous gland is not homogeneous but represents a mixture of both cell fractions, proliferating and differentiating. This can also be inferred from Fig. 4.

Furthermore, nothing is known about the length of the DNA synthesizing phase in the human sebaceous gland, which would certainly affect the number of cells counted. No comparable data on mitotic figures are available.

Since cross-sectional areas are representative for the respective volumes, a surprisingly constant correlation was found to exist between gland volume and labelled basal cells. This means that the proliferative activity of a sebaceous gland is proportional to its volume. Larger glands therefore produce more cells per unit tissue than do small ones.

A few comments seem necessary concerning the undifferentiated cell pool (UCP). These cell groups are an obvious part of the sebaceous gland anatomy (Figs. 1, 2 and 3).

Serial sections revealed that the UCP formed a sponge- or coralreef-like skeleton throughout the sebaceous gland. Although recognized by previous observers (14, 15) their function remains unknown.

Our report clearly indicates that this cell-portion plays a significant role in the new cell production of the sebaceous gland. Daughter cells of the UCP are supposedly capable of differentiating into lipid cells. However, the separation of the two cell populations of the sebaceous gland (DCP and UCP) seems to be justified on the basis of their histological features and their proliferative activity. The UCP might therefore represent a peculiar accumulation of rapidly proliferating "basal cells" which supply the sebaceous gland.

ACKNOWLEDGEMENT

We gratefully acknowledge the technical assistance of Miss A. Dürre and Miss R. Bloomberg.

This study was supported by the Deutsche Forschungsgemeinschaft and the Hartford Foundation.

REFERENCES

1. Bertalanffy, F. D.: Mitotic activity and renewal rate of sebaceous gland in the rat. Anat Rec *129:* 231, 1957.
2. Bullough, W. S. & Laurence, E. B.: Chalone control of mitotic activity in sebaceous glands. Cell Tissue Kinet *3:* 291, 1970.
3. Christophers, E.: Die Regeneration der normalen und hyperplastischen Epidermis. Habilitationsschrift 1969 (München).
4. Ebling, F. J.: Hormonal control of sebaceous glands in experimental animals. *In* Advances in Biology of Skin, vol. IV (ed. W. Montagna, R. A. Ellis & A. F. Silver) pp. 200–219. Pergamon, Oxford, 1963.
5. — Factors influencing the response of the sebaceous glands of the rat to androgen. Brit J Derm *82:* 9, 1970.
6. Eisen, A. Z., Holyoke, J. B. & Lobitz, W. C.: Responses of the superficial portion of the human pilosebaceous apparatus to controlled injury. J Invest Derm *25:* 145, 1955.
7. Ellis, R. A. & Henrikson R. C.: The ultrastructure of the sebaceous glands in man. *In* Advances in Biology of Skin, vol. IV (ed. W. Montagna, R. A.

Ellis & A. F. Silver) pp. 94–109. Pergamon, Oxford, 1963.
8. Epstein, E. H. & Epstein, W. L.: New cell formation in human sebaceous glands. J Invest Derm *46:* 453, 1966.
9. Grana, A. & Bosco, M.: Il turnover delle ghiandole sebacee umane. Ann Ital Derm Clin Sper *23:* 279, 1969.
10. Hibbs, R. G.: Electron microscopy of human axillary sebaceous glands. J Invest Derm *38:* 329, 1962.
11. Hodgson-Jones, I. S., MacKenna, R. M. B. & Wheatly, V. R.: The study of human sebaceous activity. Acta Dermatovener (Stockholm) *32:* 155, 1952.
12. Horstmann, E.: Anatomie der Haut und ihrer Anhangsorgane I/1. Dermatologie und Venerologie (ed. H. A. Gottron & W. Schönfeld) pp. 42–103. Georg Thieme Verlag, Stuttgart, 1961.
13. Kligman, A. M. & Shelley, W. B.: An investigation of the biology of the human sebaceous gland. J Invest Derm *30:* 99, 1958.
14. Montagna, W.: The sebaceous glands. *In* The Structure and Function of Skin, 2nd ed. Academic Press, New York, 1962.
15. — The sebaceous glands in man. *In* Advances in Biology of Skin, vol. IV (ed. W. Montagna, R. A. Ellis & A. F. Silver) pp. 19–31. Pergamon, Oxford, 1963.
16. Pinkus, H.: Examination of the epidermis by the strip method. II. Biometric data on regeneration of the human epidermis. J Invest Derm *19:* 431, 1952.
17. Plewig, G. & Kligman, A. M.: Zellkinetische Untersuchungen bei Kopfschuppenerkrankung (Pityriasis simplex capillitii). Eine radioautographische Untersuchung. Arch Klin Exp Derm *236:* 406, 1970.
18. Plewig, G., Fulton, J. E. & Kligman, A. M.: Cellular dynamics of comedo formation in acne vulgaris. Arch Derm Forsch *241.* In press.
19. Pochi, P. & Strauss, J. S.: The effect of aging on the activity of the sebaceous gland in man. *In* Advances in Biology of Skin, vol. VI (ed. W. Montagna) pp. 121–127. Pergamon Press, Oxford, London, Edinburgh, New York, Paris, Frankfurt, 1964.
20. Ritter, R.: Über die mitotische Aktivität der Talgdrüsen während eines Haarzyklus bei Albinomäusen. Inauguraldissertation 1968, Dermatologische Universitätsklinik Marburg.
21. Rogers, G. E.: Electron microscope observations on the structure of sebaceous glands. Exp Cell Res *13:* 517, 1957.
22. Rupec, M.: Zur Ultrastruktur der Talgdrüsenzellen. Arch Klin Exp Derm *234:* 273, 1969.
23. Snedecor, G. W.: Statistical Methods, 5th ed. The Iowa State University Press, Ames, Iowa, 1962.
24. Strauss, J. S. & Kligman, A. M.: Acne: Observations on dermabrasion and the anatomy of the acne pit. Arch Derm (Chicago) *74:* 397, 1956.
25. — The pathologic dynamics of acne vulgaris. Arch Derm (Chicago) *82:* 779, 1960.
26. Strauss, J. S. & Pochi, P. E.: The hormonal control of human sebaceous glands. *In* Advances in Biology of Skin, vol. IV (ed. W. Montagna, R. A. Ellis & A. F. Silver) pp. 220–254. Pergamon, Oxford, 1963.
27. Strauss, J. S. & Pochi, P. E.: The human sebaceous gland: Its regulation by steroidal hormones and its use as an end organ for assaying androgenicity in vivo. *In* Recent Progress in Hormone Research, vol. 19, III. Academic Press, New York, 1963.
28. — Histology, histochemistry and electron microscopy of sebaceous glands in man. *In* Handbuch der Haut- und Geschlechtskrankheiten, Ergänzungswerk I/1 (ed. O. Gans & G. K. Steigleder) pp. 184–223. Springer Verlag, Berlin, 1969.
29. — Assay of anti-androgens in man by sebaceous gland response. Brit J Derm *82:* 33, 1970.
30. Sweeney, T. M., Szarnicki, R. J., Strauss, J. S. & Pochi, P. E.: The effects of estrogen and androgen on the sebaceous gland turnover time. J Invest Derm *53:* 8, 1969.
31. Van Scott, E. J. & Ekel, T. M.: Kinetics of hyperplasia in psoriasis. Arch Derm (Chicago) *88:* 373, 1963.
32. Yamada, K.: Quantitative Untersuchungen der Anhangsorgane der Haut bei dem Deutschen. Folia Anat Jap *10:* 721, 1932.

Received May 10, 1971

G. Plewig, M.D.
Department of Dermatology
8 Munich 15
Frauenlobstr. 9
BRD