The Refractoriness of the Skin of Hairless Mice to Chemical Carcinogenesis

Beppino C. Giovanella, Joyce Liegel, and Charles Heidelberger

McArdle Laboratory for Cancer Research, The Medical School, University of Wisconsin, Madison, Wisconsin 53706

SUMMARY

The sensitivity to cutaneous chemical carcinogenesis of haired and hairless mice of the same strain has been compared. 9,10-Dimethyl-1,2-benzanthracene has been used as the initiator, and 0.5% croton oil in acetone has been used as the promoter. More than 29 weeks of this treatment produced a total of only 7 papillomas in 44 hairless mice, 87 papillomas and 3 carcinomas in their 13 haired siblings, and 127 papillomas and 9 carcinomas in 69 Swiss haired mice. Thus, the skin of haired mice is much more susceptible to chemical carcinogenesis than the skin of hairless mice. Traumatization of the skin did not alter these results. Newborn “haired” and “hairless” mice have equal amounts of hair during the first 2 weeks of life. If treated in the above manner during this period, they respond identically. These results stress the importance of the hair follicle and its appendages in cutaneous chemical carcinogenesis of the mouse.

INTRODUCTION

The first indication that the presence of hair follicles plays a role in the chemical carcinogenesis of mouse skin came from the experiments of Lacassagne and Laterjet (19) in 1946. They found that scars on the skin of mice in which hair did not regrow did not give rise to epithelial tumors when painted with MCA. Tumors were easily produced, however, in scars in which hair follicles were present. Suntzeff et al. (26) observed that the skin of newborn mice is resistant to carcinogenesis when painted with a carcinogen before the formation of hair follicles. Liang (20), using whole-mount preparations of mouse skin treated with MCA, was able to locate the first appearance of epithelial hyperplasia and neoplasia in, or in the vicinity of, the pilosebaceous apparatus. Billingham et al. (3), after painting mouse skin with MCA, transplanted the epidermis onto an untreated area of dermis and grafted untreated epidermis onto the treated area of dermis. Invariably, epithelial carcinomas arose only from the areas in which the dermis had been treated, where the only epithelial structures present were the hair follicles. In 1968, Steinmuller (25), using F1 hybrids in comparable grafting experiments, elegantly demonstrated that the hair follicle is the only possible origin of such tumors.

In apparent contradiction to the findings cited above are a number of reports stating that the skin of the hairless mouse is susceptible to chemical carcinogenesis (2, 9–12, 15, 17, 21, 23). We have reinvestigated the induction of skin tumors in hairless mice by chemical carcinogens, using the induction-promotion technique. Haired and hairless mice of the same strain, differing only in the presence or absence of the hairless mutation, were exposed to the same carcinogenic stimulus at doses just below those required to produce papillomas in 100% of the haired mice, after we made sure that the hairless mice used were really hairless.

MATERIALS AND METHODS

The mice used were a homogeneous strain, bb cc hr hr or bb cc Hr hr. Throughout this paper, the former are referred to as hairless mice and the latter are referred to as haired mice. Each group was composed of siblings. This strain originated at the Jackson Laboratory, where it was bred through at least 23 generations of sister-brother matings (d bb cc Hr hr X gb bb cc Hr hr). In 1963, some animals of this strain were given to the Division of Biological and Medical Research of the Argonne National Laboratory. At the Argonne National Laboratory these animals were bred randomly, crossing haired females with hairless males. The animals for the adult experiments were obtained directly from the Argonne National Laboratory over the period of 1964 to 1968 through the kindness of Dr. Charles Auerbach or were bred in our animal room. We obtained the “newborns” by crossing haired females with hairless males. All the mice were housed in plastic cages and received water and Rockland pellets ad libitum.

DMBA (Aldrich Chemical Co., Inc., Cedar Knolls, N. J.) in distilled acetone was used as an initiator. This solution (0.1 ml containing 100 μg of DMBA) was placed on the backs of the mice with a micropipet. For promotion, a solution of 0.5% croton oil in acetone (kindly donated by Dr. R. K.

---

1This work was supported in part by Grant CA 07175 from the National Cancer Institute, NIH. A preliminary report of part of this work has appeared (13).
2Present address: The Stehlin Foundation, 834 Hermann Professional Building, Houston, Texas 77025.
3American Cancer Society Professor of Oncology.
4The abbreviations used are: MCA, 3-methylcholanthrene; DMBA, 9,10-dimethyl-1,2-benzanthracene.

Received March 2, 1970; accepted July 1, 1970.

2590 CANCER RESEARCH VOL. 30
Boutwell of this laboratory) was used; 1 to 2 drops were applied twice weekly to the adults and once a week to the “newborns.” The same batch of croton oil was used for all experiments and was kept frozen. The solutions of croton oil and DMBA were made monthly and kept in dark bottles in the refrigerator. Hairless and hairless mice were treated with the same solution.

The animals were inspected under a magnifying glass, and no hairless mouse was treated with DMBA unless there were less than 20 hairs on its back; the majority had less than 10 hairs. Animals with more hair were used as controls. The newborns (the whole litter) were treated with DMBA 3 to 16 days after birth. They were later classed as hairless or haired according to whether or not they shed their hair after the first pelage was gone (see “Discussion”). For histological examination, samples were fixed in 10% formalin, embedded in paraffin, sectioned at 5 to 7 μ, and stained with hematoxylin and eosin.

### RESULTS

For facilitation of a comparison of different experiments, our results have been tabulated in Table 1. Table 2 contains, in comparable form, the data published by others who have worked with hairless and rhino mice. Figs. 1 to 3 illustrate Experiment 1.

Fig. 1 shows the only 3 papillomas that appeared in treated hairless mice. Also pictured is a large skin sore, a lesion observed in both treated and untreated hairless mice of this strain. Some of the lesions result from leukemic infiltration of the dermis, as in the case of the sore pictured in Fig. 1. Leukemias are fairly frequent in our strain of hairless mice. In Experiment 1, 3 leukemias developed in 19 croton oil-treated controls, and 5 leukemias developed in 20 DMBA-treated animals.

Fig. 2 shows a section of skin from a treated hairless mouse in Experiment 1 with leukemia infiltration and

### Table 1

**Cutaneous carcinogenesis of hairless and haired mice**

<table>
<thead>
<tr>
<th>Experiment</th>
<th>Strain</th>
<th>Treatment</th>
<th>Age at start</th>
<th>No. and types of tumors in hairless mice</th>
<th>Control haired mice</th>
<th>No. and types of tumors in haired control mice</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>bb cc hr hr (dd), 100 μg of DMBA in acetone: 20 μg</td>
<td>Same experiment, 100 μg of DMBA in acetone: 20 μg</td>
<td>15–18 wk</td>
<td>After 14 wk CO treatment, 0 P/20; After 20 wk CO treatment, 1 P/17; After 31 wk CO treatment, 1 P/16; After 41 wk CO treatment, 3 P/8</td>
<td>9 Swiss mice: After 14 wk CO treatment, 19 P/40; After 20 wk CO treatment, 74 P/39; After 31 wk CO treatment, 34 P/37 + 5 C; After 41 wk CO treatment, 167 P/36</td>
<td>After 14 wk CO treatment, 19 P/40; After 20 wk CO treatment, 74 P/39; After 31 wk CO treatment, 34 P/37 + 5 C; After 41 wk CO treatment, 167 P/36</td>
</tr>
<tr>
<td>2</td>
<td>Same, 14 d</td>
<td>Same, but CO treatment started 3 wk after DMBA application and continued for 29 wk</td>
<td>32–36 wk</td>
<td>After 12 wk CO treatment, 0 P/12; After 29 wk CO treatment, 3 P/10 (2 near vibrissae origin, 1 on the top of the head)</td>
<td>Haired mice (15 d) of the same strain treated once.</td>
<td>After 12 wk CO treatment, 23 P/17 + 6 C; After 23 wk CO treatment, 68 P/26 + 6 C</td>
</tr>
<tr>
<td>3</td>
<td>Same, 34 newborns</td>
<td>Same, but CO treatment started 3–7 days after DMBA application and continued once a wk for 32–40 wk</td>
<td>3–16 days</td>
<td>After 29 wk, 11 P/30; maximum, 34/34 + 3 C</td>
<td>74 haired mice of the same litter as the hairless</td>
<td>After 29 wk, 71 P/64; maximum, 66 P/70 + 11 C</td>
</tr>
<tr>
<td>4</td>
<td>Same, 10 mice/group, 40 μg</td>
<td>(a) 100 μg of DMBA in 0.1 ml acetone followed by puncture 2 times/wk; (b) Same, but also 2 drops of 0.5% CO in acetone after each puncture (c) Punctured once, just before DMBA application, then CO 2 times/wk without puncturing (d) As in c., but also punctured twice weekly before CO application</td>
<td>32–36 wk</td>
<td>None</td>
<td>None</td>
<td></td>
</tr>
</tbody>
</table>

The abbreviations used are: CO, croton oil; P, papillomas; C, carcinomas.
### Table 2

**Date from literature**

<table>
<thead>
<tr>
<th>Reference</th>
<th>Hairless mice</th>
<th>Treatment</th>
<th>Age</th>
<th>Incidence and types of tumors observed in treated hairless mice</th>
<th>Control haired mice</th>
<th>Incidence and types of tumors observed in treated haired mice</th>
</tr>
</thead>
<tbody>
<tr>
<td>2(1936)</td>
<td>Mixed ancestry; &quot;naked&quot; with occasional patches of fur; 34 animals</td>
<td>“Turning” 3 times a wk with a benzene extract of coal tar for 120 days. Does not state.</td>
<td>Not stated. Animals observed until death; survivors up to 740 days</td>
<td>18% with carcinomas at 200 days; 55% with carcinomas at 1 yr. calculated on survivors at 120 days.</td>
<td>Hairy mice of the same strain</td>
<td>Same incidence of papillomas as in the hairless. 17/23 males and 12/23 females developed squamous cell carcinomas; also 5/13 males and 8/23 females developed fibrosarcomas</td>
</tr>
<tr>
<td>9(1951)</td>
<td>hr, approximately 50 animals</td>
<td>Painted weekly with 0.25% MCA in ether for 20 wk. Does not state.</td>
<td>6 wk at the start. Animals observed until death</td>
<td>All the animals developed single or multiple papillomas. 17/23 males and 24/25 females also developed squamous cell carcinomas</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>23(1954)</td>
<td>hr/hr, genotype cr as bb dd pp hr/hr, 24 animals</td>
<td>Painted once with 0.5% MCA in benzene. Does not state.</td>
<td>1.5 to 22 mo. at the start. Animals observed until death for 18 mo.</td>
<td>145 skin &quot;growths&quot; in 19/24 mice. All 19 were 6.5 mo. old or younger when treatment started. Many sebaceous adenomas, a few papillomas, and 4 carcinomas</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>16(1964)</td>
<td>hr/hr, 30 animals in each group, 15 males and 15 females</td>
<td>MCA in benzene once; Group a. 10 µg; Group b. 5 µg; Group c. 3 µg; Group d. 1.25 µg; Group e. 1000 µg</td>
<td>8 to 10 wk at the start. Animals observed for 18 mo.</td>
<td>5% with papillomas % with carcinomas</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>16(1964)</td>
<td>hr/hr, 30 animals in each group, 15 males and 15 females</td>
<td>MCA in benzene; 5 applications at 3-day intervals. Total dose: Group a. 80 µg; Group b. 40 µg; Group c. 20 µg; Group d. 10 µg; Group e. 5 µg</td>
<td>8 to 10 wk at the start. Animals observed for 18 mo.</td>
<td>5% with papillomas % with carcinomas</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>11(1965)</td>
<td>C57BL hairless, 12 animals</td>
<td>Painted once with 500 µg of DMBA in benzene. Mice observed for more than 6 mo.</td>
<td>Not stated. Animals observed for more than 6 mo.</td>
<td>Many hundreds of tumors, predominantly papillomas in the 12 hairless, 6 haired and 6 rhino mice treated. No differences between these mice are stated</td>
<td>6 haired mice of the same strain as the hairless treated with DMBA, as were the hairless</td>
<td>Not stated. Animals developed different numbers of benign tumors at 12 wk.</td>
</tr>
<tr>
<td>10(1965)</td>
<td>Inbred hairless mice, 42 animals</td>
<td>500 µg DMBA in acetone</td>
<td>7 to 12 wk at the start</td>
<td>5 tumors in 3/41 mice after 30 wk; 3 tumors in 3/30 mice after 50 wk. Type of tumors not stated</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2(1969)</td>
<td>Mice homozygous for hairlessness, 12 animals</td>
<td>DMBA in acetone weekly for a total of 2.5 µg</td>
<td>6 to 10 mo. at the start; animals observed for 8 mo.</td>
<td>On average, 15 papillomas/mouse; 4/10 mice surviving more than 10 wk developed squamous cell carcinomas</td>
<td>24 female F1 BALB/cGa X 129/RaGa</td>
<td>On average, 15 papillomas/mouse; 9/12 mice surviving more than 10 wk developed squamous cell carcinomas</td>
</tr>
<tr>
<td>17(1965)</td>
<td>C57BL hairless, 10 animals</td>
<td>Group a (4 mice) received 8 µg of DMBA in mineral oil in 4 applications; Group b (4 mice) received 6 µg of DMBA in 3 applications; Group c (2 mice) received 150 µg of DMBA in acetone in 3 applications</td>
<td>10 to 20 wk at the start; observed for 18 mo.</td>
<td>7/8 of Groups a and b developed pigmented benign tumors, 10 to 30 in each mouse. Most of the animals developed also squamous cell carcinomas</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>12(1965)</td>
<td>BALB/cHud. hr/hr x C57BL/6Ch. Progeny selected for non-agouti black and brother-sex imbed for 10 generations. 20 animals</td>
<td>Group a received 500 µg of DMBA in mineral oil on 10 animals; Group b received 375 µg of DMBA in mineral oil on 10 animals</td>
<td>Group a. 10 to 12 mo. at the start; Group b. 2 mo. at the start. Observed for 9 wk</td>
<td>Group a, 54 papillomas in 9 survivors at 9 wk; Group b, 125 papillomas in 10 survivors at 9 wk</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>12(1965)</td>
<td>Same as above, 18 animals</td>
<td>Group a received 50 µg of DMBA in benzene-mineral oil (8 animals); Group b, same (10 animals)</td>
<td>Group a, 10 to 12 mo. at the start; Group b. 2 mo. at the start; observed for 9 wk</td>
<td>Group a, 14 papillomas in 6 survivors at 9 wk; Group b, 67 papillomas in 10 survivors at 9 wk</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>12(1965)</td>
<td>Same as above, 10 animals</td>
<td>10 µg DMBA in benzene-mineral oil</td>
<td>2 mo. at the start. Observed for 9 wk.</td>
<td>18 papillomas in 10 survivors at 9 wk (these are the same animals in Group b of the previous experiment. The 2 doses were applied to 2 different areas, equal in size, of the back)</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>
Hairless Mouse Skin Resistance to Carcinogenesis

destruction of the dermis. Extensive leukemic invasion of the liver in the same mouse is illustrated in Fig. 3. This animal had a large, running skin sore (Fig. 1), an enlarged liver (2.2 g), an enlarged spleen (0.7 g), and nodules in the lungs.

Treatment was initiated in the control Swiss mice of Group A 5 to 7 days before eruption of new hair. Twenty-three papillomas and 6 carcinomas appeared in 27 mice at 41 weeks. Treatment was initiated in mice of Group B 3 to 5 days after eruption of new hair. In 1953, Andresen and Engelbreth-Holm (1) demonstrated that haired mouse skin is more sensitive to chemical carcinogenesis during the resting phase. In 1956, Klinken-Rasmussen (18) showed that a minimum yield of papillomas was obtained when DMBA was applied 0 to 5 days before eruption of new hair, and a maximum yield resulted after application of the same carcinogen 1 to 6 days after eruption of new hair. This experiment was performed primarily for the purpose of demonstrating that our solutions actually contained carcinogenic substances.

The hairless and haired mice in Experiment 2 belong to the same strain. The difference between the 2 groups was quite striking. In the hairless group, only 3 papillomas were present, all outside the area of painting; 1 was on the top of the head and 2 were near the origin of the vibrissae. In the haired group, 87 papillomas and 3 carcinomas developed. Thus, these haired counterparts of the hairless mice of the same strain are very susceptible to tumor induction.

Fig. 4 illustrates a section of skin from a 32-week-old haired mouse; 2 hair follicles are shown. By contrast, Fig. 5 shows a section of skin from a hairless mouse of the same age. The lack of hair follicles and the large sebaceous cysts are evident.

Fig. 6 shows a papilloma in a haired mouse from Experiment 3. A papilloma in a hairless mouse from Experiment 3 and the skin which surrounds it are shown in Fig. 7. Note the great abundance of utriculi (residues of the hair canal) in this area. If we compare this to the hairless skin pictured in Fig. 5, we see that the former, in which the papilloma arose, was not truly hairless. Fig. 8 shows an epidermal carcinoma in a hairless mouse from Experiment 3. Fig. 9 illustrates the skin in the immediate proximity of this tumor. Again, note the number and development of utriculi, showing that the skin in which this carcinoma appeared was not really hairless.

We began treatment of the newborn mice bred in this laboratory when they were 3 to 16 days old and the hairless mice could not be distinguished from the haired mice. The maximum number of tumors obtained in Experiment 3 (Table 1) was 34 papillomas and 3 carcinomas in 34 mice that subsequently became hairless and 66 papillomas and 11 carcinomas in 70 mice that remained hairless. It is apparent that these animals responded identically because they were equally haired when the initiator was applied. These results, as compared with the paucity of tumors induced in adult, truly hairless mice, stress the importance of the hair follicle in cutaneous chemical carcinogenesis.

Experiment 4 (Table 1) was designed to determine whether trauma has any effect on skin carcinogenesis in hairless mice. The instrument we used for traumatization was a 1-inch square of wood from which 80 needles protruded. We found that traumatization of the skin of hairless mice does not increase the production of tumors, whether applied before or after initiation, with or without promotion with croton oil.

DISCUSSION

The hairless (hr hr) mutation has been independently observed more than once in mice. The majority of the hairless mice used for carcinogenesis experiments in the U. S. and Europe are descendants of the so-called Crew mice. These mice originated from a pair of wild hairless mice found in an aviary in London and bred by Brooke (5). In 1924, Brooke sent a hairless male and several heterozygous haired females to Dr. F. A. E. Crew of the University of Edinburgh (6, 7). By 1930, after overcoming many difficulties in breeding, Crew had succeeded in establishing a healthy strain of hairless mice. He reported (6) that the hairless mutant character is a simple recessive and described the characteristics of the strain (7).

Studies on the structure of hairless mouse skin have been carried out by Mann and Strale (22), Montagna et al. (24), and Iversen and Iversen (16). The homozygous hairless mouse produces a normal first pelage after birth, but, in contrast to the haired mouse, it does not develop normal replacement hairs (7). The few scattered hairs that do grow afterward develop from abnormal tylotrich follicles (22), which are larger than the other pelage follicles. The number of tylotrichs decreases as the hairless mouse ages, and by 1.5 years of age they are all lost. However, during this period, the hairless mouse has rudimentary hair cycles (8, 16). A characteristic feature of hairless mouse skin is the presence of numerous sebaceous cysts (Fig. 5), which originate from the residue of the pilosebaceous apparatus (24). It is important to consider that even in areas of the skin where hair is not present, there are epithelial remnants of the pilosebaceous apparatus, such as the utriculi, which are residues of the hair canal. These residues in both the hairless and rhino mouse (another hairless mutation) become increasingly scarce as the animal ages or undergoes sebaceous differentiation (12, 23). It has been observed in both rhino (12) and hairless (23) mice that, with increase in age, the sensitivity of the skin to carcinogenic chemicals diminishes. However, this observation has not been correlated with the loss of hair follicles or the epithelial structures related to them.

Cursory examination of the literature reported in Table 2 shows the difficulties involved in comparing data. First, hairlessness is due to a mutant gene and does not define a strain. At present, many strains exist that carry this character; some of them are more defined than others, and some are more inbred than others.

It is well known that strains of haired mice differ enormously in their sensitivity to carcinogenic chemicals applied to the skin. Using the initiation-promotion technique (25 μg of DMBA as initiator and croton oil twice a week as promoter), Boutwell (4) reported an average of 0.5 papillomas/mouse in the least susceptible Swiss mice from the 7 colonies he tested, as compared to 10.6/mouse in the most sensitive. Malignant tumors developed in 70% of the most
susceptible mice and in only 17% of the most resistant. The cause of these variations in susceptibility to chemical carcinogenesis is unknown. It is also not known how the introduction of the hairless mutation would affect the skin of different strains, except for the fact that they will undergo a gross loss of hair. It is therefore evident that meaningful comparisons of the susceptibility of haired and hairless mice to cutaneous chemical carcinogenesis can be made only between mice of the same strain. Table 2 shows that only Deringer (9) and Forbes (11) used this experimental design. Unfortunately, Deringer (9) started treating her mice very early (6 weeks after birth), when hair follicles and epithelial residues of the pilosebaceous apparatus are still present and numerous in the skin. She also used saturation conditions of treatment (weekly painting with a solution of MCA for 20 weeks), which resulted in 100% incidence of papillomas in both the “hairless” and haired mice and a high incidence of malignant tumors in both. Forbes (11) did not give any numbers or descriptions of the tumors he obtained, nor did he state the age of the animals used in his experiment.

The very careful experiments of Iversen and Iversen (15) lack controls of haired mice of the same strain. Nevertheless, the incidence of papillomas is rather high. This can be explained by the early age at which the mice were treated, when the experimenters themselves showed that hair was still present (16), as were epithelial remnants of the pilosebaceous apparatus. Our results are probably in good agreement with those obtained by Epstein (10). He treated 42 hairless mice once with 500 μg of DMBA and obtained only 5 papillomas; this indicates considerable resistance to carcinogenesis. The studies of others summarized in Table 2 were reported too ambiguously to enable us to draw any conclusions. They are shown in order to present a complete survey of the research done on this subject.

It is evident from our results that a profound difference in susceptibility to chemical cutaneous carcinogenesis between hairless and haired mice of the same strain can be demonstrated when nonsaturation conditions are utilized. This difference is evident, however, only in adult mice. In the newborn, all of which are haired, this discrepancy does not exist.

In our studies, under identical conditions, the maximum number of papillomas obtained per mouse were 0.37 in adult hairless females, 0.30 in adult hairless males, and 6.7 in adult haired males. However, 3 of the 6 papillomas obtained in the hairless mice were in haired unpainted areas. This incidence of papillomas is approximately equal to that of the most resistant strain tested by Boutwell (4), whereas our hairless mice had an incidence which was roughly equivalent to that of the most susceptible strains, with the exception of the one bred especially for sensitivity to chemical carcinogenesis.

Malignant epithelial tumors of the skin were not observed in the adult hairless mice and were few in the hairless ones. However, these mice were observed for only 31 weeks after application of DMBA, which is a very short time for cancers to become manifest. During the first 2 weeks of life, the future hairless mice cannot be differentiated from their future haired littermates, because at this stage they have equal amounts of hair. When we initiated treatment for the entire litter during this period, we obtained equal numbers of papillomas in those animals that matured into hairless mice and those that were haired after maturation.

The insensitivity to chemical carcinogenesis of hairless mouse skin is not due to a lack of penetration of the skin by the carcinogen. This has been proved by the fact that when radioactive DMBA was applied to the skin of Swiss hairless mice and to hairless female mice, the radioactivity bound to proteins and DNA (which was extracted from epidermis and dermis) was slightly higher in the hairless mice than in the haired ones (14). Similarly, labeled phorbol ester (kindly provided by Professor E. Hecker, Heidelberg, Germany) enters the skin (unpublished results). However, since acetone spreads more on hairless than on haired mouse skin, the effective dose of hydrocarbon and croton oil per unit area may have been slightly less in the hairless mice.

Trauma applied before or after application of DMBA, with or without croton oil treatment, did not alter the refractoriness of the hairless skin to carcinogenesis. The results of all these experiments give support to the hypothesis that in the hairless skin there is a drastic reduction in the number of cells capable of undergoing neoplastic transformation. The logical deduction is to identify these target cells with those of the hair follicle and its infundibulum—in other words, with the epithelial cells of the piliary apparatus.

REFERENCES

Hairless Mouse Skin Resistance to Carcinogenesis

The Refractoriness of the Skin of Hairless Mice to Chemical Carcinogenesis

Beppino C. Giovanella, Joyce Liegel and Charles Heidelberger

Cancer Res 1970;30:2590-2597.

Updated version

Access the most recent version of this article at:
http://cancerres.aacrjournals.org/content/30/10/2590

E-mail alerts

Sign up to receive free email-alerts related to this article or journal.

Reprints and Subscriptions

To order reprints of this article or to subscribe to the journal, contact the AACR Publications Department at pubs@aacr.org.

Permissions

To request permission to re-use all or part of this article, contact the AACR Publications Department at permissions@aacr.org.