contain various ACTH peptides other than α-MSH peptides. Some degree of cross reactivity between the 2 antisera used cannot be excluded since N-terminal fragments of the tetracosapeptide including α-MSH, inhibited complement fixation of the anti-β^{1-24}-corticotropin with the antigen conjugate to a very small degree[9].

By re-staining and comparing identical fields, the fluorescing 'corticotrophs' of the pars anterior were clearly identified as PAS-positive cells of the basophil series (Figure 2). PAS-staining was diffuse, rather weak, and no granules were seen. These cells, though tinctorially similar, could be easily distinguished from the more centrally located thyrotrophs[15]. They are most probably related to the R-type mucoid cells of the human anterior pituitary which are considered to contain ACTH[7,16]. In contrast to the view taken by other investigators[3] we conclude therefore that β-corticotropin is produced by a similar, probably identical cell type in various mammalian species.

Zusammenfassung. Unter Verwendung eines spezifischen Anti-β^{1-24}-Corticotropin-Serums vom Kaninchen wurde β-Corticotropin immunhistologisch in der Rattenhypophyse nachgewiesen. Neben den Epithelien der Pars intermedia konnte kortikotropes Hormon in einem besonderen, mukoiden Zelltypus der Adenohypophyse lokalisiert werden.

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Induction of Pigmentary Changes in the Skin of the Mongolian Gerbil by Chemical Carcinogens

Although considerable insight has been gained concerning the many unique features of skin carcinogenesis in the Syrian and Chinese hamsters, little comparable attention has been given to the related Mongolian gerbil (*Meriones unguiculatus*)[1-5]. It has been reported that 7,12-dimethylbenz(*a*)anthracene (DMBA) applied topically to the skin of gerbils produces papillomas, sarcomas and carcinomas, but further details, particularly relating to their pigmentary system, have not been published[6]. This communication demonstrates that DMBA and croton oil when applied to the hairy (trunk) skin of adult gerbils elicit striking pigmentary changes which may or may not be associated with developing neoplasms.

A total of 16 gerbils 3 months of age were divided into 4 groups each consisting of 3 males and 1 female. The experimental groups (G. 1–4) received the following treatments for periods up to 6 months: (G. 1) 1 ml of acetone applied once a week, (G. 2) 1 ml of 1% croton oil-in-acetone applied 3 times a week, (G. 3) 1 ml of 0.1% DMBA-in-acetone applied once a week, and (G. 4) 1 ml of 0.1% DMBA-in-acetone once a week for 4 weeks followed by 1 ml of 1% croton oil-in-acetone 3 times a week. Each solution was released on the shaved dorsa of the test animals from a calibrated syringe. A few animals were killed during the period of treatment, the remainder at its termination. Standard histological procedures were followed in preparing paraffin sections and whole mounts of representative skin specimens. The normal histology of the skin was determined in an additional 12 adult gerbils.

With the exception of the melanocyte system, the normal histology of the hairy (trunk) skin of the gerbil has been described elsewhere[7,8]. Our observations suggest that active melanocytes are largely restricted to the hair bulbs and occasionally the outer root sheaths of growing (anagen) hair follicles. Active melanocytes are absent from the basal layer of the thin, interfollicular trunk epidermis. The hair follicles are systematically arranged to form small groups in the dorsal skin. Variable numbers of networks of dermal melanocytes are present surrounding groups of hair follicles (Figure 1). The melanocytes which form the perifollicular networks also vary in number and as a consequence may completely or only partly encircle a particular group of follicles. The fusiform dermal melanocytes are closely applied to the sebaceous glands and connective tissue sheaths of the hair follicles. The perifollicular networks may occur singly or several adja-

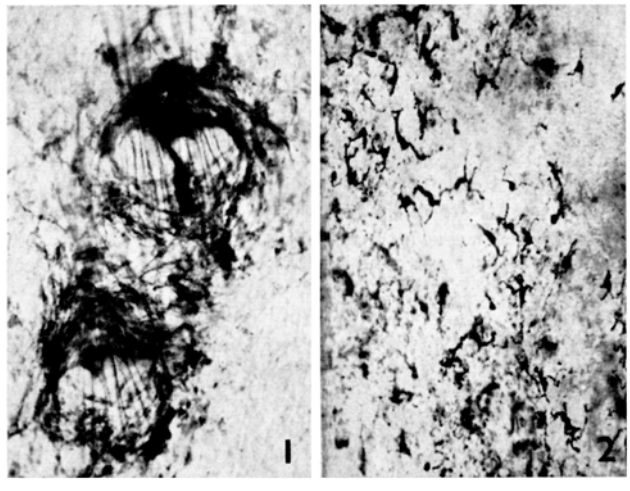

Fig. 1. Perifollicular networks of melanocytes in normal skin. × 200.
Fig. 2. Melanogenic epidermal melanocytes in DMBA-treated skin. × 200.

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cent ones may be joined together by interfollicular dermal melanocytes to produce pigmented 'islands'. In some regions the melanocytes form diffuse dermal networks which lack significant condensations about hair follicles. The repeated application of acetone (G. 1) does not elicit a departure from this picture of the normal skin.

Hyperpigmentation of the dorsal trunk skin progressively emerges in gerbils treated with croton oil-in-acetone (G. 2). It is clear that the darkening results from a marked increase in the population of active dermal melanocytes. From the pectoral hump to the base of the tail, the region over which the croton oil is most consistently applied, almost all hair follicle groups are surrounded by networks of dermal melanocytes and great numbers of melanocytes extend between them giving rise to an almost uniform meshwork. No active melanocytes are observed in the thickened interfollicular epidermis. No papillomas or other tumors have been found in the gerbils treated with croton oil for periods up to 6 months.

Numerous papillomas do develop in gerbils treated with DMBA-in-acetone (G. 3). The papillomas are most numerous on the treated dorsum but also occur in the ventrum which receives DMBA through spread from the dorsum. Melanocytes are often found in the dermis beneath papillomas, and less frequently in their hyperplastic epithelia. In addition, there is a rather spotty distribution of melanogenic epidermal melanocytes in the non-papillomatous, painted epidermis (Figure 2). As in the croton oil-treated animals there is a striking increase in the numbers of dermal perifollicular melanocyte networks and dermal interfollicular melanocytes.

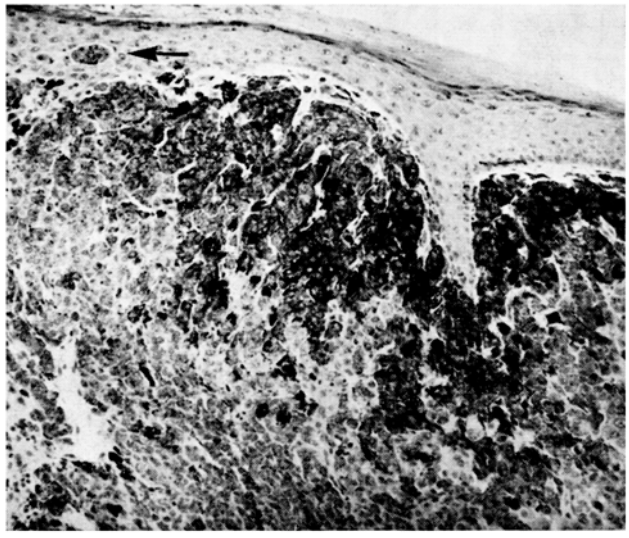

Fig. 3. Dermal melanotic tumor in skin treated with DMBA and croton oil. A small group of tumor cells (arrow) appears to be located in the overlying hyperplastic epidermis. × 200.

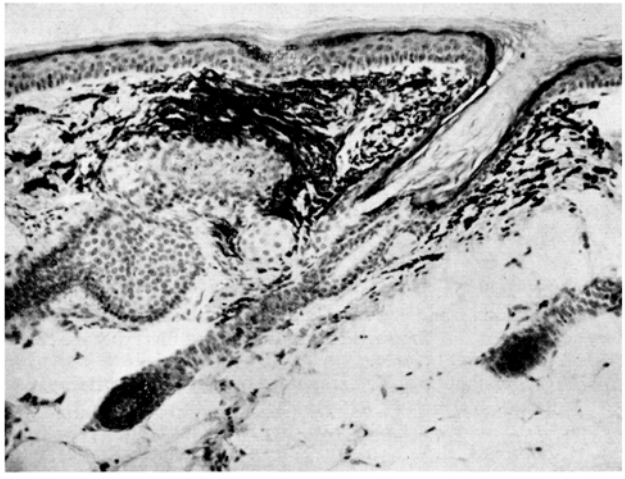

Fig. 4. Dermal melanocytes in croton oil treated skin, illustrating their distribution around and between hair follicles. × 200.

Results similar to those obtained with DMBA alone are noted in animals treated with both DMBA and croton oil (G. 4). The only 'melanocytic' tumor found thus far developed in a DMBA-croton oil treated female gerbil. The elevated dermal tumor had a maximum diameter of 5 mm at the time of removal and was characterized by a perifollicular orientation (Figure 3). From its arrangement, there is the suggestion that the tumor was derived from dermal perifollicular melanocytes (Figure 4).

The distribution of dermal melanocytes in the Mongolian gerbil embodies distinctive features of both Syrian and Chinese hamsters where the patterns are respectively, predominantly 'perifollicular' and 'diffuse-interfollicular'[2-5]. The responses of their dermal melanocytes to croton oil and DMBA are very similar to those reported previously for the Syrian hamster[9]. In both species the source of the increased numbers of melanogenic dermal melanocytes elicited by these agents remains to be established[2-5,9]. Unlike the Mongolian gerbil, DMBA does not appear to be effective in eliciting the appearance of significant numbers of epidermal melanocytes in the hairy skin of hamsters[2-5]. In general histology the 'melanocytic' tumor described here appears most comparable to the DMBA-induced, blue nevus-like tumors in Syrian hamsters and may have a similar origin, possibly from dermal melanocytes[2-5,9] or neural elements[10] associated with hair follicles[11].

Zusammenfassung. Die wiederholte Auftragung von Krotonöl oder von 7,12-Dimethylbenz(*a*)-Anthrazen (DMBA) ruft beim erwachsenen mongolischen Gerbillus eine deutliche Überpigmentierung der behaarten Bauchhaut hervor. In beiden Fällen geht die Überpigmentierung vornehmlich auf eine Vermehrung der Zahl der Hautmelanozyten zurück, die die Haarfollikel umgeben und sich zwischen diesen befinden. DMBA erzeugt im Gegensatz zu Krotonöl zahlreiche Papillome und aktive Melanozyten innerhalb der interfollikulären Oberhaut. In einem Fall hat sich bei einem mit DMBA and Krotonöl behandelten Gerbillus eine melanozytische Hautgeschwulst entwickelt.

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