Hair Regeneration in the Mouse After Application of Anti-Cancer Agent, Particularly in Terms of Epithelial-Mesenchymal Interaction

12.1 Anti-Cancer Agents and Hair Loss

Most anti-cancer agents currently in use are aimed at suppressing the growth of cancer cells and the accretion of tumors. Since the mechanism of cellular growth is the same in both normal and cancer cells, most of these agents can exert toxic effects on normal cells, especially on bone marrow mucous membrane and epithelial cells, which divide rather rapidly during the S phase. The anti-cancer agents may infiltrate the nucleolus and toxically transform the DNA structure. Sebaceous epithelial cells and hair matrix cells are therefore greatly affected by such agents. The phenomenon of hair loss is an often observed side effect of anti-cancer agents.

Inaba et al. (1991) and Inaba and Inaba (1992a) studied the effects of various anti-cancer agents on the pilosebaceous unit; the effects of methotrexate, 1.3-bis [2-chlorethyll-1-nitrosourea (BCNU), 5-fluorouracil (5-Fu), daunomycin, cytarabin, and cyclophosphamide on the hair follicle were examined.

It was found that the process of hair regeneration after the follicle had been damaged by the anti-cancer agent could be fully elucidated by the common hair cycle theory (Montagna and Parakkal 1974) alone. We conducted a study of the process of hair regeneration. The epithelial-mesenchymal interaction is an especially important factor in hair growth and, therefore, the regeneration of mesenchymal cells (dermal papilla) was the major subject of our study.

In experiments in which various anti-cancer agents were applied, we used female ICR Swiss mice about 65 days old, in good health, and with hair follicles on the back in telogen stage. Solutions containing various anti-cancer agents were applied twice daily for 7 days.

12.2 Regeneration of Hair Follicle After Application of Anti-Cancer Agent

We attempted to study the process of regeneration by applying an anti-cancer agent (methotrexate, etc.) to mouse body skin surface, thus experimentally creating telogen hair follicles (Inaba 1985). It has been thought that the new hair bud (germ) in the regeneration process begins to form from remnants of the dermal papilla or from a secondary hair germ in telogen stage (Fig. 12.1a,b). However, the authors recognize from recent studies (Inaba et al. 1991) that the regeneration of the hair germ does not necessarily occur from a secondary hair germ and the remnants of the dermal papilla, but that it can be formed from the upper isthmal portion close to the duct opening of the sebaceous glands (Fig. 12.1b).

These findings are explained as follows. As shown in Figs. 12.1a and 12.2a, the lower portion of the single hair indicates that this is a typical club hair in the telogen stage. In the medium portion of the follicle, the sebaceous gland cells and their nuclei can be observed. From between the two lobes of the sebaceous gland, i.e., from the upper isthmal portion, the epithelial cells (hair germ) regenerate as if to wrap around the lower portion of the club hair. No hair germ seems to be seen at the lower end of the telogen follicle (Fig. 12.1b). As already described in Section 1.5.2.3, no mass of mesenchymal cells can be seen at the lower portion of the telogen hair follicle.
In Figure 12.2, a more advanced hair bud also regenerates from the upper isthmal portion. A mass of mesenchymal cells can be seen at the lower tip of the newly-formed epithelial bud. From these mesenchymal cells the future dermal papilla may be formed later. Figure 12.3 shows regeneration of the hair peg stage: a club hair can be seen at the lower end of the telogen hair follicle. The lower hair follicle surrounding the club hair has atrophied and thinned. No presence of a hair germ, as asserted by Montagna, can be seen. The hair germ does not seem to have regenerated from the rem-