

merged in growth medium generally do not display the homeostatic interaction seen in cell cultures that have organizational structure similar to that observed in vivo. As a result of these and other observations, some investigators are developing in vitro models using primary cells isolated from living tissue. Attempts are also made to reconstruct the in situ microenvironment of the original tissue as closely as possible. It is hoped that this approach will contribute to obtaining more valid information in assaying the toxicity of xenobiotics.

The skin is divided into two main parts: the dermis or supportive connective tissue containing blood vessels, nerves, etc.; and the epidermis, which is the outermost structure of the skin and which is most responsible for protecting the body from external chemical and physical agents. We feel that an ideal in vitro system for studying the mechanism of action of chemicals, and for screening chemicals to determine their potential toxicity to humans, would be one that mimics the human epidermis both in morphological and in biochemical structure. Such a system, therefore, should meet the following criteria:

1. Morphologically, it must exhibit all of the stages of epidermal differentiation as seen in intact skin. This should result in keratinization of the outer cell layers as a result of ordered, step-by-step differentiation or orthokeratosis. Also, most of the unique morphological markers of the epidermis should be produced.
2. Biochemical markers of epidermal differentiation should be exhibited as it takes place in situ. Among those changes are
 - a. Progressive cell surface alterations in the keratinocytes as they differentiate
 - b. The production of specific keratin peptides found in terminally differentiated keratinocytes
 - c. The synthesis of a specific epidermal histidine-rich protein found only in that tissue

The cell type that is most responsible for the organized epidermis is the keratinocyte. Other cells such as melanocytes, Langerhan cells, and macrophages are also present, but they are not involved in forming the anatomical barrier that is characteristic of the epidermis. The *basal cells*, which are the only keratinocytes capable of proliferation, form a single layer above the dermis. This layer is connected to the underlying dermis by the basement membrane. Basal cells differentiate to *spinous cells* which form multilayers immediately above the basal layer. Keratinocytes in the next