the presence of multiple, broad lamellations in the interstices of several types of mammalian keratinizing epithelia (5–7). Several other lines of indirect evidence also supported such structural heterogeneity, including lipid histochemistry of frozen sections (6), as well as the ability of SC to be dispersed by certain organic solvents (14,15). Definitive evidence for the compartmentalization of lipids came with the isolation of SC membrane "sandwiches," containing trapped intercellular lipids. These preparations (16):(1) comprised about 50% lipid by weight, and accounted for over 80% of SC lipid; (2) displayed the same lipid profile as whole SC; (3) contained the same broad lamellae on freeze-fracture as are present in the interstices of whole SC; and (4) generated the same ordered x-ray diffraction pattern previously ascribed to the "interfilamentous lipid matrix" (17). More recently, the colocalization of lipid catabolic enzymes to SC membrane domains, both by ultrastructural cytochemistry and by enzyme biochemistry, can be considered further evidence for the structural heterogeneity of mammalian SC (18–20).

B. Localization of the Barrier

The localization of the barrier continued to be debated: Is the entire SC functionally competent, or does the principal barrier reside in the lower layers? Tracer perfusion studies, as early as 1969, showed that water-soluble molecules, injected into the dermis, do not reach the SC (21,22). Outward percolation halted in the outer SG, at intercellular sites engorged with discharged lamellar body contents (5). These studies, although admittedly employing tracers considerably larger than the water molecule itself, pointed to the presence of a barrier in the outer SG. Direct evidence of the barrier capabilities of different layers of the SC came with the recent isolation of intact sheets of porcine stratum compactum, after prior enzymatic stripping of the stratum disjunctum (23). Whereas these studies did not address the capacity of the stratum disjunctum to contribute to barrier function, they did demonstrate the functional integrity of the stratum compactum.

II. EPIDERMAL DIFFERENTIATION

The ultimate goal of epidermal differentiation is the production of the stratum corneum, a process more correctly called cornification rather than keratinization.

A. Major Structural Components

Modern research in epidermal cellular and molecular biology now recognizes four distinct cellular events that occur during the process