

EpiDerm™ Full Thickness (EpiDermFT), a Full Thickness Skin Equivalent with a Fully Developed Basement Membrane.

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Paracrine signaling between dermal fibroblasts (FB) and epidermal keratinocytes (KC) is believed to modulate skin responses during contact irritant or allergic reactions. Dermal FB also play an important role in photo-aging and photo-damage, wound healing and cancer progression. To enable in vitro study of these and other dermal phenomena in which FB-KC interactions are important, a full thickness skin model composed of a FB-containing dermis/KC-containing epidermis was developed.

Normal human epidermal KC and dermal FB were cultured to produce highly differentiated full-thickness tissues extending wall-to-wall in cell culture inserts. Histologic examination of the tissue shows a collagen dermis populated by numerous viable FB and an epidermis consisting of stratified KC including basal, spinous, granular and stratum corneum components.

Examination of ultrastructure at the dermal/epidermal junction by transmission electron microscopy revealed a well-developed basement membrane. Hemidesmosomes were observed at the basal membranes of KC, with associated tonofilaments extending into the cytoplasm. Well-defined, continuous lamina densa, lamina lucida and fine anchoring filaments were present beneath the basal KC. Anchoring fibrils with characteristic striated structure connected the lamina densa to the underlying collagen matrix. Immunohistochemical analysis of basement membrane proteins was also performed. Protein markers of hemidesmosomes (alpha6 integrin), lamina lucida (laminin 5), lamina densa (collagen IV) and anchoring fibrils (collagen VII) were specifically localized to the dermal/epidermal junction.

EpiDerm-FT overcomes shortcomings of previous models in terms of providing a wall to wall tissue as well as appropriate in vivo-like basement membrane development. These attributes will enable more realistic in vitro toxicological studies of dermal/epidermal phenomena.

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