

Features

- Psoriatic Human Tissue Phenotype
- 3D, Highly Differentiated
- Serum-Free Media System
- Highly Reproducible
- Easily-handled Cell Culture Inserts
- Quantifiable, Objective Endpoints
- Ideal for Drug Screening and Basic Studies
- Cost Effective Alternative to Clinical Testing

The Psoriasis Model

Psoriasis is a chronic inflammatory skin disease characterized by epidermal hyperplasia (Acanthosis) with elongated ridges and abnormal differentiation of epidermal keratinocytes, dermal angiogenesis, abnormal accumulation of polymorphonuclear leukocytes, infiltration of activated T cells and dendritic cells (DC), and increased cytokine levels. To enable *in vitro* study of psoriasis and screen therapeutic candidates for safety and efficacy, Mattek has developed an organotypic psoriasis tissue model (SOR-300-FT).

The psoriasis tissue model is cultured using normal human epidermal keratinocytes and psoriatic fibroblasts harvested from psoriasis lesions (Figs. 1A and 1B). The cells are cultured on specially prepared cell culture inserts using serum free medium to form a multilayered, highly differentiated tissue. The SOR-300-FT tissues adopt a psoriatic phenotype as evidenced by increased basal cell proliferation, expression of psoriasis-specific markers (Fig. 4), and elevated release of cytokines related to psoriasis (Fig. 5). Morphologically, the tissue model closely parallels lesional psoriatic human tissues. This model provides researchers with a useful, *in vitro* means to assess the safety and efficacy of lead therapeutic compounds and to study other basic psoriasis biology phenomena.

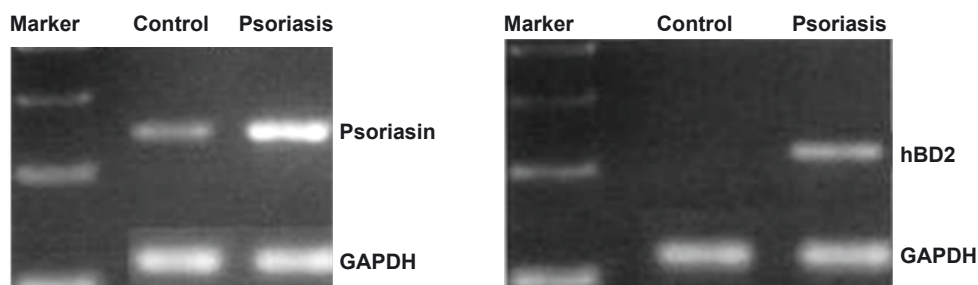


Figure 2: RT-PCR showing upregulation of the antimicrobial peptides human β -defensin-2 (HBD2) and psoriasin by the psoriasis (SOR-300-FT) and normal human skin (EFT-300-FT) models.

Histology of Psoriasis

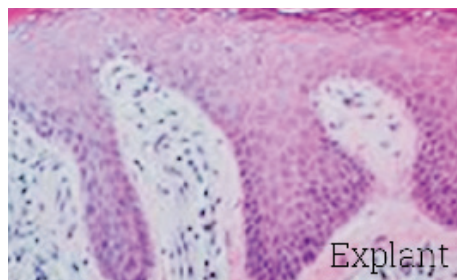


Figure 1. H&E stained histological (formalin fixed) cross-sections of: *in vitro* reconstructed psoriasis tissue model (SOR-300-FT) containing normal human keratinocytes and psoriatic fibroblasts, and psoriasis-involved skin explants.

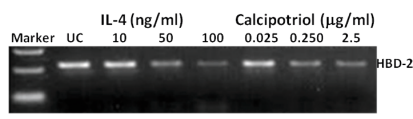


Figure 3. RT-PCR results showing effect of different concentrations of IL-4 and calcipotriol on HBD-2 expression in the psoriatic tissue model (SOR-300-FT). Marker = 100-bp ladder; UC = untreated psoriatic tissue model.

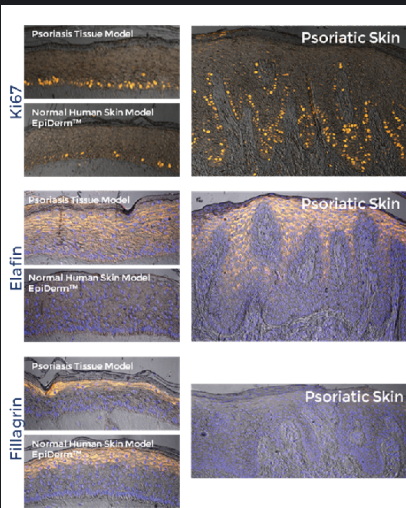


Figure 4. Immunohistochemistry showing expression of psoriasis associated markers by the psoriasis model (SOR-300-FT) and psoriasis explant tissues. Shown: Increased basal cell proliferation (Ki67), increased expression of elafin, and decreased expression of filaggrin.

The psoriasis tissue model (SOR-300-FT) exhibits a psoriatic phenotype as evidenced by increased expression of psoriasis-associated markers including human β -defensin-2 (HBD2) (Fig. 2), psoriasin (Fig. 2), SKALP/elafin (Fig. 4), activated STAT3, keratinocyte hyperproliferative cells (Ki67 staining (Fig. 4) and proinflammatory cytokines/ chemokines such as IL-6, IL-8, GM-CSF, and IP-10 (Fig. 5).

Various drug development and toxicology laboratories are actively seeking alternatives to expensive clinical or whole animal testing. The availability of a relevant psoriasis model will serve as a tool to study drug candidate toxicity, cutaneous cellular and molecular biology features of psoriasis, cell-cell interactions, and keratinocyte responses. Figure 3 shows that calcipotriol, a common anti-psoriasis agent, reduces HBD2 expression. Such an assay, along with other straightforward protocols, can be used to predict the responsiveness and irritancy of new psoriasis drug formulations.

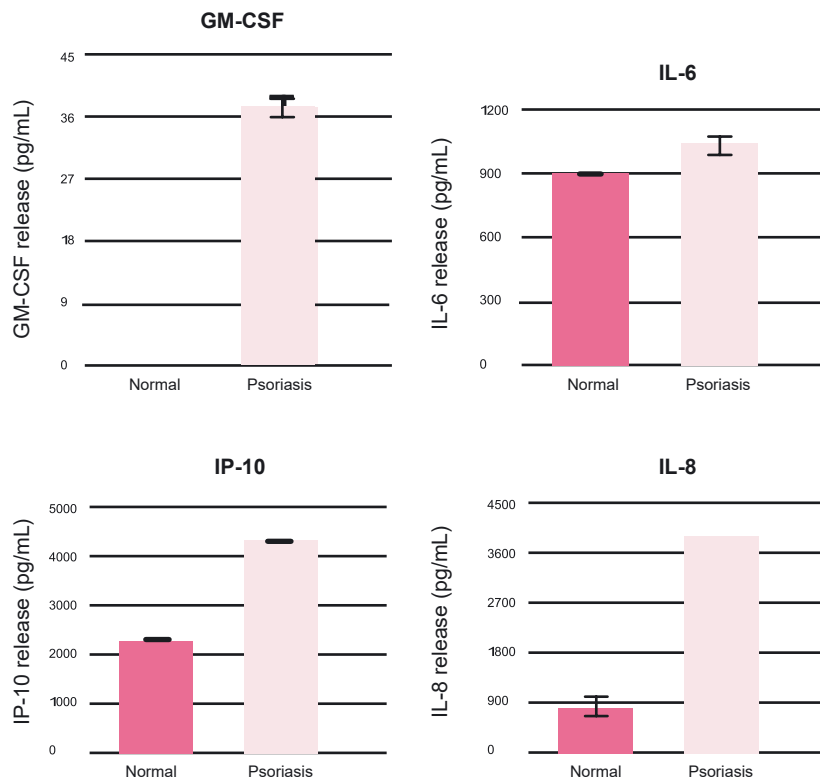


Figure 5. ELISA results showing cytokine release levels by psoriasis tissue (SOR-300-FT) versus normal human skin model (EpiDerm-FT).