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EpiVaginal | Data Sheet

Features

- Human vaginal-ectocervical tissues
- 3-dimensional, highly differentiated
- Contain normal human cells
- Serum-free medium, highly reproducible
- Easily handled cell culture inserts
- Quantifiable, objective endpoints
- Infectable with HIV-1 and other sexually transmitted pathogens
- Cost effective alternative to animal and pre-clinical testing

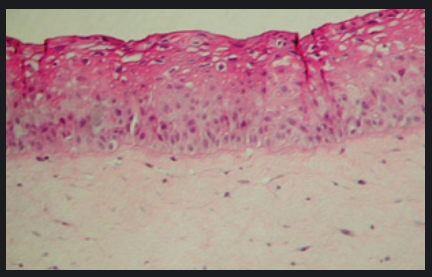

Figure 2. H&E stained histological cross-sections of full-thickness EpiVaginal tissues. The VEC-100-FT tissue consists of VEC epithelial cells cultured atop a lamina propria (LP) collagen matrix that contains fibroblasts. The VLC-100-FT consists of VEC epithelial and dendritic cells in the epithelial layers and contains both fibroblasts and dendritic cells in the LP.

The EpiVaginal Model

To facilitate the study of vaginal-ectocervical (VEC) toxicity, pathologies, and basic mucosal phenomena, Mattek has developed the EpiVaginal series of tissue models. EpiVaginal tissues are based on normal, human-derived VEC epithelial cells. Four types of EpiVaginal are offered:

1.) VEC-100 (Figure 1): An epithelial tissue containing epithelial VEC cells,

2.) VLC-100 (Figure 1): An epithelial tissue containing epithelial VEC and immuno-competent dendritic cells,

3.) VEC-100-FT (Figure 2): A full thickness version of VEC-100 which includes VEC epithelial cells and a fibroblast-containing lamina propria, and

4.) VLC-100-FT (Figure 2): An immuno-competent version of the VEC-100-FT which includes dendritic cells and a fibroblast containing lamina propia.

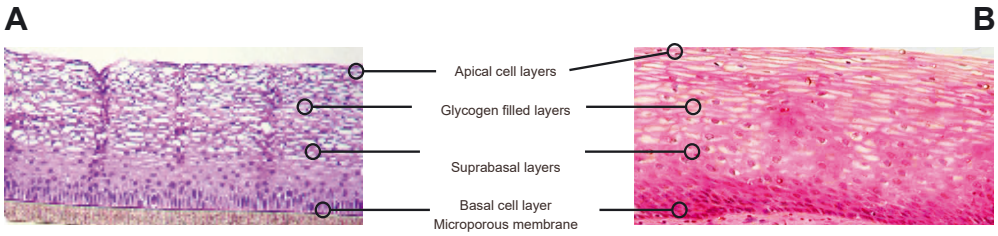

Figure 1. H&E stained histological (formalin fixed) cross sections of: A) VEC-100 *in vitro* reconstructed epithelial tissue models containing normal human cells, and B) vaginal explant tissue. Both *in vitro* and *in vivo* tissues show nucleated basal and suprabasal cell layers followed by layers in which nuclei are lost and filled with glycogen.

All VEC tissues are cultured on specially prepared cell culture inserts and are multilayered and highly differentiated. The tissues closely parallel native human tissues, thus providing a useful *in vitro* means to assess toxicity, innate immune responses, sexually transmitted infections, and other basic vaginal phenomena.

The EpiVaginal tissue models exhibit *in vivo*-like morphological and growth characteristics which are uniform and highly reproducible. EpiVaginal is a multilayered tissue consisting of an organized basal layer and multiple non-cornified layers analogous to native human vaginal-ectocervical tissue (Figures 1 - 2). The tissue expresses cytokeratin K14 in the basal and supra basal layers and cytokeratin K13 in the suprabasal tissue layers (Figure 3).

Various industrial and toxicology laboratories are actively seeking alternatives to expensive clinical or whole animal testing. The protocols for using EpiVaginal are clear and straightforward. Feminine hygiene, personal care, and pharmaceutical companies have initiated *in vitro* toxicology testing to evaluate their raw materials and final product formulations.

Figure 4 shows the effects of formulations containing the common spermicide and active ingredient, nonoxynol-9 (N9), on the VEC-100-FT tissue. Tissue viability (MTT assay) (Figure 4A) and cytokine release (IL-1b) (Figure 4B) were measured. As shown therein, with increasing N9 concentration, the tissue viability decreases and the IL-1b release increases. Such assays can be used to predict toxicity of vaginal care products, microbicides, and other chemical agents.

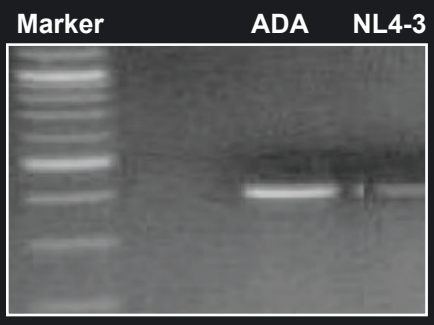

Figure 5. HIV-1 infection of VLC-100 tissue following topical exposure (24hr) to 60,000 CPM of HIV-1 ADA or NL4-3 virus. After exposure, tissues were washed 3X and then cultured for an additional 24 hr. Cellular DNA was then extracted and HIV-1 transcripts were detected using HIV-1 gag specific primer pairs.

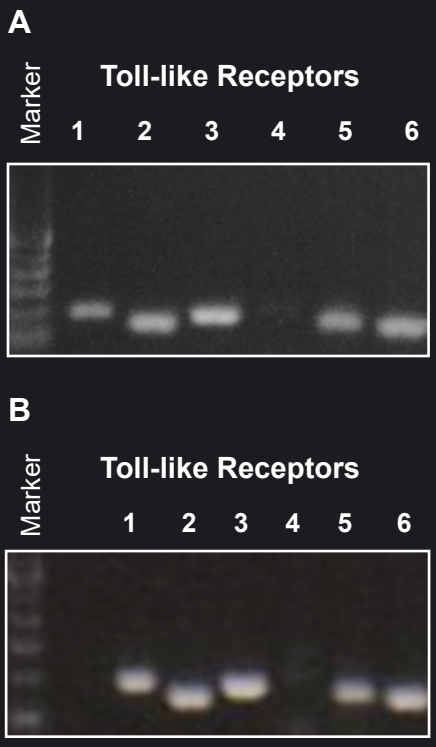

Figure 6. RT PCR showing Toll-like Receptor (TLR) expression for:
A) organotypic vaginal-ectocervical (VEC) tissue model and
B) Human cervical tissue explant.

Straightforward protocols are available for harvesting RNA to analyze gene expression (See Figure 6 for Toll-like receptor expression) or for measuring cytokines released into the culture medium (analyzed using ELISA assays). Companies and researchers utilize antibiotic/antifungal free EpiVaginal tissue (VEC-100-AFAB) to grow various opportunistic infections and pathogenic microbes in order to study their effects on the vaginal tissues. In addition, the VLC models are infectable with HIV-1 (Figure 5) and can be used to study HIV infection, transmission, and microbicides intended to prevent heterosexual passage of HIV. Finally, the tissue is amply suited to study a broad variety of pathogens that invade the vaginal-ectocervical environment along with prophylactic remedies thereto.

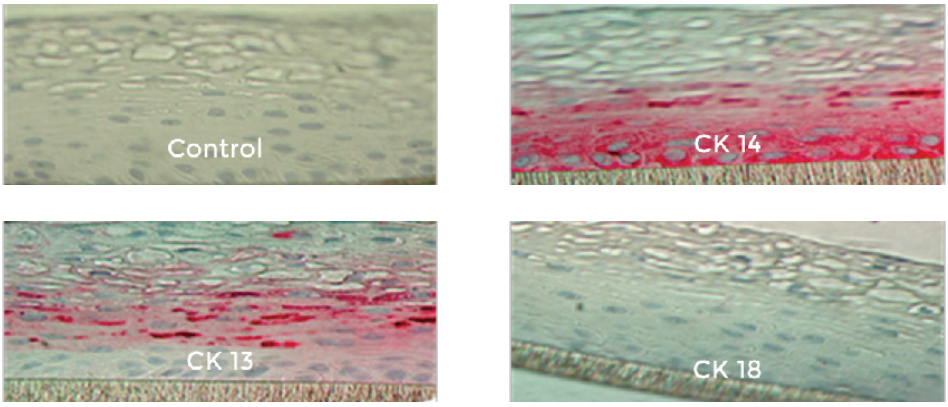

Figure 3. Formalin fixed cross-sections of the VEC-100 tissue immuno-stained for cytokeratins, CK13, CK14, & CK18. Basal cells are stained by CK14 and supra-basal cells by CK13; no cells are stained by CK18.

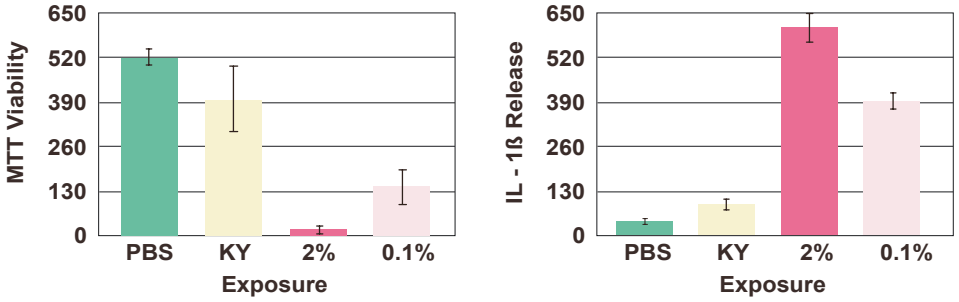

Figure 4. Viability (A) and cytokine release (B) of full thickness vaginal-ectocervical (VEC-100-FT) tissue model following exposure (18 hr) to formulations containing the common spermicide, nonoxynol-9 (N9): a) PBS control, b) KY Jelly (KY, 0% N9), c) KY N9 (2%), and d) N9 (0.1%). As viability of the tissue decreases, the IL-1β release increases.

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