

# **Recombinant Protein and Peptides to Boost Epithelial Barrier Function and Prevent Infections**

Cherpes Lab investigators discovered that recombinant ephrin-A3 or agonist ephrin-A3-derived peptides promote expression of cell-cell adhesion molecules in epithelial surfaces and improve epithelial barrier function. Topical administration of these agents in female genital tract of mice with impaired genital mucosal barrier function (i.e., mice treated with synthetic progestins or ovariectomized mice) increases genital mucosal barrier function of treated animals and decrease susceptibility to genital infections.

These discoveries have the potential to benefit women using progestin-only agents (e.g., Depo-Provera) for contraception, women that are menopausal and postmenopausal, and women with ovarian failure due to chemotherapy. In particular, decreased genital epithelial barrier function is an important risk factor for genital HIV transmission, and recombinant ephrin-A3 or agonist ephrin-A3-derived peptides enhance genital epithelial barrier function.

The researchers also found that topical administration of these agents decreases allergen-specific IgE levels in a mouse model of epicutaneous sensitization-induced atopic dermatitis. As such, these new therapeutics show promise to boost epithelial barrier function in a variety of clinical settings.

## **Stage of Research**

- Developed lead compounds that promote increased epithelial barrier function.
- Showed that topical administration of these compounds in mice prevents genital tissue penetration of small molecules, proteins, and infectious pathogens.
- Work to develop methods for sustained release of these molecules is ongoing.

## Applications

- Enhance barrier function at epithelial surfaces, including skin and genital mucosa.
- Reduce susceptibility to genital pathogens, including HSV and HIV, through the promotion of genital mucosal barrier function.
- Women using injectable progestins or experiencing the genitourinary syndrome of menopause.
- Decrease sensitization in atopic dermatitis (i.e., therapeutic potential for allergic diseases).

## Advantages

- Low-cost production of proteins and peptides described in this invention.
- Topical administration of therapeutic agents with easily adaptable to topical delivery or release from intravaginal rings.
- Non-estrogen treatment for the genitourinary syndrome of menopause.

## Publications

- Nirk E, Quispe Calla et al [Ovariectomized mice and postmenopausal women exhibit analogous loss of genital epithelial integrity](#) *Tissue Barriers* 11 Jan 2021.
- Quispe Calla NE, Vicetti Miguel RD, Boyaka PN, Hall-Stoodley L, Kaur B, Trout W, Pavelko SD, Cherpes TL. [Medroxyprogesterone acetate and levonorgestrel increase genital mucosal permeability and enhance susceptibility to genital herpes simplex virus type 2 infection](#) *Mucosal Immunol* 2016 Nov;9(6):1571-158.

## Patents

- Published Application: [WO2021071979](#)

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