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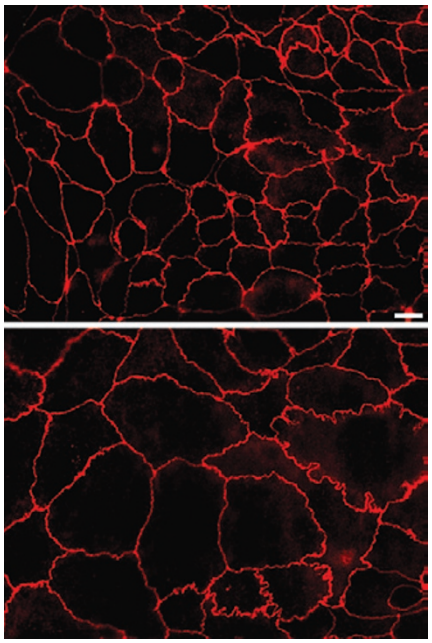
NEUROGASTROENTEROLOGY

A role for enteric glial cells in mucosal healing

Enteric glial cells enhance the repair of the intestinal epithelial barrier, partly by promoting epithelial restititution and intestinal epithelial cell spreading. "This study reinforces the concept that enteric glial cells are a central cellular component of the intestinal epithelial barrier microenvironment and that they have a major protective role towards the intestinal epithelial barrier," says Michel Neunlist, corresponding author.

The enteric nervous system, which is composed of enteric neurons and enteric glial cells, regulates various intestinal epithelial barrier functions. Enteric glial cells, in particular, enhance the differentiation of intestinal epithelial cells and increase intestinal epithelial barrier resistance. However, the role of enteric glial cells in mucosal healing, which is essential for maintaining the structure and function of the intestinal epithelial barrier, remains to be elucidated.

Ganciclovir ablates enteric glial cells in glial fibrillary acidic protein–herpes simplex virus thymidine kinase (GFAP–Tk) transgenic mice, so Neunlist and colleagues administered ganciclovir plus either dextran sulfate sodium (DSS) or diclofenac to GFAP–Tk transgenic mice and nontransgenic mice. In GFAP–Tk transgenic mice, DSS-induced mucosal injury was more severe and healing of diclofenac-induced mucosal lesions was delayed.



Human intestinal epithelial cells cultured without (top) or with (bottom) enteric glial cells. Scale bar: 20 μm. Courtesy of INSERM UMR 913.

By using an *in vitro* noncontact co-culture model, the researchers demonstrated that wound surface areas produced in response to mechanical injury were reduced when human intestinal epithelial cells were cultured with enteric glial cells, compared with when intestinal epithelial cells were cultured alone. The promotion of epithelial restitution by enteric glial cells was confirmed to involve increased intestinal epithelial cell spreading.

As focal adhesion kinase (FAK) regulates epithelial wound healing, Neunlist *et al.* investigated whether enteric glial cells acted via activation of FAK-dependent signaling pathways—they did. Inhibition of FAK substantially reduced enteric-glial cell-induced intestinal epithelial cell spreading. The researchers also identified soluble proEGF as a crucial glial-derived mediator of the effects on epithelial cell spreading and wound repair.

"A major question is whether gastrointestinal diseases with an altered repair process, such as IBD, can be associated with dysfunctions of enteric glial cells," concludes Neunlist. "In this context, we plan to characterize enteric glial cell lesions in human gastrointestinal diseases."

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Original article Van Landeghem, L. *et al.* Enteric glia promote intestinal mucosal healing via activation of focal adhesion kinase and release of proEGF. *Am. J. Physiol. Gastrointest. Liver Physiol.* doi:10.1152/ajpgi.00427.2010