ANTIBODY RESPONSES

FcRn — not just for the kids

IgG is the predominant antibody isotype found in the female genital tract and serves as an important defence mechanism against genital tract infections. In a recent study, Zili *et al.* have shown that the neonatal Fc receptor (FcRn), which is crucial for delivering protective maternal antibodies to the fetus and newborns, also delivers IgG to the female genital tract and promotes protective immunity at this site.

It is well appreciated that FcRn functions in adults to maintain serum levels of IgG. Therefore, the authors hypothesized that FcRn might also contribute to the transport of IgG across the genital epithelium. Initial screens showed that mRNA encoding FcRn could be detected in human female genital epithelial cell lines, and subsequent immunostaining experiments using tissue sections confirmed that FcRn is expressed at high levels by uterine and vaginal epithelial cells in both humans and mice. Using cell monolayers prepared from an FcRn-

expressing human uterine cell line, the authors showed that IgG could be transported in both luminal and abluminal directions by these cells. However, transport of IgG was not observed following FcRn knock-down, and chicken IgY (which is structurally similar to IgG but does not bind FcRn) was not transported across the cell monolayers.

Next, the authors switched to a mouse system to explore the *in vivo* functions of FcRn in the genital tract. Notably, significantly higher levels of IgG were found in vaginal washings from wild-type mice than in vaginal washings from FcRn-deficient animals. Furthermore, in experiments using labelled antibody, systemically delivered IgG could be subsequently detected in vaginal washings from wild-type but not FcRn-deficient mice. Labelled IgG delivered by an intravaginal route was also subsequently detected in the serum of wild-type but not FcRn-deficient mice, supporting the authors' *in vitro* observations that FcRn can promote

bidirectional transport of IgG across genital tract epithelium.

Finally, Zili *et al.* explored whether this transport function of FcRn has implications for immune protection in the genital tract. Strikingly, the systemic delivery of IgG specific for herpes simplex virus type 2 (HSV-2) protected wild-type but not FcRn-deficient mice from a lethal intravaginal HSV-2 infection.

These data suggest that IgG transfer to the genital tract is not simply passive, as historically thought, but involves active transport by FcRn. This study has important implications for the development of vaccines, as it suggests that boosting systemic or local IgG responses could contribute to immune protection in the genital tract.

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ORIGINAL RESEARCH PAPER Zili, L. *et al.*
Transfer of IgG in the female genital tract by
MHC class I-related neonatal Fc receptor (FcRn)
confers protective immunity to vaginal infection.
Proc. Natl Acad. Sci. USA 28 Feb 2011
(doi:10.1073/pnas.1012861108)

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