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IN BRIEF

CELLULAR MICROBIOLOGY

Many pathogens, one host receptor

Efficient binding to and entry into host cells is a crucial step for many pathogens to establish infection. Epstein–Barr virus (EBV) predominantly infects human B cells and epithelial cells by fusion of the viral envelope with the host cell membrane. Although the mechanism of entry into B cells has been well documented, the mechanism for entry into epithelial cells has remained elusive. Now, in two studies, Zhang, Li, Wang *et al.* and Chen *et al.* identify ephrin type-A receptor 2 (EPHA2) as an EBV epithelial cell receptor. CRISPR–Cas9-mediated knockout markedly reduced fusion and infection of epithelial cells with EBV, whereas overexpression of the receptor increased fusion and infection, suggesting that EPHA2 is important for EBV infection of epithelial cells. In agreement with this, antibodies against EPHA2, an EPHA2 ligand and an EPHA2 inhibitor all efficiently blocked EBV epithelial cell infection. The authors were also able to show that the EBV entry glycoproteins gH–gL and gB are involved in binding to EPHA2. In another study, Swidergall *et al.* show that EPHA2 functions as a non-classical pattern-recognition receptor in oral epithelial cells to sense the presence of high levels of β-glucans on the surface of *Candida albicans*. They showed that EPHA2 interacts directly with β-glucans from *C. albicans* as well as from other fungi, including *Aspergillus fumigatus*. Activation of EPHA2 not only contributes to receptor-induced endocytosis of *C. albicans* but also leads to the activation of signalling pathways in oral epithelial cells and the production of pro-inflammatory cytokines and defence peptides. Finally, Aaron, Jamklang *et al.* reported that the EPHA2 signalling pathway promotes the migration of the fungal pathogen *Cryptococcus neoformans* across the blood–brain barrier. The authors report that *C. neoformans* activates EPHA2 in brain endothelial cells, which enhances the transcellular migration of the fungus across brain endothelial cells in an *in vitro* model of the blood–brain barrier, which may be dependent on CD44.

ORIGINAL ARTICLES Zhang, H., Li, Y., Wang, H-B. *et al.* Ephrin receptor A2 is an epithelial cell receptor for Epstein–Barr virus entry. *Nat. Microbiol.* http://dx.doi.org/10.1038/s41564-017-0080-8 (2018) | Chen, J. *et al.* Ephrin receptor A2 is a functional entry receptor for Epstein–Barr virus. *Nat. Microbiol.* http://dx.doi.org/10.1038/s41564-017-0081-7 (2018) | Swidergall, M. *et al.* EphA2 is an epithelial cell pattern recognition receptor for fungal β-glucans. *Nat. Microbiol.* **3**, 53–61 (2017) | Aaron, P. A., Jamklang, M. *et al.* The human blood-brain barrier internalizes *Cryptococcus neoformans* via the EphA2-tyrosine kinase receptor. *Cellular Microbiol.* http://dx.doi.org/10.1111/cmi.12811 (2017)

BACTERIAL PATHOGENESIS

Clostridium difficile is sweet on trehalose

Two epidemic, phylogenetically distant lineages of *Clostridium difficile* recently emerged and have been linked to increased virulence and mortality. Collins *et al.* show that two epidemic ribotypes (RT027 and RT078) have acquired the ability to metabolize low concentrations of the disaccharide trehalose. RT027 contains a single point mutation in the trehalose repressor that increases its sensitivity to trehalose and leads to the expression of the TreA enzyme, which is involved in trehalose metabolism. The data indicate that increased disease severity of RT027 is possibly due to increased toxin production. RT078 acquired four genes involved in trehalose metabolism, including a trehalose transporter that is necessary and sufficient for growth on low concentrations of trehalose and confers a competitive advantage over other lineages in the presence of trehalose. The authors propose that the use of trehalose in the human diet had a role in the emergence of these epidemic and hypervirulent strains.

ORIGINAL ARTICLE Collins, J. *et al.* Dietary trehalose enhances virulence of epidemic *Clostridium difficile*. *Nature* http://dx.doi.org/10.1038/nature25178 (2018)