HOST RESPONSE

Sifting out virulent bacteria

> *C. rodentium* infection induces the generation of IgG antibodies that bind to LEE virulence factors

Gut colonization by the two human pathogens enterohemorrhagic *Escherichia coli* (EHEC) and enteropathogenic *E. coli* (EPEC), and by the related mouse pathogen *Citrobacter rodentium*, is dependent on expression of the locus for enterocyte effacement (LEE) virulence factors, which enable epithelial attachment and subversion of host immunity. In mice infected with *C. rodentium*, which are a model for human *E. coli* infection, luminal immunoglobulin G (IgG) contributes to the clearance of LEE-expressing virulent bacteria after 12 days post infection, but the exact role of IgG in this process has been unclear. Kamada *et al.* now show that IgG selectively targets virulent *C. rodentium* through the recognition of LEE virulence factors.

To establish whether the adaptive immune system is responsible for the clearance of virulent *C. rodentium*, quasi-monoclonal mice (which lack specific antibodies) were infected with *C. rodentium*; in contrast to wild-type mice, these mice succumbed to infection, which suggested that humoral immunity is crucial for elimination of *C. rodentium*. Indeed, IgG and IgA (but not IgM) antibodies were detected in wild-type mice following infection, and *in vivo* and *in vitro* binding assays established that IgG (but not IgA) antibodies bind to virulent *C. rodentium*.

Further experiments showed that IgG binding to a *ler* (LEE-encoded regulator) mutant strain, which does not express LEE virulence factors, was strongly diminished both *in vivo* and *in vitro* compared with binding to wild-type *C. rodentium*. Furthermore, immunoblotting showed that IgG from infected mice exhibited reactivity to multiple *C. rodentium* proteins, including the LEE virulence factor intimin, but that this reactivity was greatly reduced in *ler* mutants. Together, these data suggest that the adaptive immune system specifically recognizes virulent *C. rodentium* through the binding of IgG to LEE virulence factors.

The authors also demonstrated a crucial role for neutrophils in the eradication of virulent *C. rodentium*. Neutrophil-deficient mice succumbed to infection after 14 days, whereas control mice survived; furthermore, unlike in the control mice, a decrease in *ler* expression in the *C. rodentium* population was not observed in neutrophil-deficient mice, which indicated that virulent bacteria were not eradicated, despite the presence of IgG specific for the pathogen.

Collectively, these data show that *C. rodentium* infection induces the generation of IgG antibodies that bind to LEE virulence factors, which targets virulent bacteria for engulfment and elimination by neutrophils.

Naomi Attar

IMAGE100

ORIGINAL RESEARCH PAPER Kamada, N. *et al.* Humoral immunity in the gut selectively targets phenotypically virulent attaching-and-effacing bacteria for intraluminal elimination. *Cell Host Microbe* http://dx.doi.org/10.1016/j.chom.2015.04.001 (2015)