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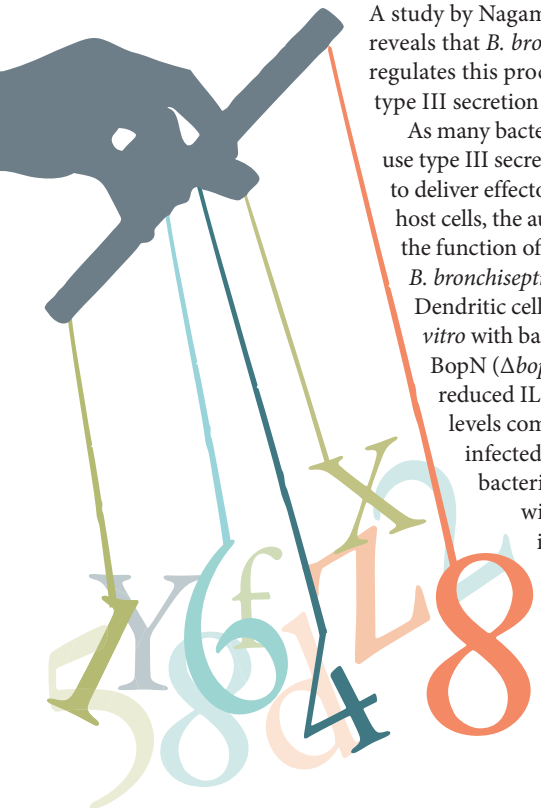
IMMUNE EVASION

Manipulating inflammation



Similarly to many bacterial pathogens, *Bordetella bronchiseptica*, which has been used for the study of *Bordetella pertussis* pathogenesis, manipulates the host immune response to promote its own survival by enhancing the production of the anti-inflammatory cytokine interleukin-10 (IL-10).

A study by Nagamatsu *et al.* now reveals that *B. bronchiseptica* regulates this process through the type III secretion effector BopN.

As many bacterial pathogens use type III secretion systems to deliver effector proteins into host cells, the authors examined the function of BopN during *B. bronchiseptica* infection. Dendritic cells infected *in vitro* with bacteria lacking BopN (Δ*bopN*) showed reduced IL-10 mRNA levels compared with cells infected with wild-type bacteria. Consistent with this, mice infected with Δ*bopN* bacteria produced significantly lower levels of IL-10 and higher levels of the pro-inflammatory cytokine interferon-γ (which is suppressed by IL-10) and had higher survival rates than mice infected with wild-type bacteria. These findings indicate an integral role for BopN in mediating IL-10 production and promoting bacterial survival.

So how does *B. bronchiseptica* increase IL-10 production? Mitogen-activated protein kinase (MAPK) and nuclear factor-κB (NF-κB) signalling pathways are known to be modulated during *B. bronchiseptica* infection and to affect the expression of cytokines, including IL-10. Indeed, introduction of BopN into a cell line triggered MAPK dephosphorylation, which coincided with increased IL-10 mRNA levels. Moreover, BopN translocated to the nucleus and altered the localization of the NF-κB subunits p50 and p65. Specifically, BopN enhanced the nuclear translocation of p50 (which is known to upregulate IL-10) and blocked that of p65. These changes in NF-κB localization could be the mechanism by which BopN increases IL-10 production. Treatment of dendritic cells with an inhibitor of nuclear export reduced IL-10 production in cells infected with wild-type bacteria, but Δ*bopN*-infected cells did not produce IL-10 in the presence or absence of the inhibitor.

These findings reveal that *B. bronchiseptica* increases IL-10 production through BopN, leading to decreased pro-inflammatory cytokine secretion and increased bacterial survival. As *B. pertussis* BopN shares 99% sequence identity with *B. bronchiseptica* BopN (which indicates that they might function in a similar way), BopN could be a therapeutic target for the treatment of whooping cough.

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ORIGINAL RESEARCH PAPERS Nagamatsu, K. *et al. Bordetella* evades the host immune system by inducing IL-10 through a type III effector, BopN. *J. Exp. Med.* 14 Dec 2009 (doi:10.1084/jem.20090494)