Survival of *Salmonella* inside activated macrophages – why bacteria will not understand the word NO?

In the current issue of *Microbiology*, Dipshikha Chakravorty and colleagues (Das *et al.*, 2009) provide insight into the molecular mechanisms that account for the persistence of the facultative intracellular pathogen *Salmonella* within the host phagocytes. It is well known that bacterial pathogens are able to manipulate cellular signalling, vesicle trafficking and the cytoskeleton to create a pleasant environment suiting their demands. For these wicked purposes, *Salmonella* wields strategic weapons, such as type III secretion systems, to inject persuasive protein effectors into the cytoplasm of the victim cells chosen as a home, namely enterocytes on our intestinal mucosa. *Salmonella* Typhimurium, the most studied among the multiple *Salmonella enterica* serovars, and a valid model for all of them, expresses two different type III secretion systems encoded by discrete pathogenicity islands (SPI-1 and SPI-2). The one encoded by SPI-2 is devoted to ensuring intracellular survival. For the bacterium, there are two scenarios that require intracellular survival: in the first scenario the bacterium chooses its host cell target, forcing its own internalization into non-professional phagocytes by making use of its SPI-1; in the second scenario the bacterium is chosen by a professional phagocyte that is duly programmed to eliminate it. The second setting is obviously less advantageous for the pathogen, because activated macrophages, the toughest enemies of *Salmonella*, will bring into play chemical weapons, such as nitric oxide (NO) among other items in the arsenal that is poured into maturing phagosomes. In their paper, Das *et al.* reveal that *Salmonella* uses the nitrite transporter NirC to quench NO production by NO synthase (iNOS) (Fig. 1). Since NO has a repressing effect on SPI-2 expression, this enhances the chances of bacterial cells to survive inside

Fig. 1. *Salmonella* says 'no' to NO.

macrophages. The investigators have shown that NirC does indeed play a role in the virulence of *Salmonella* in an oral infection mouse model, and that such advantage is related to the effects of the nitrite transporter on iNOS products. Their results reveal a novel virulence determinant and provide a nice explanation for the relative resistance of *Salmonella* to oxidative stress in the phagosome.

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REFERENCE

Das, P., Lahiri, A., Lahiri, A. & Chakravorty, D. (2009). Novel role of the nitrite transporter NirC in *Salmonella* pathogenesis: SPI2-dependent suppression of inducible nitric oxide synthase in activated macrophages. *Microbiology* 155, 2476–2489.

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