

Meeting abstract

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"Switch to kill, switch to survive" – bacterial toxins modifying Rho GTPases

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Various bacterial protein toxins act on eukaryotic cells by targeting switches involved in cellular signalling and/or control of the cytoskeleton. Of particular importance as targets are molecular switches of the Rho GTPase family. The GTPase switches have crucial functions in innate and adapted immunity and play pivotal roles in the biology of infection, which explains their preferred targeting by toxins. The toxins activate or inactivate Rho GTPases by different modes of action. Cytotoxic necrotizing factors (CNFs) from *E. coli* and *Yersinia* species activate Rho GTPases by deamidation of a glutamine residue, which is involved in the switch-off mechanism of the GTPases. Activation of RhoA is caused by *Pasteurella multocida* toxin secondary to activation of the heterotrimeric G proteins G_q and $G_{12/13}$. On the other hand, the *Yersinia* effector protein YopT, which acts as a cysteine-specific protease to cleave the lipid anchor of GTPases, inactivates Rho GTPases. C3 exotoxins inactivate RhoA, B and C by ADP-ribosylation at Asn41 thereby preventing activation of Rho, stabilizing the Rho-GDI complex and inhibiting signalling. Large clostridial toxins, including *C. difficile* toxin A and B, inactivate various Rho GTPases by glucosylation. The mode of action of *C. difficile* toxins and their structure-function relationship will be discussed in detail.