

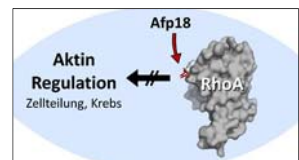
Bacterial toxins - specific inhibitors of Rho family members

PaTox & Afp18 modify Rho GTPases by tyrosine mono-O-glycosylation to result in inhibition of Rho signaling

Technology

Several bacterial protein toxins and effectors are known to target host proteins by glycosylation. The use of Rho-specific toxins and the discovery of pharmacological inhibitors of Rho signaling were essential to uncover developmental as well as disease-related mechanisms.

Here, we report on bacterial toxins (PaTox & Afp18) that specifically target particular Rho family members (i.e. Afp18 = RhoA, but not Rac and Cdc42 & PaTox = RhoA, -B, -C, Rac1, -2, -3 and Cdc42 but other GTPases of the Rho, Ras or Rab families not modified) by tyrosine mono-O-glycosylation, thereby inhibiting downstream signaling via an impaired interaction with diverse regulator and effector proteins and, eventually, leading to actin disassembly, blockade of phagocytosis and mammalian-cell death.



Interference with host-cell signaling by specific tyrosine glycosylation of particular Rho proteins holds great therapeutic potential, since often Rho family related diseases are defined by upregulated Rho protein functions, i.e. trigger initiation, progression and metastatic spread of tumors.

Innovation

- Early stage but promising novel cancer therapy potential
- Broad DE patent application
- Grant expected in 2016

Main Application

- Rho family dependent diseases
 - Diverse Cancers
 - Neurodegenerative disease and neuronal dysfunction

Developmental Status

- Sound pack of pre-clinical data (cell lines & vertebrates)

⇒ **Wanted:** Cooperation partner for further pre-clinical evaluation

► PaTox: **Jank et al (2013)**, Nature Struct Mol Biol, 20(11):1273-80
"A bacterial toxin catalyzing tyrosine glycosylation of Rho ..."

► Afp18: **Jank et al (2015)**, Nature Communications, 6:7807
"Tyrosine glycosylation of Rho by Yersinia toxin ..."

► **Jank et al (2015)**, FASEB J, 29(7):2789-802
"... Photorhabdus asymbiotica toxin is crucial for cell toxicity."

Responsible Scientists

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