New mechanism of bacterial pathogenesis discovered

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Scientists have identified a new mechanism of bacterial pathogenesis. The results of the research project, partly funded by the Academy of Finland, have been published in the journal *Proceedings of the National Academy of Sciences* (PNAS).

Bacteria that cause chronic infections have an amazing but yet poorly known ability to subvert immune response, live and produce offspring, enter and wake up from a dormant phase to cause, in some instances, deadly complications.

Bartonella bacteria cause chronic infections in mammals (incl. humans), and are typically transmitted to new hosts mainly by arthropod vectors such as fleas, lice and ticks, but also via direct tissue trauma (e.g. cat scratches).

One very notable feature of these bacteria is their ability to cause vasoproliferative tumours that resemble Kaposi's sarcoma in patients suffering from immunodeficiency (e.g. AIDS, aggressive cancer treatments, organ transplantation). If left untreated, these foci of inflammation maintain a chronic infection and contribute to transmitting bacteria to new hosts.

In his research, biologist Arto Pulliainen (University of Turku) has demonstrated that Bartonella henselae injects a protein called BepA into vascular endothelial cells and that this protein manipulates cAMP-mediated cell signalling using a previously unknown mechanism.

BepA directly binds the host cell adenylyl cyclase, which is an enzyme responsible for the production of cAMP. However, the binding of BepA to the adenylyl cyclase does not activate cAMP production per se, but the adenylyl cyclase rather becomes more sensitive to its natural activator, stimulatory G-protein (Gαs). The cellular concentration of cAMP increases and prevents the death of the host cell. BepA significantly prolongs the lifespan of the host cell and partly contributes to the formation of vasoproliferative tumours.

Several bacterial species are known to manipulate host cell functions via cAMP-mediated cell signalling. The symptoms are typically very strong and may even be deadly. The best-known example is Vibrio cholerae and its cholera toxin, which modifies Gαs into a permanently adenylyl cyclase-stimulating form. BepA, in turn, manipulates host cell signalling in a subtle sophisticated manner, which is ideal for chronic persistence of Bartonella henselae in the infected vascular endothelium.

The research has been carried out at the Universities of Basel and Turku.

More information: Pulliainen, A.T., Pieles, K., Brand, C.S., Hauert, B., Böhm, A., Quebatte, M., Webf, A., Gstaiger, M., Aebersold, R., Dessauer, C.W. and Dehio, C. (2012). "Bacterial effector binds host cell adenylyl cyclase to potentiate Gαs-dependent cAMP production". PNAS 109:9581-9586.

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