

# Gene against bacterial attack unravelled

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Dutch researcher Joost Wiersinga from AMC Medical Center in Amsterdam has unravelled a genetic defense mechanism against the lethal bacteria *Burkholderia pseudomallei*. The research is the next step towards a vaccine against this bacterium suitable for bioweapons.

Humans have an innate defence system against deadly bacteria. However, how the step from gene to anti-bacterial effect occurs in the body is not yet known. To date, *B. Pseudomallei*, a bacterium suitable for bioweapons, had managed to elude medics. It can remain hidden in the human body for many years without being detected by the immune system. The bacteria can suddenly become activated and spread throughout the body, resulting in the patient dying from blood poisoning. AMC physician Joost Wiersinga and the Laboratory for Experimental Internal Medicine discovered which gene-protein combination renders the lethal bacteria *B. pseudomallei* harmless.

Wiersinga focussed on the so-called Toll-like receptors. These are the proteins that initiate the fight against pathogens. There are currently ten known Toll-like receptors which are located on the outside of immune cells, our body's defence system. The toll-like receptors jointly function as a 10-figure alarm code. Upon coming into contact with the immune cell each bacterium enters its own Toll code. For known pathogens this sets off an alarm in the immune system and the defence mechanism is activated. Yet *B. pseudomallei* fools the system by entering the code of a harmless bacterium. As a result the body's defence system remains on standby.

Yet some people are resistant: they become infected but not ill. Wiersinga found a genetic cause for this resistance. He discovered which toll receptor can fend off *B. pseudomallei*. He did this by rearing mice DNA in which the gene for Toll2 production was switched on and off. 'The group where the gene for Toll2 was switched off, survived the bacterial infection', says Wiersinga. 'The other receptor that we investigated, Toll4, had no effect - even though for the past ten years medics had regarded this as the most important receptor.' The ultimate aim of this study is to develop a vaccine.

Source: Netherlands Organization for Scientific Research

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