Old vaccine trains immune system

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Credit: National Cancer Institute

Not only the acquired immune system but also the innate immune system has a memory. And the BCG vaccine against tuberculosis can stimulate this memory. After a BCG vaccination the innate immune system responds better to a wide range of other infections. Mihai Netea and colleagues from Radboud university medical center discovered and described how that works. They think that the old vaccine could be useful for specific target groups, such as the elderly.

BCG, a vaccine against tuberculosis, was discovered in the 1920s and is one of the most used vaccines worldwide. In the Netherlands, the vaccine no longer falls within the national vaccination program. Now that it is known that the vaccine can give a boost to the innate immune system, Mihai Netea and his colleagues are calling for more research to determine whether the vaccine can prevent infections in certain risk groups.

During a bacterial infection, monocytes penetrate the infected tissue where they differentiate/ change into macrophages. These carry out the first line of defense: the destruction of the intruder. Monocytes and macrophages are two important white blood cells of the innate immune system. They respond quickly but attack certain pathogens less specifically. The acquired immune system responds more slowly to an unknown intruder but is specifically targeted at a specific intruder. Furthermore, the acquired immune system has a memory so that it responds faster to the same threat. For a long time it was thought that this memory was an exclusive characteristic of the acquired immune system. However research by Mihai Netea has revealed that this is not the case. The innate immune system also has a memory but this is not specific. Netea and his colleagues refer to this as 'trained immunity'.

Hidden DNA

Shortly after the introduction of the BCG vaccine it was noticed that not only tuberculosis occurred less frequently but that young children also died less due to other pathogens. On September 22, 2015 Johanneke Kleinnijenhuis from Netea's group will defend her doctoral thesis for her research into a biological explanation for the non-specific effects of BCG. In volunteers who received a BCG vaccination, she observed an increase in cytokine production (proteins that control immune cells) and in the number of receptors that play a role during the recognition of intruders. This effect was sustained until three months after vaccination.

The scientists discovered that this was because the DNA required was more easily reachable. Netea: "The DNA needs to be read out for the required proteins to be produced. Prior to the vaccination the DNA was hidden so to speak and was consequently difficult to read out. Vaccination ensures that the DNA is exposed."

The researchers also examined the effect in an animal model. Mice without cells from the acquired immune system were administered a potentially lethal quantity of the fungus Candida albicans. One part of the group received a BCG vaccination two weeks before this and the other part received a placebo. The BCG-vaccinated animals all survived the fungal infection, whereas in the placebo group more than half of the animals died. As a result of this study the researchers concluded that the effects can be ascribed to the innate immune system.

According to the researchers, the trainability of cells from the innate immune system opens up many opportunities for applications. Netea: "I do not think it is worthwhile introducing BCG again on a large-scale but it would be useful to target it at specific groups. One such example is elderly people who are discharged from hospital and who often experience a relapse when they are back home again. Another possible use is as a booster for other vaccines." In the coming years the researchers want to investigate such applications.

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