Studying immune response to aluminum salts can explain how these chemicals boost vaccine's efficacy

June 28 2017

Adjuvants are often included in vaccines to stimulate the immune system and so make a vaccine more effective. Now an A*STAR team, led by Alessandra Mortellaro from the Singapore Immunology Network, has explained a new immune pathway of a commonly used vaccine adjuvant, aluminum salts or 'alum'.

Components of disease-causing microorganisms contained in vaccines are not always sufficient to elicit a strong immune response. In some cases, unrelated chemicals, called adjuvants, are needed to further stimulate the immune system. The A*STAR team has taken up the challenge of explaining this enigma, known as the "immunologist's dirty little secret".

The immunity-boosting effect of alum was discovered in the 1920s: scientists in London found that aluminum potassium sulfate enhanced the efficacy of diphtheria vaccines considerably. Nowadays, alum is included in inoculations against various diseases, including common ones such as seasonal flu, tetanus and human papillomavirus infection. Paradoxically, despite the fact that millions of doses of aluminum-containing jabs have helped prevent and eradicate several pathologies, the details of alum's mechanism of action are not fully confirmed.

Mortellaro's team discovered that alum triggers immune cells called dendritic cells (DCs), to release IL-2 proteins. These act as a bridge

between innate immunity and immunological memory. The former defends the organism against any foreign substances entering the body, while the latter is specific for a certain infectious agent and can quickly detect and attack it upon subsequent encounters.

By injecting an alum-adjuvated vaccine to mice which are either able or unable to produce DC-derived IL2, the team found that this protein is required to spark immune protection and memory against the vaccination's target.

"We found that the release of DC-derived IL-2, promoted by alum, produces the typical signs of an efficient long-term immunization, where white blood T cells help other immune cells (B cells) to differentiate into antibody-producing cells," explains Mortellaro. Specifically, the researchers found an increase in both in the number of CD4+ T cells and of antibodies specific for the antigen present in the vaccine.

The release of DC-specific IL-2 is the last step of a molecular pathway, of which A*STAR scientists clarified the specifics. "It is an immune pathway shared by mouse and man, so these findings on alum and mouse immunity could be translated into the clinic," Mortellaro points out. "Moreover, we can leverage the knowledge about this pathway to improve vaccine formulation and development, and to test whether new adjuvants and alum alternatives have the same effect on DCs."

More information: Hanif Javanmard Khameneh et al. The Syk–NFAT–IL-2 Pathway in Dendritic Cells Is Required for Optimal Sterile Immunity Elicited by Alum Adjuvants, *The Journal of Immunology* (2016). DOI: 10.4049/jimmunol.1600420

Provided by Agency for Science, Technology and Research (A*STAR),

Singapore