Autoimmune Disorders

How Our Immune Response to Bacteria is ‘Hurting’ Us

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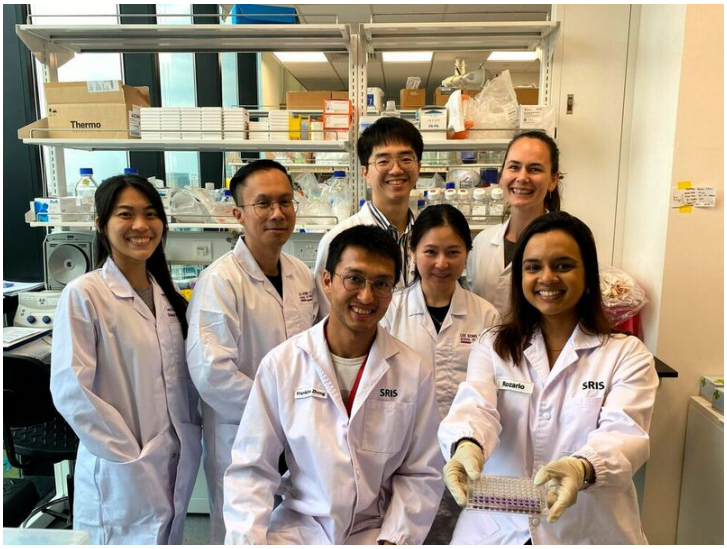
Researchers co-led by NTU Singapore’s Lee Kong Chian School of Medicine and the University of Toulouse, France, have uncovered how bacteria and their toxins prompt the human immune response, leading to inflammation.



(L-R) The team of researchers from NTU’s Lee Kong Chian School of Medicine (LKC Medicine), consisting of PhD student Miss Rae Chua, Research Associate Mr Muhammad Jasrie Firdaus, Mr Toh Gee Ann, Visiting Research Fellow Dr Anna Constance Vind, Assistant Professor Franklin Zhong Lei, Research Associate Miss Shirley Ding Suet Lee, and PhD student Miss Pritisha Rozario.
(Source: NTU Singpaore)

Inflammation plays a crucial role in fighting infections and healing injuries, but when it is persistent, it can also contribute to adverse side effects in chronic diseases such as heart disease and diabetes.

Inflammation can also trigger autoimmune disorders such as lupus, when the immune system mistakenly attacks the body's tissues, causing widespread inflammation and damage to organs like the joints, skin, brain, lungs, kidneys, and blood vessels.

Writing in the Proceedings of the National Academy of Sciences (PNAS), the researchers report a direct link between the molecules that move ions in and out of cells, known as ionophores, the consequent change of the salt content within human cells, and inflammation.

In the study, the researchers found that when the level of potassium ions within cells falls below a certain level, the cells kickstart an immune response and release strong pro-inflammatory molecules, such as those which can lead to the sensation of pain and fever and contribute to the tissue damage caused by infections.

Past research has shown that a human gene known as NLRP3 is essential to control this process in the blood. Now, the NTU Singapore and University of Toulouse study demonstrates for the first time that this process is controlled by a pair of genes known as NLRP1 and ZAKα in human organs such as the skin, lungs, and nose.

Lead author Assistant Professor Franklin Zhong from NTU's Lee Kong Chian School of Medicine (LKC Medicine), said: "Cells use a lot of energy to move sodium and potassium ions across their membranes, maintaining a specific ion balance between the interior of the cells and the external environment. This balance is crucial for normal cell functions. Problems with this balance can lead to diseases like neurological disorders and heart failure."

> *"Our study demonstrates that the human innate immune system has evolved multiple ways to sense disruptions of the cellular ion balance. This discovery helps us see how cells defend themselves when the balance of ions goes haywire, particularly when under pathogen attack. Our findings present a new piece in the puzzle of how our immune system functions and it could open doors to better treatments for diseases such as severe bacterial or viral infections."*
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> Franklin Zhong, LKC Medicine

The research team will continue their research to delve deeper into our immune responses, exploring how these signals might pave the way for tailored therapies that bolster the body's capacity to combat infections with precision.

They hope the ongoing research will contribute to developing more effective treatments for infectious diseases.

Original Article: Mechanistic basis for potassium efflux–driven activation of the human NLRP1 inflammasome; Proceedings of the National Academy of Sciences; DOI:10.1073/pnas.2309579121

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