



Influenza virus.

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Antiviral defence

Understanding the role of a messenger

A key component of the innate immune response may improve vaccines and anti-tumour assistance

The first line of defence against pathogen infection, known as ‘innate immunity’, could be boosted using synthetic copies of a small signalling molecule, called phosphatidylinositol-5-phosphate (PtdIns5P), which has been investigated by NAIST researchers.

The molecule could be paired with adjuvants, substances added to vaccines to provide additional assistance in fighting off infection. “This research suggests the possibility for developing a new vaccine adjuvant,” says Taro Kawai, who led the NAIST team.

“Innate immunity is also important in anti-tumour immunity and so in future we hope we can also develop anti-tumour adjuvants.”

When a virus invades the body, various parts are recognized by receptor molecules. These trigger inside the cells complex multi-step signalling pathways that activate elements of the innate immune system. It is a general

defence system not directed at any specific microorganisms; unlike ‘acquired immunity’, which produces targeted antibodies against unique invaders.

One of the most prominent aspects of innate immunity triggered by the signalling pathways is the production of interferon proteins. These are so-named because they can interfere with the multiplication of viruses and stimulate other cells into fighting the infection.

Kawai and colleagues at the NAIST Graduate School of Biological Sciences and other research centres in Japan investigated a part of the innate immune response that stimulates the production of type 1 interferon. The pathway leading to this interferon was known to involve two crucial proteins: a transcription factor that regulates gene activity, known as interferon regulatory factor-3 (IRF3); and an enzyme called TBK1 that adds phosphate groups to IRF3 during the interferon-producing pathway.

The researchers say that the detailed mechanisms for regulating what they call

“the TBK1-IRF3 axis” remain unclear, but they have been able to identify that ptdIns5P plays a crucial role. In particular, the work has revealed that PtdIns5P acts as a molecule that carries a signal from receptors into other parts of the cell, a process known as “second messenger” activity.

Kawai explains that using this insight to create a new vaccine adjuvant will require a suitable synthetic analogue of PtdIns5P, to make the adjuvant soluble in water and able to penetrate into cells. The team has already made and tested one such analogue and found that it can boost immune responses in mice.

Turning to a wider possibility, Kawai adds, “Innate immunity is also important in anti-tumour immunity and so in future we hope we can also develop anti-tumour adjuvants.”

Reference

1. Kawasaki, T., Takemura, N., Standley, D. M., Akira, S. & Kawai, T. The second messenger phosphatidylinositol-5-phosphate facilitates antiviral innate immune signaling. *Cell Host & Microbe* **14**, 148–158 (2013).