A new way to stimulate the immune system and fight infection

January 20 2012

A study carried out by Eric Vivier and Sophie Ugolini at the Marseille-Luminy Centre for Immunology has just reveal a gene in mice which, when mutated, can stimulate the immune system to help fight against tumors and viral infections. Whilst this gene was known to activate one of the body's first lines of defense (Natural Killer, or 'NK' cells), paradoxically, when deactivated it makes these NK cells hypersensitive to the warning signals sent out by diseased cells.

These new data are an essential step towards understanding the operation of these key cells in the immune system, and they could provide a new therapeutic approach to fighting infection. They also suggest that the operation of NK cells must be precisely regulated to guarantee an optimum immune reaction. Details of this work are published in the 20 January 2012 issue of the journal *Science*.

Our bodies are subject to attack by many different infectious particles (bacteria, viruses, etc.), which surround us in our everyday environment. Various immune cells are activated to fight off these attacks: the first response is from the innate immune cells1, which gradually give way to the memory B and T lymphocytes of the adaptive immune system. The Natural Killer (NK) cells are a part of this first line of defence of the organism. They can selectively kill tumour cells or cells infected by microbes whilst secreting chemical messengers known as cytokines, which stimulate and direct the response of the B and T lymphocytes.

Following the launch of a major genetics programme a few years ago,

scientists succeeded in revealing a gene whose deactivation causes heightened functioning of the NK cells (see figure below). This gene, called Ncr1, contributes to the manufacture of the receptor NKp46, which is present on the surface of NK cells. Surprisingly, its role in activating the NK cells has been known for several years.

'NK cells go through various stages of development before combating microorganisms or tumour cells,' explains Sophie Ugolini, joint author of the paper. 'Without this receptor, the NK cells are more reactive and therefore more effective when they encounter the attackers of the organism."

To test the therapeutic potential of their discovery, the scientists blocked the NKp46 receptor using a drug (in this case, a monoclonal antibody). As in the genetics experiments, this treatment that blocks NKp46 makes the NK cells much more effective.

'Our aim now is to further explore the underlying biological mechanisms and to work in collaboration with the biopharmaceutical industry and the hospital to evaluate the medical potential of this new type of treatment, particularly for patients whose immune system has already been weakened, such as patients with an immunodeficiency and those who have had a bone marrow transplant or chemotherapy,' concludes Eric Vivier.

1 Innate immunity is a front-line defence system against tumours and microbes. It immediately acts against microbial agents that come into contact with an organism. Innate immunity is present in all living organisms, and plays an essential role in activating the adaptive response in vertebrates. This compartment of immunity hit the headlines recently when Jules Hoffman of France, Canadian Ralph Steinman, and Bruce Beutler from the USA (another co-author of this paper) received the Nobel Prize for their work on innate immunity and its close links with

the adaptive immune system.

More information: "Tuning of Natural Killer Cell Reactivity by NKp46 and Helios Calibrates T Cell Responses" *Science*, Jan 20, 2012.

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