Paris, 6 October 2016

**Press release**

**New immunotherapy-based approach for post-transplant leukaemia relapse**

An Inserm team from the Mondor Institute for Biomedical Research (IMRB) has just identified a key switch in the immune response, and proposes a new immunotherapy-based approach for combating leukaemia. And maybe other cancers in time. This work is published in the journal *Blood*.

Towards a new immunotherapy for cancer? That may well emerge from the work carried out at Inserm Unit 955, “Mondor Institute for Biomedical Research” (IMRB) by a team led by Prof. José Cohen, Coordinator of the Clinical Investigation Centre – Biotherapy at Henri Mondor Hospital AP-HP, results of which have just been published in *Blood*. Although it works on the treatment of leukaemias, this team has discovered a key to the regulation of the immune system that makes it possible to stimulate T lymphocyte action, and probably increase the elimination of malignant cells.

It was their work on graft versus host disease, a serious complication in leukaemia patients who receive blood cell transplants, that set them on the track. This complication is due to the recipient’s cells being attacked by overactive T cells present in the transplant. Moreover the researchers found that the presence in the transplant of T regulatory cells (T regs), a specific subpopulation of T lymphocytes, the role of which is to down-regulate the immune response, limited this phenomenon. In a mouse model, when they injected additional T regs during transplantation, they prevented the transplant from attacking the host. They therefore decided to go further, and find out how these T reg cells were controlled.

**TNFR2, an immune response switch**

To do this, they performed different experiments, and finally demonstrated the existence of a closed circuit between conventional T lymphocytes and T reg lymphocytes, involving a key receptor called TNFR2. When conventional T lymphocytes are active, they secrete tumour necrosis factor (TNF), which binds to the TNFR2 receptors present on the surface of T regs. This signal stimulates the latter, which then inhibit the conventional T lymphocyte response. Conversely, when the TNFR2 receptor is blocked, T regs become inactive and T lymphocytes are activated.

“This TNFR2 receptor acts on the immune response just like a real switch. When it is in the ‘on’ position, it inhibits it. When it is in the ‘off’ position, it stimulates it,” explains José Cohen, who supervised this work. Having made this discovery, the researchers now intend to block this TNFR2 receptor in an attempt to improve the immune response against cancer, which will have direct application in immunotherapies. “The role of immunotherapy is to target ‘check-points’ in the immune response in order lift inhibition and allow it to more effectively...”
eliminate malignant cells. The treatments currently available are specific for a population of T lymphocytes known as effectors, while we propose a new target, the regulators. These treatments could therefore be complementary," adds the researcher.

The team has already filed a patent to protect the exploitation of this receptor in the context of post-transplant leukaemia relapse. The idea is now to develop a human anti-TNFR2 antibody to test this therapeutic strategy in a so-called "humanised" mouse model. If the results are conclusive, clinical trials will be conducted. At the same time, this approach is being evaluated for other types of cancers, including solid tumours, by the team led by Dr Benoit Salomon (CIMI-Paris), a co-author of the study.

Source

Control of GVHD by regulatory T cells depends on TNF produced by T cells and TNFR2 expressed by regulatory T cells
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Blood http://dx.doi.org/10.1182/blood-2016-02-700849

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