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PRESS RELEASE

The Yin and Yang of Low-dose Irradiation on Hematopoiesis

A team of researchers from CEA, Inserm, and the Paris-Sud and Paris Diderot universities has shown that exposure to low doses of irradiation (0.02 Gy) leads of a loss of hematopoietic stem cell[1] (HSC) function. The team has also shown that irradiation at this low dose facilitates efficient bone marrow transplantation without myeloablation[2]. These results, published in *Cell Reports* on September 26, 2017, show both the positive and negative aspects of low doses of irradiation.

What are the consequences of exposure to low doses of ionizing radiation, for example during medical examinations using X-rays? Previous epidemiological studies associated exposure to low doses of irradiation (<0.1 Gy) with an increased frequency of hematologic disease onset. However, no biological link between exposure to low doses of irradiation and hematopoietic cell abnormalities had been shown. The results obtained by the researchers from CEA, Inserm, and the Paris-Sud and Paris Diderot universities show that low-dose irradiation of HSCs, cells at the origin of all blood cells, leads to a decrease in HSC number and function. These effects on the stem cells can also be observed *in vivo* in inflammation and may lead to a deficiency in blood cell production and the risk of aplastic anemia[3] or leukemic transformation.

This team has used this property to test a new protocol to facilitate efficient bone marrow transplantation without the need for myeloablation. Indeed, the protocol, currently used during autologous bone marrow transplantation[4] involves the use of drug treatment to destroy the patient's bone marrow prior to the transplant (myeloablation), a procedure which is unfortunately associated with a number of side effects. On the basis of their observations, the researchers have shown that a very low dose of irradiation, a dose used in medical imaging, preceded by a treatment that is currently used in the clinical setting and which removes the HSCs from the bone marrow, would facilitate efficient bone marrow transplantation without myeloablation.

These results point to the need for careful management when performing medical imaging, particularly in patients presenting signs of inflammation. It could also

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[1] Bone marrow stem cells that produce blood cells: red cells, white cells and platelets.
[2] Drug treatment to destroy the patient's own bone marrow prior to transplant.
[3] Insufficiency of the bone marrow to produce the various blood cell lines caused by more or less lasting HSC rarefaction.
[4] In gene therapy, autologous transplant consists of taking a patient's HSCs and reconstituting his hematopoiesis with his own, genetically modified stem cells.

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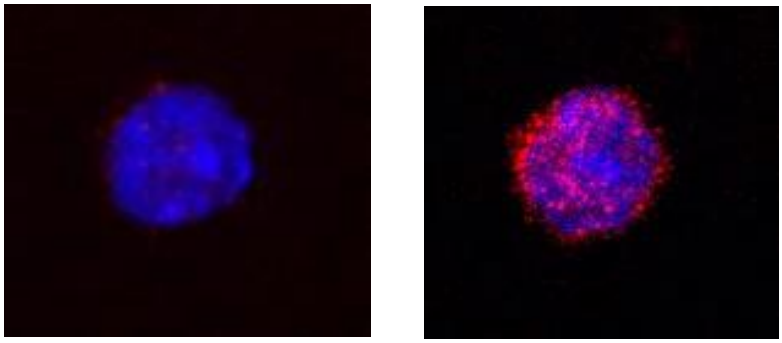
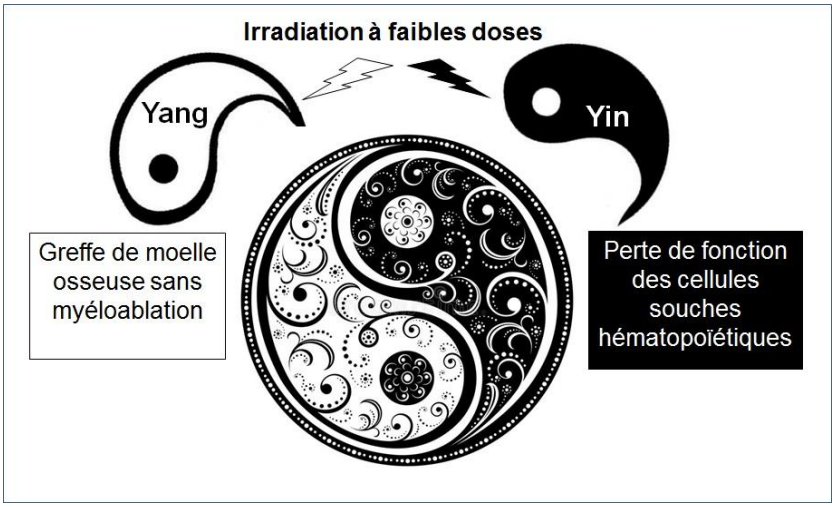
provide major therapeutic benefit to patients who are candidates for autologous bone marrow transplantation, particularly when a gene therapy protocol is used.



Hematopoietic stem cells (HSCs), non-irradiated (left) and irradiated (right) at a dose of 0.02 Gy. In blue the nucleus and in red the activated and nuclear Nrf2 protein, indicator of HSC response to oxidative stress caused by irradiation at a dose of 0.02 Gy.



Irradiation à faibles doses	Low-dose irradiation
Yang	Yang
Yin	Yin
Greffe de moelle osseusse sans myéloablation	Bone marrow transplant without myeloablation
Perte de fonction des cellules souches hématopoiétiques	Loss of hematopoietic stem cell function

References : **Low-dose irradiation promotes persistent oxidative stress and decreases self-renewal in Hematopoietic Stem Cells**, *Cell Reports*, 26/09/2017

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