Subject 5 : **Flash irradiation: beneficial or not for non-specific immunity?**

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Flash irradiation is developing in cancer medicine because it appears to be less harmful for healthy tissues surrounding the tumor than traditional radiotherapy. It is thus possible to increase the doses and promote the risk-benefit ratio imposed by radiotherapy. However, traditional radiotherapy decreases immune defenses, making the subject more susceptible to bacterial and viral diseases. In the "Dynamics and Functioning of Redox Proteins and Oxidant Stress" team (ICP, Orsay), we are studying the effects of continuous gamma irradiation on human neutrophils (1) and on models of neutrophils, PLB-985 (2) . We have shown that the lifespan of neutrophils decreases with irradiation, but above all that irradiation initiates an activation of the enzyme NADPH oxidase NOX2, which produces superoxide ions, precursors of reduced oxygen species (ROS). It is well known that irradiation produces tissue inflammation. Our results would indicate that part of these processes would be linked to the activation of neutrophils and therefore would involve non-specific immunity. The "Elementary chemical acts by pulsed radiolysis" team (ICP, Orsay) specializes in pulsed radiolysis (Elyse). Our two teams have, to date, never collaborated, but have the ambition, on the basis of their respective expertise, to use the Elyse assembly to deliver ultra-short pulses (a few picoseconds) to neutrophils or model cells. accelerated electrons. Our objective is to demonstrate whether flash irradiation causes the same phenomena as those observed with traditional irradiation on cells of the immune system. The cells are isolated from donor human blood (agreement with the French Blood Establishment) using methods mastered by the team. These cells will be subjected to flash irradiation. The dosimetry will be made according to the methods of chemistry under radiation (radiolysis of thiocyanate solutions), which gives an extremely precise measurement of the dose and the dose rate. Sophie Le Caer's team (UMR 3685 NIMBE, CEA) specializes in continuous and pulsed radiolysis in confined environments. His experience will be valuable for understanding what happens inside a neutrophil, a confined environment par excellence. This project will examine i) the lifespan of neutrophils as a function of dose (from 0 to 50Gy); ii) the state of the NADPH oxidase enzyme and its possible activation; iii) the production of superoxide ions.

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