Soutenance de thèse

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"Development of platinum based nanoparticles to enhance cancer cell killing by gamma rays and carbon ion radiation"

Radiotherapy based on the use of high energy photons (X-rays) is the most common approach in cancer treatment. However, its implementation is limited by the tolerance of healthy tissue. Therefore, it is of major interest the development of new techniques and protocols to improve the effect of radiation within the tumor. In this perspective, the hadrontherapy (tumor irradiation by protons or carbon ions) is considered as one of the most promising techniques due to the energy deposition of ions in depth, which is maximum at the end of the track. However, the use of this modality remains restricted by the lower but significant damage induced to the normal tissue located at the entrance of the ion beam.

To improve the performance of radiation therapies, a new strategy based on the combination of metallic nanoparticles with ionizing radiations was studied. This approach has been developed by the group. Indeed, nanoparticles present a remarkable surface chemistry that allows their functionalization with ligands which make them less recognized by macrophages allowing an important accumulation into the tumors.

The goal of my work was thus to develop platinum based nanoparticles (mono- and bimetallic Pt NPs) to enhance the effect of radiations (photons and carbon ions) into the cells. A novel one-step method of synthesis combining radiolysis and *in situ* PEGylation was optimized. This method enabled to obtain stable biocompatible NPs with a uniform size and shape (metallic core diameter close to 3 nm).

The biological impact of these new Pt NPs was evaluated in two human cancer cell lines. It has been observed that non-toxic Pt NPs have an internalization pathway that strongly depends on the cell line. These are, in all cases, exclusively localized in the cytoplasm. The Pt NPs developed in this work significantly enhanced cancer cell killing, particularly when medical carbon ions are used to irradiate.

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The molecular mechanisms underlying this effect were investigated through the use of a bio-nanoprobe. The experiments showed that NPs are responsible for the increase of nanometric damage, lesions that can be lethal to cells. This effect is attributed to an electronic activation processes and to the reneutralisation of NPs, which generates a strong perturbation in the surrounding nanometer volume producing highly reactive and toxic free radical clusters.

In conclusion, this work at the interface of physics, chemistry and biology shows the potential of platinum NPs to improve the eradication of cancer cells by radiation.

Vendredi 25 novembre 2016 à 14h30

Bât 210 – Amphi 1 (2ème étage)

Université Paris-Sud, 91405 Orsay Cedex

La soutenance sera suivie d'un pot auquel vous êtes chaleureusement conviés.