Soutenance de thèse

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Nanoparticles for radiotherapy and protontherapy : internalization and localization in human cell lines and impact on radiation effects

Radiation therapy is one of the main modalities for cancer treatment. However, its use is limited due to damage induced in healthy tissues and radioresistance in some cases. However, improvements are needed to improve tumor targeting and treatment effectiveness. One of the proposed improvements is the use of nanoparticles composed of high-atomic number elements that have the property of amplifying the effect of ionizing radiation. Gold nanoparticles are one of the most promising agents, because of their low toxicity and the possibility of binding molecules on their surface. The effectiveness of small gold nanoparticles functionalized with DTDTPA (< 3 nm) has been proven. However, little data exists on the link between the amplification effects in respect to the internalization dynamics and their location in cells. This work focused on studying the internalization and excretion dynamics of these nanoparticles, as well as their location in different cancer cell lines and in human fibroblasts.

An attempt to correlate the radiation effects with these data is proposed. The results obtained in this work show that the dynamics of absorption and excretion, as well as the predominant internalization pathways of gold nanoparticles, strongly depend on the cell line. The amount of internalized gold, resulting from these mechanisms, also varies. These internalization mechanisms impact the localization of nanoparticles in the various subcellular organelles, due to the specific internalization pathways. Finally, a link is proposed between the intracellular localization of gold nanoparticles and their colocalization with subcellular organelles.

In conclusion, these results indicate that the effectiveness of nanoparticles depends on the cancerous line that is treated. Although in vivo experiments are still needed to validate these results, this work proposes original methods for rapid characterization and prediction of the effects of agents on cells.

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