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Radiobiology of molecular radionuclide therapy: contribution of targeted and non-targeted effects

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Radionuclide therapy consists of the selective irradiation of tumour cells deriving from a radiolabelled molecule or device, specifically located at the tumour site. The consequent effect, on both tumours and normal tissues involved, depends not only on the modality of absorbed dose delivery but also on the specific characteristics of the irradiated tissue and of its microenvironment. Radiobiology helps to clarify the underlying mechanisms and to predict the dose-response relationship. Whilst developed for external beam radiotherapy to the extent that it is used routinely to guide fractionation, radiobiological principles are only beginning to be explored for targeted radionuclide therapy. In this respect, it is important to determine the contribution of targeted effects, which are dose-related, and of non-targeted including bystander and systemic effects of targeted radionuclide therapy. In the last decade, our team investigated the contribution of non-targeted cytotoxic and genotoxic effects in vitro and in vivo (WT C57BL/6J and athymic nude mice) during alpha (212Pb/212Bi, 213Bi) and Auger (125I) radioimmunotherapy (RIT). We confirmed that non-targeted effects play a central role in Auger and alpha RIT and that drugs modifying cholesterol metabolism can modify RIT efficacy.

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