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Radiosensitization by Au nanoparticles

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Over the last couple of decades, nanoparticles have attracted considerable interest for their possible use and exploitation in a wide range of applications. For radiotherapy, doping cancerous cells with high Z materials represents an ideal way to boost the dose to the tumour volume without compromising the dose to the healthy normal surrounding tissues. Gold nanoparticles (GNPs) in particular can be easily functionalized to be preferentially uptaken by specific tumour cells offering very selecting targeting strategies. Enhancement of radiosensitivity in GNP doped cells has been reported with some contradiction in literature especially for high energy X-rays where no physical dose enhancement is expected. Further investigations on the nanoparticle-cell interactions are therefore required to improve our understanding at the nano- and molecular-scale and optimise the use of GNPs in radiotherapy.
A mathematical model based on the Local Effect Model (LEM) used for heavy ions indicates that radiosensitization is not just due to a dose enhancement factor but complex lesions may be created in proximity of the nanoparticles by showers of secondary Auger electrons. Through clonogenic cell survival assays, we have confirmed a radiosensitising effect for a panel of cancer cell lines (MDA-231s, DU145s and T98s) in the presence of GNPs but no for normal human fibroblasts (AGO-1522). Interestingly, these cell lines differ greatly on the type of cell death induced when exposed to GNPs and radiation as seen by Annexin/PI flow cytometry analysis. The different levels of radiosensitization are likely to be due to differential GNP uptake as well as different mechanisms triggered by the nanoparticles uptake. The GNPs alone have been shown to cause DNA damage in MDA-231s and DU145s but not in T98Gs while pilot data from microbeam experiments show that cytoplasmic irradiation alone in the presence of GNPs results in significant increase of DNA damage, suggesting cytoplasmic organelles are sensitive to GNPs and irradiation. Further data indicates that the observed increased DNA damage and radiosensitisation is due to the depolarisation of mitochondria directly caused by significant increases in reactive oxygen species upon exposure to gold nanoparticles. Radiosensitization caused by GNPs seems therefore be the result of combination of physical (dose and lesion complexity enhancement) and biological effects (mitochondria inactivation).

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