The role of thioredoxin reductase in gold nanoparticle radiosensitization effects

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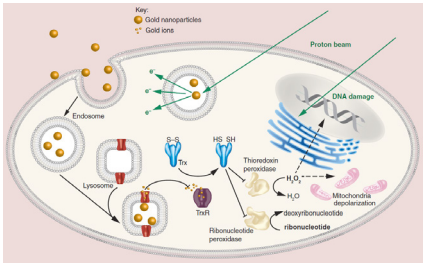
Aim: To identify new mechanisms responsible for the radiosensitization effect of gold nanoparticles (GNPs).

Materials & Methods: Five different cell lines were incubated with homemade 10 nm GNPs 24h before to be exposed to 25 keV/µm protons or 225 kV X-rays.

Findings: GNP incubation with lung carcinoma cells led to a time-dependent mitochondria membrane depolarization, oxidative stress and to X-ray and proton radiosensitization. Moreover, a marked inhibition of thioredoxin reductase (TrxR) was observed. Irradiation of cells invalidated for TrxR evidenced a radiosensitization effect, suggesting that this enzyme is a potential GNP target. Furthermore, we reported that this TrxR activity reduction is cell type-dependent and lead to differences in cell response to X-ray irradiation. Correlation analyses demonstrated that GNP uptake and TrxR activity inhibition are associated to GNP radiosensitization effect. Finally, Kaplan-Meier analyses suggested that high TrxR expression is correlated to low patient survival in four different types of cancer.

Conclusions: We suggest that GNPs play a radiosensitizer role by weakening detoxification systems. All together, these results enable a better understanding of GNP radiosensitization mechanisms which remain a mandatory step towards further use in clinic. Moreover, they highlight the potential application of this new treatment in a personalized medicine context opening up novel promising strategies for the development of nanotechnologies associated to radiotherapy.



Biography

Sebastien Penninckx got a master's degree in chemistry at Free University of Brussels (Belgium). He then defended his PhD thesis in physics and biology at University of Namur (Belgium) in February 2019. In recent years, he has built bridges between nanotechnology and biophysics in close collaboration with transdisciplinary teams in the research institute NARILIS in the UNamur. During his PhD thesis, he has spent 3 months at UC Berkeley (California, USA) and NASA Ames Research Center (USA) where he studied cancer risk prediction for astronauts exposed to ionizing radiations during spacecraft missions.

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