TUNING ENGINEERED NANOMATERIALS FOR CANCER TREATMENT WITH REACTIVE OXYGEN SPECIES

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Engineered nanomaterials that produce reactive oxygen species while exposed to X- and gamma rays offer promise of a novel cancer treatment strategy. Similar to photodynamic therapy (PDT) but suitable for deep tumours, the new approach called X-PDT is highly effective at clinically low radiation doses. The X-PDT nanomaterials can enhance cancer radiotherapy, by increasing its selectivity, and decreasing side effects. Additionally, the nanomaterial platform offers therapeutically valuable functionalities such as molecular targeting, the capability for drug/gene delivery, adaptive responses allowing triggering of drug release and more. The potential of such nanomaterials to be combined with radiotherapy has been widely recognised, as apparent in an explosion of new advances in X-PDT. So far, the field seems to develop organically, by a combinatorial approach, and optimally designed materials and quantitative approaches remain scarce. In order for further breakthroughs to be made, and to facilitate clinical translation the applicable principles and fundamentals should be articulated. We will introduce mechanisms and principles underpinning rational material design for X-PDT. The understanding of these principles will enable novel ways to optimise the ROS yields and the ensuing cytotoxicity which is directly related to therapy success. The X-PDT nanomaterials will be discussed though the lens of catalytical processes at solid surfaces. Drawing on analogies between photo- and radio-catalysis, we propose that future authors build on selected advances in the areas of clean energy, water splitting and environmental remediation.

Traditionally, in PDT photosensitizer drugs act as molecular catalysts. In the X-PDT approach, catalysis takes place on the solid surface of nanomaterials. Many aspects of such surfaces are well established in solid state physics, but disciplinary barriers prevent wider utilisation of that knowledge to build optimised X-PDT agents. We discuss optimising of charge transfer catalysis where ROS are formed by redox reactions. The alternative process of energy transfer catalysis is also highly relevant, while much less understood; we discuss resonant tuning of X-PDT offered by energy transfer processes which offers unprecendented amplification.

Functionalisations and coatings are a ubiquitous feature of engineered nanomaterials and these layers can be used for facile tuning of X-PDT. We discuss how ionic organisation of fluid at the solid-liquid interface affects the potential profile, and how this, in turn, allows to easily adjust the matching of electron and hole energies with relevant redox potentials.

We then focus on nanomaterials where coatings contain clinical photosensitizers (a development analogous to surface-immobilised organocatalysts in chemistry). These offer additional dimension to optimise X-PDT, as they can utilise energy transduction (X-rays into visible light) and also Cherenkov radiation produced during radiotherapy. Furthermore we explore clinical translation of these materials where we discuss biocompatible nanocarriers (liposomes and PLGA nanoparticles) as well as mesoporous silica etc. Critically, the photosensitizers respond with ROS not only to light but also to radiation. We explain the underpinning mechanism which makes it possible to create X-PDT nanoparticles with sophisticated functionalities such as X-ray triggering exclusively from FDA-approved components, a step that brings closer their clinical translation. Finally in this section we draw attention of the reader to novel photosensitizers derived from aggregation-induced-emission (AIE) molecular species. We explain how their violation of the Kasha rule enables exceptionally high ROS yields, suggesting that they may help build uniquely powerful and clinically compatible nanoconstructs for X-PDT.

We then turn attention to cells and explore ways in which cells fight back the ROS attacks which is necessary for their survival. Effective X-PDT agents should be able to weaken or, ideally, disable this cellular protection. We focus on DNA damage and its repair, as well as on maintaining the redox status through the cellular antioxidant system based on glutathione system. Both DNA damage and the antioxidants can be interfered with using functional nanoparticles.

As a conclusion we present a roadmap for designing nanomaterials with optimised X-PDT performance.