Radionuclide stimulated nanophotosensitizers for cancer therapy

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Light-based therapeutic interventions such as photodynamic therapy (PDT) are currently used in the clinic for treating various human diseases. The exciting combination of light and light-sensitive drugs (photosensitizers, PS) offers a high degree of control to optimize therapy. Despite the promise of PDT, the shallow penetration of light in tissue confines its use to lesions that are accessible to external light source. Furthermore, the reliance on molecular oxygen to generate reactive oxygen species implies that PDT is less effective in hypoxic conditions, which characterize most solid tumours. To overcome these limitations, we developed a treatment paradigm that harnesses the ability of some radiopharmaceuticals to stimulate the production of reactive oxygen species (ROS) from nanophotosensitizers. Unlike conventional photosensitizers, nanophotosensitizers are capable of generating ROS from a variety of oxygen sources, a catalytic process that allows continuous production of cytotoxic ROS for cancer therapy (Figure 1). We have demonstrated the potential to eradicate or inhibit the growth of certain types of solid tumours.[1] Recent results further show the applicability of this treatment method to disseminated and metastatic tumours in mouse models of multiple myeloma and breast cancer.[2] A combination of radionuclide stimulation, Cerenkov radiation, and ROS generation from nanophotosensitizers synergistically overcomes the tissue depth limitation of the current external light delivery methods. The use of radiopharmaceuticals and drugs with a history of human application points to a seamless clinical translation of the new method in future.

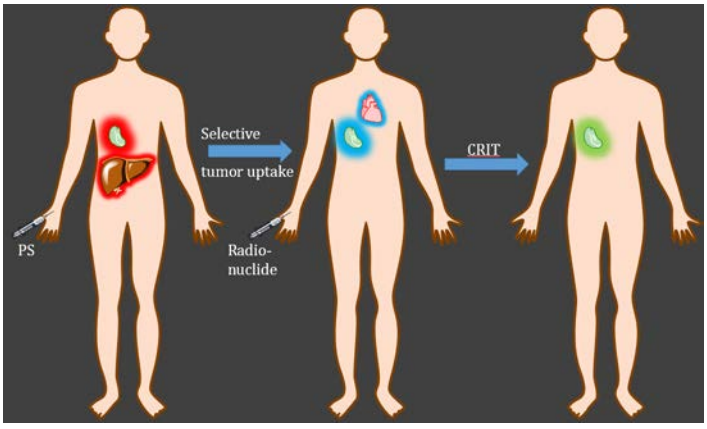

Figure 1: *Illustration of the radionuclide stimulation of cancer therapy. The PS is first administered to accumulate in cancer cells and the excretion organ, followed by injection of the radiopharmaceuticals, which selectively exerts therapeutic via multiple paths that include phototherapy*

References

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2. Kotagiri N, Cooper ML, Rettig M, Egbulefu C, Prior J, Cui G, Karmakar P, Zhou M, Yang X, Sudlow G, Marsala L, Chanswangphuwana C, Lu L, Habimana-Griffin L, Shokeen M, Xu X, Weilbaecher K, Tomasson M, Lanza G, DiPersio JF, and Achilefu S, Nat Commun. 2018, 9(1):275.