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Upconverting nanovesicles for the activation of ruthenium anti-cancer prodrugs with red light

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Propositions (Stellingen)

accompanying the thesis

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1. The activation wavelength of photochemotherapeutic drugs can be effectively shifted to the phototherapeutic window by using triplet-triplet annihilation upconversion.
This thesis, Chapter 3.

2. The oxygen sensitivity of TTA-UC, which represents its main limitation for real-world applications, can be effectively mitigated by using antioxidants.
This thesis, Chapter 8 and 9.

3. It is unacceptable to report the use of TTA-UC nanoparticles in biology without a proper discussion of the oxygen sensitivity.
Liu et al. J. Am. Chem. Soc. ***2012****, 134, 5390; Wohnhaas et al. Macromol. Biosci.* ***2011****, 11, 772; Nagai et al. ACS Biomater. Sci. Eng.* ***2015****, 1, 1206; Wang et al. Nano Lett.* ***2015****, 15, 6332.*

4. It is not justified to treat cells with aggregated silica-coated liposomes as "drug delivery system" when one fails to produce them as monodispersed particles.
This thesis, Chapter 7; Corma et al., Angew. Chem. Int. Ed. ***2009****, 48, 6247.*

5. In contrast to a high dose of blue (450 nm, 11 $kJ.cm^{-2}$) or infrared light (980 nm, > 6 $kJ.cm^{-2}$), a high dose of red light (630 nm, 38 $kJ.cm^{-2}$) does not damage mammalian tissue.
This thesis, Chapter 8; Chen et al. Chem. Eur. J. ***2015****, 21, 9165.*

6. Functionalizing ruthenium compounds with hydrophobic moieties such as alkyl tails can be useful for anchoring the complex to lipid membranes, but does not always prevent escape of the complex over time.
This thesis, Chapter 8.

7. Although polymersomes are superior to liposomes in terms of mechanical properties, membrane permeability, stability in cells, and blood circulation lifetimes, they are less suitable for attaining high TTA-UC efficiencies.
This thesis, Chapter 9; LoPresti et al. J. Mater. Chem. ***2009****, 19, 3576.*

8. It is curious that TTA-UC nanodevices receive much less attention in the literature than lanthanoid-based upconverting nanoparticles, because TTA-UC vesicles and particles are in many ways superior.

9. To reach clinical application of a photoactivated chemotherapeutic drug, many variables demand optimization: drug uptake, cellular target, light wavelength and dose, incubation time, toxicity in the dark, *et cetera*. Adding a drug delivery system to this mix may complicate these studies dramatically.
Anselmo et al. Bioeng. Transl. Med. ***2016****, 1, 10.*

10. Attributing the photocytotoxicity of dissociative ruthenium polypyridyl complexes to interaction between the metal aqua photoproduct and DNA is often unjustified.
Howerton et al. J. Am. Chem. Soc. ***2012****, 134, 8324; Sgambellone et al. J. Am. Chem. Soc.* ***2013****, 135, 11274.*

11. Microscopy offers fantastic possibilities for visualization of (nano)particles (electron microscopy) and cells (optical microscopy), but one should be wary of cherry picking. Sufficient statistics and complementary bulk measurements should provide additional evidence to confirm microscale observations.
Sahu et al. Chem. Commun. ***2012****, 48, 8835.*

12. In contrast to free-optics setups, the use of fiber-coupled optics allows for straightforwardly constructing plug-and-play spectroscopy setups.

13. Scientific publications should be supplemented with a synopsis on failed experiments in order to save the valuable research time and funding of other scientists.

14. Staying well-informed in science becomes increasingly challenging: processing the information output of the scientific community represents a tremendous task.

15. Cell incubators cannot operate in excessive ambient humidity.

16. Doing sports is an excellent remedy to overcome the mental challenges during a PhD.

Sven H. C. Askes
Leiden, September 2016