Upconverting and NIR Emitting Rare Earth based Nanostructures for NIR-Bioimaging

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Supplementary Information

Sample Overview

Table 1 gives an overview of the various Y_2O_3:Ln^{3+} and Gd_2O_3:Ln^{3+} nanostructures prepared in our group, their synthesis method, particle size as well as *in-vitro*, respectively *in-vivo* experiments that have been conducted with the respective nanostructures.

Table 1. Sample overview.

Sample	Method	Precipitant	Surfactant	Size (nm)	*in-vitro* / *in-vivo* Experiment*
Y_2O_3:Er^{3+}					
	alkaline precipitation	NH_4OH	-	100-1000	
	homogeneous precipitation	urea	SDS	500	• macrophage cytotoxicity [1]
	homogeneous precipitation	urea	-	280	• macrophage cytotoxicity [2]
	homogeneous precipitation	urea	PEG	250	• B-cell and macrophage cytotoxicity [3] • cellular uptake [3]
	homogeneous precipitation	urea	PS20	200	
	homogeneous precipitation	urea	CTAB	100	• macrophage cytotoxicity [1]
	homogeneous precipitation	urea	PAAc	40-50	• macrophage cytotoxicity [1,2] • cellular uptake [1,2]
	enzymatic precipitation	urea	-	10-30	

[1] N. Venkatachalam, T. Yamano, E. Hemmer, H. Hyodo, H. Kishimoto and K. Soga, *J. Am. Ceram. Soc.*, 2013, in print (DOI: 10.1111/jace.12476).
[2] N. Venkatachalam, Y. Okumura, K. Soga, R. Fukuda and T. Tsuji, *J. Phys.: Conf. Series*, 2009, **191**, 012002.
[3] N. Venkatachalam, E. Hemmer, T. Yamano, H. Hyodo, H. Kishimoto and K. Soga, *Prog. Cryst. Growth Charact. Mat.*, 2012, **58**, 121.

Gd_2O_3:Er^{3+},Yb^{3+}					
Rods5	hydrothermal	ammonia	-	160 x 600	• B-cell and macrophage cytotoxicity [4,5] • cellular uptake [4] • biodistribution [4] • multicolour imaging [6]
Rods12	hydrothermal	aqueous KOH	-	40 x 1000	• B-cell and macrophage cytotoxicity [5]
ParticlesAP	alkaline precipitation	Na_2CO_3	-	100-1000	• B-cell cytotoxicity [5]
ParticlesHP	homogeneous precipitation	urea	-	300	• B-cell and macrophage cytotoxicity [4,5] • biodistribution [4]
ParticlesHP-CTAB	homogeneous precipitation	urea	CTAB	120	• macrophage cytotoxicity [4,5] • cellular uptake [4] • biodistribution [4]
ParticlesHP-CTAB-PEG	homogeneous precipitation	urea	CTAB, PEG6000	80	• biodistribution [4]
ParticlesEP	enzymatic precipitation	urea	-	40	• B-cell cytotoxicity [5]
ParticlesEP-CTAB	enzymatic precipitation	urea	CTAB	30-40	
Gd_2O_3:Ho^{3+},Yb^{3+}					
ParticlesHP-CTAB-PEG	homogeneous precipitation	urea	CTAB, PEG6000	80	• biodistribution [6] • multicolour imaging [6]

* Also investigating the influence of the surface modification with PEG-*b*-PAAc on the cytotoxic behaviour

[4] E. Hemmer, H. Takeshita, T. Yamano, T. Fujiki, Y. Kohl, K. Löw, N. Venkatachalam, H. Hyodo, H. Kishimoto and K. Soga, *J. Mater. Sci.: Mater. Med.*, 2012, **23**, 2399.
[5] E. Hemmer, T. Yamano, H. Kishimoto, N. Venkatachalam, H. Hyodo and K. Soga, *Acta Biomater.*, 2013, **9**, 4734.
[6] This review

Time-Resolved Biodistribution of $Gd_2O_3:Er^{3+},Yb^{3+}$ Rods

Movie 1 shows the time-resolved distribution of the $Gd_2O_3:Er^{3+},Yb^{3+}$ nanorods (*Rods5*, modified with PEG-*b*-PAAc) in the mouse body through the blood vessel system. Integration time: 400 ms, Laser power: 4.5 W.

Preliminary Long-Term Cytotoxicity Studies

In case of $Y_2O_3:Er^{3+}$ nanoparticles, preliminary studies have been done in order to investigate the long-term effect of the nanostructures on the treated mice. Therefore, one set of mice was treated with nanoparticles (size: 250 nm, PEG-*b*-PAAc modified, single dose, 2.5 mg), while a second set of mice was untreated as control. Three weeks post-injection, the mice were sacrificed and the organs were dissected. We did not observe any abnormality in the obtained histological sections of organs of mice injected with particles when compared to the control (Figure 1). The injected mice did not show any pathological changes. For a deeper understanding of the long-term toxicity effect, respectively the effect of multi-dose injections, further experimental investigations are recently underway.

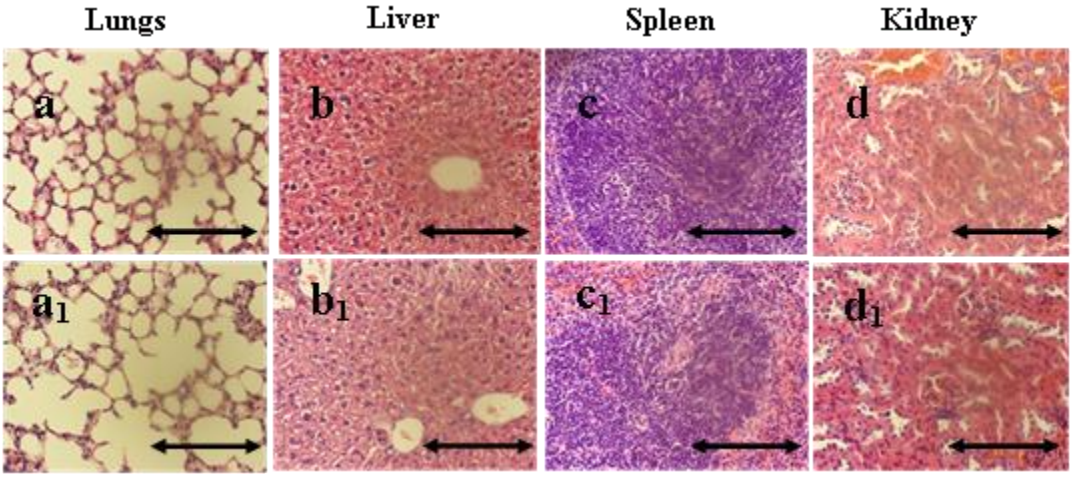

Figure 1. a)-d) Histological sections of organs from untreated mice (control). a1)-d1) Histological samples of mice three weeks post-injection (scale bar: 30μm).