PERsistent Luminescence (PERL) nanoparticles for small animal *in vivo* bioapplications

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Chemists have a wide toolbox to prepare inorganic luminescent nanoparticles that can serve as highly efficient non-bleaching optical probes. However, the weak penetration of light across the living tissues appears as a major hindrance to the use of such luminescent nanoparticles *in vivo*. First, the luminescent nanoparticles cannot be excited in the UV or visible range across the tissues and, second, their photoluminescence signal is then hidden by the tissues autofluorescence yielding a poor signal/noise ratio. Outside the UV-visible range, X-rays penetrate the tissues and *radioluminescent* nanoparticles represent an option to convert X-rays into visible/infrared light. However, their use is limited by the maximum tolerable dose. Alternatively, some infrared radiation falls into the tissues transparency windows. *Up-converting* nanoparticles, that convert 980 nm laser light into UV-visible therefore seem attractive, but they require intense laser power that causes detrimental heating to living animals. PERsistent Luminescence (PERL) nanoparticles, i.e. optical batteries, represent an exciting third option.

A PERL material is an inorganic crystalline host doped with a luminescent ion and a point defect has been introduced in a controlled manner. When illuminated by an external radiation (X-ray, UV, visible) the excitation energy is stored in the material in the form of electrons/holes trapped at point defects ("charging"). Once excitation is stopped, the ambient temperature (or the temperature of the animal body) triggers the progressive release of trapped electrons/holes, which then continuously feeds the luminescent center and yields a slowly decaying luminescence (minutes/hours).

In 2011, we pioneered $ZnGa_2O_4$:Cr (ZGO) as a near-infrared-emitting PERL material suitable for *in vivo* small animal imaging [1]. Thanks to several spectroscopies (optical, EPR, EXAFS/XANES) we elucidated the PERL mechanism of ZGO, i.e. a localized charge trapping process at antisite defects of the spinel host matrix around Cr^{3+} ions [2] [3]. This special feature confers ZGO the unique capacity of being charged not only by UV radiation but also with orange-red light. Hence, prepared by suited hydrothermal routes, 40-60 nm large ZGO nanoparticles are highly performant for small animal *in vivo* tumor imaging [4]. As the excitation is delayed relative to the emission, the technique avoids the excitation of the animal tissues and suppresses autofluorescence, yielding an excellent signal/noise ratio for optical imaging. Further, as the ZGO nanoparticles can be re-charged *in vivo* by orange/red light, the PERL signal is followed over days.

In the last decade, ZGO-based PERL nanoparticles have boomed as bioprobes in the field of small animal *in vivo* imaging and have been conveniently coupled to therapeutic agents to become outstanding theranostic nano-platforms. Notably, ZGO nanoparticles have been associated to photosensitizers (for ex. phtalocyanines) to serve as internal light sources to realize photodynamic therapy (PDT) in deep-seated tumors [5].

References

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Figures

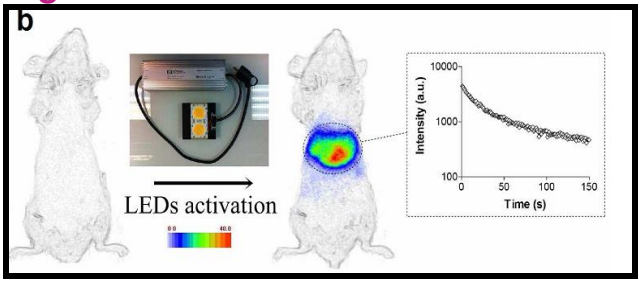

Figure 1. The detection of ZGO PERL nanoparticles after in vivo activation. Nanoparticles were first excited by UV and intravenously injected to monitor short-time biodistribution. After complete extinction of the PERL signal (in this case 15 h after the initial excitation), PERL was activated through living tissues following a 2 min orange/red LED excitation, and immediately acquired for 3 min under the photon counting system. The inset shows a persistent luminescence decay curve corresponding to the signal from the liver.