

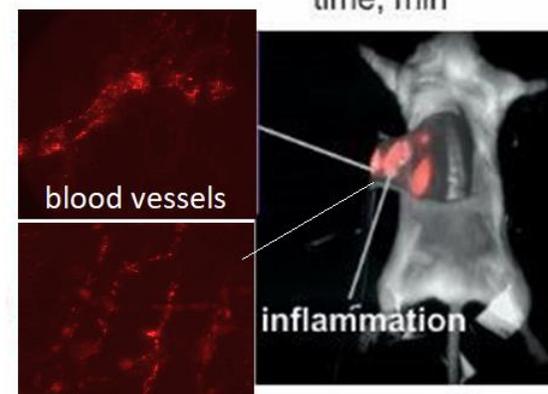
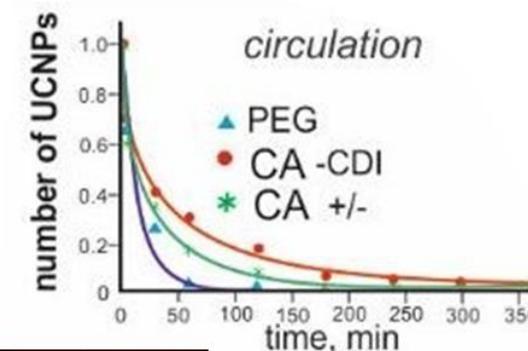
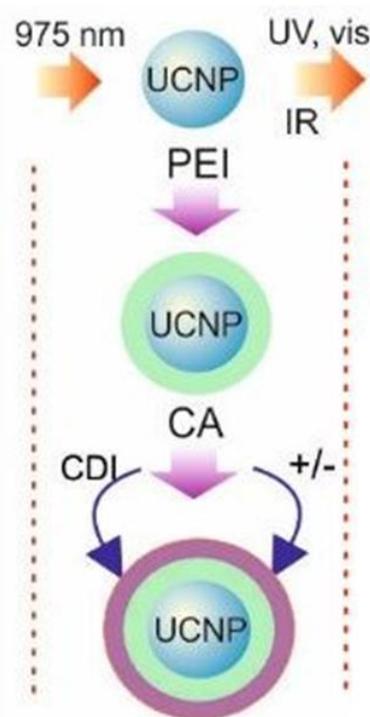
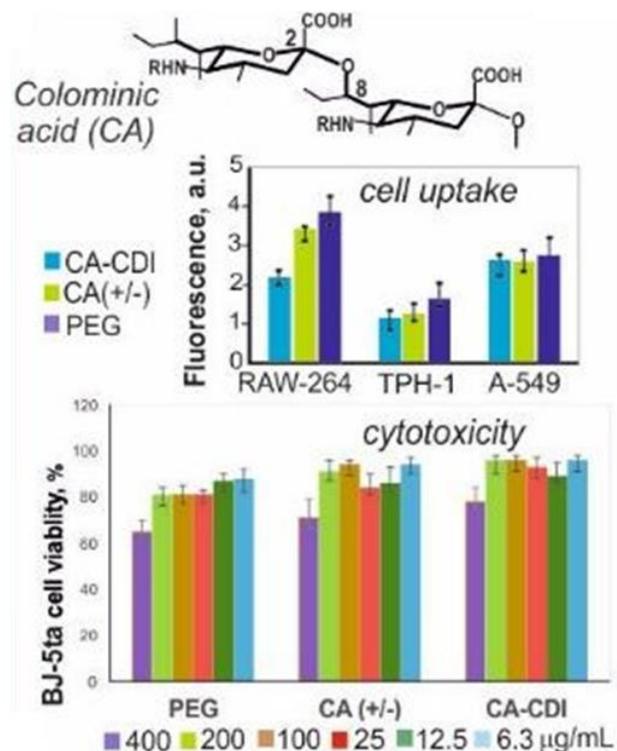
Upconversion nanoparticles as imaging nanosystems for nanodrugs distribution in vessels



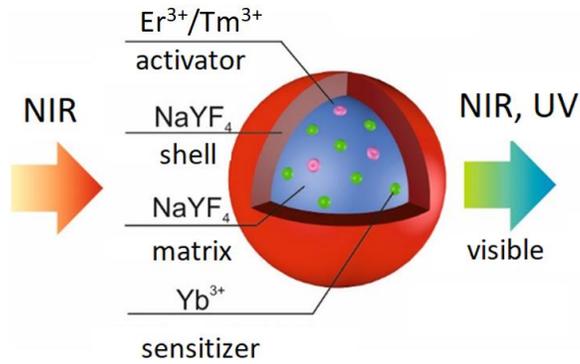
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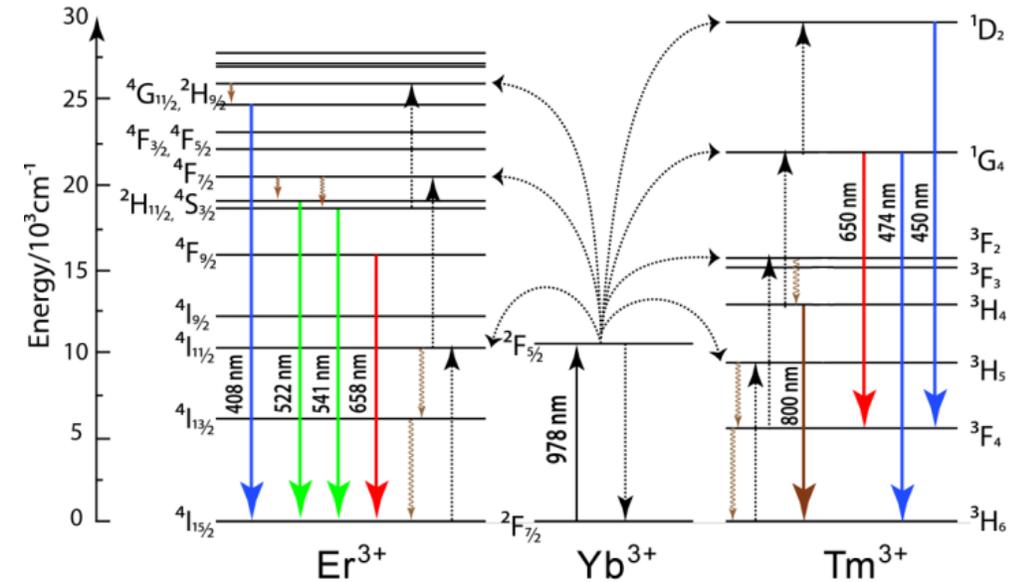
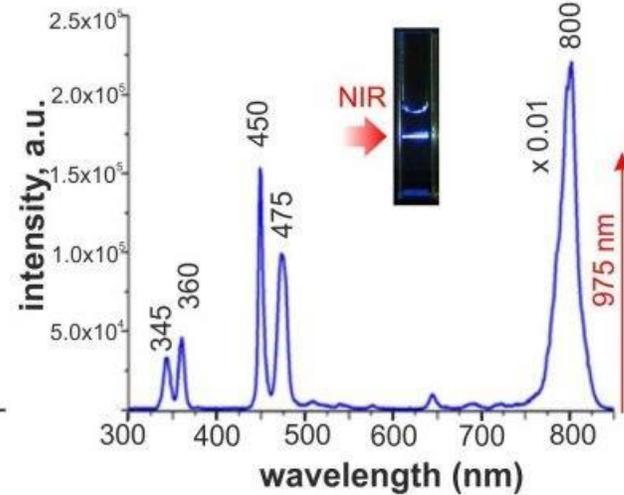
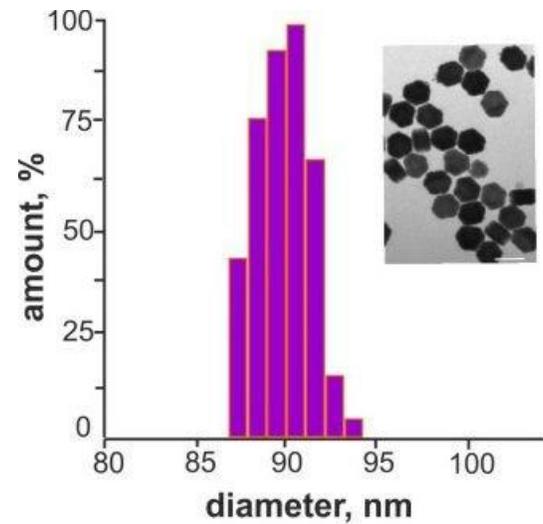


Upconversion nanoparticles



UCNPs consist of an inorganic crystalline host matrix, co-doped with a pair of trivalent lanthanide ions, usually with Yb³⁺ (as a sensitizer) and Er³⁺ or Tm³⁺ (as an activator)

NaYF₄:Yb³⁺/Tm³⁺@NaYF₄



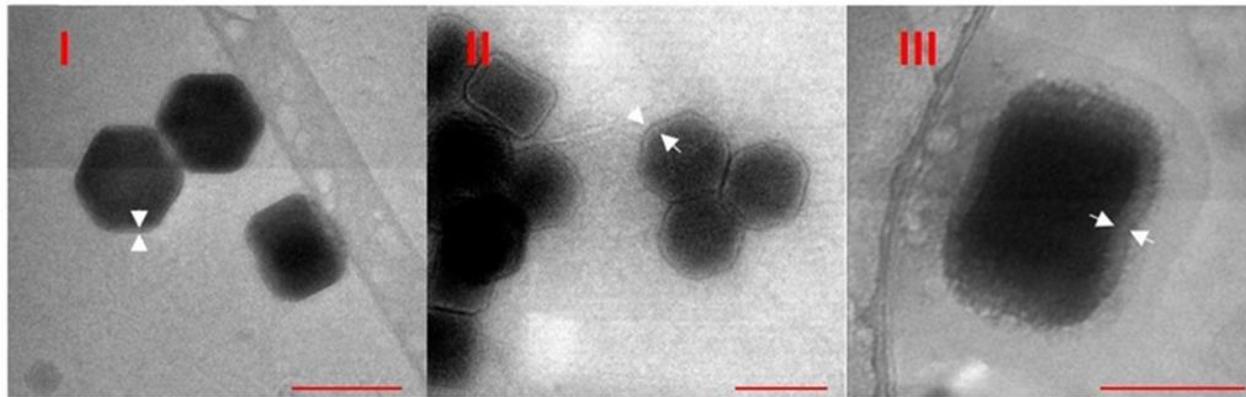
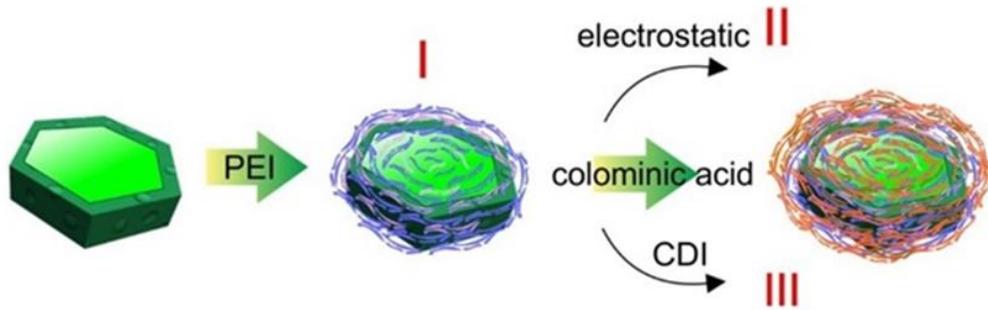
Ion Yb³⁺ absorbs a 980 nm photon and excites, then it nonradiatively transfers its energy to the neighboring Tm³⁺. The energies of these two states are very close, which enable the energy to be transferred efficiently. Thereafter, an additional energy transfer occurs from another excited Yb³⁺ to the Tm³⁺, resulting in further excitation to a higher level of Tm³⁺. That process happens till the excited Tm³⁺ emits one photon with higher energy than that of exciting photons

Size distribution histogram NaYF₄:Yb³⁺/Tm³⁺@NaYF₄ NPs and TEM image of UCNPs; spectrum of photoluminescence and image UCNPs under 975-nm excitation

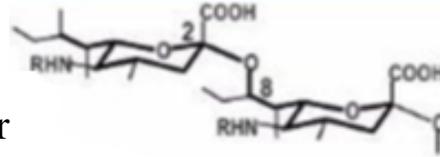
Two strategies of UCNPs modification

Colomonic acid, highly hydrophilic endogenous polymer

We developed two-step approach: 1 - hydrophilization using PEI; 2 - modification with CA based on electrostatic interactions or CDI-mediated condensation reaction

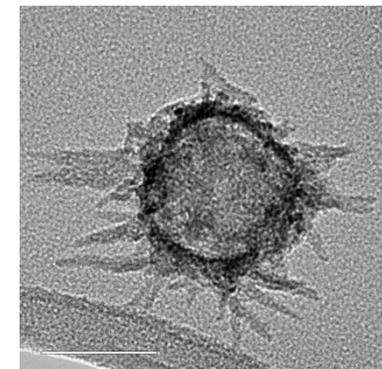
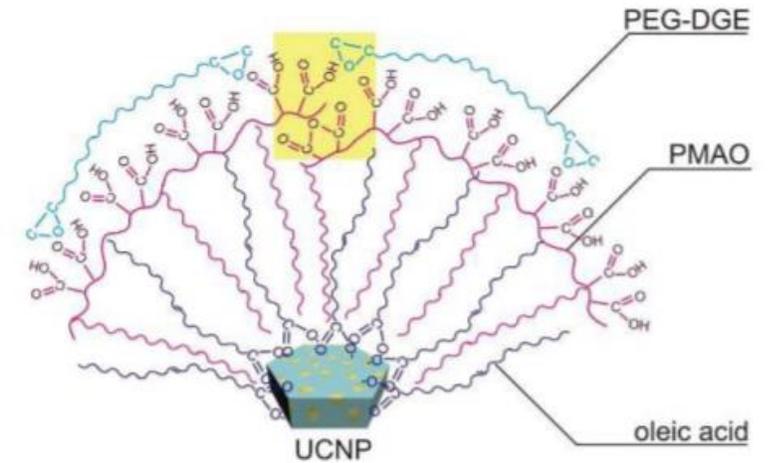
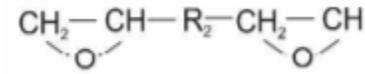


Cryo-TEM images of UCNPs at every step.



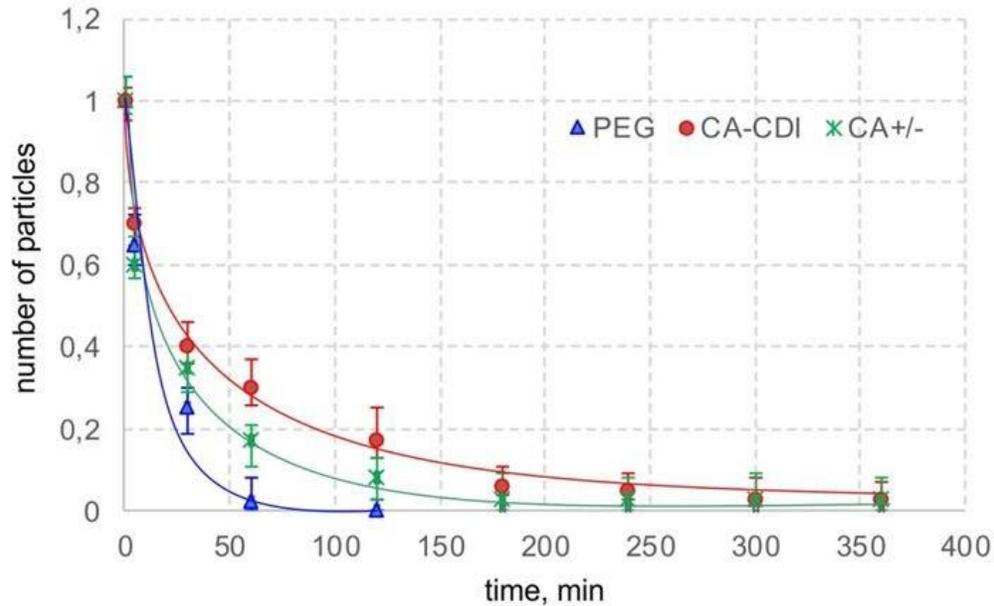
PEG modification is regarded as milestone

Scheme of UCNP modification with PMAO followed by cross-linking with PEG-DGE

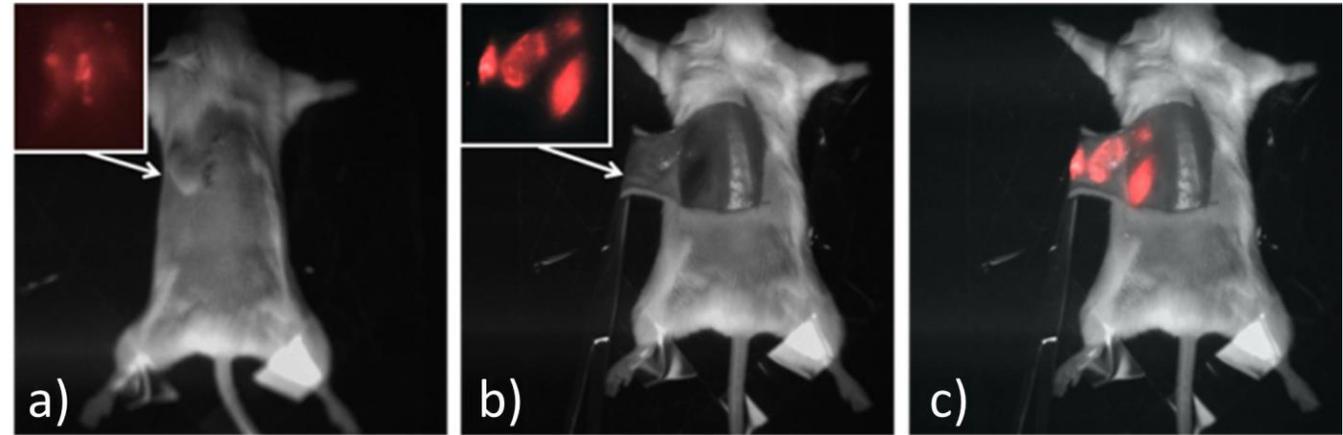


TEM image of UCNPs

In vivo experiments

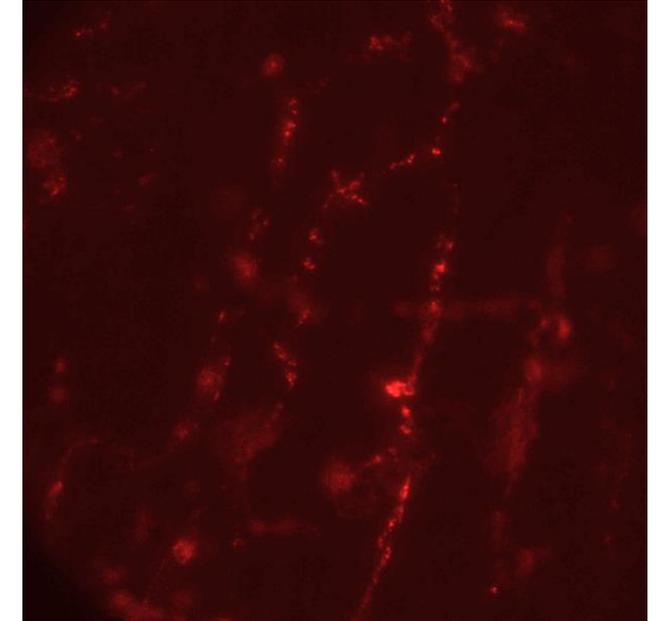
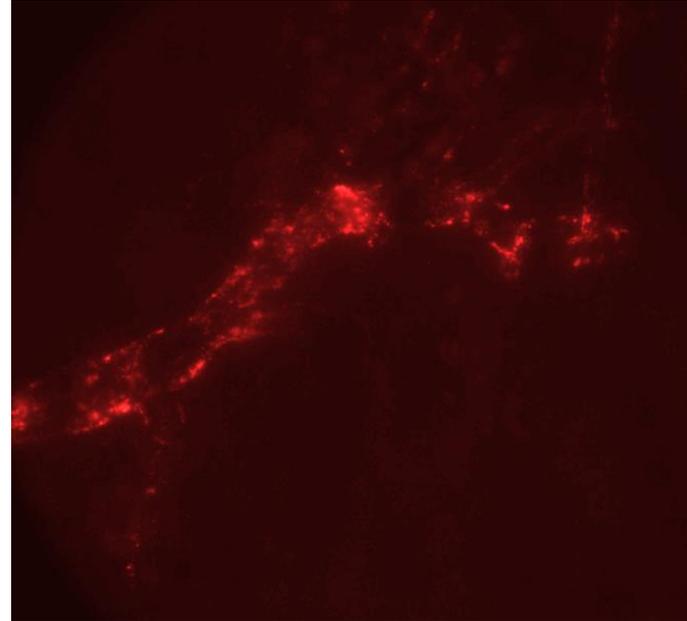
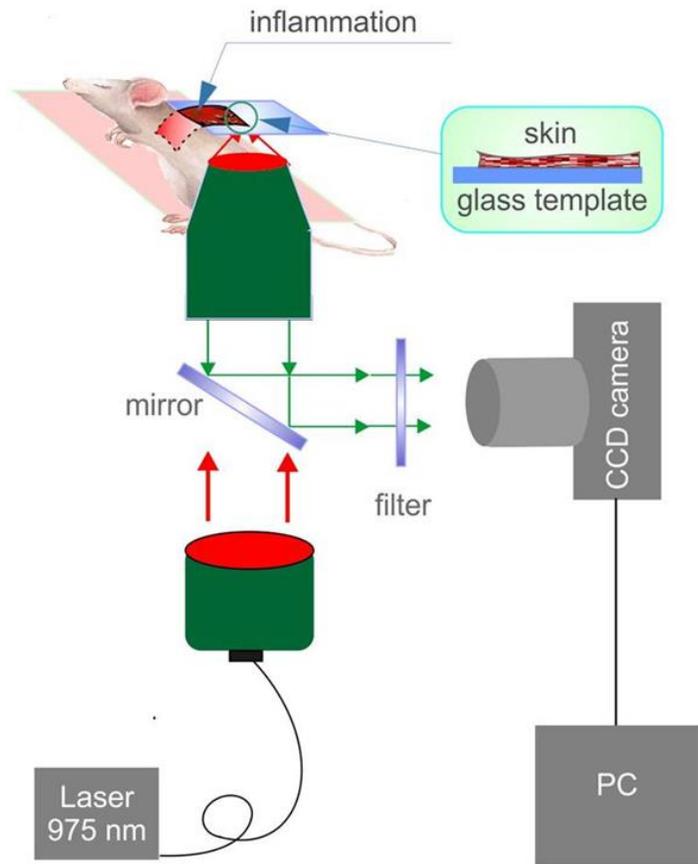


We studied *in vivo* circulation time in blood of UCNP-CA (+/-), UCNP-CA-CDI and UCNP-PEG probes. It was shown, that CA coating, prepared by both strategies, leads to almost three-fold circulation time prolongation as compared to UCNP-PEG.



We have demonstrated that UCNP-CA led to significant increase of their circulation time in blood. This effect can facilitate the passive accumulation of nanoparticles *in vivo* in inflammation model. UCNP-CA distribution in mice after injection was observed using home-built epi-luminescence imaging system. The noticeable PL signal was acquired in 12h after injection, revealing contrast compared to the surrounding tissues. After partial removing the skin and opening the inflammation site, the strong PL signal was observed. Apparently, this is associated with the inflammation angiogenesis and microvascular remodeling similar to EPR-effect in tumor.

Blood vessels bioimaging



The blood vessels imaging can be very helpful in the understanding of nanodrugs behavior in the organism and the side effects that they can cause.

The applied inflammation model and UCNP-CA enabled the visualization of large and small blood vessels. UCNPs prevailed in the place near the vessel walls, probably in the cell-free layer in the inflammation site. This arrangement is favorable for NP penetration in microcirculation. In other words, UCNPs-CA can fill significant volume of inflammation tissue, which is important for therapeutics delivery within NP nanocomplexes for treatment, photodynamic and photothermal therapy.

The scheme of home-built bioimaging system for the NP flow study in blood vessels

Thanks for attention!

Literature:

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