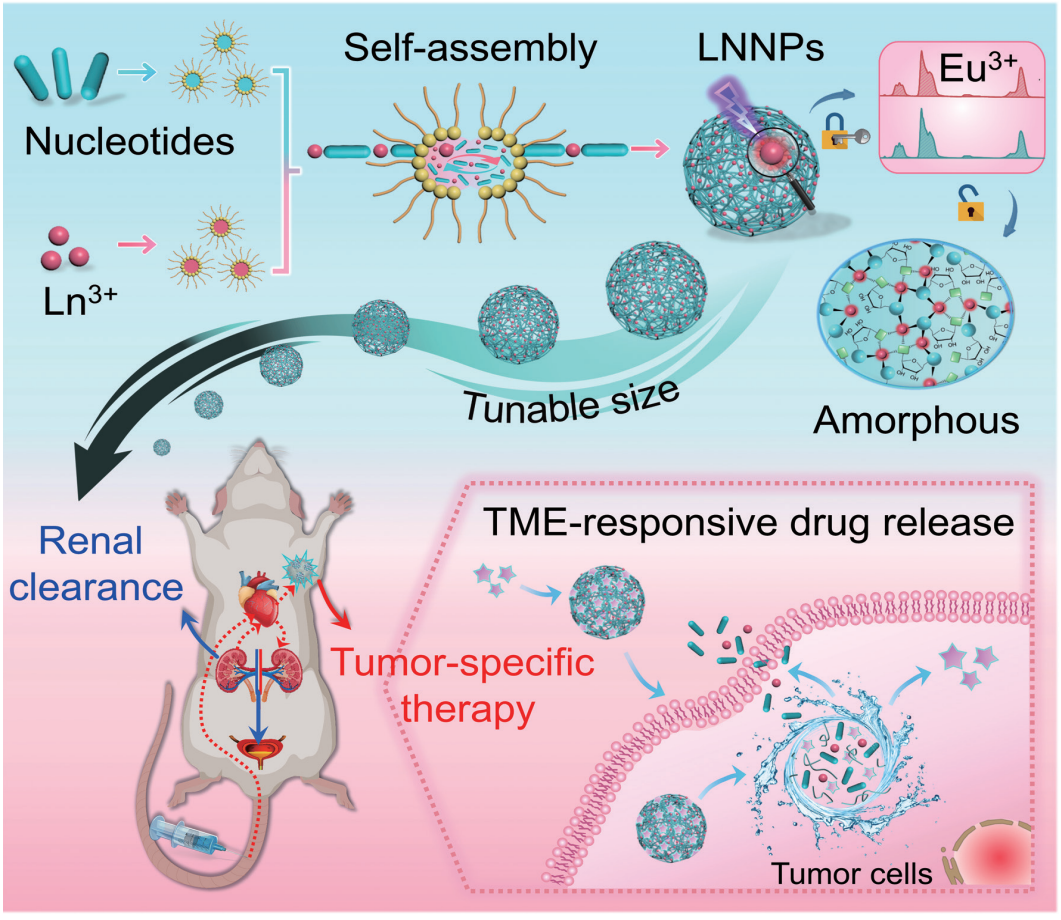
Life Sciences

Tumor-Microenvironment-Responsive Biodegradable Nanoagents Toward Precise Cancer Therapy

Nanomaterials have received considerable attention as therapeutic nanoagents in biomedical fields. Currently, the applications of conventional inorganic-organic hybrid nanoagents are severely hampered by their uncontrollable synthesis, poor tumor responsiveness, and inefficient body clearance. It remains a challenge to develop intelligent nanoagents to overcome the dilemma between efficient therapy and long-term toxicity.

In a study published in *Angew. Chem. Int. Ed.*,



Schematic illustration for the controllable synthesis of LNNPs by employing nanomicelle as a template and the TME-responsive drug delivery strategy. (Image by Prof. CHEN's group)

a research group led by Prof. CHEN Xueyuan from Fujian Institute of Research on the Structure of Matter (FJIRSM) of the Chinese Academy of Sciences developed a novel class of tumor-microenvironment (TME)-responsive biodegradable nanoagents based on self-assembled lanthanide nucleotide nanoparticles (LNNPs).

The researchers constructed amorphous LNNPs with finely tunable size (4.6-105.7 nm) and highly uniform monodispersity by employing nanomicelles as template.

Taking advantage of the porous network structure and TME-responsive biodegradable feature of LNNPs, the researchers realized highly efficient loading of drugs like doxorubicin (DOX) and stimuli-responsive drug release with the activation of H_2O_2 and acidic pH in tumor cells.

They observed the unique accumulation of ultrasmall DOX@LNNPs (sub-5 nm) in tumor with the peak level of 9.42 % ID/g at 12 h post injection, indicating their superior tumor targeting efficiency. Meanwhile, the blood circulation half-life of ultrasmall DOX@LNNPs was determined to be 3.3 h, which is superior to that of the traditional renal-clearable nanomaterials ($t_{1/2}$< 2 h).

Besides, the proposed nanoagents can be excreted from the body within 24 h via renal pathway, which fundamentally reduced the long-term toxicity *in vivo*. Benefiting from high tumor accumulation, TME-responsive drug release, and rapid renal clearance of the nanoagents, the researchers realized significantly improved chemotherapy efficacy upon targeted tumor site without evident systemic toxicity.

This study provides a novel approach to construct inorganic-organic hybrid nanoagents for nontoxic and precise cancer therapy, thereby may accelerate the exploitation and clinical translation of lanthanide-containing nanomedicine for further biomedical applications.

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Reference

Y. Yang, Y. Liu, D. Tu, M. Chen, Y. Zhang, H. Gao, X. Chen, (2022) Tumor-microenvironment-responsive biodegradable nanoagents based on lanthanide nucleotide self-assemblies toward precise cancer therapy. *Angew. Chem. Int. Ed.* 61, e202116983. doi: 10.1002/anie.202116983.