Novel Layered Double Hydroxide Nanoplatform as Ultrasensitive T_1-MRI Contrast Agent and Theranostic Agent for Mice Tumor Diagnosis and Complete Treatment

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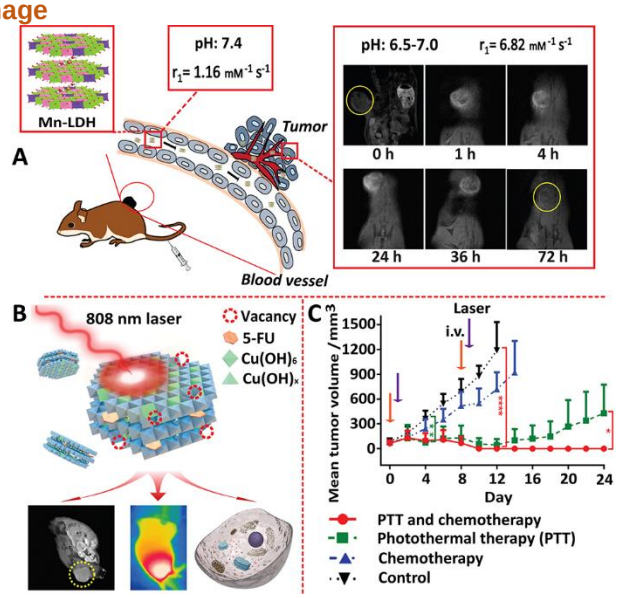
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Abstract

Recently, Mn(II)-containing nanomaterials have been explored widely as attractive alternatives to Gd(III)-based T_1-weighted magnetic resonance imaging (MRI) contrast agents (CAs) for cancer diagnosis. However, to our best knowledge, no Mn-based MRI CAs have been reported to sensitively respond to the very weakly acidic environment (pH 6.5~7.0, i.e. pH range in actual tumor microenvironment) with satisfactory imaging performance. This talk will present our recent work on devising a novel Mn-based layered double hydroxide (Mn-LDH) with outstanding T_1-MRI performance ultrasensitive to the very weak acidity (pH 6.5~7.0), and show clear MR imaging of tumor tissues in mice for at least two days (Image A). Thus, this novel Mn-LDH nanoparticle with ultrasensitive pH response, high relaxivity, and prolonged imaging time, has high potential for cancer CAs. This research has been published in *Adv. Mater.* (**2017**, *29*, 1700373). Based on this work, a further MnAl-LDH dual-functional platform has been constructed successfully as well for MRI and siRNA delivery, which has been reported and highly recommended by *Chemistry Views* and *Dual-Function Theranostic Nanoparticles* as a hot paper in *Chem. Eur. J.* (**2017**, *23*, 14299).

Furthermore, the development of biomaterials has accelerated a shift from isolated tumor diagnosis or therapy towards non-invasive imaging-guided combinational therapy. In our second exploration, novel defect-rich multifunctional Cu-LDH nanoplatform was devised delicately to perform on-target tumor theranostics via excellent T_1 weighted MR imaging-guided synergistic photothermal-/chemo-therapy with minimal impacts on normal tissues (Image B). As characterized with extended X-ray absorption fine structure and X-ray photoelectron spectroscopy, smaller Cu-LDH nanoparticles possess a considerable amount of defects around Cu cations, an advantageous microstructure that enables a high photothermal conversion of 808 nm NIR laser (53.1%). The exposure of Cu-OH octahedra on the LDH surface makes the photothermal conversion significantly acid-enhanced (53.1% at pH 7.0 vs. 81.9% at pH 5.0). This Cu peculiar microstructure also makes T_1-MRI very pH-sensitive, a desirable guide for subsequent tumor photothermal therapy. Combined photothermal therapy and chemotherapy lead to complete elimination of tumor tissues in vivo with a low agent injection dose (Image C). Therefore, this novel defect-rich Cu-LDH nanoplatform is one of promising tumor-specific nanotheranostic agents for non-invasive imaging-guided combinational therapy. This research is under revision for *Biomateirals* with very positive comments from three reviewers.

Image



Recent Publications

1. Bei Li et al (2017) Manganese-Based Layered Double Hydroxide Nanoparticles as a T_1-MRI Contrast Agent with Ultrasensitive pH Response and High Relaxivity. Adv. Mater. 29:1700373.
2. Bei Li et al (2018) Novel Theranostic Nanoplatform for Complete Mice Tumor Elimination via MR Imaging-guided Acid-enhanced Photothermo-/Chemo-therapy. Biomaterials (in revision).
3. Weiyu Chen, Huali Zuo, Bei Li et al (2018) Clay Nanoparticles Elicit Long-Term Immune Responses by Forming Biodegradable Depots for Sustained Antigen Stimulation. Small 14:1704465.
4. Huali Zuo, Weiyu Chen, Bei Li et al (2017) MnAl-Layered Double Hydroxide Nanoparticles as a Dual-functional Platform for Magnetic Resonance Imaging and siRNA Delivery. Chem. Eur. J. 23: 14299.



Biography

2015.7- present: PhD student at The University of Queensland, specializes in Layered Double Hydroxide-based Nanoparticles as Multifunctional Theranostic Agents for Cancer Treatment, under the supervision of Prof Zhi Ping (Gordon) XU.

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