Single atom-doped MOF upconversion photocatalyst for rheumatoid arthritis therapy

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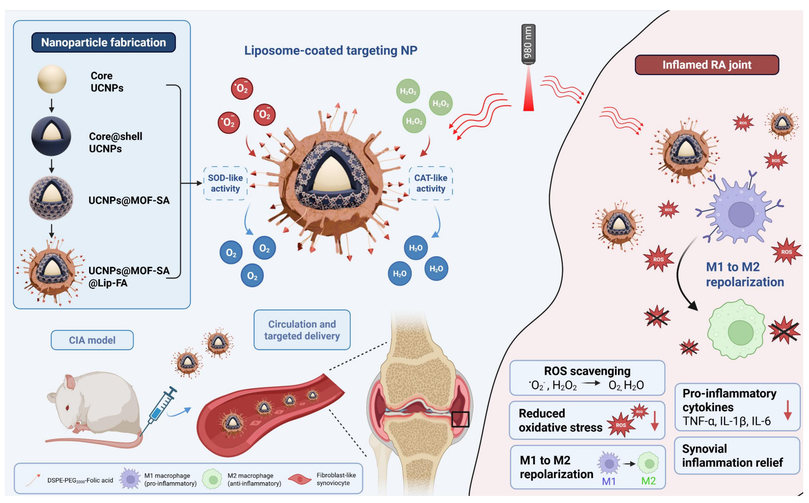
Introduction

Metal organic frameworks (MOFs) are porous and crystalline materials formed from the self-assembly between metal nodes and organic linkers. However, MOF-based materials are still in their early stages and further efforts are required to achieve performance in real-world applications. Single atom-doped MOF-coated upconversion nanoparticles (UCNPs) incorporating stimulator of interferon genes (STING) antagonist enhances catalytic activity of single atom and inhibits the inflammation pathway, showing strong potential for anti-inflammation and rheumatoid arthritis therapy.

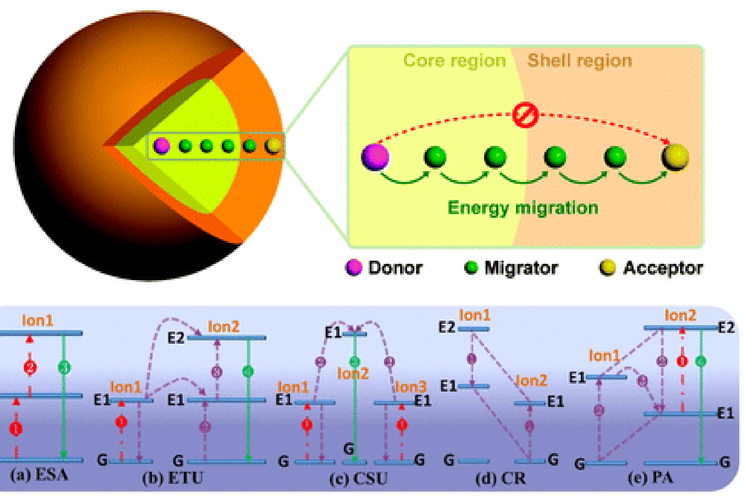
Background & Learning Objectives

- Learn the design principle of combining UCNPs with PCN shells to amplify single atom catalytic activity;
- Interpret enzyme-mimicking ROS scavenging mechanisms and their relevance to inflammation control;
- Evaluate the benefit of integrating catalytic ROS scavenging with immunomodulation (STING pathway inhibition) for synergistic anti-inflammatory therapy;



Scheme 1. Mechanism of action of ROS scavenging single-atom upconversion photocatalyst and the therapeutic effect to the rheumatoid arthritis model.

1. Principle of UCNPs



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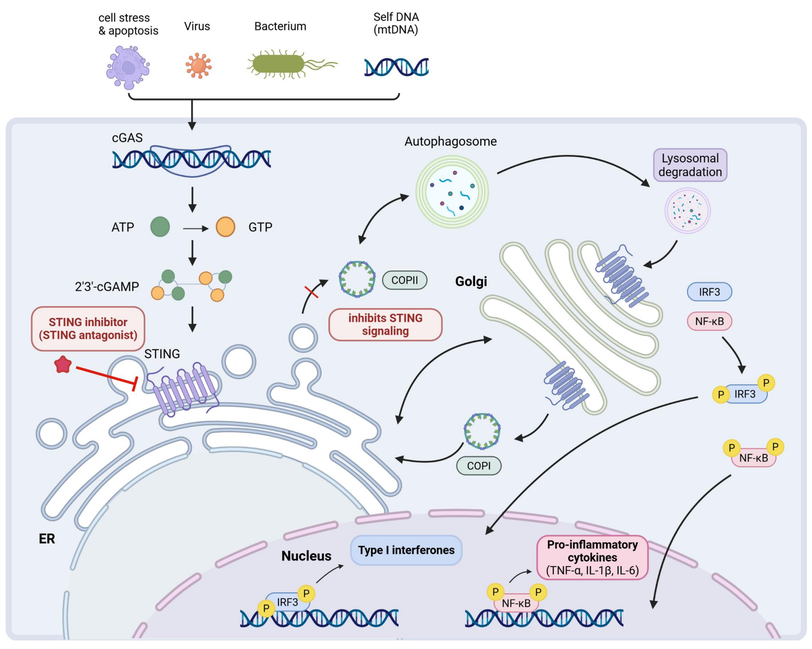
Scheme 2. Mechanism of upconversion in lanthanide-doped nanoparticles.

2. cGAS-STING pathway



Scheme 3. Schematic illustration of cGAS-STING pathway.

Results

1. Characterization of the upconversion photocatalyst UCNPs@MOF-SA@Lip

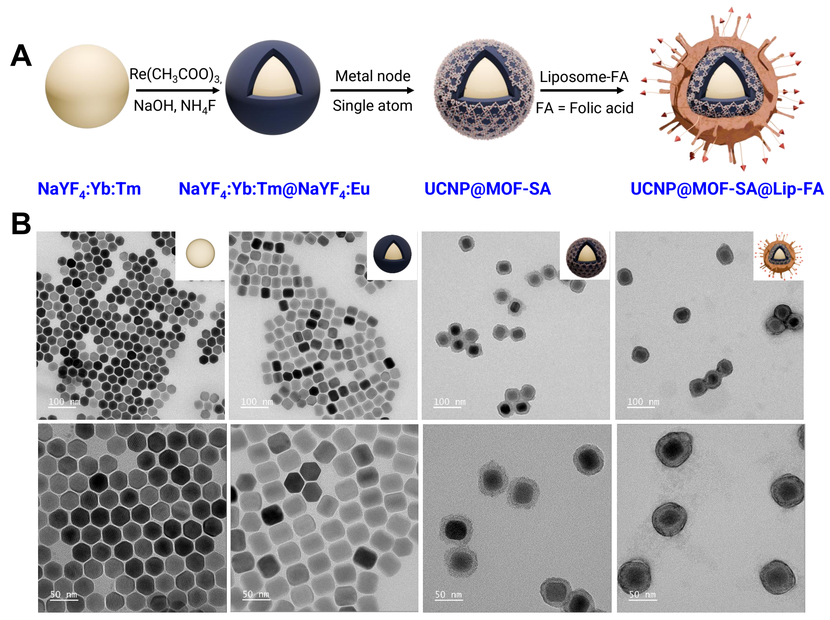


Fig 1. A. Schematic illustration of the preparation of UCNP@MOF-SA @Lip-FA; **B.** TEM images of core UCNPs; core@shell UCNPs, UCNPs@MOF-SA, and UCNP@MOF-SA@Lip-FA; **C.** Hydrodynamic size and Zeta potential of UCNPs@MOF-SA; **D.** UCL spectra of i) core UCNPs, ii) core@shell UCNPs, iii) UCNP@MOF-SA; **E.** Absorbance spectrum of UCNP@MOF-SA and UCNP@MOF

2. SOD-like activity of UCNPs@MOF-SA

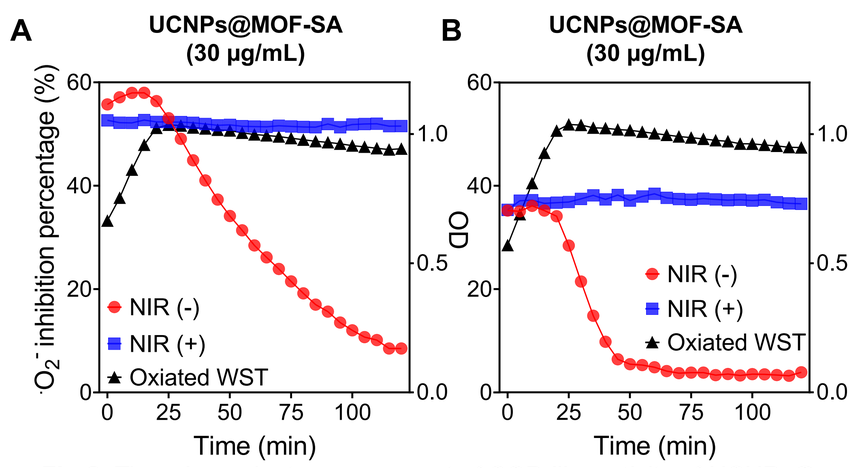


Fig 2. Time-dependent measurement of SOD-like activity of UCNPs@MOF-SA using a SOD kit with and without the 980 nm laser irradiation **A.** 30 μg/mL; **B.** 15 μg/mL.

3. CAT-like Activity and macrophage morphology

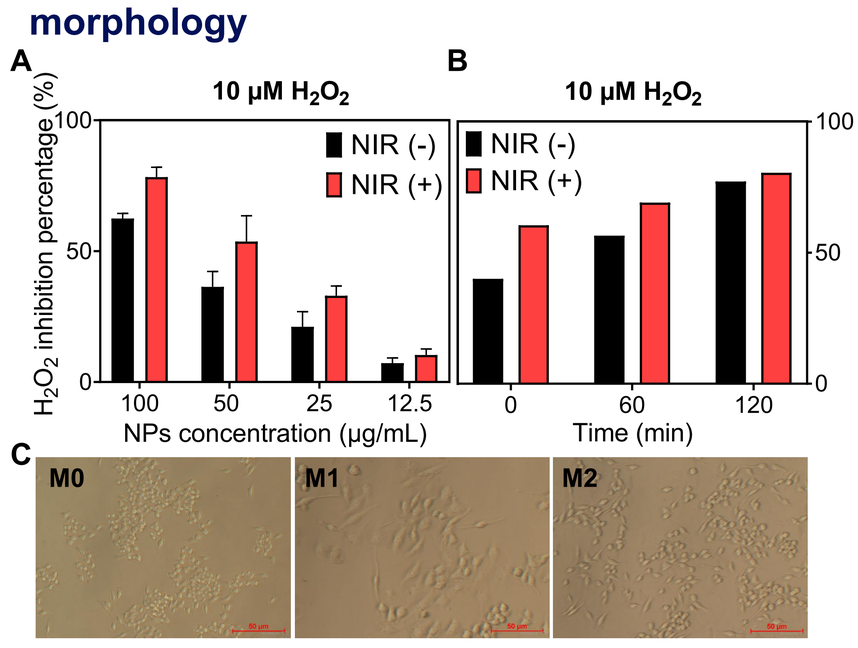


Fig 3. A. Measurement of the catalase-like activity of UCNP@MOF-SA at different concentrations at the initial time point with and without the 980 nm NIR irradiation; **B.** Time-dependent measurement of CAT-like activity of 50 μg/mL UCNP@MOF-SA; **C.** Morphology of M0, M1, M1.

4. Intracellular uptake in macrophage cells of UCNPs@MOF-SA@Lip

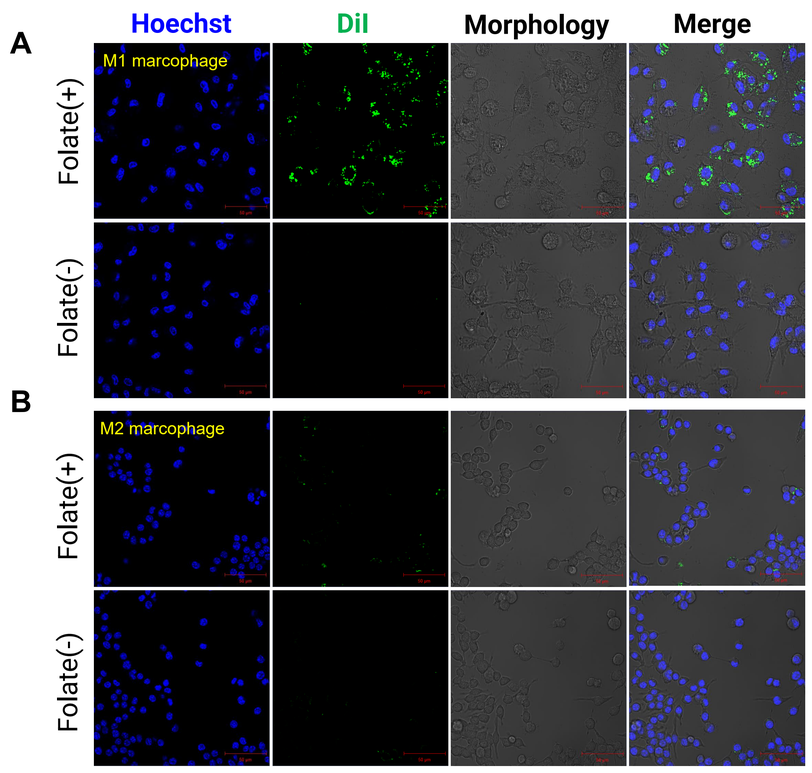


Fig 4. Intracellular uptake of UCNPs@MOF-SA@Lip with or without folate ligand in **A.** M1 and **B.** M2 macrophages.

5. Assessment of intracellular ROS levels in RAW 264.7 cells of UCNPs@MOF-SA

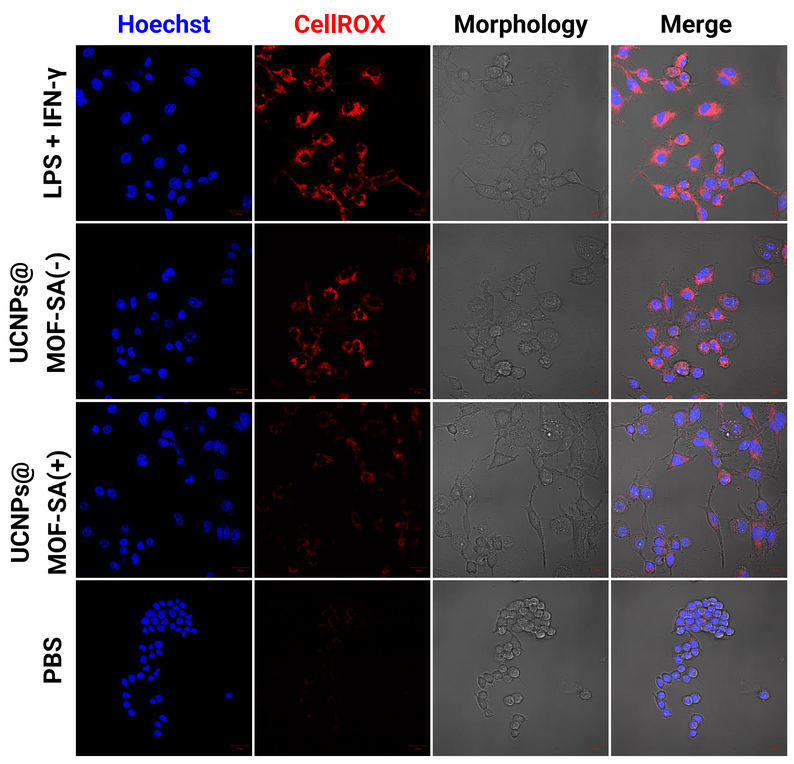


Fig 5. Intracellular ROS level with and without under 980 nm NIR irradiation. Positive control of RAW 264.7 cell (M1 macrophage) was treated LPS and INF-γ.

6. Clinical score standard for CIA Model

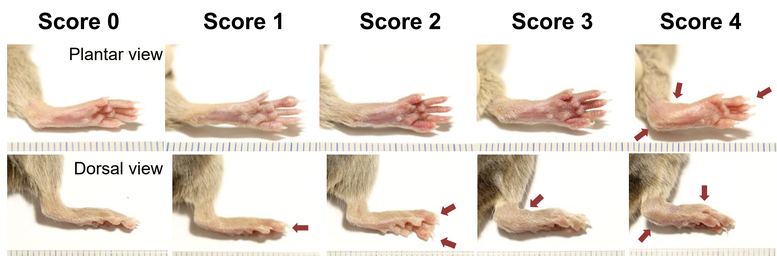


Fig 6. Scale of clinical scores for evaluation.

Conclusion

In this study, we engineered UCNP@MOF by integrating UCNPs with a single atom-doped metal organic framework , thereby increasing the density of single atom catalytic sites. This nanoplatform exhibited efficient scavenging of reactive ROS, including superoxide and hydrogen peroxide. This nanoplatform shows promising potential for effective treatment of rheumatoid arthritis.

Acknowledgments

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References

Chem. Soc. Rev., 2015, 44, 1318—1330.

Nat Rev Immunol 21, 548–569 (2021).