

The Construction Strategy of Metal MOFs and the Application of Tumor Combined Therapy

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Abstract. A tumor is a new organism formed by the abnormal, infinite proliferation of local tissue cells, in which malignant tumors will develop into cancer. In recent years, the clinical treatment of cancer has been constantly improved, but tumors have also developed a series of defense mechanisms. Metal organic frameworks (MOFs) are porous crystalline materials formed by the self-assembly of metal nodes and organic ligands. They have both inorganic rigidity and organic flexibility, and have the advantages of high specific surface area, adjustable pore size, and designable structure and function. They have become the research focus of tumor intelligent nano delivery system. In this paper, the significance of metal nodes, organic ligands and pore structures of MOFs to their functions is systematically reviewed, focusing on the principles and ideas of anti-tumor therapy based on MOFs treatment system, and the application progress of MOFs in anti-tumor combined therapy (such as chemotherapy, targeting, immunotherapy, etc.) is further summarized. At present, MOFs still have some problems, such as in vivo biological safety to be verified, large-scale synthesis being difficult, and targeting needs to be optimized. The purpose of this paper is to show the special contribution of MOFs, a new framework material, in the field of anti-tumor research, and to inspire the future synthesis of new MOFs and the establishment of a perfect combination therapy system.

Keywords: MOFs, tumor therapy, combination therapy

1. Introduction

Nano carrier materials are often used to construct intelligent delivery systems and anti-tumor research because of their nano size (1~100 nm), good biocompatibility, modifiability and high drug loading capacity. These nanomaterials can not only efficiently load small and macromolecular drugs, but also carry functional components such as immunoactive substances, photosensitizers, photothermal agents, etc., so as to achieve active targeted delivery, specific responsive release and multi-faceted therapy combination, and effectively reduce the toxicity of the delivery system while improving the therapeutic effect. However, different types of materials face some limitations in application, and the same kind of nano carrier is difficult to have the functions of high drug loading capacity, photosensitive thermal sensitivity, low biological toxicity and so on. Therefore, it is now necessary to develop a new type of intelligent nano carrier with a high drug loading rate, high

stability, good biocompatibility, multi-functional responsiveness and integration potential, so as to better achieve precise intervention in tumor treatment.

Metal organic frameworks (MOFs) are currently the research focus of nano-carrier materials. Their excellent spatial chemical structure endows them with the above functions. The synthesis methods of MOFs are various, mainly including the solvothermal method, hydrothermal method, microwave-assisted synthesis method, electrochemical deposition method and mechanochemical synthesis method. The morphology, structure and size of MOFs can be flexibly adjusted according to the functional requirements [1]. The established MOF system can not only have the intrinsic characteristics of MOFs (such as porphyrin MOFs with photosensitivity), but also introduce special functional molecules (such as targeting molecules, photosensitizers, etc.) to make it specific to the tumor environment, so as to achieve accurate and efficient delivery.

2. MOFs

Metal organic frameworks (MOFs) are a class of porous crystalline materials formed by self-assembly of metal ions or metal clusters and organic ligands through coordination bonds. They have both the rigidity of inorganic materials and the flexibility of organic materials. Their organic-inorganic hybrid structure endows them with outstanding advantages such as ultra-high specific surface area, adjustable pore size, and structural diversity, which provide broad application prospects in biological research, drug delivery, tumor diagnosis and other fields. The paper will focus on the composition and structure of MOFs, and comprehensively discuss the differences of MOFs with different metal nodes, organic frameworks and pore structures in terms of structure, function and principle of action. The following will be expanded into three parts of MOFs.

2.1. Metal node

In the structural efficiency relationship of MOFs, metal nodes are not just static linkers connecting organic ligands, but core functional units that determine the overall performance of materials. From the perspective of microstructure, metal nodes form an overall structural framework through coordination and organic frameworks, which exist in a variety of forms - either simple single metal ions (such as Zn^{2+} , Fe^{3+}) or polymetallic centers (such as Zn/Pd), or high nuclear metal clusters (such as $[\text{Zn}_4\text{O}]^{6+}$), and other organic metal framework materials.

Monometallic MOFs are the most basic form of MOFs delivery systems. Common monometallic MOFs include iron, copper, zinc, manganese, etc. The coordination ability of monometallic ions determines the spatial configuration and basic functions of MOFs, and it also affects the mechanism and path of monometallic MOFs. Fe-based MOFs undergo Fenton reaction at the tumor site, which consumes a large amount of antioxidant substances, especially glutathione (GSH), and generates highly toxic hydroxyl radicals. These radicals aggravate cellular peroxidation and oxidative damage, ultimately leading to tumor cell death. However, Zn MOFs are rapidly dissolved in cells, releasing Zn^{2+} ions explosively, and then activating the CGAs-STING pathway, connecting the body's innate immunity and adaptive immunity, and fighting tumors through the body's immune system [2].

All normal cells in the body are in a steady state, that is, the steady state of components, environment, biochemical changes and other aspects, and tumor cells are no exception. Based on the principle of single-metal-based MOFs, multi-metal-based MOFs are combined with two or more metal ions to form joint MOFs. Their mechanism of action fully includes the working principle of single metal ions. For example, using neutrophils as carriers to construct Fe/Cu MOFs nano delivery system, this kind of bimetallic MOFs can destroy the iron and copper homeostasis of tumor cells,

and induce iron death-lipid peroxidation caused by GPX4 down-regulation, and copper death-mitochondrial TCA cycle collapse caused by DLAT oligomerization. The Fenton reaction activity of bimetallic MOFs is significantly increased compared with that of single metal MOFs with a single active site. The principle is that copper ions catalyze the redox cycle of iron ions and improve the electron transfer rate [3]. There is more literature to make a comparison: Fe/Cu MOF>Fe MOF>Cu-MOF. At the same time, in recent years, the construction of Cu/Fe Bimetallic MOFs with oxygen-containing vacancy MnO_{2-x} has combined three metals, which further illustrates the research significance of polymetallic MOFs in the field of MOFs delivery systems [4].

In addition to the common metal-based MOFs, other representative MOFs systems also include MOFs systems based on high nuclear metal clusters, such as the UiO series. UiO series MOFs take Zr metal cluster as the metal center, BDC and other carboxylic acid ligands as the linker, forming a 12 coordination skeleton structure with face-centered cubic topology. UiO-66 is a typical representative of this series. UiO-66 has formed a highly rigid structural framework by virtue of its highly stable six core zirconium oxide cluster ($\text{Zr}_6\text{O}_4(\text{OH})_4$) metal center and the high coordination density of 12 coordination numbers, making it obtain excellent hydrothermal and chemical stability, successfully overcoming the shortcomings of traditional MOFs, and providing a stable physical and chemical guarantee for drug delivery, chemical process catalysis and other applications in vivo. UiO-66 has a wide range of synthetic routes to choose from: the highly crystallized product was obtained by CO heating Zr metal clusters and ligands for 24h by the solvent co-heating method; microwave-assisted synthesis is fast, and the desired product can be synthesized in a few minutes or hours; The continuous flow method achieves gram or kg scale-up and accurately controls the particle size of the product [5]. As mentioned above, MOFs with diverse structures and compositions synthesized by various synthesis methods not only expand the function of the material itself, but also provide a rich carrier basis for the design of a responsive MOFs delivery system. The most classic is pH-responsive drug delivery. In vitro experiments, UiO-66-NH₂-DOX rapidly releases about 80% of doxorubicin in tumor lysosomes in the range of pH 5.0-5.5 within 24 hours, while under the condition of pH 7.4 in normal tissues, the MOFs only release about 20% or almost no drug within 24 hours, and the structure ratio is relatively stable. The above process reflects the precise response of UiO-66MOFs to pH [5].

2.2. Organic frameworks

Metal centers and organic frameworks together form the basic structure of MOFs. The types of metal centers determine the basic functions of MOFs, while the organic framework enhances the overall role of MOFs through its interaction with metal centers and its special structure. Porphyrin, as a highly effective photosensitizer, can also be used as a ligand to construct MOFs, which not only enhances the original function of MOFs, but also makes MOFs have the characteristics of photosensitive kinetics. Fe porphyrin MOFs were constructed by the coordination of porphyrin organic framework and iron ions. The induced iron death effect was significantly stronger than that of single metal Fe-based MOFs. Because the presence of porphyrin ligands made Fe porphyrin MOFs have a photosensitive effect, photodynamic therapy (PDT) occurred under light, and reactive oxygen species (ROS) were generated. At the same time, porphyrins can convert ROS to peroxides again, providing substrates for the Fenton reaction, forming a ROS self-amplification mode. Some porphyrin derivatives can also directly bind and inhibit GPx4, destroy the antioxidant system of target cells, and further amplify the effect of iron death [6]. The change of organic framework enriches and strengthens the original functions of MOFs, while the structure of the framework itself endows MOFs with special functions. Both UiO series and NU series belong to the MOFs system of

high nuclear metal clusters. Both UiO series and NU series belong to MOFs systems based on high-nuclear metal clusters, with Zr metal clusters as the center. The UiO series is constructed with bidentate carboxylic acid ligands and a coordination number of 12, while the NU series is constructed with tetradentate carboxylic acid ligands and a coordination number of 8. The spatial topology has also changed. Thanks to the organic framework with a smaller coordination number, the central pore diameter of NU series MOFs is large, about 3nm [7]. The central pore diameter of UiO series MOFs is less than 1.5nm, which enables NU series MOFs to carry macromolecular substances such as enzymes, proteins, macromolecular drugs and so on, and enhances the scope and field of action of MOFs.

2.3. Pore structure

Metal nodes and organic frameworks are the basic components of MOFs, and they coordinate with each other to form a certain spatial structure. Among them, the pore structure is one of the most significant structures, which is also a special structure of MOFs. The pore structure of MOFs can be divided into micropores (<2 nm), mesopores (2–50 nm) and macropores (>50 nm) according to the pore size. The pore size determines the pore function. In the structural system of MOFs, the three kinds of pores play their respective roles, such as micropores providing small molecule drug carrying capacity, and mesopores carrying proteins and other macromolecules. At present, the ideal structure for tumor treatment is multi-level pores, which is similar to the relationship between multi-metal based MOFs and single-metal based MOFs.

Hierarchical pores MOFs (multi-level pores MOFs) are MOFs materials with micropores, mesopores and macropores at the same time, which can integrate the advantages of three types of pores, and are the ideal carrier for tumor drug delivery and immunotherapy. The synthesis process of hierarchical porous MOFs is from inside to outside. Hollow Prussian blue (HP) is obtained by acid etching, and then the ZIF-8 shell is grown by charge-assisted growth. HP provides a macroporous cavity and a mesoporous window for carrying macromolecular substances (described in the article as glucose oxidase Gox), and the ZIF-8 shell provides microporous loading of small molecule drug 5-fluorouracil (5-FU). This mode of zonal drug loading enables porous MOFs to obtain the ability to load a variety of drugs while achieving controlled sequential drug release [8]. After intravenous injection of this porous MOFs, it was enriched in high concentration in the tumor lesion area, and the drug release was initiated when the pH of TME was about 5.0 and high concentration glucose was added. The ZIF-8 shell first degraded and released 5-FU chemotherapeutic drugs in a slightly acidic environment. After the ZIF-8 shell was removed, Gox was released from the core. Gox catalyzed glucose to be gluconic acid in the environment, which further reduced the pH value of TME and promoted the release of more 5-FU. The whole reaction was a self-accelerating cascade reaction [8].

3. Tumor treatment and combination therapy

The conventional treatment of tumors mainly includes chemotherapy, radiotherapy, targeted therapy and immunotherapy, which is the core method of tumor treatment in the clinic. However, there are many problems in the traditional treatment mode, such as poor drug solubility, insufficient targeting, and large systemic toxicity and side effects, which seriously restrict the clinical efficacy. For the nano delivery system of MOFs, the diverse metal nodes and frameworks, as well as the complex spatial structure, give MOFs unique structural advantages. To a certain degree, MOFs show great

potential in drug loading, transportation, release and other aspects, so MOFs have become the key research object of tumor therapy.

3.1. Tumor treatment: drug loading (chemotherapy and radiotherapy), targeting and immunity

The rich pore structure of MOFs enables MOFs to carry a variety of drugs (chemotherapy and radiotherapy drugs) in drug delivery. Classic MOFs materials such as UIO 66 and ZIF 8 have been widely used in the delivery of chemotherapy drugs such as Adriamycin, 5-FU and oxaliplatin. MOFs can realize the precise release of chemotherapy drugs in tumor sites, improve the killing ability of drugs on tumor sites, and reduce the toxicity and side effects of drugs on normal tissues by responding to the acidic environment of TME with pH=6.5. At the same time, MOFs can significantly improve the solubility and stability of hydrophobic chemotherapy drugs, prolong the in vivo circulation time of drugs, thereby enhancing the killing effect of chemotherapy drugs on tumor cells. Radiotherapy is one of the conventional treatment methods for clinical malignant tumors, and tumor hypoxia and radiation resistance are the key factors restricting the efficacy of radiotherapy alone. MOFs can contain high atomic number metal nodes, which can be used as radiosensitizers to effectively catalyze the production of a large number of reactive oxygen species (ROS), thus directly enhancing the radiotherapy effect of tumor cells [9]. High atomic number metals, including Hf, Zr, Th, etc., have strong X-ray absorption ability. They can produce a large number of photons through the photoelectric effect and Compton scattering, so as to improve the local radiation ability of lesions and induce DNA double-strand breaks. Meanwhile, 3-BrPA@Hf-MOF can be loaded with glycolysis inhibitor 3-BrPA, which can be released in the lesion area, cut off ATP supply, inhibit DNA repair, and play a sensitization effect [10].

In addition, the surface of MOFs is easy to modify targeted molecules, which can realize the active targeted delivery of drugs, enrich drugs in tumor tissues, and improve the selective killing efficiency of chemotherapy and radiotherapy on tumor cells. If simply modify the surface of MOFs, it can be modified the small molecule ligand: folate, which targets folate receptor and is highly expressed in lung cancer; Hyaluronic acid (HA), targeting CD44, is highly expressed in breast cancer. These small-molecule ligands are low-cost and difficult to modify, but some receptors may also be highly expressed in normal parts of the body, so there are some problems with wrong targeting. Targeted peptide is a more accurate targeted delivery modification. A kind of MOFs in MOF core-shell structure, the shell ZIF-8 acid start degradation, the core is the NLS peptide modified drug delivery system ultra small Cu (I) Cu (II) -BTC MOF (UCMs), NLS as a nuclear localization signal peptide, actively targeted to guide UCM into the nucleus, to achieve precise drug release, 56.7% delivery efficiency and 96.4% tumor inhibition rate show the advantages of active targeting [11].

Immunotherapy is an important method of conventional treatment of cancer by activating the body's immune system to clear tumor cells. Ido immune checkpoints exist in tumors, which degrade tryptophan and inhibit effector T cells through high expression of IDO. PCP-MC-DTA MOF is loaded with 1-MT drugs. MOFs disintegrate in cells and release 1-MT. 1-MT reverses the tumor immunosuppressive microenvironment by inhibiting IDO, thereby reactivating effector T cells and reducing regulatory T cells so that the autoimmune system can reengage in anti-tumor work, enhance the body's own anti-tumor immune response, and achieve efficient and lasting anti-tumor effect [12]. In summary, under the premise of reasonable design and modification, MOFs involved in the improvement of immunotherapy has the advantages of long-lasting curative effect and low

toxicity and side effects, which can provide a new and efficient technical scheme for clinical tumor single immunotherapy.

3.2. Combination therapy

A single treatment mode may bring hidden dangers such as limited therapeutic effect, high toxicity and side effects, and tumor recurrence and metastasis. The combination of several therapies can significantly increase the therapeutic effect while overcoming some of the above problems. Thanks to the structural advantages of MOFs, MOFs have a strong modification ability, so MOFs have the potential to be used in tumor combined therapy.

3.2.1. Physical kinetics and chemical kinetics

In recent years, multimodal collaborative therapy strategy based on photodynamic therapy (PDT), photothermal therapy (PTT) and chemokinetic therapy (CDT) has become an important research direction in the field of tumor precision therapy. Among them, MOFs have become an ideal carrier for the efficient combination of the three with high specific surface area, multifunctional modification and degradability. PDT and PTT therapy rely on an external light source, and the tissue penetration ability is poor, so the ROS production efficiency is easily affected; CDT depends on endogenous H_2O_2 , and GSH in vivo can clear ROS, further reducing the curative effect. Folic acid-modified PCN-224/Pt/ Cu^{2+} (FA-PPC) achieves the combination mode of PDT+PTT+CDT, which can effectively improve the tumor treatment effect. Pt metal core can improve the efficiency of porphyrin production of 1O_2 by self-supplying oxygen. At the same time, it can achieve a rapid temperature rise under 650nm light. The tumor is thermally ablated by PTT. FA-PPC also carries Cu^{2+} , which can react with GSH, which further improves the efficiency of ROS generation and greatly enhances the anti-tumor ability in general [13]. On this basis, FA-PPC is also combined with folic acid as a target to achieve precise enrichment and monitoring. FA-PPC nano platform can enhance PDT, Pt-mediated PTT and GSH to activate CDT by self-supplying oxygen, and realize the triple combination of PDT, PTT and CDT to synergize tumor treatment [14]. It can effectively overcome the defects of limited efficacy and insufficient universality of a single treatment mode, and provides a new strategy for the development of tumor nano drugs combined with multiple therapies.

3.2.2. Combination therapy of chemotherapy

In clinical treatment, the blocking of immune checkpoints has long-term anti-tumor potential. With its unique drug loading flexibility, MOFs can release drugs orderly in the tumor microenvironment through co-loading chemotherapy drugs and immune modulators, so as to realize the combination of chemotherapy and immunotherapy. MOFs can be co-loaded with doxorubicin (DOX) and IDO1 inhibitor NLG919, which are released at pH and redox. DOX induces the release of damage-related molecules such as calreticulin, which activates the maturation of dendritic cells and T cells. NLG919 blocks tryptophan metabolism, reverses immunosuppression in TME, and simultaneously improves immune efficacy. Iron-based MOF (NH_2 -MIL-88B) can promote M1 polarization and antigen presentation of macrophages after functional modification, thereby activating the immune system [15]. On the other hand, the metal node modification of MOFs can also be linked to immunotherapy. After functionalization, iron-based MOFs can promote the polarization of tumor-associated macrophages from immunosuppressive M2 to pro-inflammatory M1, thus activating CD8⁺T cells,

significantly enhancing the antigen presentation ability, providing key support for reshaping the tumor immune microenvironment and enhancing the effect of combined therapy [16].

Studies have shown that MOFs can accurately deliver chemotherapy drugs to tumor sites through the combination of passive targeting and active targeting. Passive targeting mainly relies on tumor tissue to enhance the osmotic retention effect, while active targeting can specifically recognize highly expressed receptors on the surface of tumor cells by modifying targeted ligands such as folate, hyaluronic acid, peptides, and antibodies on the surface of MOFs, so as to achieve accurate drug delivery. For example, the targeted nanocarrier constructed based on ZIF-8 can co-carry chemotherapeutic drugs and targeted molecules, realize the responsive release of drugs under the acidic condition of the tumor microenvironment, and reduce the damage to normal tissues while improving the inhibition rate of tumor cells [17].

3.2.3. Starvation therapy combined with other therapies and the carrier role of MOFs

Starvation therapy is a way to achieve tumor treatment by blocking the nutritional supply and interfering with the energy metabolism of tumor cells, which can inhibit tumor proliferation at the nutritional level of nutrition supply. At the same time, MOFs based delivery system can organically combine starvation treatment, chemotherapy, immunotherapy and other treatment modes, increase the sensitivity of tumor cells to treatment through starvation treatment, and then enhance the biological toxicity of chemotherapy drugs and the ability of immune system with the help of the delivery ability of MOFs, to overcome the problems of limited curative effect of single treatment and easy drug resistance of tumor.

Glucose oxidase (Gox) is an enzyme that catalyzes the conversion of glucose to gluconic acid and hydrogen peroxide. When metal-based MOFs carry Gox, Gox continuously consumes glucose, making tumor cells rely on mitochondria for anaerobic respiration, and improving the sensitivity of tumor cells to chemotherapy drugs [18]. At the same time, some MOFs can also be edited as anti-PD-L1. Through combined immunotherapy, a large number of memory T cells are generated in the body, so as to achieve long-term anti-tumor immunity.

4. Existing controversies and research prospects

At present, the application of MOFs in tumor therapy still has many controversies and limitations. Firstly, the material basis of MOFs has not been fully confirmed by modern medicine, and the metabolic mechanism of their in vivo degradation products is not clear, especially since some heavy metal nodes may have potential toxicity, and the in vivo biosafety of MOFs needs further verification. Secondly, the large-scale synthesis of MOFs is difficult. The existing synthesis methods (such as the solvent co-heating method and the microwave-assisted synthesis method) are difficult to achieve low-cost and large-scale production, which limits the clinical transformation of MOFs. Thirdly, the targeting of MOFs still needs to be optimized. Some targeted modifications (such as folate modification) have off-target risks, and the precise targeting ability is insufficient. In the future, research should focus on verifying the in vivo biosafety and degradation mechanism of MOFs through modern medical technology, developing low-cost and large-scale synthesis methods, optimizing targeted modification strategies, and exploring new application forms of MOFs (such as intelligent responsive MOFs and MOF-based nanovaccines) to promote the clinical application of MOFs in tumor therapy.

5. Conclusion

MOFs, as a new type of porous crystalline material, have unique structural advantages such as adjustable metal nodes, diverse organic ligands and controllable pore structures, which make them show broad application prospects in tumor therapy. In single tumor therapy, MOFs can effectively improve the solubility and stability of drugs, realize precise targeted delivery and responsive release, enhance the curative effect of chemotherapy and radiotherapy, and regulate the body's immune system to achieve an anti-tumor effect. In combined therapy, MOFs can be used as ideal carriers to realize the combination of PDT, PTT, CDT, chemotherapy, immunotherapy and starvation therapy, which can synergistically enhance the anti-tumor effect and overcome the limitations of single treatment. Although there are still controversies and limitations in the application of MOFs in tumor therapy, with the in-depth research and technological progress, MOFs are expected to become an important part of clinical tumor comprehensive therapy, providing new ideas and schemes for tumor treatment.

References

- [1] Zhang L, Li Y, Wang X, et al. (2022). Review on Metal–Organic Framework Classification, Synthetic Approaches, and Influencing Factors: Applications in Energy, Drug Delivery, and Wastewater Treatment [J]. *ACS Omega*, 7(50): 46256–46276.
- [2] Yang N, He Z Y, Lang T Q. (2025). Drug Delivery Systems Based on Metal–Organic Frameworks for Tumor Immunotherapy [J]. *Pharmaceutics*, 17(2): 225.
- [3] Li H, Xu C, Li N, et al. (2022). Synthesis of Bimetallic Fe/Cu-MOF and Its Performance as Catalyst of Peroxymonosulfate for Degradation of Methylene Blue [J]. *Materials*, 15(20): 7252.
- [4] Chen K, Zhou A, Zhou X, et al. (2024). Cellular Trojan Horse initiates bimetallic Fe-Cu MOF-mediated synergistic Cu-proptosis and ferroptosis against malignancies [J]. *Science Advances*, 10(15): eadk3201.
- [5] Zhong X F, Sun X. (2020). Nanomedicines based on nanoscale metal-organic frameworks for cancer immunotherapy [J]. *Acta Pharmacological Sinica*, 41(7): 928–935.
- [6] Zou Y, Chen J, Luo X, et al. (2024). Porphyrin-engineered nanoscale metal-organic frameworks: enhancing photodynamic therapy and ferroptosis in oncology [J]. *Frontiers in Pharmacology*, 15: 1481168.
- [7] Pourmadadi M, Omrani Z, Forootan Z, et al. (2023). UiO-66 nanoparticles as a drug delivery system: A comprehensive review [J]. *Journal of Drug Delivery Science and Technology*, 86: 104690.
- [8] Ke Q, Jiang K, Li H, Zhang L, Chen B. (2023). Hierarchically Micro , Meso , and MacroPorous MOF Nanosystems for Localized CrossScale Dual-Biomolecule Loading and Guest-Carrier Cooperative Anticancer Therapy [J]. *ACS Nano*, 18(27): 21911–21924.
- [9] Meng X, Tan S, Chen L, et al. (2023). Multifunctional metal-organic framework (MOF)-based nanoplatforms for cancer therapy: from single to combination therapy [J]. *Theranostics*, 13(2): 624–652.
- [10] Xie Y, Xu Y, Liu Y, Mei Z, Tian J. (2026). Metal-organic framework-based radiosensitizer for cancer therapy [J]. *Coordination Chemistry Reviews*, 46: 217103.
- [11] Wang H, Fang T, Wang J, Zhang M, Mu X, Gao T, Wei T, Dai Z. (2024). Adaptive Size Evolution of an MOFs-in-MOF Nanovehicle for Enhanced Nucleus-Targeted Tumor Chemotherapy [J]. *Nano Letters*, 4(27): 10605–10613.
- [12] Dai L, Yao M, Fu Z, Li X, Zheng X, Meng S, Yuan Z, Cai K, Yang H, Zhao Y. (2022). Multifunctional metal-organic framework-based nanoreactor for starvation/oxidation improved indoleamine 2, 3-dioxygenase-blockade tumor immunotherapy [J]. *Nature Communications*, 13(1): 2688.
- [13] Wang J, Gu Y, Fan Y, Yang M. (2023). Copper-Doped Platinum/Metal-Organic Framework Nanostructures for Imaging Guided Photothermal and H₂O₂ Self-Supplying Photodynamic/Photothermal/Chemodynamic Therapy [J]. *ACS Applied Nano Materials*, 6(14): 13561–13569.
- [14] Liu Y, Wang X, Zhang W, et al. (2024). Folic acid-targeted Pt/PCN-224(Ce6) nanoplatform with self-oxygen supply for synergistic PDT/PTT/CDT trimodal cancer therapy [J]. *Journal of Nanobiotechnology*, 22(1): 178.
- [15] Dong Y, Li J, Dai Y, Zhang X, Wang T, Zhao B, Liu W, Chen L, Yang S, Du P, Jiao Z. (2025). Redox-responsive metal-organic framework nanocapsules enhance tumor chemo-immunotherapy by modulating tumor metabolic reprogramming [J]. *Materials Today Bio*, 31: 101487.

- [16] Wang T, Yang J, Ding J, Yuan Y, Wu Y, Zhang J, Rong Y, Zhou Y, Li G, Chen X, He C. (2025). A Metal–Organic Framework-Based Immune Regulating Nanocarrier Depot for Enhanced Combination Cancer Immunotherapy [J]. *ACS Nano*, 19: 23629–23646.
- [17] Chen W, Liu J, Yang Y, et al. (2021). ZIF-8 based pH-responsive nanoplatform for targeted chemotherapy delivery [J]. *ACS Applied Materials & Interfaces*, 13 (32): 37896–37907.
- [18] Zhang W, Liu Y, Wang X, Qu K, Zhu W, Cheng F, Wang L. (2025). A Self-Amplifying MOF Nanoplatform for Cancer Immunotherapy Synergizing Starvation-Enhanced Cuproptosis and cGAS–STING Activation [J]. *ACS Applied Materials & Interfaces*, 17(40): 40129–40142.