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Editorial

Supramolecular Nanotheranostics

Xiaoyuan Chen[1]✉, Gang Zheng[2]✉, Jianjun Cheng[3]✉, Yi-Yan Yang[4] ✉

1. Laboratory of Molecular Imaging and Nanomedicine (LOMIN), National Institute of Biomedical Imaging and Bioengineering (NIBIB), National Institutes of Health (NIH), Bethesda, MD 20892
2. Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, ON, Canada
3. Department of Materials Science and Engineering, University of Illinois at Urbana-Champaign, Urbana, Illinois 61801
4. Institute of Bioengineering and Nanotechnology, 31 Biopolis Way, The Nanos, 138669, Singapore

✉ Corresponding authors: shawn.chen@nih.gov (Xiaoyuan Chen), gang.zheng@uhnres.utoronto.ca (Gang Zheng), jianjunc@illinois.edu (Jianjun Cheng), yyyang@ibn.a-star.edu.sg (Yi-Yan Yang)

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Abstract

This supramolecular nanotheranostics special issue collected a total of 17 review articles and 3 research articles broadly covering the current and emerging supramolecular nanotheranostics.

Key words: Supramolecular, Nanotheranostics

The Nobel Prize in Chemistry 1987 was awarded to Cram, Lehn and Pedersen for their development and use of molecules with structure-specific interactions of high selectivity. Almost twenty years later in 2016, Nobel Prize in Chemistry recognized supramolecular chemistry and molecular recognition again by awarding Sauvage, Stoddart and Feringa for the design and synthesis of molecular machines. Supramolecular biomaterials exhibit unique properties in theranostic applications compared with the conventional artificial biomaterials, attributing to the dynamic and responsive nature of non-covalent interactions. For example, the poor solubility and stability of chemotherapeutic drugs in physiological environment can be effectively solved by taking full advantage of supramolecular chemistry and nanotechnology. By the formation of host–guest complexes with macrocyclic hosts, the anticancer drugs can be easily formulated to prepare nanomedicines showing satisfactory anti-tumor efficacy and reduced normal organ toxicity.

Theranostics journal has previous published a number of manuscripts related to self-assembly for cancer imaging and therapy [1-10]. This special issue broadly covers the current and emerging supramolecular nanotheranostics.

First, Braegelman and Webber [11] highlighted the general and phenomenological design considerations governing host–guest recognition and the specific types of chemistry which have been used and are available for different biomedical applications. They emphasize how stimuli-responsive host–guest recognition, wherein a complex form in a manner that is sensitive to, or can be governed by, externally applied triggers, disease-specific proteins and analytes, or the presence of a competing guest. Then, Yu and Chen [12] provided a comprehensive review of various host-guest molecular recognitions. The macrocyclic hosts include cyclodextrins, calixarenes, cucurbiturils, and pillararenes. The dynamic nature of the non-covalent interactions and selective host–guest complexation endow the resultant nanomaterials with intriguing properties, holding promising potentials in theranostic fields. Song et al. [13] put special emphasis on pillarenes which have rigid and symmetric structures, facile substitution, and unique host-guest properties. Reported pillarene-based supramolecular nanotheranostics can be: (a) pillarene-based hybrid supramolecular nanotheranostics upon hybridizing with porous materials such as mesoporous silica nanoparticles, metal-organic frameworks, metal nanoparticles, and other inorganic materials; (b) pillarene-based organic supramolecular therapeutic systems that include supramolecular amphiphilic systems, artificial channels, and prodrugs based on

host-guest complexes. Geng et al. [14] reported the use of amphiphilic macrocycles, particularly those bearing cationic charges and their various assemblies for gene delivery. The most prominent examples include amphiphilic cyclodextrins, calixarenes and pillararenes as non-viral vectors for gene condensation, membrane permeation and targeted delivery. Zhang et al. [15] studied the use of synthetic supramolecular receptors such as cucurbit[7]uril, sulfo-calix[4]arene and water-soluble carboxylatopillar[6]arene (WP[6]) to evaluate the antidotal effect of neuromuscular blocking agent succinylcholine (Sch). Among these, WP[6] with high binding affinity towards Sch was able to reverse Sch induced depolarization and reduce the efflux of intracellular potassium.

Liu et al. [16] highlighted the usefulness of nanoscale metal-organic frameworks (MOFs) as drug carriers, bioimaging agents, and therapeutic agents. The authors also confessed that the issue of relatively poor stability of MOFs under physiological conditions has to be solved before more broad biomedical applications of MOFs can be realized. Chu et al. [17] described the usefulness of MOF nanoparticles (MOFs) based biomineralization of various biomacromolecules such as proteins, enzymes, DNAs/RNAs, and viruses. MOFs are excellent supporting are excellent supporting matrices due to the low toxicity of polycarboxylic acids and metals, high encapsulation efficiency, and moderate synthetic conditions. Pöthig and Casini [18] illustrated how supramolecular metal-based structures can be used as scaffolds to develop multimodal theranostic agents. The host-guest chemistry of 3D self-assembled supramolecular structures can be exploited to construct supramolecular coordination complexes (SCCs) and supramolecular organometallic complexes (SOCs). One particular example that is worth mentioning is the potential of 3D-metallacages as drug delivery systems for anticancer agents. Dai et al. [19] summarize the assembly of polyphenol-based particles, including polydopamine (PDA) particles, metal-phenolic network (MPN)-based particles, and polymer-phenol particles, and their potential biomedical applications in various diagnostic and therapeutic applications.

Kim et al. [20] provided an extensive overview of how peptides and oligonucleotides can be precisely tuned to have diverse structural, mechanical, physicochemical and biological properties. The current challenges related to cellular internalization and more efficient delivery to drug targets were elaborated. Wang et al. [21] described how non-covalent interactions between nucleic acids (DNA, siRNA, miRNA, and mRNA) with peptides or nucleopeptides can be applied to construct supramolecular assemblies for gene delivery and therapy. Li et al. [22] emphasized the unique features of peptide-modulated self-assemblies for tumor supramolecular nanotheranostics, exemplified by peptide-photosensitizers, peptide-drugs, and multicomponent cooperative self-assembly, including building block design, interaction strategies and the potential relationships between their structures and properties. Chen et al. [23] discussed the elegant properties of deoxyribonucleic acid (DNA), such as accurate recognition, programmability and addressability to develop DNA-supramolecule conjugates (DSCs). DSCs can be applied for sensing, protein activity regulation, cell behavior manipulation, and biomedicine. Lee et al. [24] pointed out that protein delivery into cells is a potentially transformative tool for treating "undruggable" targets in diseases associated with protein deficiencies or mutations. This review presented promising non-viral approaches for direct delivery into the cytosol or escape from endosomal pathways.

Zhu et al. [25] reported a ferroptosis promoted photodynamic therapy (PDT) approach in which photosensitizer chlorin e6 (Ce6) and the ferroptosis inducer erastin were self-assembled into a supramolecular Ce6-erastin nanodrug through hydrogen bonding and π−π stacking. This assembly enhances anticancer actions overcomes by hypoxia-associated resistance of PDT in cancer treatment by relieving hypoxia and promoting ROS production. Thang et al. [26] reviewed light-responsive nanoparticles that have been employed for precise regulation of cellular events and disease treatments. The light-responsive nanoregulators can be manipulated to provide UV-Vis light-triggered photocleavage or photoisomerization studies, as well as near-infrared (NIR) light-mediated deep-tissue applications for stimulating cellular signal cascades and treatment of mortal diseases. He et al. [27] described aggregation-induced emission (AIEgens) and their derived supramolecular systems with unique optical properties as fluorescent probes for turn-on sensing of pathogens with high sensitivity and specificity, and for image-guided photodynamic inactivation (PDI) therapy of pathogenic infection. Cheng et al. [28] focus on describing mesoporous silica nanoparticle carriers with a large internal pore volume suitable for carrying anticancer and antibiotic drugs, and supramolecular components that function as caps that can both trap and release the drugs on-command. The design, synthesis and operation of supramolecular systems that act as stimuli-responsive pore capping devices are discussed in detail. Xu et al. [29]

developed an NF-κB-activating supramolecular nanoadjuvant (3DSNA) that is prepared by pH-triggering self-assembly of a positively charged D-configurational peptide derivative. 3DSNA adsorbs antigen through electrostatic interactions and promotes ingestion and cross-presentation of antigen, upregulates costimulatory factors (CD80 and CD86) and secretes proinflammatory cytokines (IL-6 and IL-12) by dendritic cells (DCs), accompanied by activation of the innate immune response (NF-κB signaling), resulting in long-term antigen-specific memory and effector $CD8^+$ T cells response. Such nanofiber adjuvant is superior to the conventional aluminum hydroxide adjuvant.

Finally, Valic and Zheng [30] reviewed approaches for extrapolation of nanomaterial pharmacokinetics from preclinical models to humans with a focus on allometric scaling and physiologically based pharmacokinetic (PBPK) modeling. Such practice will likely result in a more straightforward roadmap for the clinical translation of promising nanomaterials.

In summary, this timely issue touches upon molecular recognitions and host-guest chemistry, stimuli-responsive supramolecular self-assembly, bioorthogonal supramolecular catalysis, supramolecular diagnosis, new imaging methods based on supramolecular chemistry, supramolecular chemotherapy and theranostics, and controlled supramolecular drug/gene delivery. It's our hope that this special issue will stimulate more interest to develop supramolecular theranostic platforms for disease diagnosis, therapy and prognosis.

Competing Interests

The authors have declared that no competing interest exists.

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