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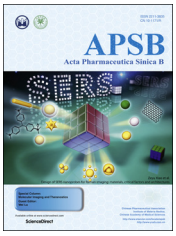

Editorial for Molecular Imaging and Theranostics

Molecular imaging has become a hot research area since the early of this century. It utilizes the molecular interaction between the imaging probes and the particular targets to image the change of the area of interest. Molecular imaging opens up the possibility of early diagnosis as well as monitoring treatment response and outcomes that tailors individualized therapies. Researches have been focused on the development of imaging probes for various imaging modalities. Thanks to the contribution of chemistry and material sciences, certain probes have been endowed with multifunctions that enable multimodal imaging or combinatorial diagnosis and therapeutics termed as theranostics. In this special column, five review articles and three research reports have been selected to illustrate the principles of design and biomedical applications of the molecular imaging probes for fluorescence imaging, Raman spectroscopic imaging, X-ray computed tomography (CT), magnetic resonance imaging (MRI), single photon emission computed tomography (SPECT) as well as their combinations.

Fluorescence imaging probes have been widely reported for biomedical imaging owing to their high sensitivity, low cost and quick imaging process especially suitable for intraoperative imaging. The fluorescein isothiocyanate (FITC)-labeled folic acid has been successfully used for fluorescence imaging-guided surgery of ovarian cancer in clinics[1]. Beyond this, the fluorescence probes can be integrated with other imaging modalities including CT, MRI, positron emission tomography (PET) and photoacoustic imaging (PAI). Dr. Wei Wang and co-authors summarized the design strategies of multimodality optical fluorescence imaging probes[2]. They also outlined the advantages and limitations of each imaging modality and provided the opinions on the multimodality imaging that would improve detection sensitivity and accuracy. Except the multimodal fluorescence imaging probes, Dr. Haiyu Hu and co-authors' review focused on the fluorogen-activating proteins (FAPs)[3]. FAPs are a class of proteins which do not fluoresce unless bound to the specific fluorogens. These fluorogens are small molecules that have high binding affinity to FAPs in nanomolarity range. Upon the interaction between the fluorogens and FAPs, the restrain of the intramolecular rotation of the fluorogens allows the molecules to fluoresce. Due to high specific binding between the fluorogens and FAPs, the FAP/fluorogen systems have been developed for both intracellular and *in vivo* molecular imaging with a serial of smart strategies.

Compared with other imaging modality, Raman imaging generates higher specificity and sensitivity derived from its fingerprint signature of Raman spectroscopy. Yet, Raman signals are too weak to be directly applied to biomedical application. It requires pronounced enhancement through substrates such as nanostructures made of noble metals. Dr. Zeyu Xiao and co-authors' review expatiated on the design strategies of the termed surface-enhanced Raman scattering (SERS) probes[4]. Particularly, they provided critics on the factors including material properties, modifying factors, and structural parameters that affect the imaging quality. These parameters are critical determinants for a successful SERS imaging. The review of Dr. Min Zhou and co-authors highlighted the recent progress of SERS nanoparticles for cancer theranostics[5]. Delicate nanostructures have been designed not only for multimodality imaging such as a combination of SERS imaging, MRI and photoacoustic imaging, but also for SERS imaging-guided cancer therapy such as the imaging-guided photodynamic therapy. Further, the SERS nanoparticle-derived biosensing was discussed. With the development of new materials, we can envision that Raman imaging will have great potential for clinical translation in the future.

CT is currently widely applied in clinical diagnosis. A radiopaque contrast agent is usually used for the imaging enhancement between the area of interest and the surrounding tissues. Although the iodinated contrast agents are clinically used, these small molecules are rapidly cleared by the kidney, resulting in higher doses applied for longer CT scans and toxicity. The review by Dr.

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Marites P. Melancon and co-authors summarized the recent progress on the development of radiopaque nanomaterials either masking the iodine or consisting of noble elements with higher Z numbers for atherosclerosis imaging[6]. Radiopaque polymeric materials are also developed for embolization and other catheterization procedures under the image guidance of X-ray fluoroscopy during an interventional treatment. In particular, Melancon's groups developed radiopaque and resorbable infera vena cava filters (IVCFs) capable of being monitored during the deployment or for long term stability.

The current column includes two research articles on the application of iodine-131 (^{131}I) which decays with a half-life of 8.02 days with β^- and γ emissions ideal for cancer imaging and therapeutics. ^{131}I is used for the clinical treatment of thyrotoxicosis (hyperthyroidism) and some types of thyroid cancer. Dr. Jian Zhang and his colleagues labeled Evans blue with ^{131}I (^{131}I-EB) and investigated its necrosis targeting property on the basis of the necrosis avidity of Evans blue[7]. The biodistribution, autoradiography and histological staining analysis as well as *in vitro* binding assay proved the necrosis-targeting effect of ^{131}I-EB, thus demonstrating the possibility of imaging the necrotic tissues generated from the disease clinically. Dr. Gang Huang and his colleagues developed the biodegradable microspheres loaded with hollow CuS nanoparticles and paclitaxel (HCuSNPs-MS-PTX), which can be directly labeled with ^{131}I[8]. ^{131}I-HCuSNPs-MS-PTX offered multimodality SPECT/CT and photoacoustic imaging to monitor the distribution of the injected agents non-invasively, as well as a combinatorial photothermal, chemo- and radio-therapies with a synergistic therapeutic effect, showing the versatility of a theranostic agent in breast cancer treatment.

In the last research communication, Dr. Haiyu Hu and her colleagues designed a nitroreductase (NTR)-enhanced MRI contrast agent, which is for the detection of NTR activity *in vitro* and in living *E. coli*[9]. The probe is selectively reduced by NTR in the presence of nicotinamide adenine dinucleotide (NADH) and converted into Dotarem (Gd-DOTA), which causes the change of the longitudinal T1 relaxivity detectable by MRI. The probe exhibits great promise for a broad application in therapeutic NTR-activated prodrug treatment in clinical research.

This special column is expected to provide the audience with the updated knowledge and the cutting-edge technology of molecular imaging and theranostics, which may facilitate either the research in the related field by utilizing the molecular imaging tools or the development of pharmaceutical theranostic agents.

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