Editorial

The Medicinal Chemistry of Targeted Tumor Imaging (II)

This issue (volume 10, number 12) and the previous issue (volume 10, number 11) of *Current Topics in Medicinal Chemistry*, dedicated to "The Medicinal Chemistry of Targeted Tumor Imaging," are aimed at describing and highlighting the state-of-the-art of current research and development in the field of molecular imaging probe development. Last issue contained a total of 5 review articles covering the chemistry of positron emission tomography (PET), single-photon emission computed tomography (SPECT), and activatable optical fluorescence imaging. The remaining 7 review articles on quantum dot based fluorescence imaging, T1 and T2 weighted MR contrast agents, gas microbubbles for contrast-enhanced ultrasound, theranostic nanoparticles, general design of cancer imaging probe and strategies to label cells for cancer are discussed in this issue.

This issue starts by a review article from Jinhao Gao *et al.* summarizing recent advances of quantum dot (QD) nanoparticle-based near-infrared fluorescence (NIR) optical imaging probes. Compared with the organic dyes and fluorescent proteins, QDs show many unique optical properties, such as symmetrical, narrow, and tunable emission spectra, superior photostability, high quantum yields, and the capacity of simultaneous excitation of multiple fluorescence colors. Based on the availability of various Cd and non-Cd based quantum dots, how the physicochemical properties, surface chemistry and bioconjugation chemistry of QDs profoundly affect the absorption, distribution, metabolism, excretion, toxicity, and tumor targeting efficiency were elaborated in this article.

The next review article by Nazila Kamaly *et al.* talked about the development and implementation of tumor targeted T1 MRI contrast agents, with an emphasis on the chemistry used to modify pre-existing clinical MRI contrast agents for targeted tumor imaging. MRI is capable of producing three dimensional images of tissues containing water with a high degree of spatial resolution. MRI contrast agents provide reliable means to enhance images and play a key role in clinical investigations. MRI contrast agents consist of molecules which incorporate a paramagnetic metal ion, most commonly Gd or iron (Fe). Image improvement arises from the modulation of longitudinal (T1) or transverse (T2) relaxation times of the surrounding bulk water protons by the coordinated metal ions. Both small molecules that carry single and nanoparticles (NPs) carrying multiple paramagnetic metal ions were discussed.

The third review article by Lise-Marie Lacroix *et al.* described the synthesis of iron based magnetic nanoparticle (MNP) contrast agents for T2-weighted MRI or as heaters for magnetic fluid hyperthermia (MFH). It first introduced the nanomagnetism and elucidated the critical parameters to optimize the superparamagnetic NPs for MRI and ferromagnetic NPs for MFH. It then further outlined the new chemistry developed for making monodisperse MNPs with controlled magnetic properties. The review finally highlighted the NP functionalization with biocompatible molecules and biological targeting agents for tumor diagnosis and therapy.

The fourth review article by Francesca Cavalieri *et al.* described the use of gas-filled microbubbles for ultrasound imaging guided cancer therapy. Combining diagnostic and therapeutic ultrasound for tumor imaging and treatment is especially attractive for reasons of simplicity and cost-effectiveness. The development of microbubbles acting as targeted and smart drug carriers is however a very challenging goal as these systems present difficult and inherent problems of stability. The methods of preparation, mechanism of action, *in vitro* and *in vivo* stability, structural/functional characterization of microbubbles were described in details. New mechanisms for ultrasound-enhanced local drug and gene delivery were also reviewed. Different strategies used to target microbubbles to regions of disease and some of the recent experiences in ultrasound image-guided therapy were illustrated.

The fifth review article by Debatosh Majumdar *et al.* summarized the current status and future prospects of using nanotechnology for targeted cancer imaging. Theragnostics (or sometimes called theranostics) is an approach based on the fusion of diagnostics and therapeutics. In theragnostics, the results of diagnostic tests are used to design and decide the appropriate targeted therapy, in which an anti-cancer drug is delivered specifically to the targeted cancer site with the help of appropriate targeting ligands. Theragnostics is also aimed to monitor the treatment response, increase the drug efficacy and

safety. This review provided a number of nanoparticle platforms for multimodality imaging and simultaneous imaging and therapy applications.

The sixth review article by Kai Chen *et al*. provided insights into molecular imaging probe design. A molecular imaging probe is an agent used to visualize, characterize and quantify biological processes in living systems. It can be referred to many other terms, such as a tracer, a contrast agent, or a molecular beacon. A successful cancer imaging probe with clinical translation potential is expected to have high affinity and specificity for the target of interest, can be detected with high sensitivity, have high tumor/background ratio, reasonable metabolic stability, low immunogenicity and toxicity, as well as relatively low cost and ease of production. It was concluded in this review that both random and rational strategies are necessary in the design and development of molecular imaging probes.

The final review article of this special issue by Hao Hong *et al*. discussed different approaches to label and track immune cells, stem cells, and cancer cells. There are two methods for cell labeling: one is direct labeling in which cells are labeled with certain tags that can be detected directly with suitable imaging device; and the other is quote-on-quote indirect cell labeling in which cells are transfected with a reporter gene. The pros and cons of each labeling strategy and imaging modality to track labeled cells *in vivo* were analyzed. Several concerns about the reliability and clinical translatability of different cell labeling techniques were commented.

I would like to take this opportunity to thank all the authors for their excellent contributions and participation in these two consecutive issues. With the rapid advances in the newly emerged molecular imaging field and ever growing needs for early diagnosis and early detection of therapy response to cancer therapy, it is our understanding and hope that the state-of-the-art chemistry and radiochemistry techniques are presented in a timely manner and will continue to serve as a useful guide for the cancer research community and other related fields in the future.

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