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Editorial

Reporter Gene Imaging in Therapy and Diagnosis

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Abstract

Noninvasive molecular imaging using reporter genes is a relatively recent field in biomedical imaging that holds great promises for disease diagnosis and therapy. As modern medicine is moving towards personalized medicine, targeted biomolecule based therapies is gaining popularity that requires careful and systematic validation. Reporter genes have emerged as important generalizable tools to overcome the shortcomings of direct evaluation of individual biomolecules and are being applied in various fields such as cell therapy, stem cell therapy, immune therapy, viral gene delivery through optical, radionuclide, magnetic resonance imaging techniques. New approaches to image protein-protein interaction, protein phosphorylation, protein folding that are crucial parameters for theranostic study using reporter genes are being developed. All these new technologies and relevant preclinical and clinical researches will determine the success of early detection and personalized therapy in the future.

Key words: reporter genes, molecular imaging

Amalgamation of therapy with diagnosis is a prime requirement in successful translation of research information from bench to bedside. 'Theranostics', a newly developed concept in biomedical science, is thus gaining popularity in pre-clinical and clinical research. The science of theranostics involves development of new probes, new delivery vectors/chemicals and new strategies of imaging in cellular and animal models. The goal of theranostics is to achieve personalized medicine with stratified patient population [1]. At preclinical stage, various reporter genes suitable for in vivo imaging using multiple modalities have become extremely useful tools for theranostic study. These imaging strategies based on genetic reporters have contributed immensely in developing better therapeutic and diagnostic procedures for disease evaluation. In this special edition, global experts on reporter gene imaging explore the potential use of various reporter genes in expanding research areas covering stem cell and immune cell mediated cell therapy and viral therapy applications using nuclear medicine imaging to MR imaging to optical imaging and activatable imaging strategy.

Various cell based strategies have been developed for delivering therapeutic dose to the disease targets. Cell therapy overcomes many deleterious effects of conventional drug therapy but requires detail validation and ethical clearance before use in human subjects. Recently stem cells are widely used for therapy due to their unprecedented power of regenerating normal tissues which is not possible by other therapeutic approaches. Gu et al. [2] elaborated the application of stem cells and induced pluripotent stem cells (iPSCs) in monitoring tumorigenicity, immunogenicity, biodistribution and how molecular imaging plays roles in answering the crucial questions about their clinical applications. Amongst all the existing imaging methods bioluminescence imaging is the most sensitive technique in small animal models

due to the high signal to noise ratio. Thus by exploiting the power of optical reporter gene based imaging strategy, Huang et al. [3] described the application of pluripotent /adult /embryonic stem cells to rectify various peripheral vascular disorders.

Modulating immune system for better treatment is a challenge and a constant focus for development of personalized medicine, particularly in cancer. In order to fully understand the efficacy of immune therapies, it is critical to understand how the treatment modulates the function of each cell type involved in the anti-cancer immune response. The development of reporter genes for tracking cell movement and function is a powerful addition to the immunologist's toolbox. In a concise review, Dubey [4] elaborated the importance of non-invasive imaging of innate and adaptive immune cells for their interaction, trafficking, location and functional analysis of immune therapy.

Successful delivery of gene of interest is crucial for any therapy and viral vectors have long been used for gene therapy. The safety, non-specific targeting, and efficiency are the major points of improvement for these vehicles. In this issue, Rojas & Thorne [5] described the therapeutic potential of a special group of virus, the oncolytic virus that selectively replicate in tumor cells. Some of these viruses are already in clinical trials and are expected soon to be approved as agents for cancer treatment in North America and Europe.

Though bioluminescence imaging confers the greatest sensitivity amongst all the imaging modalities, it still lacks the power of clinical application. Radionuclide imaging, particularly the positron emission tomography (PET) reporter genes and reporter probes emerge as the most valuable and reliable tools for gene and cell therapy from small animal models to humans. The advantages of PET reporter gene/probe combination in theranostics have been discussed in two articles by Yaghoubi et al. [6] and by Ahn B. [7]. Yaghoubi et al. comprehensively reviewed the existing PET reporter genes and the reporter probes for preclinical and clinical purposes. This review also detailed how academia and industry partnership can join hands and set the stage for evaluation of gene therapy or cell therapy trials. Ahn in his article emphasized the diagnostic and therapeutic use of sodium iodide symporter (NIS) and its evolution as a reporter gene. NIS gene mediated molecular imaging and radionuclide gene therapy is one of the most promising examples of the few theranostic genes discovered to date.

The spatio-temporal imaging of genomic and proteomic events in living subjects is the crux of molecular imaging with reporter genes. Of all the imaging modalities available magnetic resonance imaging produces best spatial resolution and generates both functional and anatomical information. Lee et al. [8] described the principle of MRI and the merits and demerits of the four existing MR reporter-based imaging approaches.

In another article, Niu and Chen [9] described the mechanistic approaches of various reporter genes with a special emphasis on developing activatable sensors to image translational molecular events such as protein-protein interactions, protein phosphorylation or protein folding. Development of such smart sensor based imaging approach is an important area in molecular imaging that has the propensity to image systems biology.

All together this special issue presents a broad spectrum of evidences on how reporter gene imaging plays vital roles in diagnosis and therapy. Advancement in theranostic science will allow moving from generalized medicine towards personalized medicine and early detection of diseases. The success and true potential of theranostics is yet to achieve in the clinical world. Advanced molecular imaging techniques with a generalized reporter gene platform would surely assist to determine the path.

Competing Interests

The authors have declared that no competing interest exists.

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