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Editorial

Cardiovascular Molecular Imaging as a Tool to Study Biology

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Over the last few decades, there have been significant advances in the understanding of the pathophysiology of cardiovascular diseases (CVD), providing new tools for diagnosis and novel treatment alternatives (e.g., medical intervention, devices). However, despite these advancements, atherosclerosis disease (ASD) and its consequences (e.g., myocardial infarction and heart failure) remain the leading causes of death and morbidity in the Western world, and progressively all around the world.[1] According to American Heart Association ASD statistics, 715,000 patients suffered a new or recurrent myocardial infarction in 2010, and 56,210 patients died of heart failure in 2009 alone.[1] Furthermore, from the financial perspective, they occupy a significant portion of a nation's health budget. In the US alone, medical care for ASD in 2012 amounted to $3126.6 billion. Thus, there is significant interest in the development of novel ways to detect disease at early stages and monitor therapy for CVD. This issue of *Theranostics* focuses on the role that molecular imaging can play in the detection, risk stratification, and monitoring of CVD and their therapies.

Molecular imaging can be briefly defined as the capability of imaging processes at the molecular level. The main strength of molecular imaging is the capacity of not only detecting organ dysfunction, but also providing insight on the mechanism that led to such dysfunction, opening the door for the understanding of the disease at the molecular level.[2,3] This technology has its roots in the nuclear medicine field, more specifically in the oncology area where it has played a significant research role for the last few decades. Currently, molecular imaging extends the nuclear medicine field and many other imaging modalities that are part of the molecular imaging chest of tools.

As previously mentioned, atherosclerosis constitutes the main cause of CVD and as such it has been of significant interest to develop ways to monitor the progression of atherosclerosis.[4,5] In this issue of *Theranostics*, Orbay et al.[6] provide a comprehensive review of the different imaging targets that have proved useful for the understanding of the development of ASD. As outline in the review, the existence of molecular imaging agents targeted to inflammation and different portions of the atherogenesis cascade has generated tremendous research. Unfortunately, most of these agents have not made it to the clinic, where ^{18}F-FDG continues to be the agent of choice for the assessment of inflammation. This particular article focuses on the use of positron emission tomography (PET) as the imaging modality. It is important to mention that although nuclear medicine has been at the forefront of molecular imaging, with PET as an example of one of the leading and most sensitive modalities, other imaging modality are entering the molecular imaging world, each one with its own strengths and weaknesses. The wide array of imaging modalities that can be used for molecular imaging in CVD is shown by the article by Wildgruber et al.,[7] which identifies the different imaging modalities that can be used for the detection of inflammation. One of the main lessons from this article is that there is no

single imaging modality that can provide all the answers, and the choice of imaging modality should be selected depending on the specific question or need in mind.

Progenitor cell (PC) therapies are being developed for myocardial salvation in ASD[8] and have been shown to improve cardiac function. Significant interest have been placed in understanding the mechanisms by which progenitor cells exert their effect. In this issue of Theranostics, Ale et al. use molecular imaging to study the effect of progenitor cells on myocardial apoptosis,[9] illustrating the potential of molecular imaging in monitoring not only the survival of progenitor cells but also their effect on the target tissue. Furthermore, the use of progenitor cells has been hampered by lack of understanding of their mechanisms of action and poor retention rates after delivery.[10,11] Molecular imaging strategies have also been used to monitor the effect of these novel therapies. The article by Kedziorek et al.[12] described a novel way to ascertain a successful delivery of progenitor cells in the myocardium. The main strength of this study lies on the use of clinically applicable and relatively easily translatable imaging modalities that will bring these approaches closer to clinical use.

Many molecular imaging strategies have been discussed in this issue of *Theranostics*, most of which are used in the animal research field, with a very few of them in clinical use, as this would require approval by the respective national agencies. The Federal Drug Administration (FDA) approval process is a long one with many difficult steps, as detailed in the article by Dr. Hung.[13] Although most researchers in the animal research field might never undergo the arduous FDA process, for clinicians or clinician investigators, it has become very important to start understanding how these regulatory agencies work and what is needed to translate imaging agents. It is possible that some of these mechanisms may change over time, but the basic principles of safety and cost/benefit ratio will remain the same and must always be considered carefully.

In summary, we are taking important initial steps in this fascinating field of molecular imaging in CVD. In the future, we would anticipate that novel imaging modalities or a new combination of existing modalities will emerge, and will continue to provide us with critical insights on the molecular basis of disease. Clinical translation in the future will depend on our progress on these fronts and the creative exploitation of the knowledge being discovered by scientists.

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