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P-TH-159: Optical Fluorescence Imaging-based Real-time Monitoring of Myocardial Tissue Regeneration

Abstract .pdf

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Sessions

Approaches in Cellular/Molecular Imaging and Tracking
목요일, 10월 17 9:30 오전
Exhibit Hall DE

Optical Fluorescence Imaging-based Real-time Monitoring of Myocardial Tissue Regeneration

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Introduction: Real-time longitudinal monitoring of living cells provides an insight in understanding the mechanism of cellular migration from the transplanted graft and its integration with that of the host tissues. Different kinds of imaging modalities using nontoxic and stable contrast agents have been explored to quantify the presence of cellular migrations from the graft to the host tissues. However, longitudinal monitoring of cells is currently limited by the lack of a stable probe in the near-infrared (NIR) window. In addition, difficulties related to the use of multimodal channels limit its application in real-time tracking of multiple cells *in vivo*, thereby demanding for an alternate approach to combat the existing challenges. The present work demonstrated long-term simultaneous tracking of multiple cells *in vivo* using 3 Charge-coupled device (3CCD) optical fluorescence imaging technique and different types of stable, nontoxic and target-specific fluorescent dyes in the NIR window. To do so, a cell-laden patch using tissue derived extracellular matrix encapsulated with endothelial cells was fabricated *via* 3D bioprinting technique and implanted at the site of myocardial infarction (MI) in a rat MI model. Furthermore, the multimodal 3CCD optical fluorescence imaging based system was employed to differentiate between healthy and ischemic zone using different contrast agents and track the cellular migration from implanted graft to host tissue. Thus, the developed imaging system having high sensitivity and multimodal capability offers a platform to longitudinally monitor living cells *in vivo*, which is pivotal for understanding biological mechanisms such as cell migration, integration and neovascularization.

Materials and Methods: To observe biological mechanisms, 3CCD optical fluorescence imaging system was employed for detecting two different target probes emitting the lights in NIR range and the other CCD sensor was used for detecting visible light from the surrounding tissue. Furthermore, target-specific contrast agents were selected to observe normal tissues, ischemic tissues, and blood vessels. In addition, cell tracker was used to label the cells to be delivered in the form of 3D bioprinted cardiac patch at the site of MI in the rat model followed by imaging with the optical system.

Results and Discussion: We demonstrated that the 3CCD optical fluorescence imaging system could detect contrast agents for respective target tissues. In addition, the 3D bioprinted cell-laden cardiac patch stained with cell tracking dye was detected *in vitro* and *in vivo*, respectively using the optical fluorescence imaging system. Prior to cardiac patch transplantation, the induced MI in the rat model was confirmed through Echocardiography. One-week post transplantation imaging result demonstrated migration of cells from the 3D bioprinted cardiac patch to the neighboring tissues at the infarcted zone. In addition, integration of the transplanted graft with that of the host tissue was well evident.

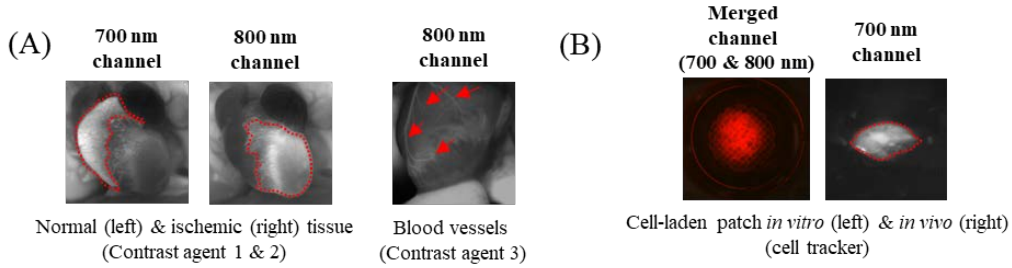

Figure 1. *Images taken with 3CCD optical fluorescence imaging system. (A) cardiac images taken after injecting target-specific contrast agents to MI murine model. (B) cell-laden cardiac patch images taken before (left) and after (right) transplantation onto the infarcted heart.*

Conclusions: The multimodal 3CCD optical fluorescence imaging system holds the potential to monitor critical biological processes that occurs upon the transplantation of a cell-printed construct at the injured site such as cellular migration, integration and neovascularization. This type of imaging techniques provides a wide platform in gaining direct evidences of the *in vivo* fate at a single as well as multi cell level, which in turn aid in understanding the physiological and pathological conditions in both preclinical and clinical studies.

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Abstract

Real-time longitudinal monitoring of living cells provides an insight in understanding the mechanism of cellular migration from the transplanted graft and its integration with that of the host tissues. Different kinds of imaging modalities using nontoxic and stable contrast agents have been explored to quantify the presence of cellular migrations from the graft to the host tissues. However, longitudinal monitoring of cells is currently limited by the lack of a stable probe in the near-infrared (NIR) window. In addition, difficulties related to the use of multimodal channels limit its application in real-time tracking of multiple cells *in vivo*, thereby demanding for an alternate approach to combat the existing challenges.

The present work demonstrated long-term simultaneous tracking of multiple cells *in vivo* using 3 charge-coupled device (3CCD) optical fluorescence imaging technique and different types of stable, nontoxic and target-specific fluorescent dyes in the NIR window.

To do so, a cell-laden patch using tissue derived extracellular matrix (dECM) encapsulated with endothelial cells was fabricated *via* 3D bioprinting technique and implanted at the site of myocardial infarction (MI) in a rat MI model. Furthermore, the multimodal 3CCD optical fluorescence imaging based system was employed to differentiate between healthy and ischemic zone using different contrast agents and track the cellular migration from implanted graft to host tissue.

Thus, the developed imaging system having high sensitivity and multimodal capability offers a platform to longitudinally monitor living cells *in vivo*, which is pivotal for understanding biological mechanisms such as cell migration, integration and neovascularization.

Conclusion

- Optical fluorescence imaging system was developed in order to monitor the regeneration of myocardial tissue after transplanting cell-laden patch.
- Myocardial infarction (M.I.) rat model was developed to observe the regeneration process in vivo environment.
- Tissue-specific near-infrared fluorescent agents for assessing the efficacy of cardiac patch were developed and selected.
- Optical stability test were performed *in vitro* and *in vivo*.
- Patch transplantation to the M.I. rat model was performed.

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