In situ three-dimensional reconstruction of mouse heart sympathetic innervation by two-photon excitation fluorescence imaging

In situ three-dimensional reconstruction of mouse heart sympathetic innervation by two-photon excitation fluorescence imaging

Freeman, Kim Renee

Name: Thesis Kim Freeman.pdf
Size: 5.126Mb
Format: PDF

Permanent Link:	http://hdl.handle.net/1805/4030
Date:	2014-02-25
Committee Chair:	Rubart-von der Lohe, Michael
Committee Members:	Atkinson, Simon Hurley, Thomas D., 1961- Gattone II, Vincent H.
Degree:	Ph.D.
Degree Year:	2013
Department:	Biomolecular Imaging and Biophysics
Grantor:	Indiana University
Keywords:	Microscopy ; Multi-photon ; Two-Photon ; TPLSM ; Confocal ; GFP ; Sympathetic Nervous System ; Cardiac ; Neuron ; Heart ; Cardiomyocyte

LC Subjects: Sympathetic nervous system -- Research -- Evaluation ; Fluorescence microscopy -- Research ; Multiphoton excitation microscopy ; Confocal microscopy ; Neurons ; Cellular signal transduction ; Muscle cells ; Myocardial infarction -- Research ; Myocardium ; Heart -- Pathophysiology ; Three-dimensional imaging in medicine -- Research -- Evaluation -- Analysis ; Two-photon absorbing materials ; Heart -- Imaging ; Cardiovascular system -- Innervation ; Neuromuscular transmission ; Mice as laboratory animals -- Research

Abstract:

The sympathetic nervous system strongly modulates the contractile and electrical function of the heart. The anatomical underpinnings that enable a spatially and temporally coordinated dissemination of sympathetic signals within the cardiac tissue are only incompletely characterized. In this work we took the first step of unraveling the in situ 3D microarchitecture of the cardiac sympathetic nervous system. Using a combination of two-photon excitation fluorescence microscopy and computer-assisted image analyses, we reconstructed the sympathetic network in a portion of the left ventricular epicardium from adult transgenic mice expressing a fluorescent reporter protein in all peripheral sympathetic neurons. The reconstruction revealed several organizational principles of the local sympathetic tree that synergize to enable a coordinated and efficient signal transfer to the target tissue. First, synaptic boutons are aligned with high density along much of axon-cell contacts. Second, axon segments are oriented parallel to the main, i.e., longitudinal, axes of their apposed cardiomyocytes, optimizing the frequency of transmitter release sites per axon/per cardiomyocyte. Third, the local network was partitioned into branched and/or looped sub-trees which extended both radially and tangentially through the image volume. Fourth, sub-trees arrange to not much overlap, giving rise to multiple annexed innervation domains of variable complexity and configuration. The sympathetic network in the epicardial border zone of a chronic myocardial infarction was observed to undergo substantive remodeling, which included almost complete loss of fibers at depths >10 µm from the surface, spatially heterogeneous gain of axons, irregularly shaped synaptic boutons, and formation of axonal plexuses composed of nested loops of variable length. In conclusion, we provide, to the best of our knowledge, the first in situ 3D reconstruction of the local cardiac sympathetic network in normal and injured mammalian myocardium. Mapping the sympathetic network connectivity will aid in elucidating its role in sympathetic signal transmisson and processing.

Description:

Indiana University-Purdue University Indianapolis (IUPUI)

This item appears in the following Collection(s)

- Biomolecular Imaging and Biophysics Program (formerly Medical Biophysics) Theses and Dissertations (/handle/1805/2013)

 Show Statistical Information (#)

My Account

- Login
- Register

Statistics

- Most Popular Items
- Statistics by Country
- Most Popular Authors