

**Stony Brook University
The Graduate School**

Doctoral Defense Announcement

Abstract

Finding Fluorescent Needles in the Cardiac Haystack: Tracking the location and fate of hMSCs with quantum dots for electrical and mechanical repair of damaged myocardium

By

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Adult myocardium has long been considered an amitotic tissue, incapable of self-repair after injury. Stem cells now show promise for restoring mechanical and electrical function to damaged heart tissue. One major limitation to studying the mechanism of stem cell action *in vivo*, however, has been the difficulty of labeling and then tracking the cells delivered in animal models. Traditional fluorescent proteins and dyes fail to illuminate exogenous cells amidst the high levels of autofluorescence in the heart. Non-invasive cell tracking methods have been developed but suffer from poor resolution. In order to fully understand the spatiotemporal distribution of stem cell clusters in the heart, as well as determine the fate of these delivered cells, the ideal cell tracking method must overcome these challenges. We have developed a novel technique using quantum dot (QD) fluorescent nanoparticles to track stem cells delivered *in vivo*. Our approach uniformly loads QDs into human mesenchymal stem cells (hMSCs) with no observed effect on cell proliferation or gene expression. Labeled cells maintain the ability to differentiate *in vitro* along adipogenic and osteogenic lineages, and terminally differentiated cells retain the QDs. QD-hMSCs can be delivered to myocardium *in vivo* and easily identified in histologic sections without immunostaining or effects from autofluorescence. After injecting QD-hMSCs into the rat ventricle *in vivo*, we have generated 3-D reconstructions of their complete distribution with single-cell resolution. Furthermore, we have tracked the fate of QD-hMSCs eight weeks after delivery to the canine heart on an extracellular matrix patch. QD-hMSCs were found to differentiate along an endothelial lineage, suggesting participation by these cells in vasculogenesis. We also identified expression of cardiac-specific markers in cells containing the QD label; in some cases, QD-hMSC-derived cells were found with morphologic hallmarks of mature cardiac myocytes, suggesting they can terminally differentiate into mature cardiac myocytes. In summary, this novel technique of stem cell labeling with QDs provides a robust method for tracking the location and fate of stem cells both *in vitro* and after delivery *in vivo*.

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