
Preface

Human hearts have a limited regenerative potential, motivating the development of the alternative treatment options for the conditions that result in the loss of beating cardiomyocytes. An example is myocardial infarction that results in a death of tens of millions of ventricular cardiomyocytes that cannot be replaced by the body. It is estimated that five to seven million patients live with myocardial infarction in North America alone. A majority of these patients do not need a surgical intervention, and medical management provides satisfactory results. However, over a period of 5 years, one-half of the patients who experience a myocardial infarction will develop heart failure, ultimately requiring heart transplantation.

The long-term goal of cardiac tissue engineering is to provide a living, beating, ideally autologous, and non-immunogenic myocardial patch that can restore the contractile function of the failing heart. The engineered tissues could also be used for preclinical drug testing to discover new targets for cardiac therapy and eliminate drugs, cardiac and noncardiac, with serious side effects. It generally involves a combination of suitable cell types, human or non-human cardiomyocytes and supporting cells, with an appropriate biomaterial made out of either synthetic or natural components and cultivation in an environment that reproduces some of the complexity of the native cardiac environment (e.g., electrical, mechanical stimulation, passive tension, or topographical cues).

This field is still young. The term cardiac tissue engineering usually refers to engineering of myocardial wall in vitro using living and beating cardiomyocytes. The pioneering papers appeared in the late 1990s, and they all utilized either neonatal rat cardiomyocytes or embryonic chick cardiomyocytes as a cell source. Since then, the field has matured significantly to include a range of approaches that all give cardiac tissues in vitro that are capable of developing contractile force and propagating electrical impulses. Advances in human embryonic stem cell research and induced pluripotent stem cell technology now provide the possibility of generating millions of bona fide human cardiomyocytes. When research in cardiac tissue engineering started some 25 years ago, the issue of a human cell source appeared insurmountable; however the researchers continued to make way, and there are many reports now on the use of human pluripotent stem cells as a source of cardiomyocytes for cardiac tissue engineering. Although early researchers thought that having purified cardiomyocytes in three-dimensional structures would be beneficial, based on analogies with monolayer studies where fibroblasts overgrow cardiomyocytes, there is a consensus in the field now that a mixed cell population is optimal for maintenance of cardiac phenotype and survival of cardiomyocytes in engineered tissues both in vitro and in vivo. The mixed population usually contains cardiomyocytes, endothelial cells, and a stromal cell type such as fibroblasts or mesenchymal stem cells. Also, there is a consensus that a form of physical stimulation, either mechanical or electrical, or passive tension is required for cardiomyocytes to achieve and maintain a differentiated phenotype and in vivo-like functional properties during in vitro cultivation.

This book gathers for the first time a collection of protocols on cardiac tissue engineering from pioneering and leading researchers around the globe. Protocols related to cell preparation, biomaterial preparation, cell seeding, and cultivation in various systems are provided.

Our goal is to enable adoption of these protocols in laboratories that are interested in entering the field as well as enable transfer of knowledge between laboratories that are already in this field. We hope that these efforts will lead to standardization, definition of best practices in cardiac tissue cultivation, and direct comparison of various production protocols using controlled in vivo studies that would ultimately lead to translational efforts. Although bio-material patches alone and hydrogels have been investigated in clinical studies focused on myocardial regeneration, a cardiac patch based on living, beating human cardiomyocytes has not yet been tested in humans. Only patches based on non-cardiomyocytes have been tested in humans with mixed results. Bringing a new therapy to the clinic is an overwhelming task, one that we must approach in a collaborative rather than competitive spirit. We hope that sharing of the best protocols in cardiac tissue engineering will enable this goal.

Toronto, ON, Canada
Medford, MA, USA

Milica Radisic
Lauren D. Black III, Ph.D.

Cardiac Tissue Engineering

Methods and Protocols

Radisic, M.; Black III, L.D. (Eds.)

2014, XII, 266 p. 77 illus., 60 illus. in color., Hardcover

ISBN: 978-1-4939-1046-5

A product of Humana Press