The greatest threat to the long-term health and well-being of people living with diabetes is cardiovascular disease. The diabetic population as a whole is two to four times more likely than non-diabetics to develop heart disease or suffer a stroke. Type 1 diabetes, which is most often diagnosed in childhood and adolescence, is particularly devastating, as one *New England Journal of Medicine* study associated it with a ten-fold increase in cardiovascular disease.

The human adult heart has about five billion heart cells, all pulsing as a coordinated orchestra with every heartbeat. These cells can be killed by high blood pressure, blood clots, heart attacks, and other byproducts of cardiovascular disease. The heart has an age-related block in its ability to make new heart cells, so that damaged cells are not replaced in the latter half of life, precisely when we need them the most. A typical patient with heart failure has lost over a billion heart cells.
Cardiac Stem Cell Therapy

Harvard Stem Cell Institute (HSCI) investigators are developing ways to make replacement heart cells and provide them with the right cues so that the new cells play as needed in the orchestra.

Heart Cell Regeneration

Both embryonic stem cells and induced pluripotent stem cells — mature cells that are manipulated back to a stem cell state — can be harnessed to create new heart cells.

The difficulty is that the heart cells made with stem cells resemble the heart cells of an infant, rather than adult heart cells. To function in adult hearts, the new heart cells must “mature” and then be able to survive within the constantly beating environment of the heart.

The scientific community has generated the technology to make heart cells that are immature, but very few heart cells derived from stem cells integrate into the normal heart tissue as mature heart cells. At the HSCI, our researchers are focused on understanding how to take these new heart cells all the way to maturity and stability, so they can be used as an effective therapy.

Rebuilding a Damaged Heart

HSCI scientists are also developing ways of using the body’s heart matrix — the rich, intricate scaffold of the heart that serves as the permanent home for our heart cells — to guide maturation and prolong the survival of heart cells derived from stem cells after implantation.

The heart matrix is like the sheet music for the heart orchestra. It tells the heart cells where to sit and how to function with their neighbors so that a heartbeat is in sync. The problem of redrawing these matrix-directed instructions from scratch once seemed too daunting to tackle.

By breaking down the heart’s scaffold material into thousands of individual chemicals, HSCI researchers hope to rebuild the environments that allow immature heart cells to mature. Armed with this knowledge, it will be possible to construct real adult heart tissue in the laboratory, as well as realistic approaches to transplanting patient-specific heart cells into their damaged organs.

Research Benefits

In addition to these ambitious projects, HSCI is pursuing interim objectives before reaching the ultimate goal of reconstructing the heart. For example, a recent study led to the identification of a blood circulating factor that declines with age but, when injected, can reverse age-related heart enlargement and accompanying heart failure. If this is successful in human studies, we will have identified a new therapeutic approach for the aging heart.

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