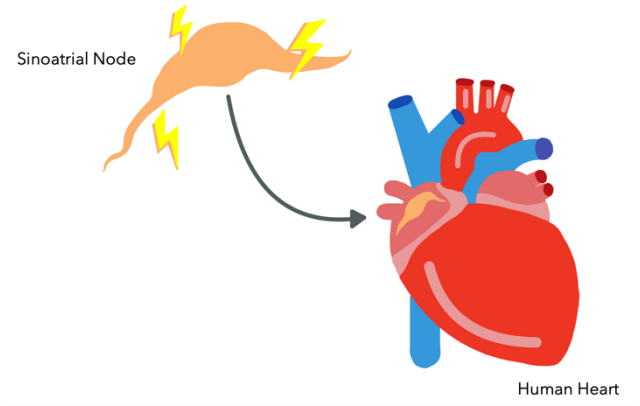
Heartfelt Innovation:
How Stem Cells Could Conduct Our Hearts' Future

By Kaitlin Van Brusselen

Have you ever found yourself captivated by the beautiful music of an orchestra and wondered, "Who is that individual gracefully waving a baton at the front of the stage?" That's the conductor! The conductor sets the pace and rhythm of the orchestra and works to create a beautiful harmony through a coordinated performance. As the conductor waves their baton through the air, the musicians watch carefully to make sure they remain in sync with one another. Without the conductor, the musicians could easily get lost and fall off beat [1]. Just as the conductor sets the tempo and rhythm of their orchestra, the human heart has its own conductor that sets the rhythm of our entire cardiovascular system—the pacemaker.



The pacemaker, also called the sinoatrial node (SA node), is a mass of heart tissue in the upper right quadrant of the heart. From this location, the SA node produces electrical impulses that travel to other chambers of the heart to elicit coordinated muscle contractions. These muscle contractions create your heartbeat. With each heartbeat, freshly oxygenated blood that flows into the heart from the lungs is immediately ejected to the rest of the body. Without the electrical impulses created by the SA node we would have no heartbeat, and our body would not get the oxygen-rich blood it needs to survive. Since survival is on the line, when the SA node begins to malfunction, immediate intervention is usually required [2, 3]. In most cases, the intervention for a misfunctioning SA node is an electronic pacemaker.

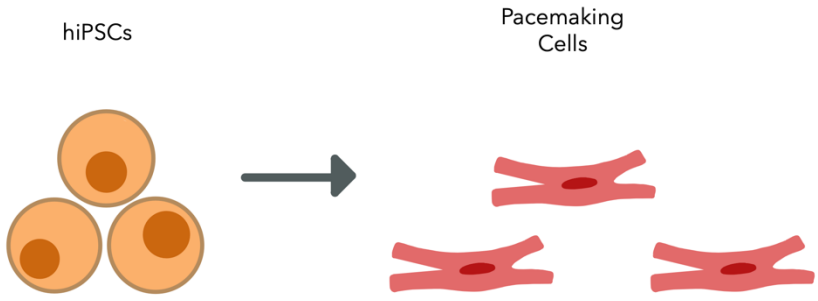
An electronic pacemaker is a small, battery powered device that has wires connecting to the chambers of the heart. The electronic pacemaker does exactly what it sounds like—it helps set the pace of the heart! The device gets implanted under the skin near the heart where it detects the natural heart rate. When the pacemaker detects an irregular heartbeat, it sends electrical signals to correct the rhythm of the heart. If an individual is suffering from an irregular heartbeat or heart failure, this device can help correct it [4].

Although the electronic pacemaker is without question a groundbreaking invention, there are still several associated risks and drawbacks, including blood clots, infection, and collapsed lungs. With this list of harmful side effects, you may be wondering why these devices are still commonly used, and why there is no potential alternative yet. After all, over one million cardiac pacemakers are implanted annually [5]! Luckily, scientists are working towards developing a new, promising alternative that overcomes these risks posed by an electronic pacemaker.

Stem cell biologists are currently conducting research into a biological pacemaker (bio-pacemaker). While that may sound fancy and complex, it is simply a pacemaker composed of biological tissue rather than electronic parts. The bio-pacemaker is intended to mimic the natural SA node in the human body. Rather than implanting an electronic device into a patient, we could potentially implant a pacemaker composed of real, living cells [6]! This is definitely an amazing concept…and you may find the science behind it even more fascinating.

The current approach to developing a bio-pacemaker focuses on the use of stem cells. Stem cells are a unique group of cells that are "unspecialized" and can divide indefinitely to produce more cells. "Unspecialized" means that these cells don't have any specialized function (like pacemaker cells' function of setting the rhythm of the heart); instead, stem cells' only function is to divide and give rise to specialized cells. In fact, there are some stem cells that can develop into any cell type in the body [7]! This begs the question, what if we could harness this ability to direct these unspecialized cells to form any cell type we desire? Believe it or not, we can do just that!

To further study and use these exceptional cells, researchers have developed human induced pluripotent stem cells (hiPSCs.) hiPSCs are a type of stem cell generated from living, human cells (usually skin cells) by re-programming them into a stem-cell like state through small molecule treatments.



One of the most amazing aspects of hiPSCs is they can be generated using skin cells from the patient, so that any cells created from the hiPSCs will be genetically identical to the patient, therefore eliminating the chance of post-implantation rejection [8, 9, 10]. The "pluripotent" in hiPSC simply means they can

become any type of cell in the human body; so, once you have generated hiPSCs you can, in theory, induce them to form any cell type of your choosing [11]!

To create a biological pacemaker, the goal is to turn hiPSCs into pacemaking cells. As I write this, scientists are working hard to optimize a protocol using small molecule treatments to guide the differentiation of hiPSCs into pacemaking cells. Incredibly, scientists have already successfully converted hiPSCs into pacemaking cells—they just need to modify the protocol to improve the yield of pacemaking cells produced [6]. Increasing yield is actually a lot harder than it sounds—but we're getting closer to the reality of a bio-pacemaker every day!

Bio-pacemakers represent an amazing advancement that would eliminate the need for electronic pacemakers and their associated risks. A genetically matched personalized conductor for the heart, bio-pacemakers will eventually allow millions of hearts to continue to produce their sweet, synchronized songs.

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