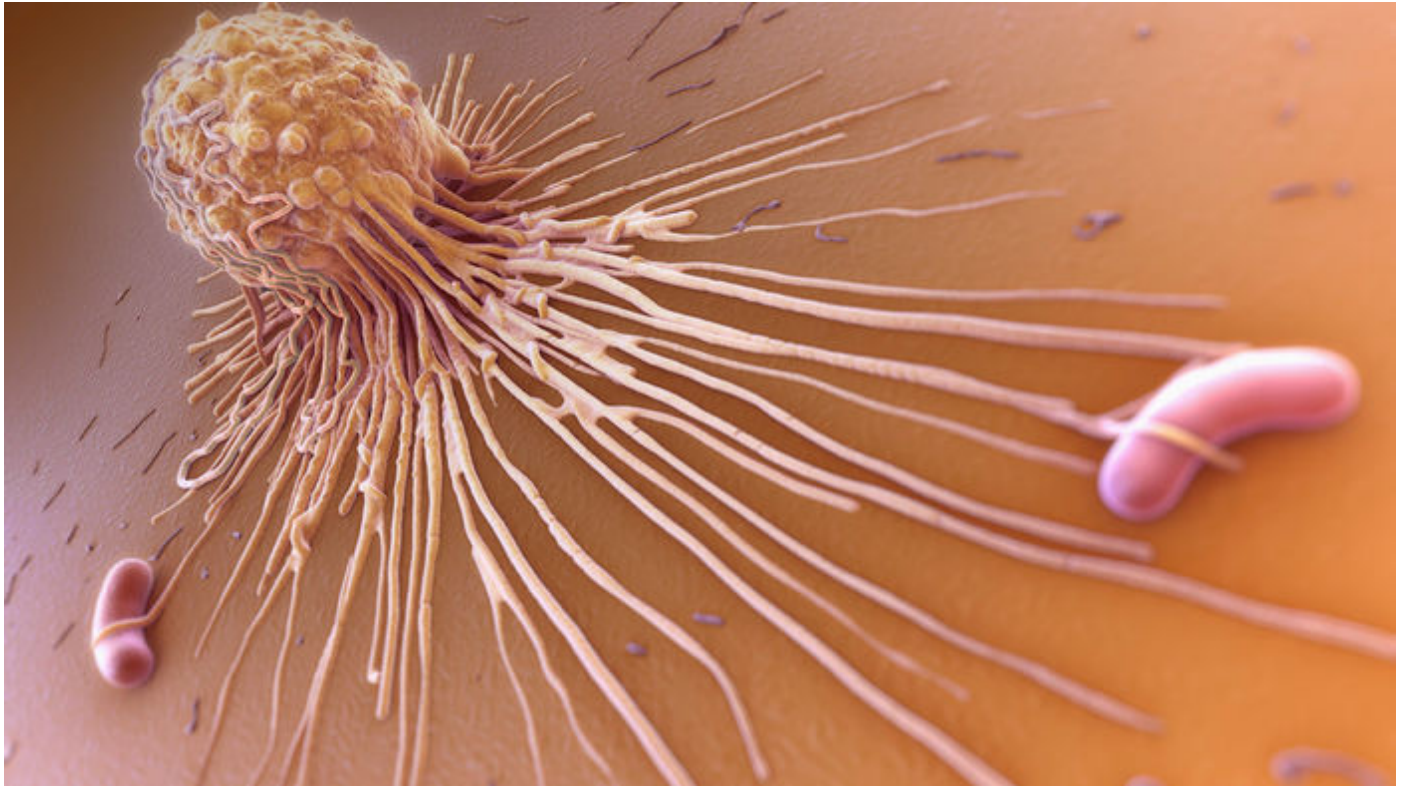


Immune cells unexpectedly help the heart keep its beat

By [Mitch Leslie](#) Apr. 20, 2017 , 12:00 PM



This macrophage is busy capturing bacteria, but its relatives may be helping your heart beat.

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The immune cells known as macrophages have a long to-do list in our bodies. They defend us from bacteria, coax wounds to heal, and perform other vital tasks. A surprising new study suggests they are also essential for the heart to beat normally. That could make macrophages prime targets for treating conditions like arrhythmias, in which the heart beats erratically.

“It’s a very careful study all the way through,” says cardiac electrophysiologist Douglas Zipes of the Indiana University School of Medicine in Indianapolis, who wasn’t connected to the research. Macrophages “are clearly playing an

important role” in the heart, he says.

A heartbeat begins when the organ’s pacemaker, a structure called the sinoatrial node, fires off an electrical impulse that disperses across the atria, the blood-collecting chambers. But to reach the ventricles, the heart’s pumping chambers, the signal needs a little help. Another structure, the atrioventricular (AV) node, relays the impulse to the ventricles, allowing them to contract. Macrophages, researchers assumed, weren’t involved.

However, the cells are prevalent in the heart, and cell biologist Matthias Nahrendorf of Harvard Medical School in Boston and colleagues wanted to determine what they did. When the team began examining mice that lacked macrophages, a technician noticed that the electrical rhythms of the animals’ hearts were abnormal. Nahrendorf says the rodents appeared to have an AV block, in which the AV node doesn’t forward the atrial signal to the ventricles.

The researchers then discovered that macrophages were common in AV nodes from mouse and human hearts. The AV node also contains many heart muscle cells that can transmit the “contract now” signal. When the researchers grew macrophages and heart muscle cells together in culture dishes, they found that the two types of cells were connected physically and synchronized electrically. Because of these interactions, macrophages made it easier for their muscular neighbors to fire, the group reports today in *Cell*.

But do macrophages have the same impact in a beating heart? To find out, the scientists studied the isolated hearts of genetically modified mice whose macrophages respond to light. The cells’ electrical charge becomes more positive, which in turn promotes firing by neighboring heart muscle cells. After spurring the animals’ hearts to beat faster with an electrical stimulus, the team used a fiber optic cable to illuminate the organ, thus prodding the macrophages. Because the heart is contracting rapidly in these experiments,

it occasionally misses a beat when the AV node fails to relay the contraction signal to the ventricles. [Fewer of these missed beats occurred in hearts whose macrophages had been stimulated by light](#), the researchers discovered. “If the light is switched on, the AV node functions better,” Nahrendorf says.

The researchers found that the AV node was also faulty in two other groups of genetically modified mice, which are missing the protein that links macrophages to heart muscle cells or that kill off their macrophages. “The net effect is that macrophages make conduction more reliable” Nahrendorf says.

For scientists studying AV node biology, “this paper really puts macrophages on the map,” says molecular and developmental biologist Vincent Christoffels of the University of Amsterdam in the Netherlands. But he notes that previous studies have implicated other non–heart muscle cells, such as fibroblasts, in the AV node’s operation. “So now we need to know how big [macrophages’] contribution is compared to other cells.”

Why the AV node needs assistance from macrophages, when the heart muscle cells it harbors conduct electrical impulses perfectly well, remains unclear, Nahrendorf says. Whatever the reason, the results raise the question of whether macrophages deserve some of the blame for conditions in which the heart rhythm is abnormal. If they do, researchers might be able to restore the heartbeat to normal by, for example, dosing macrophages with drugs that alter their behavior. Some of these drugs are already in clinical trials.

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