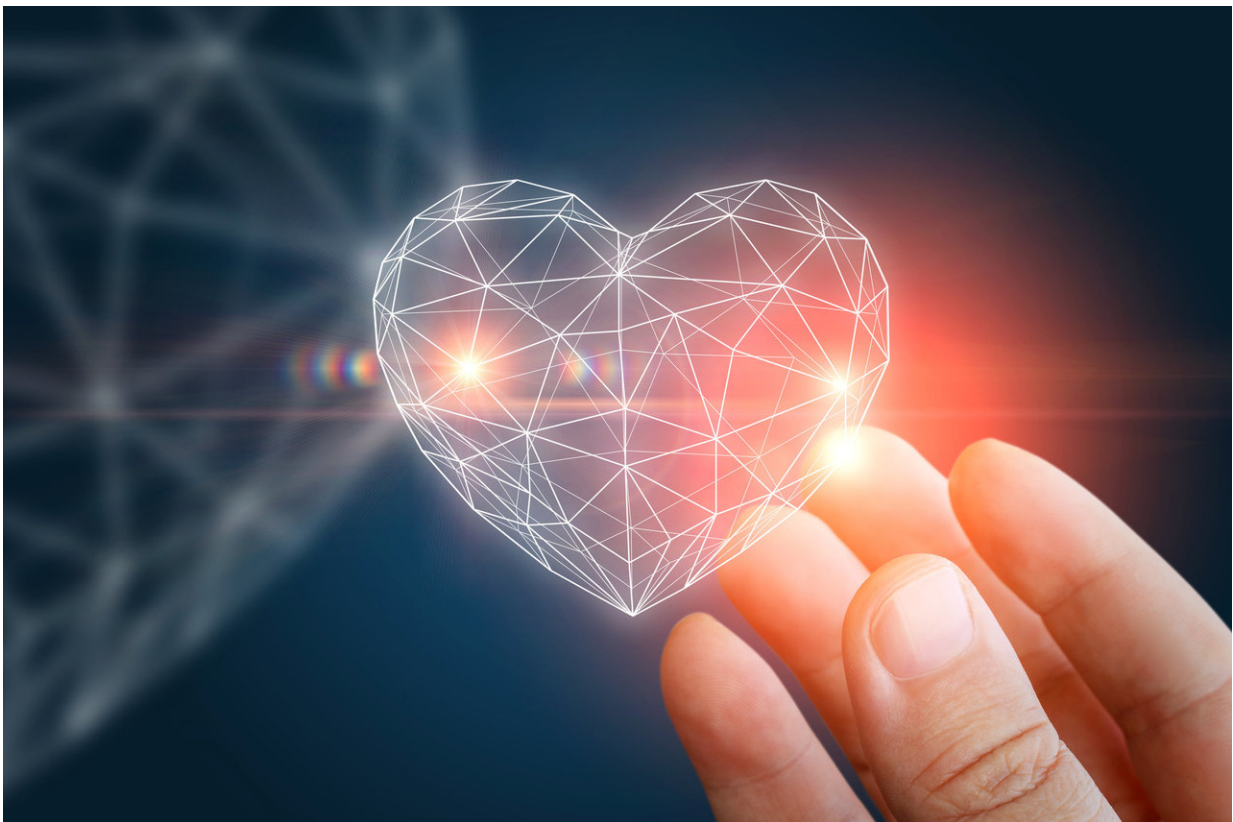


# RNA molecules predict adverse heart growth and function that can lead to atrial fibrillation

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Researchers have identified that enlargement of the left atrium of the heart is linked to abnormal activity of molecules that are associated with adverse changes in the heart's size, shape, structure, and function -- conditions that can lead to atrial fibrillation and death. Credit: Intermountain Medical Center Heart Institute.

Researchers have identified that enlargement of the left atrium of the heart is linked to abnormal activity of molecules that are associated with adverse changes in the heart's size, shape, structure, and function—conditions that can lead to atrial fibrillation and death.

The new study, conducted by researchers at the Intermountain Medical Center Heart Institute in Salt Lake City, is the first time this association has been connected to the human heart in a clinical setting.

In conducting the study, researchers noted that under stress conditions, cardiac fibroblasts, which play a role in normal cardiac function and changes in the heart, release greater quantities of exosomes, which are small pieces of cells circulating in the blood that contain cellular components and convey information to distant tissues.

The Intermountain Medical Center Heart Institute researchers found that in patients with [atrial fibrillation](#), exosomes and plasma are enriched with MicroRNA (miR)-21-3p—which is associated to abnormal enlargement of the heart muscle.

Scientists are interested in exosomes because initially they were thought to be a waste by-product as cells shed. But now researchers are learning that not only are exosomes communicators between cells, but they influence the spread of proteins, lipids, mRNA, miRNA, and DNA and are contributing factors in the development of several diseases.

"Our study gives us a better understanding of the process of how atrial fibrillation begins and advances," says Victoria Jacobs, NP, Ph.D., a member of the Intermountain Medical Center Heart Institute research team. "Once atrial fibrillation happens, we have some 'band-aids' to fix its symptoms, but we want to learn how to keep atrial fibrillation and atrial enlargement from happening in the first place."

Researchers will present results of the study at the Heart Rhythm Society's 39th annual Scientific Sessions in Boston on May 11.

While an enlarged atria may have several causes, recent studies have linked enlargement to an increased risk of atrial fibrillation. Researchers are interested in learning more about atrial fibrillation because it, along with coronary artery disease, is the number one killer of people in America. Atrial fibrillation affects more than 3.4 million Americans, primarily older adults.

Atrial fibrillation is the most common arrhythmia and is characterized by a rapid and irregular heartbeat caused when the top chambers of the heart atria quiver erratically, sometimes faster than 200 times per minute. The condition can have a significant negative impact on an individual's quality of life, causing heart palpitations, chronic fatigue, debilitating pain, and a five-fold increase in the risk of stroke.

An enlarged left atrium has been linked to atrial fibrillation, as it can prevent the heart from pumping blood properly and may increase risk of an irregular heartbeat.

Researchers at the Intermountain Medical Center Heart Institute examined biomarkers, which are biological molecules used to see how well the body responds to a treatment for a disease or condition, that could specifically predict the occurrence and severity of adverse growth in the left atrium of the heart. A basic study previously done in Germany that focused on cell cultures and small lab rodents suggested that miR-21-3p played a role in that growth. But no one has connected it to the human heart in a clinical setting until now.

"We know patients with atrial fibrillation develop thickening of [heart](#) tissue, or fibrosis," said Dr. Jacobs. "As atrial fibrillation progresses, we know there's more fibrosis in the left atrium. But this is the first time

we've shown miR-21-3p is associated with left atrial fibrillation in patients."

The researchers examined samples from 145 patients with atrial fibrillation—65% with paroxysmal atrial fibrillation, which is episodic, and 34.5% with persistent/permanent atrial fibrillation, which lasts and has different types of severity.

After researchers adjusted for age, gender, race, and atrial fibrillation subtype, miR-21-3p levels were significantly higher in the group with moderate and severe left atrial enlargement compared to the group with a normal or mildly enlarged left atrium. Blood pressure medications weren't associated with lower miR-21-3p levels nor with smaller atrium sizes.

Samples came from the Intermountain Medical Center Heart Institute's extensive bio bank, which contains a large amount of biological and medical data that's collected by taking a small amount of blood from consenting patients, then banking those samples for future research. For the study, researchers used very small amounts of plasma from the bio bank. Because microRNAs are so small and stable, they can be detected in circulating biological fluids like saliva and blood.

"We selected a group of patients based on the size of their [left atrium](#) and whether they were taking any medications," said Oxana Galenko, Ph.D., clinical research senior scientist at the Intermountain Medical Center Heart Institute. "What we found was pretty astonishing. MiR-21-3p was believed to be a by-product. No one thought the molecule had biological activity."

Because of the association of circulating levels of miR-21-3p and adverse left atrial size in atrial fibrillation patients, researchers can now direct their efforts to seeing if, or which, medications are effective in

blocking the development of left atrial enlargement.

"If we can link miR-12-3p to left atrial enlargement in patients with atrial fibrillation, we'll be able to target the medications that can best help patients," said Dr. Galenko. "Our goal is to find better, more precise, affordable, accessible ways that will help us take care of patients."

Further studies of miR-21-3p levels as a biomarker for selection and response to antiarrhythmic approaches are needed. The research team will now take the information they've collected and conduct a larger study.

"Medicine is undergoing changes and starting to realize biomarkers provide very insightful information when we look at diseases," said Dr. Jacobs. "MiR-21-3p could be a biomarker of left atrial [fibrillation](#), but it will require verification and more studies. This has also given us an idea to look further to see if there are medicines that can block the process and development of left atrial enlargement."

Provided by Intermountain Medical Center

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