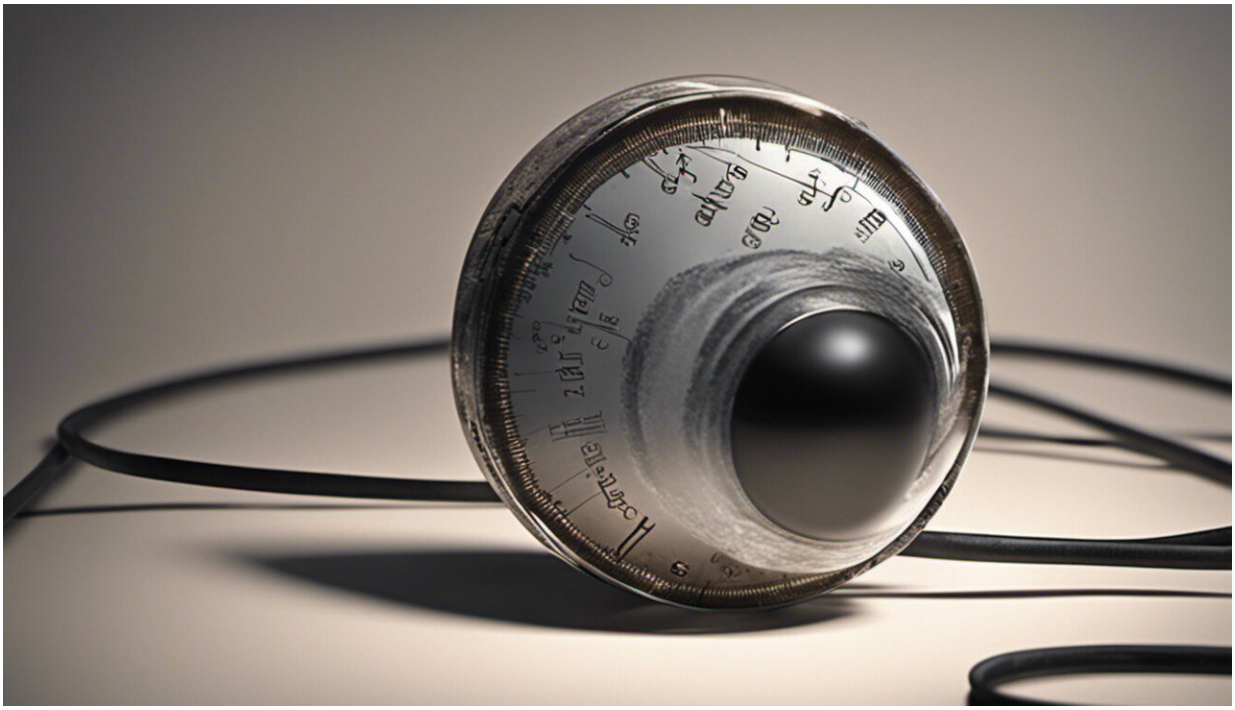
First of our three billion heartbeats is sooner than we thought

October 11 2016



Credit: AI-generated image (disclaimer)

When does our heart first start to beat? Until now, researchers thought that the first time our heart muscle contracted to beat was at eight days after conception in mice, which equates to around day 21 of a human pregnancy.

Now, a team funded by the British Heart Foundation (BHF) at the University of Oxford has demonstrated earlier beating of the heart in mouse embryos which, if extrapolated to the human heart, suggests beating as early as 16 days after conception.

In the study, published in the journal *eLife*, researchers looked at the developing mouse heart and found that the muscle started to contract as soon as it formed the cardiac crescent – an early stage in heart development. In mice, this crescent forms 7.5 days after conception, which is equivalent to day 16 in the human embryo. Previously, it was thought that the heart started to contract a stage later, when the heart appears as a linear tube.

Congenital heart disease is diagnosed in at least one in 180 births, which equates to around 4,000 each year – or 12 babies every day – in the UK. The researchers ultimately hope that by understanding more about how the heart forms in the womb, they will one day be able to prevent heart conditions that arise as a foetus develops.

By adding fluorescent markers to calcium molecules within the mouse embryo, the team was able to see at exactly which point in time the calcium tells our heart muscle cells to contract and then become coordinated enough to produce a heartbeat.

The team also found that this initiation of beating was essential for the heart to develop properly at an early stage and that a protein called NCX1 plays a key role in the generation of the calcium signals needed to produce the beating action of the heart.

The heart is the first organ to form during pregnancy and is critical in providing oxygen and nutrients to the developing embryo. The process of heart development is highly conserved between mammalian species, meaning that these findings may add considerably to our understanding

of how the human heart develops.

BHF Professor Paul Riley, who led the research at the University of Oxford's Department of Physiology, Anatomy and Genetics, said: "We are trying to better understand how the heart develops, and ultimately what causes the heart defects that develop in the womb before birth and to extrapolate to adult heart repair.

"By finding out how the heart first starts to beat and how problems can arise in heart development, we are one step closer to being able to prevent heart conditions from arising during pregnancy.

"We also hope that this new research will help us learn how the beating of new heart muscle cells might be triggered in replaced muscle after a heart attack."

Professor Riley and his team also hope that these findings will bring them closer to being able to repair damaged muscle after a heart attack.

One of the main difficulties with repairing the heart is that the new cells need to connect and synchronise their beating with the existing tissue. Just like making origami, without having the right set of instructions it becomes much more difficult to make a heart, or even parts of the heart, with the right form and function.

By finding out how and when the heart first starts to beat, the team has uncovered some of the 'instructions' that may help them transform stem cells into fully functional cardiac cells in the lab.

Professor Sir Nilesh Samani, Medical Director at the British Heart Foundation, said: "This study describes some of the very first stages in the development of a beating heart, identifies some of the key molecules involved and shows that the initiation of the beat itself has a bearing on

the further development of the heart.

"Such fundamental research is vital in understanding and ultimately preventing diseases that affect the heart."

More information: Richard CV Tyser et al. Calcium handling precedes cardiac differentiation to initiate the first heartbeat, *eLife* (2016). DOI: 10.7554/eLife.17113

Provided by University of Oxford