

Testing for 'zombie' cells could boost number of hearts for transplant

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Testing older potential organ donors for dangerous "zombie" cells could help to increase the number of hearts available for transplant, according to research presented at the <u>British Cardiovascular Society conference in Manchester</u>.



Currently, hearts from donors aged over 65 are not accepted for donation due to the likelihood of a poor clinical outcome. However, our hearts age at different rates and age isn't necessarily the best indicator of heart health.

Researchers from Newcastle University are working to develop a test which may help clinicians determine quickly whether a <u>donor heart</u> may still be suitable for <u>transplant</u>. With around 320 people currently waiting for a lifesaving heart transplant, it is hoped this new test would help to increase the number of hearts available and allow more people to get the transplant they desperately need.

The research has shown that people with <u>heart disease</u> have more senescent—or zombie—cells than those without, after they found higher levels of zombie cell markers in their blood.

Zombie cells arent dead, but they dont work as they should. They release molecules which can impact neighboring cells, turning these into zombie cells too. They also increase the amount of inflammation and cause scar tissue to form in the heart muscle. This raises the risk of developing heart and circulatory diseases.

The team now want to find out more about the "signature" that zombie cells leave in the blood and what that signature tells them about the biological as opposed to the chronical age of the heart. They think that a blood test to look for this signature in older potential donors could reveal those who have biologically young, healthy hearts that might be suitable for transplant.

Dr. Gavin Richardson, Senior lecturer and lead of the Vascular Medicine and Biology Theme at Newcastle University, is leading the research. He said, "Our work is revealing more about the clues that zombie cells leave to suggest their presence in the body. We are confident that we will be



able to use these clues to better understand which hearts from noneligible donors might be able to be used after all.

"This could be a game changer—as currently most hearts from older donors are not used for transplant, but the hope is we will be able to show that a number of these organs are suitable for transplant for people desperately waiting for a new heart."

When they looked at human heart cells in a dish, the researchers saw that the zombie cells secrete higher levels of protein called GDF15 compared to healthy cells.

Using <u>blood samples</u> from 774 people aged over 85, the researchers then found higher levels of the GDF15 protein in the blood of people with heart disease than people without—suggesting that their hearts contain more zombie cells.

The increase in GDF15 levels in the blood of people with heart disease was similar to that of another protein that is already used to diagnose heart failure—which made the researchers confident that they would be able to identify the cells associated with senescence.

The team also looked at the RNA in cells from eight donor hearts. RNA—short for <u>ribonucleic acid</u>—is similar to DNA and tells cells which proteins to make depending on the genes that are turned on. When researchers looked at another marker in these hearts linked to zombie <u>cells</u>—called p21—they found a strong link between this and another marker of heart and circulatory diseases.

The researchers believe these two molecules will form part of the zombie cell signature that could be detected through a tissue or blood tests. They're now using <u>blood</u> and tissue samples from the Quality in Organ Donation biobank and NHS Blood and Transplant to look for this



signature and find out whether it's linked to better transplant outcomes.

Professor James Leiper, associate medical director at the British Heart Foundation, said, "We are facing a <u>heart failure</u> epidemic with nearly one million people in the U.K. living with this condition—and for a small but significant number of these people the only cure we can offer is a <u>heart</u> transplant.

"We urgently need more hearts available for transplant, so it is very encouraging to hear about the work Dr. Richardson and his colleagues are doing to help meet this demand."

Derek Manas, medical director for transplantation, at NHS Blood and Transplant said, "With the need for organ donation and transplantation to happen quickly, it is helpful to explore the ways that new technologies and tests can help us assess the suitability of organs for transplant. For many reasons, hearts from donors of any age are often not suitable for transplant, so we are keen to support any research which may help us increase the number of hearts suitable for transplantation, save more lives and improve outcomes for those who are waiting."

Provided by British Heart Foundation

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