Human embryonic stem cell secretions minimized tissue injury after heart attack

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A novel way to improve survival and recovery rate after a heart attack was reported in the journal *Stem Cell Research* by scientists at Singapore's Institute of Medical Biology (IMB) and Bioprocessing Technology Institute (BTI) and The Netherlands' University Medical Center Utrecht.

This method, developed in laboratory research with pigs, is the first non-cell based therapeutic application of human embryonic stem cells (hESCs). It entails using secretions from stem cells.

In their studies with pigs, the researchers found that the administration of secretion from stem cells minimized heart injury by enhancing reperfusion therapy (angioplasty and cardiac bypass surgery) and reducing tissue death by another 60%.

Heart function was also markedly improved, the scientists report in the paper, published in the June 2008 issue of the journal.

By demonstrating the efficacy of this secretion in an experimental pig model, currently the best approximation to a human heart attack patient undergoing reperfusion therapy, the researchers say that they have addressed the longstanding problem of reperfusion injury in the most clinically relevant experimental setting.

"Using secretion instead of cells allows us to circumvent many highly intractable problems such as tumour formation, immune compatibility,

cell viability, delivery, costs and timeliness," said IMB'S Dr Lim Sai Kiang, who leads the Singapore-The Netherlands collaboration.

Unlike the more common approach of directly administering stem cells for therapy, this new method carries negligible risk of tumour formation or rejection
by the body.

In the pig research model, this approach minimised heart injury after a heart attack, a particularly important consideration since the heart has a limited ability to regenerate.

The research was carried out on pigs because it is the closest animal approximation to the human heart in terms of size, structure and function.

The findings are especially important as they show that the new method can overcome the unwanted side effects of reperfusion, currently the best therapeutic option available to heart attack patients. Reperfusion is the restoration of blood flow to the oxygen-deprived heart after a heart attack.

"This is a major discovery of clinical significance. There are some problems and issues associated with the use of stem cells to treat heart attacks and blocked arteries in the heart, and with this new method, many of these issues are removed. Potentially, we may have an important way to treat heart attacks. More tests will need to be done and human trials planned," said advisor to the Singapore researchers, Lee Chuen-Neng, M.D., who heads National University Hospital of Singapore's Department of Cardiac, Thoracic and Vascular Surgery. He also is Chair of Surgery at the National University Health System.

This discovery is all the more significant because the therapy for

reperfusion injury remains an unmet need despite three decades of huge resource investment, thousands of research papers and hundreds of experimental protocols. This preclinical study had come amidst an international call to improve the translation of preclinical experimental therapies for reperfusion injury to clinical applications.

Heart attack or myocardial infarction (MI), occurs when blood flow to part of the heart is blocked, and the heart muscle is deprived of oxygen. If allowed to persist, prolonged oxygen deprivation causes cell death and irreversible loss of heart function, and inevitably progresses to heart failure and death. To minimise heart muscle damage and preserve the pumping action of the heart after a MI, early reperfusion by standard medical treatments such as angioplasty (commonly known as "ballooning") or bypass surgery is carried out in the hospital. Despite this, most MI patients suffer additional irreversible cardiac muscle cell loss, ironically as a result of these treatments— a condition known as reperfusion injury.

As Singapore moves from basic science towards translational studies in the next phase of its biomedical push, rigorous preclinical testing and carefully designed studies such as this project would be most critical in ensuring the success of clinical trials.

Professor Birgit Lane, IMB's Executive Director, said, "This is a very exciting result from Dr. Lim and her colleagues. It paves the way for improved recovery after heart attack -- a very practical outcome from stem cell research. It is a great example of what can be achieved when doctors and scientists work closely together. By sharing their specialist skills and knowledge, they can discover and refine new approaches to curing sick people. This targeting of research to find ways of combating illness and benefiting people faster is at the heart of what we aim to do at IMB."

Source: Agency for Science, Technology and Research (A*STAR), Singapore

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