Post-mortem stem cells for regenerative medicine

Cell-based therapies offer immense potential for the treatment of a variety of diseases. Adipose-derived mesenchymal stem cells (ASCs) are abundant in adipose tissue. This is a rapidly expanding area of research and in the future, there may be a need for an alternative source of such cells in addition to live donors. Dr Takashi Saito and colleagues at Osaka Medical and Pharmaceutical University, Japan, demonstrate that post-mortem ASCs can be harvested and maintain their ability to proliferate for up to seven days, thus offering a potential alternative source of ASCs in cell-based therapy.

Regenerative medicine refers to therapies that restore and heal tissues and organs that are diseased or damaged due to trauma. Studies reveal the potential of regenerative medicine in the treatment of wounds, some cancers, and cardiovascular diseases, to name but a few. Immunomodulation is the change to immune system functioning by various compounds including cells. Introducing cells can lead to indirect effects and can induce a therapeutic response. An example is mesenchymal stem cells which are being explored for use in cardiac tissue regeneration, multiple sclerosis, and brain trauma. Stem cells are cells that can differentiate into several other types, thus offering vast therapeutic potential. Cell-based therapy is the use of live cells as a treatment. Various cell types can be used for different therapeutic indications and the cells used may be from the individual (autologous) or from a donor (allogeneic).

Many cell-based therapies are in the early stages of development, but this field is rapidly advancing. Shortages in the supply of therapeutic cells pose a challenge and there is ongoing interest in exploring ways to collect more cells derived from adult tissues. Dr Takashi Saito and colleagues at Osaka Medical and Pharmaceutical University, Japan, aimed to determine if adipose-derived mesenchymal stem cells (ASCs) can be from harvested post-mortem from cadavers. The researchers investigated the viability and proliferation potential of these cells. By doing so, they explore an alternative source of ASCs from cadavers which may be needed should future shortages arise due to increased cell-based therapy demand.

ADIPOSE-DERIVED MESENCHYMAL STEM CELLS

Mesenchymal stem cells derived from adipose tissue are called adipose-derived mesenchymal stem/stromal cells (ASCs). Laboratory studies have shown ASCs can differentiate into several mesodermal cell types such as adipocytes, chondrocytes, myoblasts, osteoblasts, as well as ectodermal and endodermal cell lines. In addition, these cells secrete cytokines, growth factors, and extracellular matrix molecules, all of which may be useful in regenerative medicine and in scenarios relating to wound healing, angiogenesis, and immunomodulation. As Saito explains, 'adipose tissue is a well-vascularised connective tissue comprising a population of ASCs. These cells are present in large numbers in adipose tissues and have anti-inflammatory and anti-fibrotic effects'.

Saito and colleagues demonstrate that postmortem ASCs have potential in cell-based therapy.

Research shows that ASCs have stronger inhibitory effects on natural killer cells CD4+ and CD8+ T cells than mesenchymal stem cells isolated from other tissues. Such anti-inflammatory properties as well as anti-fibrotic properties were demonstrated in recent research by Saito and colleagues. They explored whether ASCs can be activated to boost therapeutic effects. Their study combined human ASCs with low molecular weight heparin (hep-hASCs) and investigated its effects on ASC cellular function revealing the induction of ASC migration and proliferation. In addition, increased hepatocyte growth factor (needed for cell proliferation and survival) was noted and upregulation of immunomodulatory factors. Results confirmed the potential of hep-hASCs as a therapeutic tool in systemic lupus erythematosus (SLE), warranting further research.

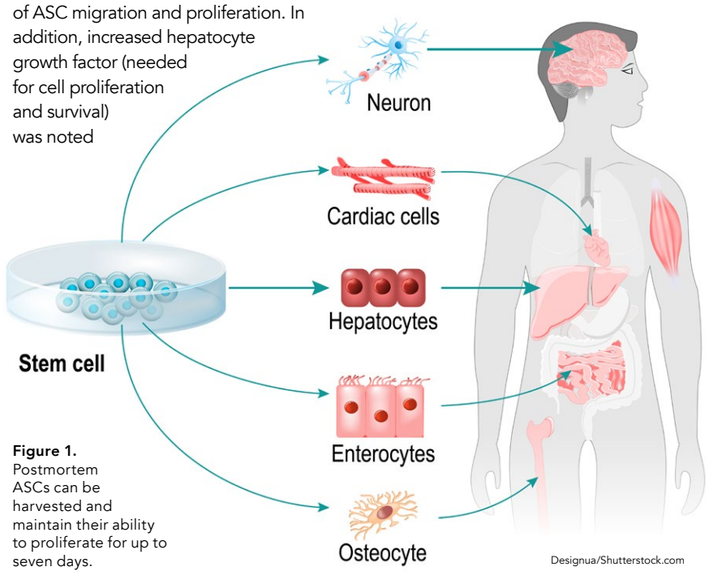

Figure 1. Postmortem ASCs can be harvested and maintain their ability to proliferate for up to seven days.

Stem cells can differentiate into several other types, thus offering vast therapeutic potential.

With extreme inflammation as a hallmark of many diseases, ASCs have significant therapeutic potential. Furthermore, ASCs are more abundant in number in adipose tissue compared to other tissues and thus easier to collect. These cells are typically collected from live individuals but have been shown to survive conditions with inadequate blood supply for a sustained period of time; therefore Saito is exploring the ability of these cells to survive and proliferate after death.

POST-MORTEM HARVESTED ADIPOSE-DERIVED MESENCHYMAL STEM CELLS

Post-mortem changes to blood flow result in insufficient supply of oxygen and nutrients, so tissue and organs cannot maintain their biological functions. However, some cells can survive for a brief period of time. One such cell type are stem cells which are currently used for regenerative therapy and forensic diagnostics.

Post-mortem stem cells have been used in transplants, but their cell viability and function deteriorate with time and studies have limited the timeframe to a maximum of three days post death. More information is needed on the quality of these stem cells after death to determine whether cells harvested post mortem are suitable for cell-based therapy use.

In a paper published in the *Journal of Forensic and Legal Medicine*, Saito studied ASC post-mortem collection and used cell-culture techniques to grow and expand these cells (culture expand) as well as investigate cell viability and proliferation. Furthermore, he determined the length of time before cell senescence (a cell's reduced potential for proliferation and differentiation). Human ASCs were derived from axillary adipose tissue (from the armpit) as this anatomical area is less susceptible to damage and autolysis than other tissues. The study analysed and compared human ASCs with those of mice, revealing that mice ASCs survived for a shorter period of time than human ASCs. Human ASCs were successfully collected and cultured from cadavers and these cells were shown to survive, adhere, and proliferate for up to seven days after death depending on the temperature and environment in which the cadavers were kept. In addition, the study showed that viable ASCs could be obtained from older individuals.

IMPLICATIONS FOR FUTURE ADIPOSE-DERIVED MESENCHYMAL STEM CELL THERAPY

This study indicates potential utility and application of ASCs cells harvested from post-mortem axilla adipose tissue for regenerative medicine and

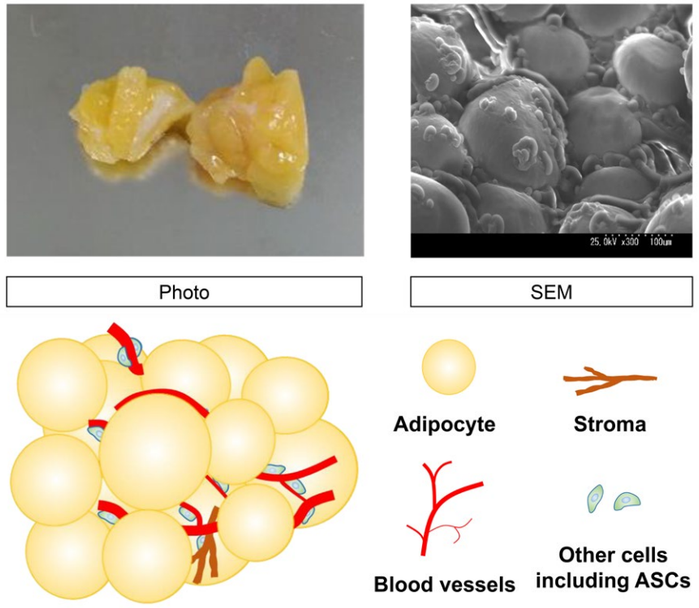

Figure 2. Adipose tissue is a well-vascularised connective tissue comprising a population of ASCs.

This study indicates potential utility and application of ASCs cells harvested from post-mortem axilla adipose tissue for regenerative medicine and forensic diagnostics.

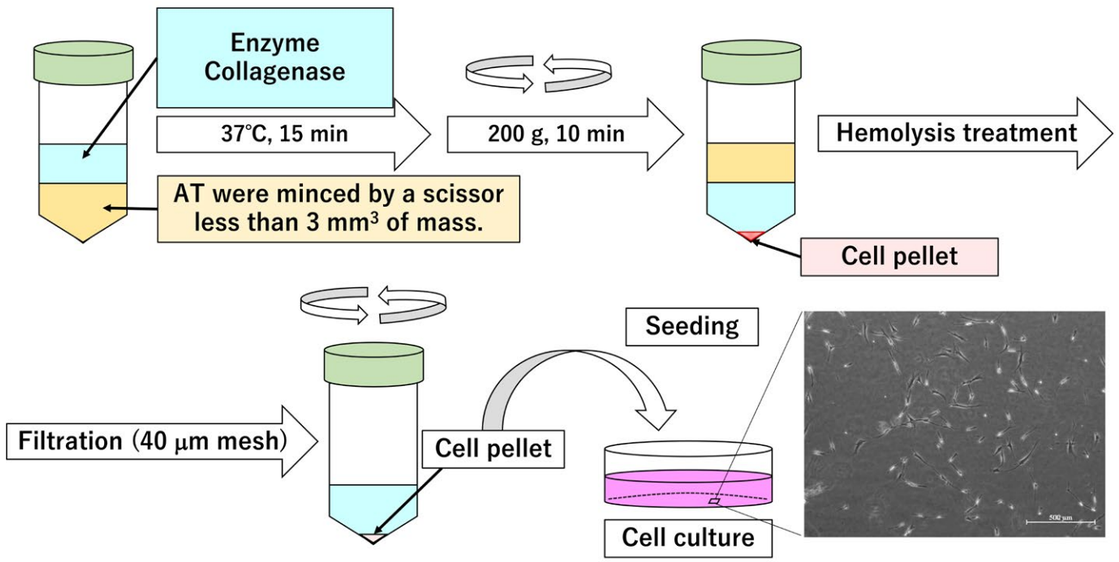

Figure 3. Enzymatic treatment and isolation of ASCs from human cadavers.

forensic diagnostics. Saito suggests that characterisation of ASCs could also help in ascertaining the time and cause of death. With proven anti-inflammatory and anti-fibrosis abilities, ASCs and such cell-based therapy has the potential to treat a variety of diseases. If this area of therapy expands and there are not enough live donors, then post-mortem ASCs may be of use with the team's research showing ASCs can be harvested days after death and maintain proliferative potential for up to seven days. Therefore, post-mortem ASCs may offer a viable and alternative stem cell source.

Saito also advises that cell banks of post-mortem ASCs could be established for stem cell transplantation from a donor to a recipient (allogeneic stem cell transplantations). However, further research is needed to optimise ASC isolation from post-mortem tissue and better characterise these cells to understand aspects such as localisation, surface antigen expression and their ability to secrete growth factors. This study has, however, demonstrated novel findings about the viability and function of post-mortem ASCs and provided a valuable indication of the future potential utility of these cells in regenerative therapy and forensic diagnostics.

Behind the Research

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Research Objectives

Takashi Saito's research investigates the control of inflammation in lesion sites using adipose-derived mesenchymal stem cells.

Detail

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Bio
Dr Takashi Saito received his PhD in engineering (Department of Biomaterials) from Kyoto University. He has been working as an assistant professor at Osaka Medical and Pharmaceutical University (formerly Osaka Medical College) from 2015 to present.

Funding
- JSPS KAKENHI, Grant-in-Aid for Young Scientists (B), PI, Grant Number 16K19303.
- JSPS KAKENHI, Grant-in-Aid for Young Scientists, PI, Grant Number 21K16312.

Collaborators
- Research colleagues who are co-authors of Dr Saito's research articles.
- Takuya Kotani, Division of Rheumatology, Department of Internal Medicine IV, Osaka Medical and Pharmaceutical University, Osaka, Japan.

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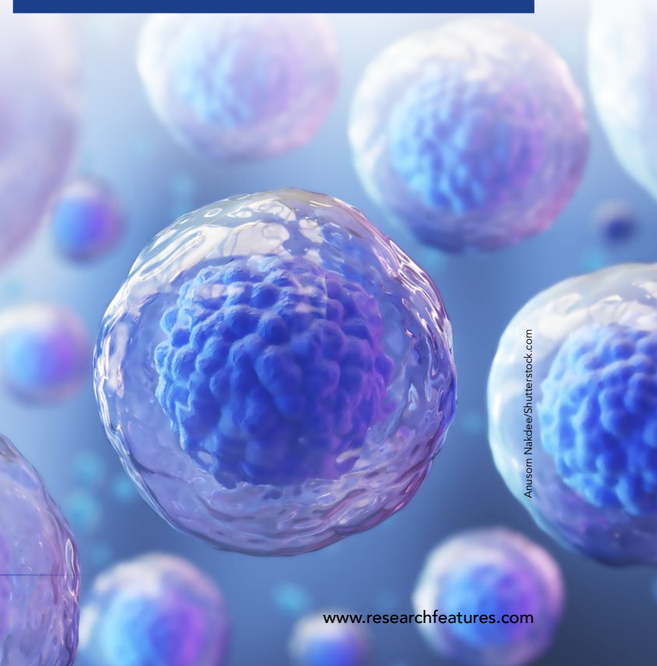
Osaka Medical and Pharmaceutical University

Personal Response

Are there plans to expand your work and investigate any other types of post-mortem stem cells?

"I will try to isolate other stem cells from post-mortem organs or tissues. I think proliferative stem cells derived from post-mortem organs or tissues can be applied to cell-based therapy. Other research groups have already successfully isolated and cultured human skeletal muscle stem cells from postmortem tissue (Latil et al, 2012)."



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