



STEM CELL THERAPY

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ABSTRACT

Stem cell therapy holds immense promise for the treatment of patients with diabetes mellitus. Research on the ability of human embryonic stem cells to differentiate into islet cells has defined the developmental stages and transcription factors involved in this process. However, the clinical applications of human embryonic stem cells are limited by ethical concerns, as well as the potential for teratoma formation. As a consequence, alternative forms of stem cell therapies, such as induced pluripotent stem cells, umbilical cord stem cells and bone marrow-derived mesenchymal stem cells, have become an area of intense study. Recent advances in stem cell therapy may turn this into a realistic treatment for diabetes in the near future.

KEYWORDS: human embryonic stem cells, pluripotent stem cells, umbilical cord stem cells and bone marrow-derived mesenchymal stem cells.

INTRODUCTION

Stem cells are biological cells found in all multicellular organisms, that can divide (through mitosis) and differentiate into diverse specialized cell types and can self-renew to produce more stem cells. In mammals, there are two broad types of stem cells: embryonic stem cells, which are isolated from the inner cell mass of blastocysts, and adult stem cells, which are found in various tissues. In adult organisms, stem cells and progenitor cells act as a repair system for the body, replenishing adult tissues. In a developing embryo, stem cells can differentiate into all the specialized cells (these are called pluripotent cells), but also maintain the normal turnover of regenerative organs, such as blood, skin, or intestinal tissues.^[1]

There are three accessible sources of autologous adult stem cells in humans.

Bone marrow, which requires extraction by *harvesting*, that is, drilling into bone (typically the femur or iliac crest), Adipose tissue (lipid cells), which requires extraction by liposuction, and Blood, which requires extraction through pheresis, wherein blood is drawn from the donor (similar to a blood donation), passed through a machine that extracts the stem cells and returns other portions of the blood to the donor.

Stem cells can also be taken from umbilical cord blood just after birth. Of all stem cell types, autologous harvesting involves the least risk. By definition, autologous cells are obtained from one's own body, just

as one may bank his or her own blood for elective surgical procedures.

Highly plastic adult stem cells are routinely used in medical therapies, for example in bone marrow transplantation. Stem cells can now be artificially grown and transformed (differentiated) into specialized cell types with characteristics consistent with cells of various tissues such as muscles or nerves through cell culture. Embryonic cell lines and autologous embryonic stem cells generated through therapeutic cloning have also been proposed as promising candidates for future therapies. Research into stem cells grew out of findings by Ernest A. McCulloch and James E. Till at the University of Toronto in the 1960s.

Amniotic fluid or liquor amnii is the nourishing and protecting liquid contained by the amniotic sac of a pregnant woman.

Recent studies show that amniotic fluid contains a considerable quantity of stem cells. These amniotic stem cells are multipotent and able to differentiate into various tissues, which may be useful for future human application. Some researchers, including Anthony Atala of Wake Forest University, a team from Harvard University, and Italian Paolo de Coppi, have found that amniotic fluid is also a plentiful source of non-embryonic stem cells. These cells have demonstrated the ability to differentiate into a number of different cell-types, including brain, liver and bone.

It is possible to conserve the stem cells extracted from amniotic fluid in private stem cells banks. Some private companies offer this service for a fee.

PROPERTIES

The classical definition of a stem cell requires that it possess two properties.

Self-renewal: the ability to go through numerous cycles of cell division while maintaining the undifferentiated state.

Potency: the capacity to differentiate into specialized cell types. In the strictest sense, this requires stem cells to be either totipotent or pluripotent—to be able to give rise to any mature cell type, although multipotent or unipotent progenitor cells are sometimes referred to as stem cells. Apart from this it is said that stem cell function is regulated in a feed back mechanism.

Self-Renewal

Two mechanisms to ensure that a stem cell population is maintained exist.

Obligatory asymmetric replication: a stem cell divides into one father cell that is identical to the original stem cell, and another daughter cell that is differentiated.

Stochastic differentiation: when one stem cell develops into two differentiated daughter cells, another stem cell

undergoes mitosis and produces two stem cells identical to the original.

Potency Definitions

Potency specifies the differentiation potential, the potential to differentiate into different cell types of the stem cell.

Totipotent (a.k.a. omnipotent) stem cells can differentiate into embryonic and extra embryonic cell types. Such cells can construct a complete, viable organism. These cells are produced from the fusion of an egg and sperm cell. Cells produced by the first few divisions of the fertilized egg are also totipotent.

Pluripotent stem cells are the descendants of totipotent cells and can differentiate into nearly all cells, i.e. cells derived from any of the three germ layers.

Multipotent stem cells can differentiate into a number of cells, but only those of a closely related family of cells.

Oligopotent stem cells can differentiate into only a few cells, such as lymphoid or myeloid stem cells.

Unipotent cells can produce only one cell type, their own, but have the property of self-renewal, which distinguishes them from non-stem cells (e.g., muscle stem cells).

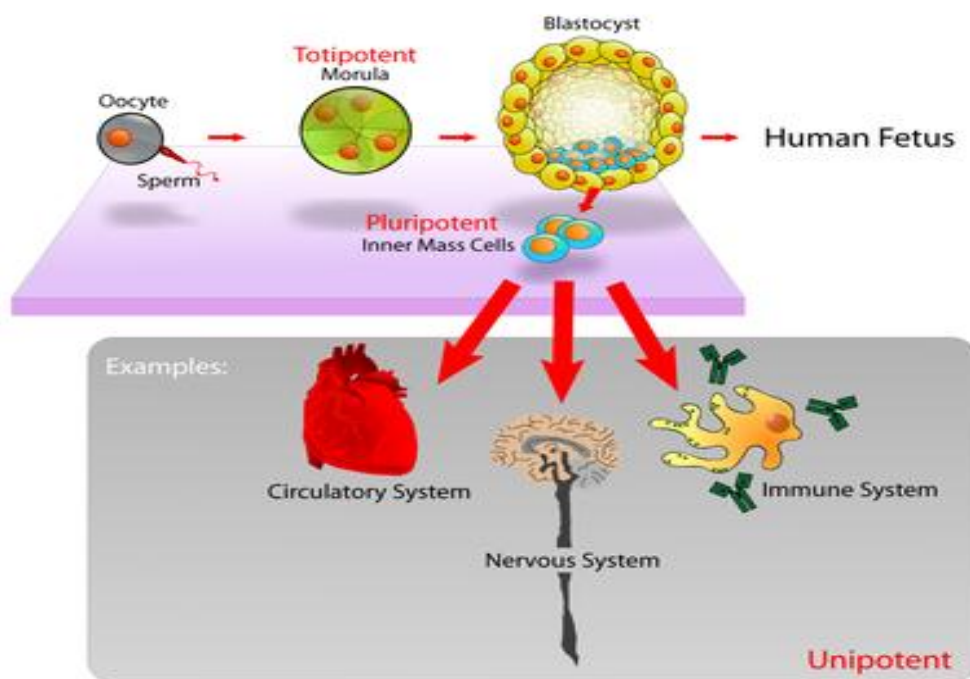


Fig.1 Potency

Unipotent

Pluripotent, embryonic stem cells originate as inner cell mass (ICM) cells within a blastocyst. These stem cells can become any tissue in the body, excluding a placenta.

Only cells from an earlier stage of the embryo, known as the morula, are totipotent, able to become all tissues in the body and the extraembryonic placenta.

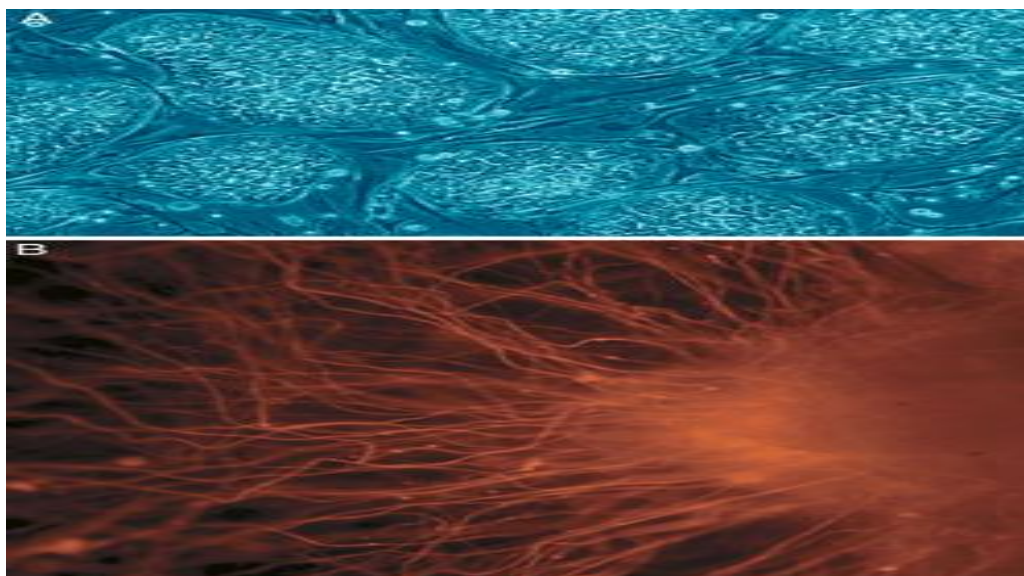


Fig 2: Human Embryonic Stem Cells.

A: Cell colonies that are not yet differentiated.

B: Nerve cell

Identification

The practical definition of a stem cell is the functional definition, a cell that has the potential to regenerate tissue over a lifetime. For example, the defining test for a bone marrow or hematopoietic stem cell (HSC) is the ability to transplant one cell and save an individual without HSCs. In this case, a stem cell must be able to produce new blood cells and immune cells over a long term, demonstrating potency. It should also be possible to isolate stem cells from the transplanted individual, which can themselves be transplanted into another individual without HSCs, demonstrating that the stem cell was able to self-renew.

Properties of stem cells can be illustrated *in vitro*, using methods such as clonogenic assays, in which single cells are assessed for their ability to differentiate and self-renew. Stem cells can also be isolated by their possession of a distinctive set of cell surface markers. However, *in vitro* culture conditions can alter the behavior of cells, making it unclear whether the cells will behave in a similar manner *in vivo*. There is considerable debate as to whether some proposed adult cell populations are truly stem cells.

TYPES OF STEM CELLS

Embryonic

Embryonic stem (ES) cell lines are cultures of cells derived from the epiblast tissue of the inner cell mass (ICM) of a blastocyst or earlier morula stage embryos. A blastocyst is an early stage embryo, approximately four to five days old in humans and consisting of 50–150 cells. ES cells are pluripotent and give rise during development to all derivatives of the three primary germ layers: ectoderm, endoderm and mesoderm. In other words, they can develop into each of the more than 200 cell types of the adult body when

given sufficient and necessary stimulation for a specific cell type. They do not contribute to the extra-embryonic membranes or the placenta. The endoderm is composed of the entire gut tube and the lungs, the ectoderm gives rise to the nervous system and skin, and the mesoderm gives rise to muscle, bone, blood—in essence, everything else that connects the endoderm to the ectoderm.

Nearly all research to date has made use of mouse embryonic stem cells (mES) or human embryonic stem cells (hES). Both have the essential stem cell characteristics, yet they require very different environments in order to maintain an undifferentiated state. Mouse ES cells are grown on a layer of gelatin as an extracellular matrix (for support) and require the presence of leukemia inhibitory factor (LIF). Human ES cells are grown on a feeder layer of mouse embryonic fibroblasts (MEFs) and require the presence of basic fibroblast growth factor (bFGF or FGF-2). Without optimal culture conditions or genetic manipulation, embryonic stem cells will rapidly differentiate.

A human embryonic stem cell is also defined by the expression of several transcription factors and cell surface proteins. The transcription factors Oct-4, Nanog, and Sox2 form the core regulatory network that ensures the suppression of genes that lead to differentiation and the maintenance of pluripotency. The cell surface antigens most commonly used to identify hES cells are the glycolipids stage specific embryonic antigen 3 and 4 and the keratan sulfate antigens Tra-1-60 and Tra-1-81. The molecular definition of a stem cell includes many more proteins and continues to be a topic of research.

There are currently no approved treatments using embryonic stem cells. The first human trial was approved

by the US Food and Drug Administration in January 2009. However, the human trial was not initiated until October 13, 2010 in Atlanta for spinal injury victims. On November 14, 2011 the company conducting the trial announced that it will discontinue further development of its stem cell programs. ES cells, being pluripotent cells, require specific signals for correct differentiation—if injected directly into another body, ES cells will differentiate into many different types of cells, causing a teratoma.

Differentiating ES cells into usable cells while avoiding transplant rejection are just a few of the hurdles that embryonic stem cell researchers still face. Many nations currently have moratoria on either ES cell research or the production of new ES cell lines. Because of their combined abilities of unlimited expansion and pluripotency, embryonic stem cells remain a theoretically potential source for regenerative medicine and tissue replacement after injury or disease.

Fetal

The primitive stem cells located in the organs of fetuses are referred to as fetal stem cells.

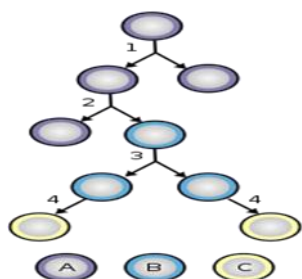


Fig.3 Primitive Stem Cells

Adult

Stem cell division and differentiation.

A: Stem cell;

B: Progenitor cell;

C: Differentiated cell;

1: Symmetric stem cell division;

2: Asymmetric stem cell division;

3: Progenitor division;

4: Terminal differentiation

Also known as somatic stem cells and germline stem cells, they can be found in children, as well as adults.

Pluripotent adult stem cells are rare and generally small in number but can be found in a number of tissues including umbilical cord blood. A great deal of adult stem cell research to date has had the aim of characterizing the capacity of the cells to divide or self-renew indefinitely and their differentiation potential. In mice, pluripotent stem cells are directly generated from adult fibroblast cultures. Unfortunately, many mice do not live long with stem cell organs.

Most adult stem cells are lineage-restricted (multipotent) and are generally referred to by their tissue origin (mesenchymal stem cell, adipose-derived stem cell, endothelial stem cell, dental pulp stem cell, etc.).

Adult stem cell treatments have been successfully used for many years to treat leukemia and related bone/blood cancers through bone marrow transplants. Adult stem cells are also used in veterinary medicine to treat tendon and ligament injuries in horses.

The use of adult stem cells in research and therapy is not as controversial as the use of embryonic stem cells, because the production of adult stem cells does not require the destruction of an embryo. Additionally, in instances where adult stem cells are obtained from the intended recipient, the risk of rejection is essentially non-existent. Consequently, more US government funding is being provided for adult stem cell research.

An extremely rich source for adult mesenchymal stem cells is the developing tooth bud of the mandibular third molar. The stem cells eventually form enamel (ectoderm), dentin, periodontal ligament, blood vessels, dental pulp, nervous tissues, and a minimum of 29 different end organs. Because of extreme ease in collection at 8–10 years of age before calcification and minimal to no morbidity, these will probably constitute a major source of cells for personal banking, research and current or future therapies. These stem cells have been shown capable of producing hepatocytes.

Amniotic

Multipotent stem cells are also found in amniotic fluid. These stem cells are very active, expand extensively without feeders and are not tumorigenic. Amniotic stem cells are multipotent and can differentiate in cells of adipogenic, osteogenic, myogenic, endothelial, hepatic and also neuronal lines. All over the world, universities and research institutes are studying amniotic fluid to discover all the qualities of amniotic stem cells, and scientists such as Anthony Atala and Giuseppe Simoni have discovered important results.

Use of stem cells from amniotic fluid overcomes the ethical objections to using human embryos as a source of cells. Roman Catholic teaching forbids the use of embryonic stem cells in experimentation; accordingly, the Vatican newspaper "Osservatore Romano" called amniotic stem cells "the future of medicine".

It is possible to collect amniotic stem cells for donors or for autologous use: the first US amniotic stem cells bank was opened in 2009 in Medford, MA, by Biocell Center Corporation and collaborates with various hospitals and universities all over the world.

Induced pluripotent

These are not adult stem cells, but rather adult cells (e.g. epithelial cells) reprogrammed to give rise to pluripotent capabilities. Using genetic reprogramming with

protein transcription factors, pluripotent stem cells equivalent to embryonic stem cells have been derived from human adult skin tissue. Shinya Yamanaka and his colleagues at Kyoto University used the transcription factors Oct3/4, Sox2, c-Myc, and Klf4 in their experiments on cells from human faces. Junying Yu, James Thomson, and their colleagues at the University of Wisconsin–Madison used a different set of factors, Oct4, Sox2, Nanog and Lin28, and carried out their experiments using cells from human foreskin. As a result of the success of these experiments, Ian Wilmut, who helped create the first cloned animal Dolly the Sheep, has announced that he will abandon somatic cell nuclear transfer as an avenue of research.

Frozen blood samples can be used as a source of induced pluripotent stem cells, opening a new avenue for obtaining the valued cells.

Lineage

To ensure self-renewal, stem cells undergo two types of cell division. Symmetric division gives rise to two identical daughter cells both endowed with stem cell properties. Asymmetric division, on the other hand, produces only one stem cell and a progenitor cell with limited self-renewal potential. Progenitors can go through several rounds of cell division before terminally differentiating into a mature cell. It is possible that the molecular distinction between symmetric and asymmetric divisions lies in differential segregation of cell membrane proteins (such as receptors) between the daughter cells.

An alternative theory is that stem cells remain undifferentiated due to environmental cues in their particular niche. Stem cells differentiate when they leave that niche or no longer receive those signals. Studies in *Drosophila* germlarium have identified the signals decapentaplegic and adherens junctions that prevent germlarium stem cells from differentiating.

Induced Pluripotent Stem Cell

The signals that lead to reprogramming of cells to an embryonic-like state are also being investigated. These signal pathways include several transcription factors including the oncogene c-Myc. Initial studies indicate that transformation of mice cells with a combination of these anti-differentiation signals can reverse differentiation and may allow adult cells to become pluripotent. However, the need to transform these cells with an oncogene may prevent the use of this approach in therapy.

Challenging the terminal nature of cellular differentiation and the integrity of lineage commitment, it was recently determined that the somatic expression of combined transcription factors can directly induce other defined somatic cell fates; researchers identified three neural-lineage-specific transcription factors that could directly convert mouse fibroblasts (skin cells) into fully

functional neurons. This "induced neurons" (iN) cell research inspires the researchers to induce other cell types implies that all cells are totipotent: with the proper tools, all cells may form all kinds of tissue.

CONTROVERSY SURROUNDING THE USE OF STEM CELLS

Embryonic stem cells and embryonic stem cell lines have received much public attention concerning the ethics of their use or non-use. Clearly, there is hope that a large number of treatment advances could occur as a result of growing and differentiating these embryonic stem cells in the laboratory. It is equally clear that each embryonic stem cell line has been derived from a human embryo created through in-vitro fertilization (IVF) or through cloning technologies, with all the attendant ethical, religious, and philosophical problems, depending upon one's perspective.

1. STEM CELL TREATMENTS

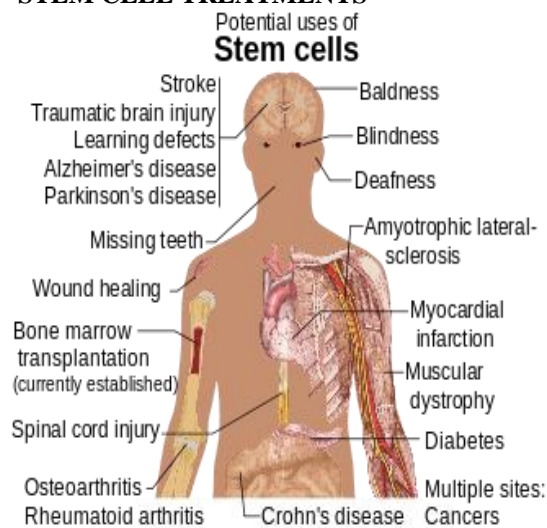


Fig.4 Stem Cell Treatments.

Stem cell treatments are a type of intervention strategy that introduces new adult stem cells into damaged tissue in order to treat disease or injury. Many medical researchers believe that stem cell treatments have the potential to change the face of human disease and alleviate suffering. The ability of stem cells to self-renew and give rise to subsequent generations with variable degrees of differentiation capacities, offers significant potential for generation of tissues that can potentially replace diseased and damaged areas in the body, with minimal risk of rejection and side effects.

A number of stem cell therapies exist, but most are at experimental stages or costly, with the notable exception of bone marrow transplantation. Medical researchers anticipate that adult and embryonic stem cells will soon be able to treat cancer, Type 1 diabetes mellitus, Parkinson's disease, Huntington's disease, Celiac Disease, cardiac failure, muscle damage and neurological disorders, and many others. Nevertheless, before stem cell therapeutics can be applied in the

clinical setting, more research is necessary to understand stem cell behavior upon transplantation as well as the mechanisms of stem cell interaction with the diseased/injured microenvironment.

POTENTIAL TREATMENTS

Brain Damage
Cancer
Spinal Cord Injury
Heart Damage
Haematopoiesis (Blood Cell Formation)
Baldness
Missing Teeth
Deafness
Blindness And Vision Impairment
Amyotrophic Lateral Sclerosis
Neural And Behavioral Birth Defects
Diabetes

Diabetes patients lose the function of insulin-producing beta cells within the pancreas. Human embryonic stem cells may be grown in cell culture and stimulated to form insulin-producing cells that can be transplanted into the patient.

The most common types of diabetes

Type 1 diabetes occurs when the body's immune system damages and then destroys beta cells. This means the levels of sugar in the blood stay high all the time, which can lead to long-term damage to the body.

Type 2 diabetes occurs when insulin no longer works correctly as a signal to the body's cells that sugar should be absorbed. This might be because cells are unresponsive to insulin, or that beta cells are producing too much or too little insulin, or a combination of both of these cases.

Complications of Diabetes

Diabetes can lead to number of health complications:

Heart Attacks
Strokes
Peripheral Artery Disease
Diabetic Retinopathy
Cataracts
Glaucoma
Diabetic Foot
Diabetic Nephropathy
Peripheral Neuropathy

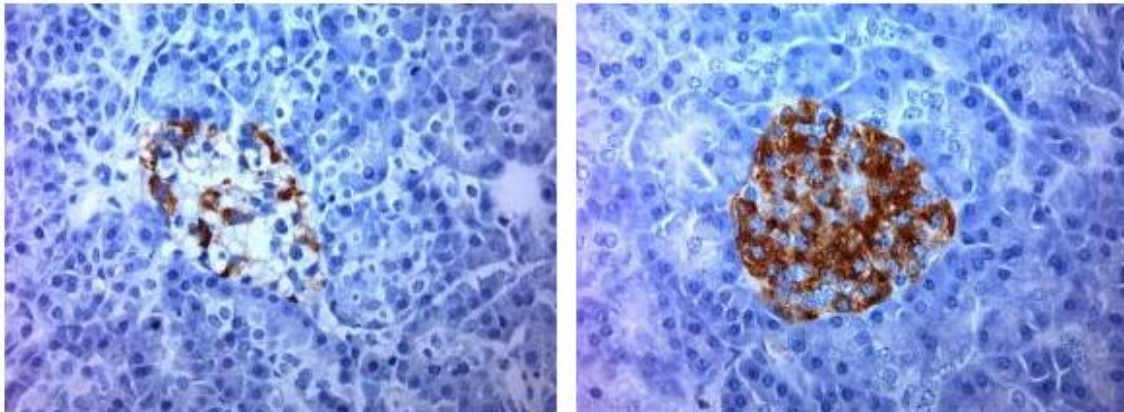
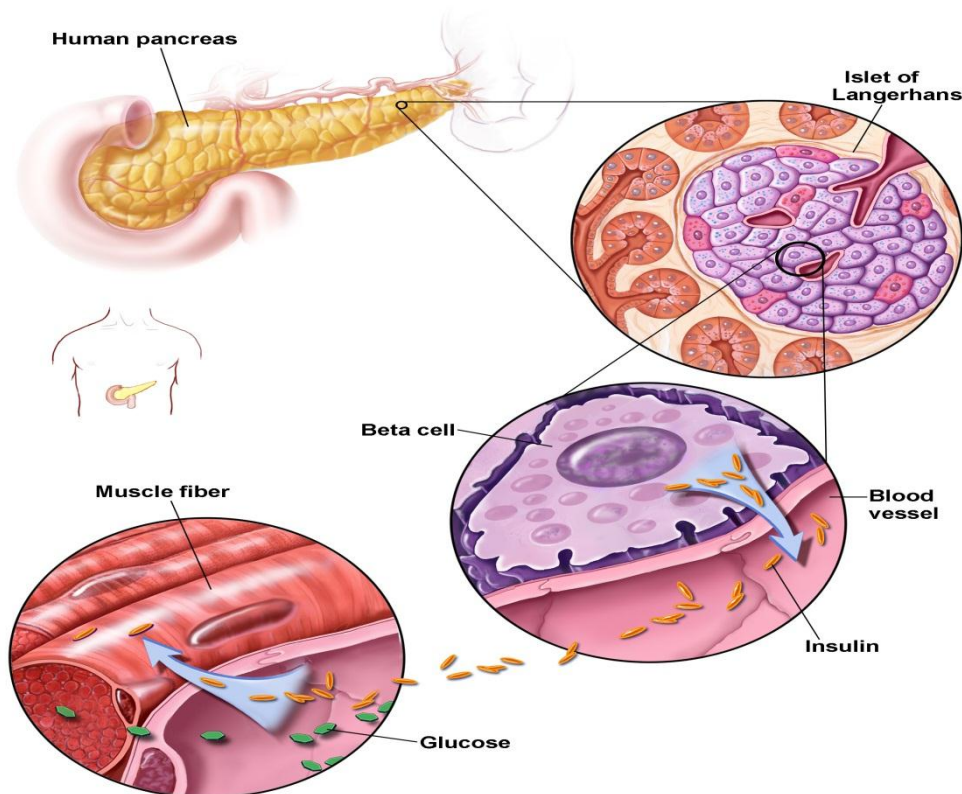


Fig 5: Seeing Diabetes.

Seeing diabetes: Images showing an islet in a person with diabetes type 1 (left) and without diabetes (right). In

the left image we can see less insulin being made (shown in brown) and swelling, as the beta cells are damaged.



© 2001 Terese Winslow (assisted by Lydia Kibiuk)

Fig 6: Islet Cycle.

Clinical success is highly dependent on the development of the following procedures:

Transplanted cells should proliferate.

Transplanted cells should differentiate in a site-specific manner.

Transplanted cells should survive in the recipient (prevention of transplant rejection).

Transplanted cells should integrate within the targeted tissue.

Transplanted cells should integrate into the host circuitry and restore function.

Current approaches to make new beta cells for therapy

Mature human pluripotent stem cells into beta cells in the lab, which are transplanted into diabetic patients.

Mature beta cells in the lab from other types of cells, for example liver cells, which are transplanted into diabetic patients.

Use drugs to trigger cells in the diabetic patient's own pancreas to produce new beta cells.

How can we protect the cells from being attacked by the immune system once they have been transplanted?

Work is underway to find the most effective way of encapsulating transplanted cells to protect them from immune attack. At the moment several research groups and commercial companies (ViaCyte and Beta-O₂Technologies) are involved in clinical phase 1 studies to create a capsule that allows for inward transport of

glucose and other nutrients and outward transport of insulin yet protecting the cells from the immune system. Work exploring drugs, vaccines or cells that reduce the immune reaction is also underway. Results of this work could create better therapies by being combined with beta cell transplantation.

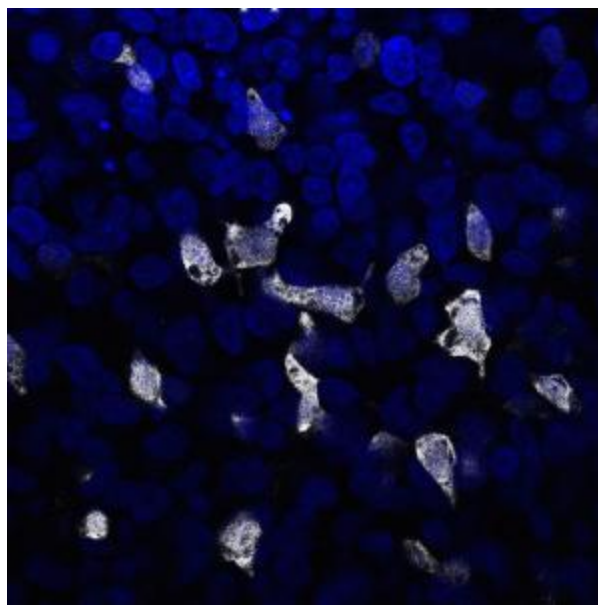


Fig 7: Insulin-producing cells made from human embryonic stem cells.

Making beta cells from pluripotent stem cells

Pluripotent cells (either embryonic stem cells or induced pluripotent stem cells) can make any cell type in the body and researchers are exploring how to direct these to make fully functional beta cells. Such cells could replace the scarce source of donor pancreatic islets of Langerhans. Researchers have so far succeeded in producing cells from human pluripotent stem cells that respond to glucose in a similar way to normal beta cells both in the laboratory and in mice. Moreover, when transplanted in diabetic mice glucose levels become normalized. These beta cells will soon be tested for safety in phase 1 clinical trials.

Making beta cells from other cells

Some researchers think it might be possible to encourage cells already present in the patient's pancreas to make new beta cells – a process normally referred to as regeneration. It is not known whether stem cells exist in the pancreas but beta cell precursors have been found in mice. Some researchers hope that if these precursors exist in the human pancreas that they may be able to find drugs that convert them into new beta cells in patients. Obviously, even if this would be possible one would also have to prevent the autoimmune destruction of the newborn beta cells. These efforts are still experimental in nature and have not reached a point where clinical trials are close.

Mimicking Diabetes in a Dish with "Vascular" Organoids

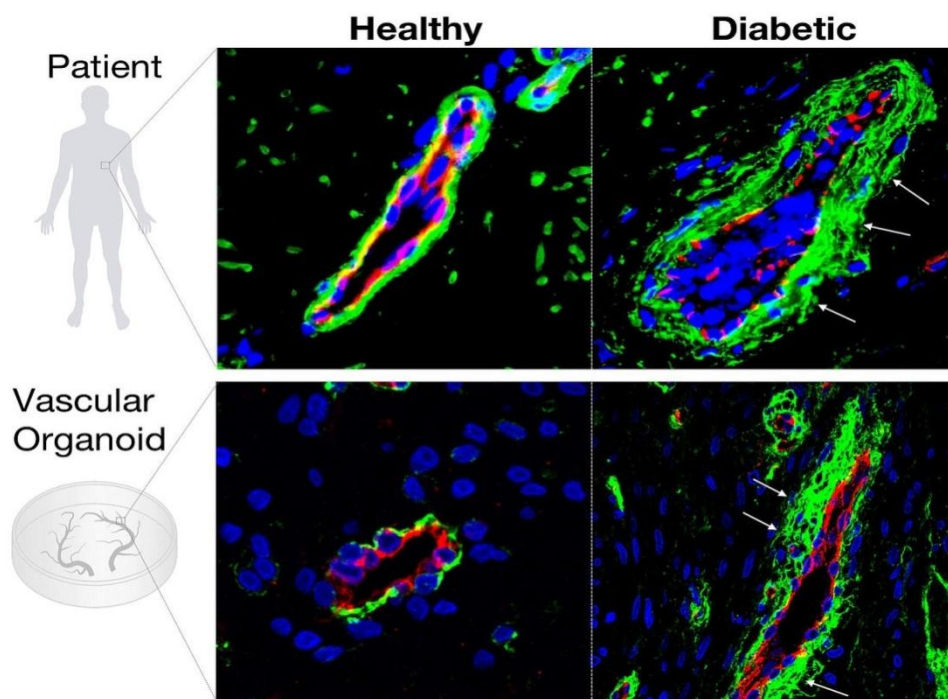


Fig 8: Vascular Organoids.

Diabetic blood vessel changes in patients and human vascular organoids. The basement membrane (green) around the blood vessels (red) is massively enlarged in diabetic patients (white arrows). This results in impaired blood vessel function and reduced supply of oxygen

Deciphering Diabetes with Human Blood Vessels from Stem Cells

Changes in blood vessels are the major cause of death and morbidity in diabetes. For the first time, scientists managed to grow perfect human blood vessels as organoids in a petri dish. This breakthrough engineering technology dramatically advances research of vascular dysfunction in diseases like diabetes, identifying a key pathway that prevents diabetic vasculopathy, as reported in the current issue of Nature.

Diabetes is increasing at an alarming rate worldwide, already affecting at least 420 million people. Another 500 million people are estimated to be pre-diabetic. The global costs of diabetes, which can lead to blindness, kidney failure, heart attacks, stroke or lower limb amputation, is estimated to be 825 billion dollars per year. Many of these diabetic symptoms are the consequence of changes in blood vessels, resulting in impaired blood circulation and oxygen supply of tissues. Despite its prevalence, very little is known about the vascular changes arising from diabetes - in part because we lack human model systems that fully recapitulate these changes. This limitation has stymied the development of much needed therapeutics.

changes and can now be used as diabetic model in the lab to identify novel therapeutics.

One of the pathogenic feature of diabetes is that blood vessels show an abnormal thickening of the basement membrane. As a result, the delivery of oxygen and nutrients to cells and tissues is strongly impaired, causing a multitude of health problems, such as kidney failure, heart attacks, strokes, blindness, and peripheral artery disease, leading to amputations. To recapitulate this pathological condition in a dish, the research team exposed the blood vessel organoids to a “diabetic” environment. “Surprisingly, we could observe a massive expansion of the basement membrane in the vascular organoids. This typical thickening of the basement membrane is strikingly similar to the vascular damage seen in diabetic patients”, says Wimmer. “Such thickening of the blood vessel walls appears to only occur when there is an intricate and very close contact between the different cell types, endothelial cells and pericytes, that make up capillaries.”

As a next step, the scientists searched for chemical compounds that could block development of the pathological phenotype in the “diabetic” lab grown vessels. They screened current anti-diabetic medications, none of which had any positive effects on these blood vessel defects, as well as multiple small-molecule inhibitors of different signaling pathways. They discovered that an inhibitor of γ -secretase could completely prevent the diabetic vasculopathies in organoids. They went on to show that the γ -secretase target Notch3 and its ligand Dll4 are key mediators of basement membrane thickening in diabetic organoids. The authors also found evidence of elevated Notch3 activity in skin blood vessel biopsies from diabetic patients.

Finally they modelled diabetic vasculopathy in diabetic mice, that were transplanted with stem cell-derived human vascular organoids and carry a functional human blood vessel tree. Intriguingly in diabetic mice, the human blood vessels showed prototypic pathologies, whereas the mouse blood vessels remained normal. Blocking γ -secretase or, in first studies, Notch3, could prevent the diabetic vasculopathies of the human blood vessels in the chimeric mice. “Mouse genetics has taught us a lot about disease mechanisms, however some aspects of human disease, such as diabetic blood vessel changes, cannot be modelled well in mice” says Donscho Kerjaschki, a pathologist of the Medical University of Vienna who was involved in the study. “Now we can model it! This allows us to identify underlying disease mechanisms and hopefully develop and test new medicines for hundreds of millions of patients with diabetes.”

“Every single organ in our body is linked with the circulatory system, and the formation of new blood vessels is a key feature for cancers to grow. There are

also many rare diseases that affect blood vessels and for instance lead to strokes and heart attacks in young people” says Penninger, founding director of IMBA, and recently appointed director of the Life Science Institute of the University of British Columbia, who is the lead author of the paper. “Vascular organoids generated from iPS cells represent a game-changing model - allowing us to unravel etiologies and treatments for a broad spectrum of vascular diseases, ranging from diabetes, Alzheimer’s disease, cardiovascular diseases, wound healing, or stroke, to cancer”.

Results of therapy: In a recent peer reviewed publication (reference #7) they outlined 15 separate human clinical trials that were conducted to treat diabetes using MSC’s that encompassed 457 patients. Every single study found MSC’s to be safe for use, with no severe or adverse reactions reported and effective for use, with patients showing measurable clinical benefit. The studies ranged from 3 months to 4 years in duration.

The US-FDA is currently tracking 21 clinical trials to treat diabetes using MSC’s and those studies encompass 926 patients. The studies are ongoing, so no results are available yet.

CONCLUSION

Stem cell therapy is an exciting and active field of biomedical research. Scientists and physicians are investigating the use of stem cells in therapies to treat a wide variety of diseases and injuries. For a stem cell therapy to be successful, a number of factors must be considered. The appropriate type of stem cell must be chosen, and the stem cells must be matched to the recipient so that they are not destroyed by the recipient's immune system. It is also critical to develop a system for effective delivery of the stem cells to the desired location in the body. Finally, devising methods to “switch on” and control the differentiation of stem cells and ensure that they develop into the desired tissue type is critical for the success of any stem cell therapy.

Researchers are currently examining the use of stem cells to regenerate damaged or diseased tissue in many conditions, including those listed below.

Heart disease
Parkinson's disease
Spinal cord injury
Diabetes mellitus
Amyotrophic lateral sclerosis
Arthritis
Burns

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