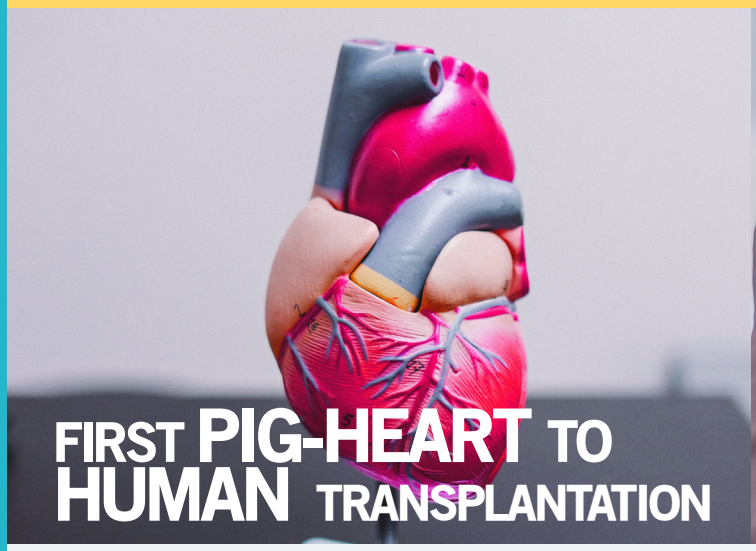

FIRST PIG-HEART TO HUMAN TRANSPLANTATION

AISLING ZENG

Currently, one treatment option for end-stage heart disease is a heart transplant, with about 3442 patients on the American transplant waiting list as of February 2022.[1,2] However, for some, a human heart transplant is not an option due to underlying conditions and other factors.[3] Xenotransplantation is a solution to address the increasing organ demand and offers an alternative for ineligible transplant patients.[4]

On January 7, 2022, surgeons from the University of Maryland successfully transplanted the first ever genetically modified pig heart into 57-year-old David Bennett.[4] This breakthrough surgery was not part of a clinical trial, but was rather a last ditch effort to save Bennett, who had been on cardiac support for two months.[4] The primary cause of concern for most transplants is organ rejection, which is addressed by administering immunosuppressive medications to the patient. Bennett's case, however, was one of the first instances in 70 years where scientists modified the donor instead of suppressing the recipient's immune system.[5] In 2005, Dr. David Cooper, a surgeon from Harvard University, was able to use CRISPR-Cas9 technology to delete the gene that encodes for galactosyltransferase, an enzyme responsible for the production of galactose-α(1,3)-galactose (Gal).[5] Gal is a sugar found on the surface of pig cells that is one of the major targets for human anti-pig antibodies.[6] This discovery was a gamechanger in the field as it successfully prevented hyperacute rejection and led to the success of Bennett's surgery.[5]

Unfortunately, 45 days post-surgery, Bennett struggled with numerous infections and ultimately passed away 2 months after the initial operation.[7] Despite this setback, the surgery was still deemed a significant step forward and surgeons are open to potentially conducting formal clinical trials involving xenotransplantation in the future.[7]

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MCMASTER RESEARCHERS DEVELOP INHALED VACCINES

AISLING ZENG

The emergence of variants throughout the progression of the COVID-19 pandemic has caused political unrest and public concern, while demonstrating the need for more long-term and robust vaccine development strategies.[1]

Recently, researchers at McMaster University developed a new vaccine that has just begun phase 1 clinical trials.[2] The vaccine is adenoviral-based with human and chimpanzee origins and expresses three SARS-CoV-2 antigens.[1] Thus far, it has been shown to confer protection against variants B.1.1.7 and B.1.351, commonly known as alpha and beta, respectively.[1] However, this vaccine has gained attention not for its efficacy, but for its non-traditional administration route: intranasal.

Respiratory vaccines, more commonly known as inhaled vaccines, have been researched for years, though few have progressed to regulatory approval and distribution.[3] Regardless, respiratory vaccines have shown promising results, especially when addressing airborne diseases such as COVID-19.[3,4] The respiratory tract's large surface area and high amount of antigen-presenting cells makes it the optimal target for pharmaceutical uptake and inducing an immunological response.[4] Additionally, since COVID-19 is transmitted via aerosols and droplet spread, respiratory vaccines confer an advantage compared to traditional intramuscular vaccines, as they are delivered straight to the pathogen's primary site of entry.[4]

Clinical trials are currently still underway, but if the results continue to show success, the approval and distribution of this inhaled vaccine could have huge implications for the trajectory of the pandemic and how researchers approach vaccine development in the future.

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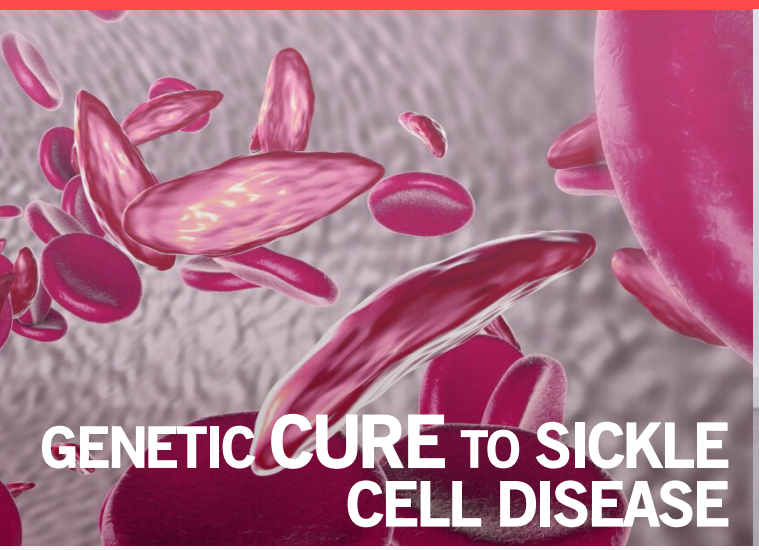

GENETIC CURE TO SICKLE CELL DISEASE

DALRAJ DHILLON

Sickle cell disease (SCD) is a group of genetic disorders pertaining to the malformation of hemoglobin and consequent dysmorphia of red blood cells (RBCs).[1] SCD is the result of a single nucleotide polymorphism to the beta-globin gene, resulting in the replacement of glutamate with valine at position 6 and the subsequent formation of hemoglobin S (HbS) instead of the normal hemoglobin A (HbA).[2] At high blood oxygen concentrations, the structure of HbS appears normal, however, HbS polymerizes at low concentrations to form fibrous precipitates which alter the RBC into a crescent shape.[3] These malformed RBCs tend to readily cohere, resulting in frequent clotting and associated excruciating pain crises.[4] While SCD can be cured with a donor bone marrow transplant, the use of this therapy has the best chance of success in patients who have a closely matched donor, which is difficult to find for many patients.[5] However, recent clinical trials have assessed the use of a viral vector gene therapy, which uses the patient's own stem cells in order to minimize rejection. This treatment, Lentiglobin, involves the transduction of CD34+ hematopoietic stem cells recovered from the patient with a lentiviral vector (BB305) that encodes for HbA.[6] The single-dose reinfusion of the stem cells into the patient's blood was shown to result in sustained HbA production, reduced hemolysis, immense reduction in pain crises 4-32 months following injection, and limited adverse effects.[6] While further studies will be conducted to further assess efficacy and safety, the success of this trial marks an immense step forward in the field of gene therapy for SCD and other genetic blood disorders.

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QUADRICEPS TENDON GRAFT FOR ACL RECONSTRUCTION

DALRAJ DHILLON

Throughout history, the most common practice for anterior cruciate ligament (ACL) reconstruction was through the use of a bone-patellar tendon-bone (BPTB) graft.[1] The widespread use of this graft arises from its many benefits, including its similar structure and composition to the ACL, relative ease of harvesting, notable strength, and a low incidence of reinjury.[2] Despite these many advantages, BPTB graft harvesting involves the harvesting of both the patellar tendon and part of the patella. This intrusive harvesting approach commonly leads to harvest-site morbidity, usually manifesting as diminished knee mobility and chronic anterior knee pain.[2,3] While manageable, this presents a major barrier to returning to optimal performance and function of the joint and has led to longer recovery periods for professional athletes when compared to other graft repairs.[4] To alleviate these drawbacks, the use of a quadriceps tendon (QT) graft in ACL reconstruction has gained popularity. Compared to the BPTB graft, the QT graft has a 70% higher biomechanical load, and 20% more collagen fibrils per cross sectional area.[5] In addition to structural prowess of the QT, graft harvesting is very minimally invasive and does not involve any bone harvesting.[5] A meta-analysis of clinical trials and observational studies revealed that QT graft ACL repairs bear no significant differences in graft failure compared to BPTB graft, yet significantly lowers the rate of donor site morbidity.[6] While still gaining traction as a viable graft for ACL reconstruction, the quality-of-life benefits, coupled with a negligible difference in graft performance, may lend the QT graft as the preferred choice for orthopedic surgeons for ACL reconstruction in the future.

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