ALTERNATE HORIZONS PLATFORM

Did Old McDonald have a human heart?

Nitisha Moodley

SPECIAL EDITION - 'SCINTILLATING SURGERY AND SCIENCE'

Hearing the phrase "Old McDonald" brings a surge of memories from my childhood. I remember the nursery rhyme having a cow, chickens, and most of all, a pig at the end. Never would I have thought that the last animal in a children's nursery rhyme would potentially be the frontrunner and saviour for millions of heart-transplant patients worldwide.

On January 7, 2022, the University of Maryland School of Medicine team of surgeons performed a heart transplant of a genetically modified pig heart into David Bennet, a 57-year-old man who had been on cardiac support for two years.[2] The work of the medical team, led by Muhammad Mohiuddin, has allowed for a cardinal step forward in the world of surgery and science, by gaining a critical understanding of xenotransplants, defined as the transferring of animal organs and/or tissues into a human recipient.[4]

Another recorded xenotransplantation was a surgery that was performed in 2021, by the University of Langone Health in New York, that involved transplanting the kidneys of a pig that was also genetically modified.[1] What makes Mohiuddin's team's surgery a hallmark, in comparison to the surgeons from the University of Langone Health, is that they performed a xenotransplant surgery on a patient who had a chance at recovery and survival post-operatively, whereas Langone Health transplanted the kidneys into two patients who were declared legally dead, with no responsive brain function, although they were being sustained as a result of ventilators.[1] The bodies of the legally dead patients did not reject the kidneys[1], but the main objective of such surgeries is to observe the effects of xenotransplantation and whether it can lead to an improved quality of life, beyond hospitalization.

Though the xenotransplant of Mohiuddin and his colleagues proved to be successful, it resulted in the unfortunate passing of Bennet, two months post-surgery.[3] His passing comes with the concerns that Carl G. Groth expressed in his article, published in the *Indian Journal of Urology*.[1] The article raises the concern of the body's rejection of the pig organs as a result of a vigorous immune response to porcine antigens. The article further goes on to say that an antigenic determinant, which is generated by alpha 1-3 galactosyl transferase enzyme, is responsible for the cell's rejection of pig organs, as it will lead to the body firing off vascular injuries to the tissues.[1]

However, as unfortunate as Bennet's passing was, his contribution to medicine and science provided the platform needed in this field for surgery to be pushed past more boundaries and shake the ground of the body of surgery as it is. The efforts of Mohiuddin and the University of Maryland's School of Medicine are a testament to what can be accomplished when creativity is used.

When this article was published and the story made headline news, I was dumbfounded in nothing but awe that such a thing as this ground-breaking surgery even existed. I remember learning about and dissecting the heart in my high school biology days. My teacher had mentioned that we would be working on pigs' hearts because it is similar to the human heart.

Now being at the University of Pretoria and studying as an undergraduate in Human Genetics, what makes this surgery so much more sentimental to me is the fact that I can actually understand and somewhat explain to a novice of science and medical innovations, why this surgery is so revolutionary. Biochemistry lectures have enabled me to put somewhat of a face to the enzyme alpha 1-3 galactosyltransferase, which is responsible for the immune response when it comes to xenotransplantations. It is characterised as being an enzyme that transfers functional groups within a cell and is comprised of galactose, which is one of the main six-carbon sugars. Groth states that "[r]ecently, however, research groups in Boston and Pittsburgh succeeded in cloning pigs and in this context, were able to eliminate the gene that encodes alpha-galactosyltransferase."

These "gal-knockout pigs" do not express the gal epitope".[1] The words "clone" and "knock-out", are words that every genetics student is accustomed to. Excitement erupts in me knowing that the concepts I am learning to master as a training scientist, who is aspiring to

work in medical research, have such a fundamental role in real-life surgery and medicine. The overlap of concepts and what seems like an endless amount of theory sometimes makes me want to sigh in exasperation. However, after reading the article on Mohiuddin's work and studying the concepts encountered in my genetics, biochemistry and physiology modules, this was transformed into gratitude. These are the beginnings of the scintillating complexity of surgery.

After this magnificent marvel of surgery discussed above, there can only be hope that just like the wonders of science were pioneered by those scientists and doctors of the past, so too is this surgery with science laying the pioneering ground for training doctors and scientists to reshape the face of surgery and medicine for years to come. I may just tell my students that I lecture in the future, that Old McDonald might not have had a human heart.

References

[1.] Groth, C.G. 2007.The potential advantages of transplanting organs from pig to man: A transplant surgeon's view. *Indian J Urol*,23:305-310

[2.] Reardon, S. 2022. First pig-to-human heart transplant: What can scientists learn?. *Nature*, 601:305-306

[3.] Salam, E. and agencies. 2022. First person to receive heart transplant from pig dies, says Maryland hospital. *The Guardian*. [Online] Available from: https://www.theguardian.com/us-news/2022/mar/09/first-person-heart-transplant-pig-dies-david-bennett. (Accessed 26 September 2022).

[4.] Koplon, S. 2022. Xenotransplantation: what it is, why it matters and where it is going. [Online] Available from: https://www.uab.edu/news/youcanuse/item/12581-xenotransplantation-what-it-is-why-it-matters-and-where-it-is-going. (Accessed 26 September 2022).