EDITORIAL

Cardiac Xenotransplantation.

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In an article published by Pietro Bajona et al. in the Annals of Thoracic Surgery in 2016, in which the distinguished surgeon, transplant pioneer and xenotransplant researcher David K.C. Cooper et al. [1], the authors stated: "when pig hearts could be successfully transplanted into patients with end-stage heart failure; the problem of the availability of organs for transplantation will be solved."

This powerful statement began to gain strength after the recent news the first days of January 2022 when the media reported the successful performance of a porcine to human heart transplant at the University of Maryland Hospital Center, United States of America, by the respected surgeon Bartley Griffith and coworkers [2]. The news took the world by surprise, especially to the medical community. Many of us who have devoted ourselves for years to the study and treatment of terminal heart diseases, did not anticipate that during the last few years the research programs for the development of transgenic animals would have been resumed. During the 1990's there was a slowdown in research of transgenic animals for transplantation purposes since it was demonstrated that the porcine retrovirus (PERV) was capable of infecting human cell with the risk of transmission of swine diseases to immunosuppressed humans and the possibility of consequent pandemics [3].

Today, after many years since those first attempts to transplant organs between different species made by Hardy, Reemtsma, Baruah and Bailey among others; and after the media reported the successful procedure carried out by Griffith and coworkers, other cases have also come to light, such as the two kidney transplants from genetically modified pigs and transplanted into brain-dead human patients, one in New York and the other in Alabama; resulting in adequate function for more than 50 hours [4].

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Regarding the transplant, it is a reality that the surgical teams had to familiarize themselves with the anatomy of the porcine heart, which shows several important morphological differences that need to be mastered so that the implant is properly aligned; thus avoiding early or late failure as a consequence of a surgical error [5].

From the immunological point of view, in the pig, unlike the human vascular endothelium where the ABO and Rh blood group antigens are expressed, a galactose oligosaccharide commonly called *GAL* is expressed and responsible for the hyperacute rejection of the porcine xenograft. Within minutes of the implant the host antibodies recognize this antigen and activate a very aggressive complement mediated reaction [6].

We can define that the technical obstacles are solved by us surgeons in the experimental surgery laboratories, but the immunological and antigenic obstacles typical of each species require complex genetic manipulations that have been achieved during all these years thanks to the interaction of several university centers of the world with the collaboration of the pharmaceutical industry; likewise, several generations of virus-free transgenic animals have been raised, thus reducing the risk of zoonoses. For this particular case, a group of scientists from the University of Maryland and the Revivicor company achieved ten genetic changes in pigs. three were directed exclusively at blocking the synthesis of sugars from porcine surface antigens. They were also able to add six human genes, two with anti-inflammatory properties, two that regulate the coagulation cascade and another two that produce regulatory proteins that help modulate the immune response. Finally, the porcine growth hormone receptor gene was modified to prevent the organ from continuing to grow after being transplanted [7,8].

Finally and as we can see, the recent xenotransplant published by the media represents a new milestone in modern medicine, since the patient survived the procedure and did not presented hyperacute rejection. He is still alive today

though in critical condition; which effectively and objectively represents the beginning of a new horizon for patients in need of a heart transplant. Probably it will take several years before the use of xenografts becomes a common practice. Regarding mechanical cardiac support, last week I had the opportunity to witness the experimental implantation of a novel continuous but pulsatile flow device, the Bivacor Total Artificial Heart; by doctors O.H. Frazier and Billy Cohn at the Texas Heart Institute, whom in turn commented that despite the great achievement represented by xenotransplantation performed by Dr. Barth Griffith, there is still an important niche for mechanical cardiac support, especially in patients with acute pathology and for all those chronic patients who, due to immunological idiosyncrasy or recent cancer, cannot undergo any type of transplant [9].

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