GENETIC MODIFICATIONS FOR XENOTRANSPLANTATION

1. Government License Rights

[0001] This invention was made with government support under ~~grant number P01~~ AI045897 awarded by ~~National Institute of Allergy and Infectious Diseases (NIAID),~~ the National Institutes of Health (NIH). The government has certain rights in the invention.

2. Cross-Reference to Related Applications

[0002] This application claims the benefit of U.S. Serial No. 63/075,285 filed September 7, 2020, and U.S. Serial No. 63/108,986 filed November 3, 2020, the disclosure of each of which is incorporated by reference herein in its entirety.

3. Reference to Sequence Listing Submitted Electronically

[0003] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on August 26, 2021, is named 14648-015-228_Sequence_Listing.txt and is 42,743 bytes in size.

4. Field

[0004] Provided herein are recombinant miniature swine (*e.g.*, GalT knockout miniature swine) expressing human CD47 in a tissue specific fashion. Also provided are kidneys isolated from a miniature swine, wherein the glomeruli of the kidney express human CD47 at a level higher than the level of human CD47 expression in the tubules of the kidney. Furthermore, provided herein are methods of transplanting such swine kidneys with glomeruli-specific expression of human CD47 from recombinant miniature swine into human recipients. In certain aspects, provided herein are methods of transplantation comprising transplanting hematopoietic stem cells expressing human CD47 from a first donor animal (*e.g.*, a miniature swine) and a kidney expressing human CD47 in the glomeruli from a second donor animal (*e.g.*, a miniature swine) to a recipient (*e.g.*, a human recipient).

5. Background

[0005] The severe shortage of allogeneic donors currently limits the number of organ transplants performed. This supply-demand disparity may be corrected by the use of organs from other species (xenografts). In view of the ethical issues and impracticalities associated