More than bacon: Genetic alterations in pig tissue may allow for human transplantation

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A sizzling genetic discovery by Chinese scientists may one day allow pig tissue to be transplanted successfully into humans. Their research presented in the *Journal of Leukocyte Biology* represents a major step forward toward filling the shortage of vital organs for human transplantation. At the core of their work, they showed that altering or overexpressing the human programmed death ligand-1 (PD-L1) molecule in the endothelial cells of pig arteries reduces the conditions that lead to rejection. This strongly suggests that humans could receive altered porcine organs with fewer complications.

"Genetically engineered pigs may someday overcome the severe donor organ shortage, and save human lives," said Qing Ding, Ph.D., co-study author from the Shanghai Institute of Immunology at the Shanghai Jiaotong University School of Medicine in Shanghai, China.

To make the discovery, scientists conducted experiments using two groups of pig vascular endothelial cells. The first group was genetically engineered to express human PD-L1, while the second group was normal. When both sets of cells were exposed to human lymphocytes, lower rejection response occurred in the group with the altered gene, while higher rejection responses were seen in the normal cells. Study results suggest that human PD-L1 could be used as a novel therapeutic agent to enhance tolerance of xenotransplants and also supports the possibility of using human PD-L1 transgenic pigs as xenotransplant donors. Using this type of genetic engineering technique could potentially overcome current challenges related to successful pig/human

transplant rejection.

"Xenotransplantation has the potential to fill a huge gap between the number of available human donor tissue and number of needy recipients," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology, "but our understanding of the pathways that might enhance the acceptance and physiological function of organs from animals such as pigs remains incomplete. The study by Dr. Ding and his colleagues is a very substantial step forward in defining a key immunoregulatory pathway that could be targeted in this setting."

More information: Qing Ding, Liming Lu, Xiaorong Zhou, Yun Zhou, and Kuang-Yen Chou. Human PD-L1-overexpressing porcine vascular endothelial cells induce functionally suppressive human CD4+CD25hiFoxp3+ Treg cells . *J Leukoc Biol* July 2011 90:77-86; doi:10.1189/jlb.1210691

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