Medical Xpress

Antibody shows promise for preventing organ rejection after transplantation

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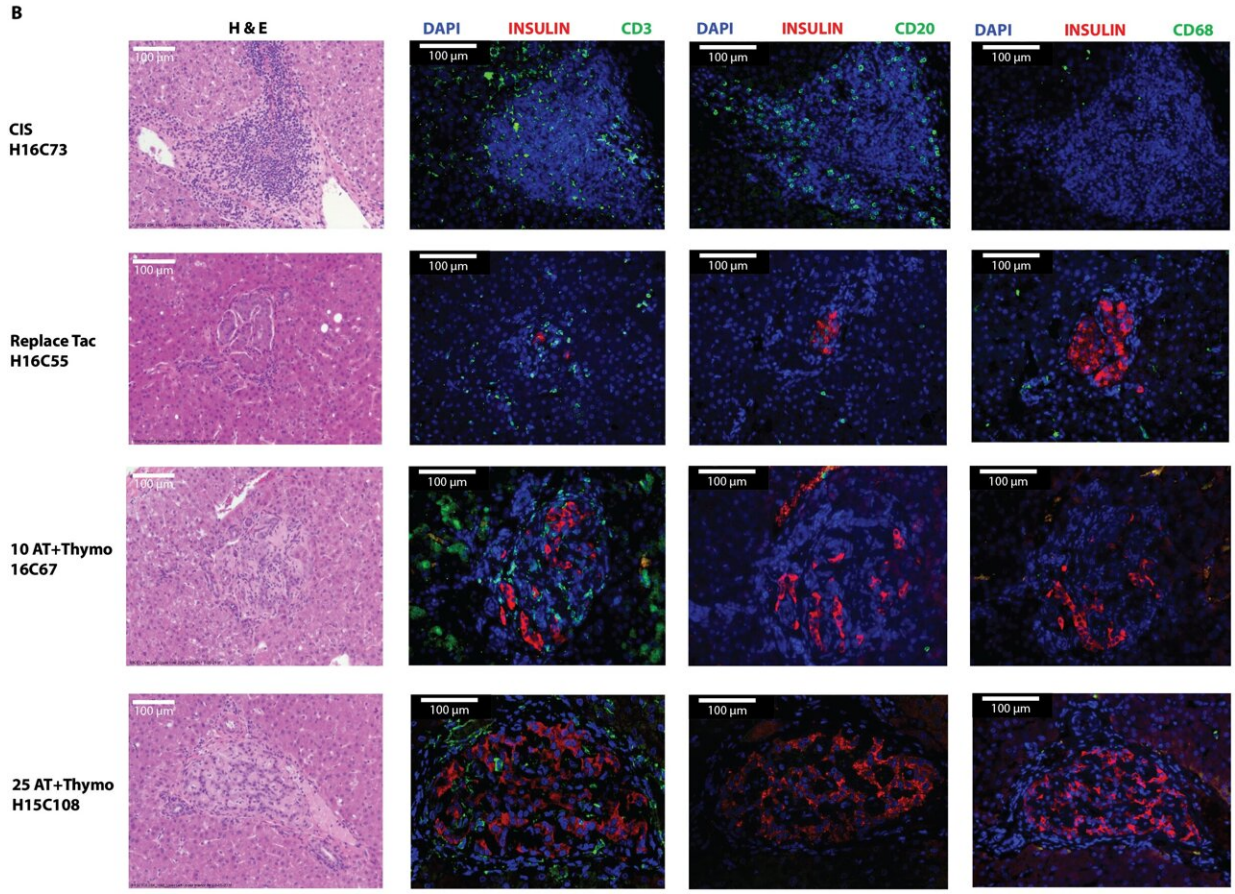

A B cell flow crossmatch performed before and after islet transplant. No animals developed donor-specific antibodies after islet transplantation. Credit: Kenyon, et al, *Science Translational Medicine*, 2023

A man-made antibody successfully prevented organ rejection when tested in primates that had undergone a kidney transplant, Duke Health researchers report.

The finding clears the way for the new monoclonal antibody to move forward in human clinical trials. Results of the study appear online Aug. 30 in the journal *Science Translational Medicine*.

"Current medications to prevent organ rejection are good overall, but they have a lot of side effects," said lead author Imran J. Anwar, M.D., a surgical research fellow in Duke's Department of Surgery. "These therapies suppress the immune system, putting patients at risk of infections and organ damage, and many cause non-immune complications such as diabetes and high blood pressure.

"The push over the last 30 to 40 years has been to develop new, less toxic drugs," Anwar said. "We are hopeful this antibody moves us closer to that goal."

Anwar and colleagues, including co-senior author Allan Kirk, M.D., Ph.D., chair of the Department of Surgery, focused on a monoclonal antibody identified as AT-1501. It was engineered to minimize the risk of blood clots, which had become problematic for an earlier version of this therapy.

In studies using primates that had undergone kidney transplantation, AT-1501 prevented rejection without the need for additional immunosuppressive drugs or promoting blood clots, confirming its immunosuppressive potential.

In animals that had undergone islet transplantation, AT-1501 alone did not lead to uniform rejection control, but it was effective in combination with existing immunosuppressive agents. The combination therapies in

islet transplantation led to uniform islet graft survival without weight loss or infections that can typically arise. The islet transplants were performed by Norma Kenyon, Ph.D., co-senior author and professor at the University of Miami.

"These data support AT-1501 as a safe and effective agent to promote both islet and kidney transplant survival and function and allow us to advance into clinical trials right away," Kirk said. "This less toxic approach has been pursued for over 20 years, and I think we are finally at a turning point. This could be a great advance for people in need of organ transplants."

In addition to Kirk and Anwar, study authors include Dora M. Berman, Isabel DeLaura, Qimeng Gao, Melissa A. Willman, Allison Miller, Alan Gill, Cindy Gill, Steve Perrin, Camillo Ricordi, Philip Ruiz, Mingqing Song, Joseph M Ladowski, and Norma S. Kenyon.

Anelixis Therapeutics, now Eledon Pharmaceuticals, is developing AT-1501 for kidney and islet cell transplant.

More information: Imran Anwar et al, The anti-CD40L monoclonal antibody AT-1501 promotes islet and kidney allograft survival and function in nonhuman primates, *Science Translational Medicine* (2023). DOI: 10.1126/scitranslmed.adf6376. www.science.org/doi/10.1126/scitranslmed.adf6376

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