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Short Communication

A transplant compatible with all patients: A salvage underway

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Finding compatible organs is not an easy task..!

Approximately 100,000 people are on organ transplant waiting lists in the United States and less than a third of patients on the list received an organ in 2017. ABO blood types, which are determined by the presence of A and B antigens on our cells, must be matched for transplants to avoid immunological rejection of the donor's organ in the recipient. The requirement to match these antigens diminishes the likelihood of finding a matching donor, lengthening wait times. Antigens A, B, both, or none are present in people with blood groups A, B, AB, and O, respectively. Although patients with blood type AB can get blood or organs from all other blood types, people with blood type O can only receive blood or organs from individuals of the same blood group, immunological rejection can result from transfusions or transplants between mismatched blood types.

Organs for these patients must be compatible with their key cell surface antigens and patient-donor blood types are one of the characteristics that must be matched. Because it's so difficult to locate matches, not only will a patient have to wait longer, but also the donated lungs will be wasted due to incompatibility. Currently, transplanting lungs with the wrong blood type triggers an immunological response and the organ's rejection by the host. Henceforth, the patients with gradually failing organs frequently wait years for a life-saving transplant, and some will die because they will never receive an appropriately matched donor.

New research suggests that the blood type of some given lungs could be changed before transplant, resulting in a larger pool of universal donor lungs and shorter wait times for individuals in need. A study has shown that blood type conversion in donor organs for transplantation can be done safely. This discovery is a crucial step toward the development of universal type O organs, which would dramatically enhance organ allocation fairness and reduce mortality for individuals on the waiting list.

A study by Wang A et al., employed two enzymes that can cleave sugars from A and B antigens on red blood cells, transforming them into universal type O cells namely FpGalNAc deacetylase and FpGalactosaminidase, to convert blood type A lungs to blood group O lungs during ex vivo lung perfusion. This discovery is crucial in developing the universal blood-type organs used in the current work, which uses the EVLP circuit to deliver these enzymes to the lungs. It is reported that FpGalNAc deacetylase and FpGalactosaminidase, when used together, have been shown to efficiently convert group A (ABO-A) red blood cells (RBCs) to group O red blood cells (RBCs) (ABO-O). Ex vivo i. e outside of the body, under a plastic dome, lung perfusion is used to investigate the safety and preclinical efficacy of utilizing these enzymes to remove A antigen (A-Ag) from human donor lungs (ex vivo lung perfusion, EVLP). The EVLP system, which was employed in Cypel's lab study, circulates nourishing fluids through organs, allowing them to be warmed to body temperature and healed before transplanting. For this investigation, the scientists employed non-transplantable human donor lungs from type A donors. They used an enzymatic solution to cleanse one of the donor's lungs of A antigens while leaving the other untreated [1].

They conducted a study on eight blood type A lungs. They used the enzyme combination under laboratory conditions which resulted in 97% of antigen A removal from the bloodstream in mere 4 h without any detectable toxicity or harm to the organ. Without the surface antigen, the graft looks to be blood group O and is nearly universally termed neutral. Three of the freshly "neutral" lungs (free from antigen A) were then immersed in plasma to mimic a transplant. The amount of antibody damage observed was modest, implying that the transformed lungs were accepted rather than rejected, at least in the early stages. When compared to control lungs, the treatment of the donor's lungs reduced antibody binding, complement deposition, and antibody-mediated damage. This technique has the potential to increase ABO-incompatible lung transplantation and improve organ allocation fairness. Because no patient has yet had an organ treated according to this approach transplanted, there is still a lot of unknown information concerning the organ's viability and the body's reaction. The researchers,

Abbreviations: EVLP, Ex vivo lung perfusion; PRA, Panel reactive antibody; HLA, Human leukocyte antigen.

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on the other hand, replicated a transplant between persons who are ordinarily incompatible [1] Moving forward, researchers want to explore antigen re-expression kinetics and long-term post-transplant impacts of the organ donor enzymatic therapy using similar transgenic mice and also working on a clinical trial proposal to put the technology to the test in humans.

The implementation of the same in the real-time clinical trial with human subjects and in the practice poses various kinds of challenges. As we may surpass the major challenge with universal compatibility making of ABO groups, HLA incompatibility contributes to the next common cause for rejection. The best match for the recipient is to have zero mismatches with 12 out of s12 antigens matching. If the patient has a very common HLA type, it is possible for all 12 markers to match. These are better assessed by panel reactive antibody (PRA). There is much new advancement in therapeutic apheresis to manage both pre-transplant and post-transplant immunological barriers. They are plasmapheresis, immunoadsorption, extracorporeal photopheresis, etc. More studies need to be encouraged in the real-time setting of universal compatibility and the efficacy of various techniques to manage immunological rejection.

If this innovation works out, researchers believe that the treatment could potentially boost the number of blood group O donor's lungs from the current 55% to more than 80%. Since, patients with blood type O, for example, have a 20% higher risk of dying while waiting for a matching donor. By eliminating the blood type-A antigens, the treatment prevents the auto-immune reaction from occurring and if all organs are converted to universal type O, that barrier will be fully removed.

More research is needed before this method can be approved for use on real people, but the early signals are very promising.

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Author's contributions

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Declaration of competing interest

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Reference

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