

MUTANT ALPHA-1-ANTITRYPSIN COMPOSITIONS

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Technology

Human Alpha1-antitrypsin (hAAT) is a serum glycoprotein presently prescribed for patients with genetic AAT deficiency. It is administered in the form of a plasma-derived affinity-purified protein. Research in Prof. Eli Lewis's lab, has had success in protecting islet grafts between strains of the same species for a while by using hAAT in combination with A Temporary T-cell depletion given before transplantation (sometime referred to as ATG). On its own, temporary T-cell depletion affords merely a delay in graft rejection. However, unexpectedly, when alpha1 was administered to animals in combination with the temporary T-cell depletion approach using anti-CD4 or anti-CD8 antibodies, islet Xenotransplant grafts were accepted between species.

Application

For individuals with type 1 diabetes (T1D), current treatment revolves around insulin administration. But despite nearly 100 years of clinical use, injections of insulin are still far from attaining control over glucose levels; in fact, patients exhibit dangerously high blood glucose levels over 60% of their day. Pancreatic islets are where our insulin is made, and these become the target of an immune attack during T1D. For the past decade, human islets have been isolated from human donors and given to diabetic hosts in a rather simple and non-invasive surgical procedure. Under these conditions, perfectly stable glucose levels are achieved, mostly with no need for further injections of insulin. However, the problem of the immune attack against the grafts is yet unresolved, and even if it were to be soon resolved, we simply don't have enough donors to go around. As a solution to the shortage in organs, animal donors have been considered, such as the pig, and regulatory authorities have recently approved clinical trials using pigs as islet donors.

Today, over 100,000 people are on the organ transplant waiting list in the US alone, with one new person added to the list every 10 minutes. So it's no wonder there is a global organ shortage, with patients dying every day because of a lack of available organs. With today's abundance in pig islets for human grafting, one has to tackle a much more aggressive immune response, the response mounted against another species.

Advantages

- **Safety**—the very same protein has a remarkable safety record when administered to a small population of individuals with a rare genetic deficiency.
- **Novel MoA**- the synergy between the anti-inflammatory hAAT and a pure T-cell drug ATG, points at some under-examined aspects of the novel suggested MoA.

Patent PCT