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**Speaker's Abstract**

# Immune Tolerance in Diabetes


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Europe and USA are facing a dramatic increase in the incidence of autoimmune Type 1 diabetes (T1D), especially in young children. In T1D, the body's own immune cells gradually destroy the insulin-producing beta cells of the pancreas. The disease has a strong genetic component and is influenced by environmental factors. The main trigger, however, is ultimately a false reaction of the immune system in which the immune cells do not distinguish between foreign and endogenous components. Normally, $Foxp3^+$ regulatory T(Treg) cells move to the scene and prevent an attack on the body's own cells. Therefore Treg cells are referred to as the "blue helmets, the peacekeeping troops of the immune system" in order to maintain a state called immune tolerance. However, in T1D, sufficient numbers of these "blue helmets" are lacking to carry out this function. Consequently, insulin-producing beta cells are destroyed by the pathologically activated immune cells. Therefore, concepts are urgently needed that strengthen the "peacekeeping troops" to restore immune tolerance.

The development of human Treg induction strategies to interfere with autoimmunity is still in its infancy. Now, using novel humanized models we show that induction of human insulin-specific Tregs, which then can impede the attack of the immune system on the insulin-producing cells, can be achieved *in vivo*. Moreover, we provide first evidence that in humans increased frequencies of insulin-specific $Foxp3^+$Tregs are associated with profound delays in progression to T1D. These results directly support the rationale of developing insulin-specific Treg induction strategies in humans. These findings highlight that a mechanistic dissection of human tolerance induction together with a modeling of islet autoimmunity in humanized mice opens new avenues for the development of innovative precision medicines aimed at the safe and specific manipulation of $Foxp3^+$Tregs in children at risk of developing T1D.


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