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Oral *Salmonella*-Based Vaccine for Type 1 Diabetes

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Type 1 diabetes (T1D) is a metabolic disease caused by the autoimmune destruction of pancreatic insulin-producing beta-cells due to loss of tolerance to specific self-antigens (autoantigens). A promising approach to restore immune balance is the oral administration of diabetic autoantigens which diminishes the islet-specific destructive responses and induces regulatory responses. We recently reported the development of an oral vaccine for T1D based on live attenuated *Salmonella* expressing preproinsulin (PPI) as the autoantigen combined with host cell expression of TGFβ. We showed that oral vaccination with the combined PPI+TGFβ prevented the onset of diabetes in non-obese diabetic (NOD) mice. In this study we extended this approach by evaluating another autoantigen, GAD65, as well as the addition of a complementary treatment, partial T-cell ablation with anti-CD3. Our results showed that GAD65+TGFβ and the combination of PPI with TGFβ+IL10 and a sub-therapeutic dose of anti-CD3 prevented diabetes in the NOD mice and restored normal glucose tolerance. We also found the oral combination therapy of PPI+TGFβ+IL10 combined with anti-CD3 effectively reversed diabetes in the majority of diabetic NOD mice after replacement of arginine with glutamic acid (R22E) and glutamic acid to glycine (E21G) in Insulin B9-23. Initially we have shown that combined vaccine therapy increases the Tregs in splenocytes, and local Tregs in PLN and pancreas of vaccinated NOD mice. Additionally, the combination therapy significantly increased regulatory cytokines (IL10 and IL2) and inhibited the inflammatory IFNγ. Together these results indicated that the vaccine suppressed the autoimmunity and increased regulatory mechanisms leading to a conclusion that a *Salmonella*-based oral vaccine expressing autoantigens in combination with tolerogenic cytokines is a promising therapy for the prevention and treatment of T1D.

Biography:

Dr. Mohamed I. Husseiny, completed his master of microbiology and immunology from Faculty of Pharmacy, Zagazig University, Egypt. He received his Ph.D from Institute for Clinical Microbiology, Immunology and Hygiene, Friedrich-Alexander University, Germany and postdoctoral studies from LA Biomed at Harbor-UCLA Medical Center, California, and Childrens Hospital Los Angeles at USC California. Currently he is an Assistant Research Professor at Beckman Research institute of City of Hope, California, USA he is working with *Salmonella*-based vaccine for over 16 years and I published this methodology in reputed journals.