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Type 1 Diabetes (T1D) reversal by neuropeptide therapy– A Phase-1 progress report

Our Diabetes Research Program focused on neuronal elements in T1D pathogenesis. We found that in T1D mouse models as well as patients, 1.) a major subset of autoimmune targets have neuronal derivation; 2.) TRPV1 (transient receptor potential, vanilloid-1, a Ca⁺⁺channel) mutations are a core disease-prerequisite, which consequent deficiency of TRPV1-dependent neuropeptides such as substance P (sP). Hypofunctional/hyposecretory mutations in T1D-prone NOD mice have analogs in T1D patients: human TRPV1 (chromosome 17) is polymorphic with possibly thousands of varied alleles, but we found the exclusive presence of the same, 4 alleles in over 50 patients. The sole exception was one T1D patient, carrying non-polymorphic, African TRPV1. Single nucleotide polymorphisms (SNP) Analysis of 1000-Genomes data showed 59 severe SNP mutations TRPV1(2.3%). Remarkably, there were 159 TRPV1 SNPs in our first 21 T1D patients, clustered mainly in 6 of 28 genomic PCR fragments sequenced, and this trend is sustained in 28 additional patients. Collectively, these data emphasize similarities between NOD mice and patients, with TRPV1 clearly a prominent if not the major element. T1D is reversed in NOD mice for months following a single pancreatic sP injection via the celiac artery, a routine medical access route in Interventional Image-Guided therapies (IGT). Recently, substantial reserves of pre-beta-cells with re-differentiation of functionality were discovered well after T1D onset. Here we describe our approved translational trial, designed to determine if and at what dose sP can reverse human T1D.

Biography

Prof. H Michael Dosch received all his schooling & training in, then, West Germany, graduating with the German MD, PhD degree in 1970 from Phillips University in Marburg/Lahn. In 1974 he began postdoctoral training at Toronto University, Canada, joined the Faculty 1977 and was promoted to full Professor of Pediatrics and Immunology. His core interest molecular & cellular elements of (mostly) Type-1 Diabetes documented in over 500 often high profile articles.

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