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Type 1 Diabetes: Prediction and progression

K M Gillespie, A E Long, I Wilson, D J Becker, I M Libman, F S Wong, A K Steck, M J Rewers, P Achenbach and A J K Williams
University of Cambridge, UK

Multiple islet autoimmunity increases risk of diabetes but not all individuals positive for two or more islet autoantibodies progress to disease within a decade. The SNAIL study seeks to harmonize data from longitudinal studies to identify the characteristics of slow progression to type-1 diabetes. Samples from 125 individuals with multiple islet autoantibodies (IAA, GADA, IA-2A and ZnT8A) for more than 10 years without progression were available from four studies (Bart-Oxford (BOX), UK; BABYDIAB, Germany; DAISY and Pittsburgh Diabetes, USA). Individuals enrolled in BOX provided "Rapid Progressor" (diagnosed <age 5 years) and at diagnosis samples. Intermediate HLA-Class II risk was more frequent in slow (61%) than Rapid Progressors (49%) with a reciprocal reduction in high risk genotypes (24% vs. 48%; pCorr=0.005) but none carried protective HLA DQ6. Slow Progressors carried fewer HLA-Class I B risk alleles (48%) than Rapid Progressors (86%; pCorr<0.001). Of 35 Slow Progressors with longitudinal data available, only 13 (37%) retained multiple autoantibodies after 10 years (p<0.001). A reduction in positivity for IAA and GADA was observed (p<0.001 and p=0.016 respectively) and in levels of GADA, IA-2A and ZnT8A even when autoantibody positive status was maintained (p<0.05 for all). In addition, Slow Progressors had lower levels of IA-2AIgG subclasses than individuals sampled close to diagnosis (p<0.05). Multiple autoantibody positivity is not maintained in some Slow Progressors suggesting regulation of the autoimmune response. Continued immuno-phenotyping of these individuals is required to elucidate the mechanisms underlying a decreased humoral response and delayed progression.

Biography

K M Gillespie is a Molecular Biologist with a long term interest in the genetic mechanisms underlying autoimmunity. She has joined the Diabetes and Metabolism Unit in 1998 as a Non-Clinical Lecturer having worked previously as a Post-doctoral Researcher at the Academic Renal Unit in Bristol and at the Department of Medicine, University of Cambridge. Her current research projects include further analysis of the novel observation that maternal cells have the capacity to differentiate into functional pancreatic beta cells, studies into the role of NK cells in autoimmune diabetes and the immunogenetic characterization of Diabetes in Down's Syndrome. She has research interests in autoimmunity, genetic mechanisms, maternal cells, functional pancreatic beta cells, NK cells, autoimmune diabetes and diabetes.

K.M.Gillespie@bristol.ac.uk

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