The Environmental Determinants of Diabetes in the Young (TEDDY): genetic criteria and international diabetes risk screening of 421 000 infants.

**Abstract:**

The Environmental Determinants of Diabetes in the Young (TEDDY) study seeks to identify environmental factors influencing the development of type 1 diabetes (T1D) using intensive follow-up of children at elevated genetic risk. This study requires a cost-effective yet accurate screening strategy to identify the high-risk cohort. The TEDDY cohort was identified through newborn screening using human leukocyte antigen (HLA) class II genes based on criteria established with pre-TEDDY data. HLA typing was completed at six international centers using different genotyping methods that can achieve >98% accuracy. TEDDY developed separate inclusion criteria for the general population (GP) and first-degree relatives (FDRs) of T1D patients. The FDR eligibility includes nine haplogenotypes (DR3/4, DR4/4, DR4/8, DR3/3, DR4/4b, DR4/1, DR4/13, DR4/9, and DR3/9) for broad HLA diversity, whereas the GP eligibility includes only the first four haplogenotypes with DRB1*0403 as an exclusion allele. TEDDY has screened 414 714 GP infants, of which 19 906 (4.8%) were eligible, whereas 1415 of the 6333 screened FDR infants (22.2%) were eligible. High-resolution confirmation testing of the eligible subjects indicated that the low-cost and low-resolution genotyping techniques employed at the screening centers yielded an accuracy of 99%. There were considerable variations in eligibility rates among the centers for GP (3.5-7.4%) and FDR (19-32%) subjects. The eligibility rates among US ethnic groups were 0.9, 1.3, 5.0, and 6.9% for Asians, Black, Caucasians, and Hispanics, respectively. Different low-cost and low-resolution genotyping methods are useful for the efficient and accurate identification of a high-risk cohort for follow-up based on the TEDDY HLA inclusion criteria.