HelmholtzZentrum münchen
German Research Center for Environmental Health

Scientific Highlight   October 2014

☐ co-ordinated with the Director of the Institute / Research Unit

Institute of Diabetes Research Type 1 (IDF 1)

PSP-Element:
G-502 100–001/ G-508600-005

Person to contact for further enquiries:
Christiane Winkler, christiane.winkler@helmholtz-muenchen.de, Tel. -3745

Title of the highlight:
Feature ranking of type 1 diabetes susceptibility genes improves prediction of type 1 diabetes

Keywords:
Type 1 Diabetes, Type 1 Diabetes susceptibility genes

Central statement of the highlight in one sentence:
We identified a weighted risk model with 10 selected SNPs that improves prediction of type 1 diabetes and therefore could be considered for recruitment of infants into studies of early type 1 diabetes natural history or prevention.

Text of the highlight:
More than 40 regions of the human genome confer susceptibility for type 1 diabetes and could be used to establish population screening strategies. The aim of our study was to identify weighted sets of SNP combinations for type 1 diabetes prediction. Therefore, we applied multivariable logistic regression and Bayesian feature selection to the Type 1 Diabetes Genetics Consortium (T1DGC) dataset with genotyping of HLA plus 40 SNPs within other type 1 diabetes-associated gene regions in 4,574 cases and 1,207 controls. We tested the weighted models in an independent validation set (765 cases, 423 controls), and assessed their performance in 1,772 prospectively followed children.
We could show, that the inclusion of 40 non-HLA gene SNPs significantly improved the prediction of type 1 diabetes over that provided by HLA alone ($p=3.1\times10^{-25}$), with a receiver operating characteristic AUC of 0.87 in the T1DGC set, and 0.84 in the validation set. Feature selection identified HLA plus nine SNPs from the PTPN22, INS, IL2RA, ERBB3, ORMDL3, BACH2, IL27, GLIS3 and RNLS genes that could achieve similar prediction accuracy as the total SNP set. Application of this ten SNP model to prospectively followed children was able to improve risk stratification over that achieved by HLA genotype alone.

In conclusion, we provided a weighted risk model with selected SNPs that could be considered for recruitment of infants into studies of early type 1 diabetes natural history or appropriately safe prevention.

Taking account of the HMGU mission:
We were able to improve prediction for type 1 diabetes by multiple logistic regression and feature ranking analysis methods on large susceptibility SNP sets. We suggest that these approaches and weighted SNP genotype models similar to those that we have identified could be used for selection of cohorts of at-risk children in natural history and appropriately safe prevention studies.

The internal HMGU co-operation partners with whom the highlight was compiled, if appropriate:
ICB