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Building and validating a prediction model for pediatric type-1 diabetes risk using next generation targeted sequencing of class II HLA genes

Aim: It is of interest to predict possible lifetime risk of Type-1 Diabetes (T1D) in young children for recruiting high-risk subjects into longitudinal studies of effective prevention strategies.

Method: Utilizing a case-control study in Sweden, we applied a recently developed Next Generation Targeted Sequencing (NGTS) technology to genotype class II genes and applied an Object-Oriented Regression (OOR) to build and validate a prediction model for T1D.

Result: In the training set, estimated risk scores were significantly different between patients and controls ($P=8.12 \times 10^{-92}$) and the Area Under the Curve (AUC) from the Receiver Operating Characteristic (ROC) analysis was 0.917. Using the validation data set, we validated the result with AUC of 0.886. Combining both training and validation data resulted in a predictive model with AUC of 0.903. Further, we performed a biological validation by correlating risk scores with six islet autoantibodies and found that the risk score was significantly correlated with IA-2A (Z-score=3.628, $P<0.001$). When applying this prediction model to the Swedish population, where the lifetime T1D risk ranges from 0.5% to 2%, we anticipate identifying about 20,000 high-risk subjects after testing all newborns and this calculation would identify about 80% of all patients expected to develop T1D in their lifetime.

Conclusion: Through both empirical and biological validation, we have established a prediction model for estimating lifetime T1D risk, using class II HLA. This prediction model should prove useful for future investigations to identify high-risk subjects for prevention research in high-risk populations.

Biography

Lue Ping Zhao has earned his BS in Computer Science (Shanghai University of Science and Technology), MS-candidate in Health Statistics (Fudan Medical University), MS/Ph.D. in Biostatistics (University of Washington) and Postdoc training in Biostatistics (Harvard University). Currently, he is a full member at Fred Hutchinson Cancer Research Center and an affiliated Professor at University of Washington. As a senior investigator in Biostatistics, Dr. Zhao has participated in many national and international studies, and has published extensively in biostatistical applications to clinical, genetic and epidemiological studies. In the past ten years, he has devoted major research interests in hematopoietic stem cell transplantation (HSCT) research, autoimmune disease etiology research, in particular, type 1 diabetes, and vaccine development for disease prevention and treatment. As a data scientist, his research interests largely center on three topics: 1) investigation of MHC/HLA genes and their roles in development of autoimmune diseases, 2) development of novel data science strategies (designs and data analytics) to enable complex data analyses with real world data from clinics, and 3) building risk prediction models for early detection, screening or prognostic assessment. Zhao's prolific developments have profited from his work at the finest research institutions, including Fred Hutchinson Cancer Research Center, University of Washington and Harvard University, and also from collaborating with prominent geneticists, biologists, physicians and epidemiologists, in addition to working with some best biostatisticians as mentors or collaborators.

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