AD-0557: Effects of β -cell function genetic variants on predicting glucose tolerance deterioration in a 9 year prospective cohort study in Chinese

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Aims

The relative contribution of β -cell function and insulin sensitivity in the pathogenesis of type 2 diabetes (T2D) are not fully understood. We investigated the role of genetic variants of β -cell function in deterioration of glucose tolerance, from a 9-year prospective cohort in the Chinese population.

Methods

We first genotyped 89 SNPs associated T2D in a cross-sectional population in China and found that 40 SNPs had a significant association with diabetes risk ($P<0.05$). Then, multiple linear regression showed that the 12 of 40 SNPs were significantly associated with β -cell function indicated by HOMA- β , Stumvoll1st and 2nd index. Then, a β -genetic risk score model (β -GRS) was constructed to assess its predicting effects on incidence rate of T2D and impaired glucose regulation (IGR) in a community-based 9-year prospective cohort (N=2495), including 2192 normal glucose tolerance and 303 IGR patients at baseline through Logistic, Cox and multiple linear regression tests.

Results

During 9-year follow up, 260 develop T2D and 326 developed IGR. 12 SNPs of 40 were associated with β -cell function indicated as HOMA- β , Stumvoll 1st and 2nd phase insulin secretion indices (Table 1). β -GRS was constructed by summing up the alleles negatively associated with β -cell function. β -GRS could predict incidence of T2D and IGR in the logistic regression (OR 1.236, 95% CI 1.094, 1.395, $P=0.0006$) as well as in the Cox model (HR 1.038, 95% CI 1.002, 1.078, $P=0.041$) after adjusting for age, sex, body mass index (BMI) at baseline (Figure 1). In addition, β -GRS also predict change in β -cell function (Stumvoll 1st : $P=0.0259$, Stumvoll 2nd : $P=0.0083$, respectively) during the 9-year follow-up period (Figure 2). As β -GRS increase, β -cell compensatory function decrease.

Conclusion

β -GRS could predict deterioration of glucose tolerance in the Chinese population. Chinese population are susceptible to type 2 diabetes due to their poor β -cell function.

Table 1 12 SNPs associated with β -cell function

SNP	Gene	Traits	Negatively allele	β (SE)	P value
rs340874	PROX1	Stumvoll 1 st	G	-0.0062 (0.0037)	0.0893
rs16856187	G6PC2	Stumvoll 1 st	A	-0.0087 (0.0039)	0.0263
rs10229583	PAX4	Stumvoll 1 st	G	-0.0080 (0.0047)	0.0894
rs10906115	CDC123	Stumvoll 1 st	A	-0.0068 (0.0036)	0.0605
rs2237892	KCNQ1	Stumvoll 1 st	C	-0.0070 (0.0038)	0.0629
		Stumvoll 2 nd	C	-0.0073 (0.0034)	0.0295
rs7041847	GLIS3	Stumvoll 1 st	A	-0.0062 (0.0036)	0.0865
		HOMA- β	A	-0.0147 (0.0086)	0.0862
rs13389219	GRB14	Stumvoll 2 nd	T	-0.0096 (0.0051)	0.0617
rs1801282	PPAR γ	Stumvoll 2 nd	G	-0.0111 (0.0064)	0.0829
rs864745	JAZF1	Stumvoll 2 nd	A	-0.0067 (0.0039)	0.0830
rs8042680	PRC1	Stumvoll 2 nd	A	-0.0319 (0.0185)	0.0848
rs13266634	SLC30A8	HOMA- β	C	-0.0155 (0.0084)	0.0643
rs13342232	SLC16A11	HOMA- β	G	-0.0421 (0.0130)	0.0013

Figure 1 Predicting effects of β -GRS on incidence of T2D and IGR

Figure 2 Predicting effects of β -GRS on quantitative traits