Supplementary Table 1. Performance of gene expression prediction models built

Prediction performance (R^2)	**All**	**Protein**	**lncRNAs**	**miRNAs**
≥0.01	8479	6788	1690	1
≥0.04	5623	4495	1127	1
≥0.09	3350	2656	693	1
≥0.16	2010	1602	408	0

Protein: Protein coding genes; lncRNAs: long non-coding RNAs; miRNAs: microRNAs.

Supplementary Table 2. Twenty-five lambda pairs and the corresponding prediction performance in the tuning set for prediction models of the 13 associated genes

gene	pair1	pair2	pair3	pair4	pair5	pair6	pair7	pair8	pair9	pair10	pair11	pair12	pair13	pair14	pair15	pair16	pair17	pair18	pair19	pair20	pair21	pair22	pair23	pair24	pair25
SFT2D1	lambda1=0.009; lambda2=0.009; r2_tuning=0.066	lambda1=0.009; lambda2=0.258; r2_tuning=0.276	lambda1=0.009; lambda2=0.508; r2_tuning=0.29	lambda1=0.009; lambda2=0.757; r2_tuning=0.282	lambda1=0.009; lambda2=1.006; r2_tuning=0.27	lambda1=0.258; lambda2=0.009; r2_tuning=0.075	lambda1=0.258; lambda2=0.258; r2_tuning=0.28	lambda1=0.258; lambda2=0.508; r2_tuning=0.29	lambda1=0.258; lambda2=0.757; r2_tuning=0.282	lambda1=0.258; lambda2=1.006; r2_tuning=0.27	lambda1=0.508; lambda2=0.009; r2_tuning=0.084	lambda1=0.508; lambda2=0.258; r2_tuning=0.282	lambda1=0.508; lambda2=0.508; r2_tuning=0.29	lambda1=0.508; lambda2=0.757; r2_tuning=0.281	lambda1=0.508; lambda2=1.006; r2_tuning=0.269	lambda1=0.757; lambda2=0.009; r2_tuning=0.091	lambda1=0.757; lambda2=0.258; r2_tuning=0.283	lambda1=0.757; lambda2=0.508; r2_tuning=0.289	lambda1=0.757; lambda2=0.757; r2_tuning=0.281	lambda1=0.757; lambda2=1.006; r2_tuning=0.269	lambda1=1.006; lambda2=0.009; r2_tuning=0.099	lambda1=1.006; lambda2=0.258; r2_tuning=0.285	lambda1=1.006; lambda2=0.508; r2_tuning=0.289	lambda1=1.006; lambda2=0.757; r2_tuning=0.281	lambda1=1.006; lambda2=1.006; r2_tuning=0.269
MTMR6	lambda1=0.007; lambda2=0.007; r2_tuning=0.081	lambda1=0.007; lambda2=0.299; r2_tuning=0.3	lambda1=0.007; lambda2=0.59; r2_tuning=0.283	lambda1=0.007; lambda2=0.882; r2_tuning=0.254	lambda1=0.007; lambda2=1.174; r2_tuning=0.254	lambda1=0.299; lambda2=0.007; r2_tuning=0.092	lambda1=0.299; lambda2=0.299; r2_tuning=0.301	lambda1=0.299; lambda2=0.59; r2_tuning=0.282	lambda1=0.299; lambda2=0.882; r2_tuning=0.254	lambda1=0.299; lambda2=1.174; r2_tuning=0.254	lambda1=0.59; lambda2=0.007; r2_tuning=0.102	lambda1=0.59; lambda2=0.299; r2_tuning=0.301	lambda1=0.59; lambda2=0.59; r2_tuning=0.281	lambda1=0.59; lambda2=0.882; r2_tuning=0.254	lambda1=0.59; lambda2=1.174; r2_tuning=0.254	lambda1=0.882; lambda2=0.007; r2_tuning=0.111	lambda1=0.882; lambda2=0.299; r2_tuning=0.301	lambda1=0.882; lambda2=0.59; r2_tuning=0.28	lambda1=0.882; lambda2=0.882; r2_tuning=0.254	lambda1=0.882; lambda2=1.174; r2_tuning=0.254	lambda1=1.174; lambda2=0.007; r2_tuning=0.119	lambda1=1.174; lambda2=0.299; r2_tuning=0.301	lambda1=1.174; lambda2=0.59; r2_tuning=0.279	lambda1=1.174; lambda2=0.882; r2_tuning=0.254	lambda1=1.174; lambda2=1.174; r2_tuning=0.254
ACOT2	lambda1=0.009; lambda2=0.009; r2_tuning=0.207	lambda1=0.009; lambda2=0.292; r2_tuning=0.336	lambda1=0.009; lambda2=0.574; r2_tuning=0.305	lambda1=0.009; lambda2=0.856; r2_tuning=0.282	lambda1=0.009; lambda2=1.139; r2_tuning=0.265	lambda1=0.292; lambda2=0.009; r2_tuning=0.216	lambda1=0.292; lambda2=0.292; r2_tuning=0.335	lambda1=0.292; lambda2=0.574; r2_tuning=0.304	lambda1=0.292; lambda2=0.856; r2_tuning=0.282	lambda1=0.292; lambda2=1.139; r2_tuning=0.264	lambda1=0.574; lambda2=0.009; r2_tuning=0.224	lambda1=0.574; lambda2=0.292; r2_tuning=0.335	lambda1=0.574; lambda2=0.574; r2_tuning=0.303	lambda1=0.574; lambda2=0.856; r2_tuning=0.281	lambda1=0.574; lambda2=1.139; r2_tuning=0.264	lambda1=0.856; lambda2=0.009; r2_tuning=0.231	lambda1=0.856; lambda2=0.292; r2_tuning=0.334	lambda1=0.856; lambda2=0.574; r2_tuning=0.302	lambda1=0.856; lambda2=0.856; r2_tuning=0.281	lambda1=0.856; lambda2=1.139; r2_tuning=0.263	lambda1=1.139; lambda2=0.009; r2_tuning=0.238	lambda1=1.139; lambda2=0.292; r2_tuning=0.333	lambda1=1.139; lambda2=0.574; r2_tuning=0.301	lambda1=1.139; lambda2=0.856; r2_tuning=0.28	lambda1=1.139; lambda2=1.139; r2_tuning=0.262
STARD3	lambda1=0.009; lambda2=0.009; r2_tuning=0.096	lambda1=0.009; lambda2=0.195; r2_tuning=0.227	lambda1=0.009; lambda2=0.382; r2_tuning=0.255	lambda1=0.009; lambda2=0.569; r2_tuning=0.254	lambda1=0.009; lambda2=0.755; r2_tuning=0.253	lambda1=0.195; lambda2=0.009; r2_tuning=0.102	lambda1=0.195; lambda2=0.195; r2_tuning=0.229	lambda1=0.195; lambda2=0.382; r2_tuning=0.255	lambda1=0.195; lambda2=0.569; r2_tuning=0.254	lambda1=0.195; lambda2=0.755; r2_tuning=0.253	lambda1=0.382; lambda2=0.009; r2_tuning=0.107	lambda1=0.382; lambda2=0.195; r2_tuning=0.231	lambda1=0.382; lambda2=0.382; r2_tuning=0.255	lambda1=0.382; lambda2=0.569; r2_tuning=0.254	lambda1=0.382; lambda2=0.755; r2_tuning=0.253	lambda1=0.569; lambda2=0.009; r2_tuning=0.112	lambda1=0.569; lambda2=0.195; r2_tuning=0.233	lambda1=0.569; lambda2=0.382; r2_tuning=0.255	lambda1=0.569; lambda2=0.569; r2_tuning=0.253	lambda1=0.569; lambda2=0.755; r2_tuning=0.253	lambda1=0.755; lambda2=0.009; r2_tuning=0.116	lambda1=0.755; lambda2=0.195; r2_tuning=0.235	lambda1=0.755; lambda2=0.382; r2_tuning=0.255	lambda1=0.755; lambda2=0.569; r2_tuning=0.253	lambda1=0.755; lambda2=0.755; r2_tuning=0.253
GSDMB	lambda1=0.008; lambda2=0.008; r2_tuning=0.131	lambda1=0.008; lambda2=0.338; r2_tuning=0.29	lambda1=0.008; lambda2=0.667; r2_tuning=0.271	lambda1=0.008; lambda2=0.997; r2_tuning=0.256	lambda1=0.008; lambda2=1.327; r2_tuning=0.252	lambda1=0.338; lambda2=0.008; r2_tuning=0.142	lambda1=0.338; lambda2=0.338; r2_tuning=0.29	lambda1=0.338; lambda2=0.667; r2_tuning=0.27	lambda1=0.338; lambda2=0.997; r2_tuning=0.255	lambda1=0.338; lambda2=1.327; r2_tuning=0.252	lambda1=0.667; lambda2=0.008; r2_tuning=0.153	lambda1=0.667; lambda2=0.338; r2_tuning=0.289	lambda1=0.667; lambda2=0.667; r2_tuning=0.27	lambda1=0.667; lambda2=0.997; r2_tuning=0.255	lambda1=0.667; lambda2=1.327; r2_tuning=0.252	lambda1=0.997; lambda2=0.008; r2_tuning=0.164	lambda1=0.997; lambda2=0.338; r2_tuning=0.288	lambda1=0.997; lambda2=0.667; r2_tuning=0.269	lambda1=0.997; lambda2=0.997; r2_tuning=0.254	lambda1=0.997; lambda2=1.327; r2_tuning=0.252	lambda1=1.327; lambda2=0.008; r2_tuning=0.173	lambda1=1.327; lambda2=0.338; r2_tuning=0.287	lambda1=1.327; lambda2=0.667; r2_tuning=0.269	lambda1=1.327; lambda2=0.997; r2_tuning=0.254	lambda1=1.327; lambda2=1.327; r2_tuning=0.252
ADAM33	lambda1=0.008; lambda2=0.008; r2_tuning=0.093	lambda1=0.008; lambda2=0.358; r2_tuning=0.308	lambda1=0.008; lambda2=0.708; r2_tuning=0.284	lambda1=0.008; lambda2=1.058; r2_tuning=0.26	lambda1=0.008; lambda2=1.408; r2_tuning=0.253	lambda1=0.358; lambda2=0.008; r2_tuning=0.105	lambda1=0.358; lambda2=0.358; r2_tuning=0.307	lambda1=0.358; lambda2=0.708; r2_tuning=0.283	lambda1=0.358; lambda2=1.058; r2_tuning=0.26	lambda1=0.358; lambda2=1.408; r2_tuning=0.253	lambda1=0.708; lambda2=0.008; r2_tuning=0.116	lambda1=0.708; lambda2=0.358; r2_tuning=0.307	lambda1=0.708; lambda2=0.708; r2_tuning=0.282	lambda1=0.708; lambda2=1.058; r2_tuning=0.259	lambda1=0.708; lambda2=1.408; r2_tuning=0.253	lambda1=1.058; lambda2=0.008; r2_tuning=0.127	lambda1=1.058; lambda2=0.358; r2_tuning=0.306	lambda1=1.058; lambda2=0.708; r2_tuning=0.282	lambda1=1.058; lambda2=1.058; r2_tuning=0.258	lambda1=1.058; lambda2=1.408; r2_tuning=0.253	lambda1=1.408; lambda2=0.008; r2_tuning=0.139	lambda1=1.408; lambda2=0.358; r2_tuning=0.306	lambda1=1.408; lambda2=0.708; r2_tuning=0.281	lambda1=1.408; lambda2=1.058; r2_tuning=0.258	lambda1=1.408; lambda2=1.408; r2_tuning=0.253
INHBA	lambda1=0.007; lambda2=0.007; r2_tuning=0.071	lambda1=0.007; lambda2=0.325; r2_tuning=0.256	lambda1=0.007; lambda2=0.644; r2_tuning=0.253	lambda1=0.007; lambda2=0.962; r2_tuning=0.253	lambda1=0.007; lambda2=1.28; r2_tuning=0.253	lambda1=0.325; lambda2=0.007; r2_tuning=0.081	lambda1=0.325; lambda2=0.325; r2_tuning=0.257	lambda1=0.325; lambda2=0.644; r2_tuning=0.253	lambda1=0.325; lambda2=0.962; r2_tuning=0.253	lambda1=0.325; lambda2=1.28; r2_tuning=0.253	lambda1=0.644; lambda2=0.007; r2_tuning=0.089	lambda1=0.644; lambda2=0.325; r2_tuning=0.257	lambda1=0.644; lambda2=0.644; r2_tuning=0.253	lambda1=0.644; lambda2=0.962; r2_tuning=0.253	lambda1=0.644; lambda2=1.28; r2_tuning=0.253	lambda1=0.962; lambda2=0.007; r2_tuning=0.096	lambda1=0.962; lambda2=0.325; r2_tuning=0.258	lambda1=0.962; lambda2=0.644; r2_tuning=0.253	lambda1=0.962; lambda2=0.962; r2_tuning=0.253	lambda1=0.962; lambda2=1.28; r2_tuning=0.253	lambda1=1.28; lambda2=0.007; r2_tuning=0.103	lambda1=1.28; lambda2=0.325; r2_tuning=0.258	lambda1=1.28; lambda2=0.644; r2_tuning=0.253	lambda1=1.28; lambda2=0.962; r2_tuning=0.253	lambda1=1.28; lambda2=1.28; r2_tuning=0.253
SMC2	lambda1=0.013; lambda2=0.013; r2_tuning=0.174	lambda1=0.013; lambda2=0.4; r2_tuning=0.354	lambda1=0.013; lambda2=0.787; r2_tuning=0.342	lambda1=0.013; lambda2=1.174; r2_tuning=0.32	lambda1=0.013; lambda2=1.561; r2_tuning=0.29	lambda1=0.4; lambda2=0.013; r2_tuning=0.188	lambda1=0.4; lambda2=0.4; r2_tuning=0.354	lambda1=0.4; lambda2=0.787; r2_tuning=0.342	lambda1=0.4; lambda2=1.174; r2_tuning=0.319	lambda1=0.4; lambda2=1.561; r2_tuning=0.289	lambda1=0.787; lambda2=0.013; r2_tuning=0.2	lambda1=0.787; lambda2=0.4; r2_tuning=0.354	lambda1=0.787; lambda2=0.787; r2_tuning=0.341	lambda1=0.787; lambda2=1.174; r2_tuning=0.318	lambda1=0.787; lambda2=1.561; r2_tuning=0.288	lambda1=1.174; lambda2=0.013; r2_tuning=0.211	lambda1=1.174; lambda2=0.4; r2_tuning=0.354	lambda1=1.174; lambda2=0.787; r2_tuning=0.34	lambda1=1.174; lambda2=1.174; r2_tuning=0.317	lambda1=1.174; lambda2=1.561; r2_tuning=0.287	lambda1=1.561; lambda2=0.013; r2_tuning=0.222	lambda1=1.561; lambda2=0.4; r2_tuning=0.354	lambda1=1.561; lambda2=0.787; r2_tuning=0.34	lambda1=1.561; lambda2=1.174; r2_tuning=0.316	lambda1=1.561; lambda2=1.561; r2_tuning=0.286
ABO	lambda1=0.01; lambda2=0.01; r2_tuning=0.225	lambda1=0.01; lambda2=0.359; r2_tuning=0.426	lambda1=0.01; lambda2=0.708; r2_tuning=0.371	lambda1=0.01; lambda2=1.057; r2_tuning=0.333	lambda1=0.01; lambda2=1.407; r2_tuning=0.285	lambda1=0.359; lambda2=0.01; r2_tuning=0.243	lambda1=0.359; lambda2=0.359; r2_tuning=0.425	lambda1=0.359; lambda2=0.708; r2_tuning=0.37	lambda1=0.359; lambda2=1.057; r2_tuning=0.332	lambda1=0.359; lambda2=1.407; r2_tuning=0.284	lambda1=0.708; lambda2=0.01; r2_tuning=0.257	lambda1=0.708; lambda2=0.359; r2_tuning=0.423	lambda1=0.708; lambda2=0.708; r2_tuning=0.369	lambda1=0.708; lambda2=1.057; r2_tuning=0.331	lambda1=0.708; lambda2=1.407; r2_tuning=0.282	lambda1=1.057; lambda2=0.01; r2_tuning=0.271	lambda1=1.057; lambda2=0.359; r2_tuning=0.422	lambda1=1.057; lambda2=0.708; r2_tuning=0.368	lambda1=1.057; lambda2=1.057; r2_tuning=0.329	lambda1=1.057; lambda2=1.407; r2_tuning=0.28	lambda1=1.407; lambda2=0.01; r2_tuning=0.284	lambda1=1.407; lambda2=0.359; r2_tuning=0.42	lambda1=1.407; lambda2=0.708; r2_tuning=0.367	lambda1=1.407; lambda2=1.057; r2_tuning=0.328	lambda1=1.407; lambda2=1.407; r2_tuning=0.278
PDX1	lambda1=0.02; lambda2=0.02; r2_tuning=0.087	lambda1=0.02; lambda2=0.158; r2_tuning=0.259	lambda1=0.02; lambda2=0.296; r2_tuning=0.258	lambda1=0.02; lambda2=0.434; r2_tuning=0.254	lambda1=0.02; lambda2=0.572; r2_tuning=0.254	lambda1=0.158; lambda2=0.02; r2_tuning=0.09	lambda1=0.158; lambda2=0.158; r2_tuning=0.259	lambda1=0.158; lambda2=0.296; r2_tuning=0.258	lambda1=0.158; lambda2=0.434; r2_tuning=0.254	lambda1=0.158; lambda2=0.572; r2_tuning=0.254	lambda1=0.296; lambda2=0.02; r2_tuning=0.094	lambda1=0.296; lambda2=0.158; r2_tuning=0.26	lambda1=0.296; lambda2=0.296; r2_tuning=0.258	lambda1=0.296; lambda2=0.434; r2_tuning=0.254	lambda1=0.296; lambda2=0.572; r2_tuning=0.254	lambda1=0.434; lambda2=0.02; r2_tuning=0.097	lambda1=0.434; lambda2=0.158; r2_tuning=0.26	lambda1=0.434; lambda2=0.296; r2_tuning=0.257	lambda1=0.434; lambda2=0.434; r2_tuning=0.254	lambda1=0.434; lambda2=0.572; r2_tuning=0.254	lambda1=0.572; lambda2=0.02; r2_tuning=0.101	lambda1=0.572; lambda2=0.158; r2_tuning=0.261	lambda1=0.572; lambda2=0.296; r2_tuning=0.257	lambda1=0.572; lambda2=0.434; r2_tuning=0.254	lambda1=0.572; lambda2=0.572; r2_tuning=0.254
RCCD1	lambda1=0.011; lambda2=0.011; r2_tuning=0.178	lambda1=0.011; lambda2=0.365; r2_tuning=0.381	lambda1=0.011; lambda2=0.718; r2_tuning=0.348	lambda1=0.011; lambda2=1.071; r2_tuning=0.313	lambda1=0.011; lambda2=1.424; r2_tuning=0.273	lambda1=0.365; lambda2=0.011; r2_tuning=0.191	lambda1=0.365; lambda2=0.365; r2_tuning=0.38	lambda1=0.365; lambda2=0.718; r2_tuning=0.347	lambda1=0.365; lambda2=1.071; r2_tuning=0.312	lambda1=0.365; lambda2=1.424; r2_tuning=0.271	lambda1=0.718; lambda2=0.011; r2_tuning=0.203	lambda1=0.718; lambda2=0.365; r2_tuning=0.38	lambda1=0.718; lambda2=0.718; r2_tuning=0.346	lambda1=0.718; lambda2=1.071; r2_tuning=0.31	lambda1=0.718; lambda2=1.424; r2_tuning=0.27	lambda1=1.071; lambda2=0.011; r2_tuning=0.215	lambda1=1.071; lambda2=0.365; r2_tuning=0.379	lambda1=1.071; lambda2=0.718; r2_tuning=0.345	lambda1=1.071; lambda2=1.071; r2_tuning=0.309	lambda1=1.071; lambda2=1.424; r2_tuning=0.268	lambda1=1.424; lambda2=0.011; r2_tuning=0.227	lambda1=1.424; lambda2=0.365; r2_tuning=0.379	lambda1=1.424; lambda2=0.718; r2_tuning=0.343	lambda1=1.424; lambda2=1.071; r2_tuning=0.308	lambda1=1.424; lambda2=1.424; r2_tuning=0.267
CFDP1	lambda1=0.011; lambda2=0.011; r2_tuning=0.111	lambda1=0.011; lambda2=0.283; r2_tuning=0.292	lambda1=0.011; lambda2=0.555; r2_tuning=0.289	lambda1=0.011; lambda2=0.827; r2_tuning=0.275	lambda1=0.011; lambda2=1.099; r2_tuning=0.259	lambda1=0.283; lambda2=0.011; r2_tuning=0.12	lambda1=0.283; lambda2=0.283; r2_tuning=0.294	lambda1=0.283; lambda2=0.555; r2_tuning=0.288	lambda1=0.283; lambda2=0.827; r2_tuning=0.274	lambda1=0.283; lambda2=1.099; r2_tuning=0.259	lambda1=0.555; lambda2=0.011; r2_tuning=0.128	lambda1=0.555; lambda2=0.283; r2_tuning=0.295	lambda1=0.555; lambda2=0.555; r2_tuning=0.288	lambda1=0.555; lambda2=0.827; r2_tuning=0.274	lambda1=0.555; lambda2=1.099; r2_tuning=0.258	lambda1=0.827; lambda2=0.011; r2_tuning=0.136	lambda1=0.827; lambda2=0.283; r2_tuning=0.296	lambda1=0.827; lambda2=0.555; r2_tuning=0.288	lambda1=0.827; lambda2=0.827; r2_tuning=0.273	lambda1=0.827; lambda2=1.099; r2_tuning=0.258	lambda1=1.099; lambda2=0.011; r2_tuning=0.143	lambda1=1.099; lambda2=0.283; r2_tuning=0.296	lambda1=1.099; lambda2=0.555; r2_tuning=0.287	lambda1=1.099; lambda2=0.827; r2_tuning=0.273	lambda1=1.099; lambda2=1.099; r2_tuning=0.257
PGAP3	lambda1=0.008; lambda2=0.008; r2_tuning=0.132	lambda1=0.008; lambda2=0.3; r2_tuning=0.303	lambda1=0.008; lambda2=0.591; r2_tuning=0.297	lambda1=0.008; lambda2=0.883; r2_tuning=0.285	lambda1=0.008; lambda2=1.174; r2_tuning=0.269	lambda1=0.3; lambda2=0.008; r2_tuning=0.141	lambda1=0.3; lambda2=0.3; r2_tuning=0.303	lambda1=0.3; lambda2=0.591; r2_tuning=0.297	lambda1=0.3; lambda2=0.883; r2_tuning=0.285	lambda1=0.3; lambda2=1.174; r2_tuning=0.268	lambda1=0.591; lambda2=0.008; r2_tuning=0.15	lambda1=0.591; lambda2=0.3; r2_tuning=0.304	lambda1=0.591; lambda2=0.591; r2_tuning=0.297	lambda1=0.591; lambda2=0.883; r2_tuning=0.284	lambda1=0.591; lambda2=1.174; r2_tuning=0.268	lambda1=0.883; lambda2=0.008; r2_tuning=0.159	lambda1=0.883; lambda2=0.3; r2_tuning=0.304	lambda1=0.883; lambda2=0.591; r2_tuning=0.296	lambda1=0.883; lambda2=0.883; r2_tuning=0.284	lambda1=0.883; lambda2=1.174; r2_tuning=0.267	lambda1=1.174; lambda2=0.008; r2_tuning=0.166	lambda1=1.174; lambda2=0.3; r2_tuning=0.303	lambda1=1.174; lambda2=0.591; r2_tuning=0.296	lambda1=1.174; lambda2=0.883; r2_tuning=0.283	lambda1=1.174; lambda2=1.174; r2_tuning=0.266

Supplementary Table 3. Associations of age, sex, top principle components, and assessed pancreatic cancer risk variants with pancreatic cancer risk in conditional analyses of 13 associated genes

Variable	*SFT2D1*		*MTMR6*		*ACOT2*		*STARD3*		*GSDMB*		*ADAM33*		*INHBA*		*SMC2*		*ABO*		*PDX1*		*RCCD1*		*CFDP1*		*PGAP3*	
	coefficient	*P* value	coefficient	*P* value	coefficient	*P* value	coefficient	*P* value	coefficient	*P* value	coefficient	*P* value	coefficient	*P* value	coefficient	*P* value	coefficient	*P* value	coefficient	*P* value	coefficient	*P* value	coefficient	*P* value	coefficient	*P* value
Gender of male	-3.93×10^{-4}	0.99	2.34×10^{-3}	0.95	-1.39×10^{-3}	0.97	-3.76×10^{-4}	0.99	1.36×10^{-3}	0.97	-4.78×10^{-4}	0.99	1.16×10^{-4}	1.00	-6.06×10^{-4}	0.99	3.25×10^{-4}	0.99	1.22×10^{-4}	1.00	3.34×10^{-4}	0.99	-7.65×10^{-4}	0.98	-1.70×10^{-4}	1.00
Age < 50	-0.17	0.01	-0.17	0.01	-0.17	0.01	-0.17	0.01	-0.17	0.01	-0.17	0.01	-0.17	0.01	-0.17	0.01	-0.17	0.01	-0.17	0.01	-0.17	0.01	-0.17	9.87×10^{-3}	-0.17	0.01
50 ≤ Age < 60	-0.14	2.78×10^{-3}	-0.14	3.07×10^{-3}	-0.14	3.03×10^{-3}	-1.40	2.72×10^{-3}	-0.14	2.23×10^{-3}	-0.14	3.11×10^{-3}	-0.14	2.79×10^{-3}	-0.14	3.28×10^{-3}	-0.14	2.77×10^{-3}	-0.14	2.67×10^{-3}	-0.14	2.59×10^{-3}	-0.14	2.46×10^{-3}	-0.14	2.71×10^{-3}
70 ≤ Age < 80	0.03	0.41	0.04	0.41	0.04	0.39	0.04	0.40	0.03	0.42	0.04	0.36	0.04	0.39	0.03	0.43	0.04	0.40	0.03	0.41	0.03	0.41	0.04	0.38	0.04	0.40
Age ≥ 80	0.28	4.43×10^{-5}	0.28	3.74×10^{-5}	0.28	3.98×10^{-5}	0.28	4.38×10^{-5}	0.28	4.06×10^{-5}	0.28	4.23×10^{-5}	0.28	4.07×10^{-5}	0.29	3.66×10^{-5}	0.28	4.49×10^{-5}	0.28	4.37×10^{-5}	0.28	4.06×10^{-5}	0.29	3.52×10^{-5}	0.28	4.67×10^{-5}
PC1	-13.75	1.17×10^{-10}	-14.11	3.73×10^{-11}	-13.78	1.09×10^{-10}	-14.10	3.97×10^{-11}	-13.65	1.62×10^{-10}	-14.29	2.09×10^{-11}	-14.14	3.32×10^{-11}	-14.15	3.35×10^{-11}	-13.98	5.70×10^{-11}	-14.12	3.49×10^{-11}	-14.10	3.82×10^{-11}	-14.26	2.30×10^{-11}	-14.02	4.91×10^{-11}
PC2	1.37	0.52	1.46	0.49	1.01	0.63	0.92	0.67	1.07	0.61	0.98	0.64	1.26	0.55	1.09	0.61	1.21	0.57	1.23	0.56	0.94	0.66	1.22	0.56	0.99	0.64
PC3	0.74	0.72	1.12	0.59	0.76	0.71	1.26	0.55	1.07	0.61	0.83	0.69	1.06	0.61	0.99	0.63	0.82	0.69	0.91	0.66	0.99	0.63	-0.90	0.67	1.26	0.55
PC4	8.49	6.11×10^{-5}	8.56	5.39×10^{-5}	8.32	8.51×10^{-5}	7.71	2.85×10^{-4}	7.83	2.21×10^{-4}	8.09	1.35×10^{-4}	8.35	8.12×10^{-5}	7.93	1.84×10^{-4}	8.28	9.17×10^{-5}	8.25	9.80×10^{-5}	8.37	7.86×10^{-5}	7.82	2.25×10^{-4}	7.73	2.74×10^{-4}
PC5	-2.18	0.30	-2.01	0.34	-1.99	0.34	-2.27	0.28	-2.39	0.25	-2.23	0.29	-2.24	0.29	-2.71	0.20	-2.26	0.28	-2.26	0.28	-2.11	0.31	-2.09	0.32	-2.29	0.27
PC6	1.79	0.39	1.86	0.37	2.16	0.29	1.96	0.34	1.79	0.39	1.88	0.36	1.90	0.36	2.13	0.30	1.97	0.34	1.91	0.36	1.78	0.39	1.68	0.42	1.91	0.35
PC7	-2.93	0.15	-2.91	0.16	-2.56	0.21	-3.05	0.14	-2.88	0.16	-2.88	0.16	-2.98	0.15	-3.03	0.14	-2.92	0.16	-2.87	0.16	-2.99	0.15	-3.02	0.14	-3.02	0.14
PC8	-5.95	4.94×10^{-3}	-6.01	4.50×10^{-3}	-5.94	4.98×10^{-3}	-5.67	7.37×10^{-3}	-5.85	5.70×10^{-3}	-5.81	6.03×10^{-3}	-5.93	5.07×10^{-3}	-5.91	5.21×10^{-3}	-5.90	5.28×10^{-3}	-5.85	5.71×10^{-3}	-6.07	4.16×10^{-3}	-5.93	5.10×10^{-3}	-5.66	7.48×10^{-3}
PC9	4.44	0.04	4.63	0.03	4.49	0.03	4.41	0.04	4.54	0.03	4.57	0.03	4.56	0.03	4.44	0.04	4.50	0.03	4.52	0.03	4.52	0.03	4.41	0.04	4.41	0.04
PC10	-4.19	0.04	-4.14	0.04	-4.00	0.05	-4.11	0.05	-4.13	0.05	-4.04	0.05	-4.14	0.04	-4.21	0.04	-4.16	0.04	-4.15	0.04	-4.19	0.04	-4.12	0.05	-4.10	0.05
rs2816938	0.14	3.32×10^{-6}	0.13	3.50×10^{-6}	0.14	3.26×10^{-6}	0.13	3.35×10^{-6}	0.14	3.17×10^{-6}	0.14	3.11×10^{-6}	0.13	3.67×10^{-6}	0.13	4.11×10^{-6}	0.14	3.26×10^{-6}	0.14	3.24×10^{-6}	0.14	3.05×10^{-6}	0.14	2.37×10^{-6}	0.14	3.13×10^{-6}
rs3790844	-0.16	1.44×10^{-6}	-0.16	1.74×10^{-6}	-0.16	1.72×10^{-6}	-0.16	1.34×10^{-6}	-0.16	1.04×10^{-6}	-0.16	1.92×10^{-6}	-0.16	1.35×10^{-6}	-0.16	1.08×10^{-6}	-0.16	1.38×10^{-6}	-0.16	1.39×10^{-6}	-0.16	1.58×10^{-6}	-0.16	1.44×10^{-6}	-0.16	1.37×10^{-6}
rs1486134	0.11	1.67×10^{-5}	0.11	1.68×10^{-5}	0.11	1.70×10^{-5}	0.11	1.50×10^{-5}	0.11	1.48×10^{-5}	0.11	1.49×10^{-5}	0.11	1.57×10^{-5}	0.11	1.38×10^{-5}	0.11	1.46×10^{-5}	0.11	1.48×10^{-5}	0.11	1.34×10^{-5}	0.11	1.26×10^{-5}	0.11	1.50×10^{-5}
rs9854771	-0.12	1.27×10^{-6}	-0.12	1.22×10^{-6}	-0.13	1.03×10^{-6}	-0.12	1.27×10^{-6}	-0.12	1.14×10^{-6}	-0.12	1.16×10^{-6}	-0.12	1.29×10^{-6}	-0.12	1.39×10^{-6}	-0.12	1.30×10^{-6}	-0.12	1.30×10^{-6}	-0.12	1.36×10^{-6}	-0.12	1.39×10^{-6}	-0.12	1.24×10^{-6}
rs2736098	-0.17	3.27×10^{-5}	-0.17	2.86×10^{-5}	-0.17	2.98×10^{-5}	-0.17	4.07×10^{-5}	-0.17	3.13×10^{-5}	-0.17	4.01×10^{-5}	-0.17	3.45×10^{-5}	-0.17	3.26×10^{-5}	-0.17	3.72×10^{-5}	-0.17	3.49×10^{-5}	-0.17	4.11×10^{-5}	-0.17	3.21×10^{-5}	-0.17	3.92×10^{-5}
rs35226131	-0.28	4.26×10^{-3}	-0.28	5.10×10^{-3}	-0.28	4.70×10^{-3}	-0.28	4.73×10^{-3}	-0.28	4.64×10^{-3}	-0.28	4.61×10^{-3}	-0.28	4.40×10^{-3}	-0.28	4.82×10^{-3}	-0.28	4.62×10^{-3}	-0.28	4.74×10^{-3}	-0.28	4.50×10^{-3}	-0.29	3.86×10^{-3}	-0.28	4.82×10^{-3}
rs401681	0.09	5.37×10^{-3}	0.10	4.14×10^{-3}	0.10	3.62×10^{-3}	0.10	4.06×10^{-3}	0.10	4.00×10^{-3}	0.10	4.02×10^{-3}	0.10	4.05×10^{-3}	0.10	4.63×10^{-3}	0.10	4.05×10^{-3}	0.10	3.96×10^{-3}	0.96	4.44×10^{-3}	0.95	4.68×10^{-3}	0.10	4.04×10^{-3}
rs17688601	0.14	5.29×10^{-7}	-0.13	7.42×10^{-7}	-0.13	7.61×10^{-7}	-0.14	5.05×10^{-7}	-0.14	6.24×10^{-7}	-0.14	5.56×10^{-7}	-0.09	9.07×10^{-3}	-0.14	7.08×10^{-7}	-0.14	4.94×10^{-7}	-0.14	5.22×10^{-7}	-0.14	4.48×10^{-7}	-0.14	5.79×10^{-7}	-0.14	5.09×10^{-7}
rs78417682	-0.17	1.09×10^{-5}	-0.17	1.52×10^{-5}	-0.17	1.19×10^{-5}	-0.17	1.02×10^{-5}	-0.18	8.98×10^{-6}	-0.17	1.84×10^{-5}	-0.17	1.31×10^{-5}	-0.17	1.40×10^{-5}	-0.17	1.15×10^{-5}	-0.17	1.18×10^{-5}	-0.17	1.08×10^{-5}	-0.17	1.30×10^{-5}	-0.17	1.04×10^{-5}
rs6971499	-0.17	2.36×10^{-6}	-0.17	2.88×10^{-6}	-0.17	2.31×10^{-6}	-0.17	3.55×10^{-6}	-0.17	2.91×10^{-6}	-0.17	2.73×10^{-6}	-0.17	2.66×10^{-6}	-0.17	3.20×10^{-6}	-0.17	2.68×10^{-6}	-0.17	2.76×10^{-6}	-0.17	3.07×10^{-6}	-0.17	2.95×10^{-6}	-0.17	3.30×10^{-6}
rs2941471	-0.10	2.96×10^{-5}	-0.10	2.85×10^{-5}	-0.10	2.84×10^{-5}	-0.10	3.03×10^{-5}	-0.10	3.32×10^{-5}	-0.10	3.49×10^{-5}	-0.10	2.70×10^{-5}	-0.10	3.12×10^{-5}	-0.10	3.15×10^{-5}	-0.10	3.13×10^{-5}	-0.10	3.89×10^{-5}	-0.10	2.85×10^{-5}	-0.10	3.03×10^{-5}
rs10094872	0.09	5.22×10^{-3}	0.09	4.84×10^{-3}	0.09	4.48×10^{-3}	0.10	4.35×10^{-3}	0.10	4.05×10^{-3}	0.10	4.41×10^{-3}	0.10	4.28×10^{-3}	0.09	5.11×10^{-3}	0.10	4.77×10^{-3}	0.09	4.61×10^{-3}	0.10	4.30×10^{-3}	0.95	4.37×10^{-3}	0.10	4.38×10^{-3}
rs1561927	-0.10	1.44×10^{-4}	-0.11	1.17×10^{-4}	-0.11	1.35×10^{-4}	-0.10	1.64×10^{-4}	-0.10	1.53×10^{-4}	-0.10	1.43×10^{-4}	-0.10	1.42×10^{-4}	-0.10	1.44×10^{-4}	-0.10	1.32×10^{-4}	-0.11	1.39×10^{-4}	-0.10	1.47×10^{-4}	-0.11	1.17×10^{-4}	-0.10	1.74×10^{-4}
rs505922	0.25	$< 2 \times 10^{-16}$	0.25	$< 2 \times 10^{-16}$	-0.25	$< 2.00 \times 10^{-16}$	0.25	$< 2.00\times 10^{-16}$	0.25	$< 2.00\times 10^{-16}$	0.25	$< 2.00\times 10^{-16}$	0.25	$< 2.00\times 10^{-16}$	0.25	$< 2.00\times 10^{-16}$	0.27	2.37×10^{-15}	0.25	$< 2.00\times 10^{-16}$	0.25	$< 2.00\times 10^{-16}$	0.24	$< 2.00\times 10^{-16}$	0.25	$< 2.00\times 10^{-16}$
rs9581943	0.15	3.34×10^{-9}	0.15	4.62×10^{-9}	0.15	3.67×10^{-9}	0.15	3.48×10^{-9}	0.15	4.44×10^{-9}	0.15	4.99×10^{-9}	0.15	4.35×10^{-9}	0.15	3.47×10^{-9}	0.15	3.43×10^{-9}	0.06	0.45	0.15	2.97×10^{-9}	0.15	4.58×10^{-9}	0.15	3.55×10^{-9}
rs9543325	0.21	1.10×10^{-15}	0.21	7.58×10^{-16}	0.21	7.18×10^{-16}	0.21	8.80×10^{-16}	0.21	1.09×10^{-15}	0.21	7.09×10^{-16}	0.21	7.33×10^{-16}	0.21	1.06×10^{-15}	0.21	8.41×10^{-16}	0.21	8.02×10^{-16}	0.21	1.28×10^{-15}	0.21	4.16×10^{-16}	0.21	8.55×10^{-16}
rs7190458	0.16	0.03	0.16	0.03	0.16	0.03	0.16	0.03	0.16	0.03	0.16	0.03	0.16	0.03	0.16	0.03	0.16	0.03	0.16	0.03	0.16	0.03	0.07	0.40	0.16	0.03
rs4795218	-0.12	1.68×10^{-4}	-0.12	1.77×10^{-4}	-0.12	1.08×10^{-4}	-0.12	1.25×10^{-4}	-0.12	1.23×10^{-4}	-0.12	1.74×10^{-4}	-0.12	1.50×10^{-4}	-0.12	1.35×10^{-4}	-0.12	1.49×10^{-4}	-0.12	$1.49 \times 10^{-}$	-0.12	1.43×10^{-4}	-0.12	1.90×10^{-4}	-0.12	1.22×10^{-4}
rs11655237	0.19	4.34×10^{-5}	0.19	3.01×10^{-5}	0.19	4.00×10^{-5}	0.19	2.98×10^{-5}	0.19	3.43×10^{-5}	0.19	4.27×10^{-5}	0.19	3.51×10^{-5}	0.19	3.10×10^{-5}	0.19	3.73×10^{-5}	0.19	3.74×10^{-5}	0.19	3.89×10^{-5}	0.19	3.98×10^{-5}	0.19	2.88×10^{-5}
rs1517037	-0.13	6.72×10^{-5}	-0.13	5.97×10^{-5}	-0.13	6.69×10^{-5}	-0.12	6.85×10^{-5}	-0.12	6.87×10^{-5}	-0.12	6.87×10^{-5}	-0.13	6.25×10^{-5}	-0.12	6.84×10^{-5}	-0.13	6.43×10^{-5}	-0.13	6.63×10^{-5}	-0.13	5.52×10^{-5}	-0.13	6.63×10^{-5}	-0.13	6.80×10^{-5}
rs16986825	0.14	1.60×10^{-5}	0.14	1.66×10^{-5}	0.14	1.54×10^{-5}	0.14	1.36×10^{-5}	0.14	1.34×10^{-5}	0.14	1.22×10^{-5}	0.14	1.54×10^{-5}	0.14	1.55×10^{-5}	0.14	1.40×10^{-5}	0.14	1.32×10^{-5}	0.14	1.24×10^{-5}	0.14	8.81×10^{-6}	0.14	1.32×10^{-5}

Supplementary Table 4. The functions of *RCCD1*, and *CFDP1* and their reported links with human cancers

Region	**Gene name**	**Functions**	**Cancer**	**References (PMID)**
15q26.1	*RCCD1*	The RCCD1 (RCC1 domain-containing protein 1) protein plays an important role in regulating alpha-tubulin deacetylation and cytoskeletal microtubule stability, thereby promoting cell migration and TGF-beta-induced epithelial to mesenchymal transition (EMT).	Lung cancer	31582214
				28455245
			Breast cancer	28362817
			Ovarian cancer	27432226
16q23.1	*CFDP1*	Gene *CFDP1* (Craniofacial development protein 1) is 139,815 bp long with 7 exons and 6 introns and maps to chromosome 16 in the band 16q22.2-q22.3. *CFDP1* gene expression has been detected in a wide range of cancer tissues.	Esophageal adenocarcinoma	31891614
			Angiotropic melanoma	23275074

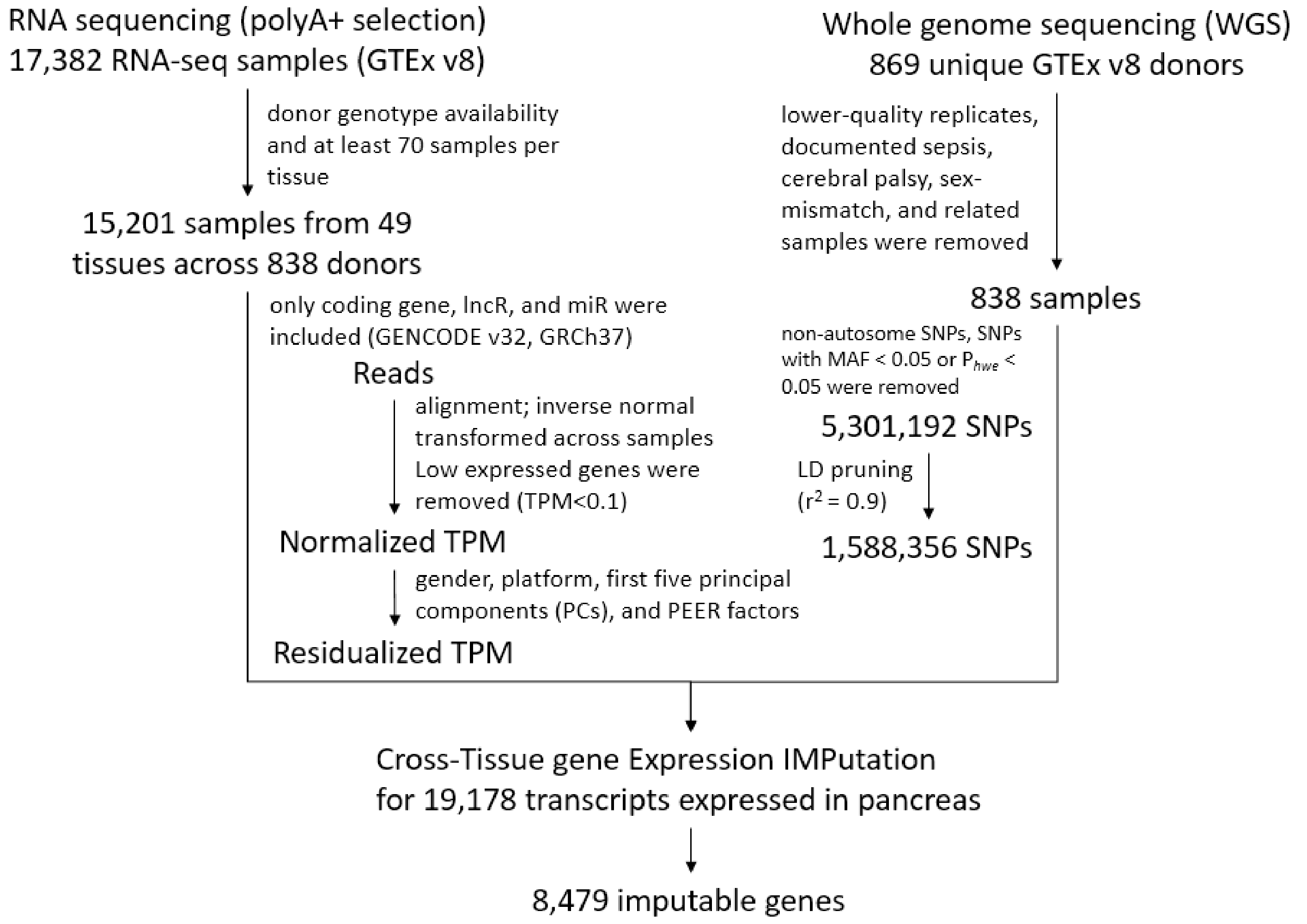
Supplementary Table 5. Associations of genes identified in Zhong et al. with pancreatic cancer risk in the present study

Previous TWAS (Zhong et al.)						The present study		
Region	Gene name	Approach	Training tissue	Z	*P* value after FDR	OR	95% CI	*P* value
1p36.12	*CELA3B*	FUSION	GTEx pancreas	-3.98	6.89×10^{-5}	1.02	0.09-11.49	0.99
		FUSION	Combined pancreas	-4.62	3.80×10^{-6}			
		MetaXcan	GTEx pancreas	-4.43	9.38×10^{-6}			
		MetaXcan	Combined pancreas	-4.29	1.83×10^{-5}			
5p15.33	*TERT*	SMulTiXcan	Cross tissue	-8.24 to 4.20	5.80×10^{-18}	No prediction model with $R^2 \geq 0.01$ built		
5p15.33	*CLPTM1L*	SMulTiXcan	Cross tissue	-8.33 to 0.91	1.48×10^{-16}	No prediction model with $R^2 \geq 0.01$ built		
5p15.33	*ZDHHC11B*	SMulTiXcan	Cross tissue	-1.6 to 3.13	3.18×10^{-6}	1.21	0.94-1.56	0.13
7p14.1	*INHBA*	MetaXcan	GTEx pancreas	-5.11	3.20×10^{-7}	0.56	0.47-0.68	8.44×10^{-7}
		SMulTiXcan	Cross tissue	-5.11 to -0.72	4.10×10^{-6}			
9p31.1	*SMC2*	FUSION	Combined pancreas	4.95	7.52×10^{-7}	2.80	2.04-3.83	7.71×10^{-8}
		MetaXcan	Combined pancreas	4.93	8.19×10^{-7}			
		SMulTiXcan	Cross tissue	-3.34 to 5.35	8.50×10^{-6}			
9p31.1	*SMC2-AS1*	SMulTiXcan	Cross tissue	-4.9 to 4.8	1.39×10^{-5}	No prediction model with $R^2 \geq 0.01$ built		
9q34.2	*ABO*	FUSION	LTG pancreas	9.38	6.71×10^{-21}	1.25	1.17-1.33	1.38×10^{-8}
		FUSION	GTEx pancreas	6.96	3.44×10^{-12}			
		FUSION	Combined pancreas	7.55	4.34×10^{-14}			
		MetaXcan	LTG pancreas	10.72	8.07×10^{-27}			

		MetaXcan	GTEx pancreas	7.08	1.41×10^{-12}			
		MetaXcan	Combined pancreas	7.65	2.05×10^{-14}			
10q23.31	*RP11-80H5.9*	SMulTiXcan	Cross tissue	-2.21 to 4.4	8.23×10^{-6}	No prediction model with $R^2 \geq 0.01$ built		
12q13.13	*SMUG1*	FUSION	GTEx pancreas	-4.04	5.40×10^{-5}	0.90	0.84-0.96	3.04×10^{-3}
13q12.2	*PDX1*	MetaXcan	GTEx pancreas	-7.18	6.85×10^{-13}	0.50	0.42-0.60	5.29×10^{-10}
		SMulTiXcan	Cross tissue	-7.18 to -6.59	4.87×10^{-12}			
13q22.1	*KLF5*	FUSION	GTEx pancreas	4.91	9.17×10^{-7}	No prediction model with $R^2 \geq 0.01$ built		
		FUSION	Combined pancreas	5.92	3.15×10^{-9}			
14q32.33	*BTBD6*	FUSION	GTEx pancreas	4.06	4.98×10^{-5}	1.52	1.14-2.02	4.56×10^{-3}
		FUSION	Combined pancreas	4.00	6.30×10^{-5}			
15q23	*HEXA*	FUSION	Combined pancreas	-4.02	5.68×10^{-5}	No prediction model with $R^2 \geq 0.01$ built		
15q26.1	*RCCD1*	FUSION	LTG pancreas	-3.98	6.94×10^{-5}	0.85	0.79-0.91	2.48×10^{-4}
		FUSION	GTEx pancreas	-4.04	5.38×10^{-5}			
		FUSION	Combined pancreas	-3.99	6.52×10^{-5}			
16q23.1	*WDR59*	FUSION	Combined pancreas	-4.70	2.54×10^{-6}	No prediction model with $R^2 \geq 0.01$ built		
16q23.1	*CFDP1*	FUSION	LTG pancreas	6.07	1.26×10^{-9}	1.51	1.33-1.72	1.29×10^{-7}
		FUSION	Combined pancreas	5.76	8.47×10^{-9}			
		MetaXcan	Combined pancreas	5.58	2.40×10^{-8}			
		SMulTiXcan	Cross tissue	2.50 to 6.89	2.02×10^{-8}			

16q23.1	*BCAR1*	SMulTiXcan	Cross tissue	-5.60 to 6.49	1.94×10^{-7}	No prediction model with $R^2 \geq 0.01$ built		
16q23.1	*TMEM170A*	SMulTiXcan	Cross tissue	-3.69 to 2.86	1.21×10^{-5}	No prediction model with $R^2 \geq 0.01$ built		
17q12	*PNMT*	FUSION	LTG pancreas	4.86	1.20×10^{-6}	No prediction model with $R^2 \geq 0.01$ built		
17q12	*CDK12*	FUSION	GTEx pancreas	-4.05	5.15×10^{-5}	No prediction model with $R^2 \geq 0.01$ built		
17q12	*PGAP3*	FUSION	LTG pancreas	3.91	9.11×10^{-5}	1.19	1.10-1.29	3.32×10^{-4}
		FUSION	GTEx pancreas	3.98	6.96×10^{-5}			
		MetaXcan	GTEx pancreas	4.11	3.03×10^{-5}			
		MetaXcan	Combined pancreas	4.17	2.98×10^{-5}			
17q22	*SUPT4H1*	FUSION	GTEx pancreas	4.12	3.72×10^{-5}	1.19	0.97-1.46	0.099
		MetaXcan	GTEx pancreas	4.11	3.90×10^{-5}			
18q11.22	*RP11-888D10.3*	MetaXcan	GTEx pancreas	-4.07	4.67×10^{-5}	No prediction model with $R^2 \geq 0.01$ built		
19p13.11	*PGPEP1*	MetaXcan	Combined pancreas	-4.13	3.67×10^{-5}	0.81	0.73-0.90	1.46×10^{-4}

Supplementary Figure 1. **The flowchart of quality control and prediction model training in the reference dataset.** GTEx v8 was used as the reference dataset to build the prediction model. More details can be found in the preprint of the v8 release (1). Totally 838 samples and 49 tissues were included in the model training. The weights were jointly estimated by (penalized) regressing the residual of gene expression on genotypes.



Reference

1. Aguet F, Barbeira, A. N., Bonazzola, R., Brown, A., Castel, S. E., Jo, B., et al. The GTEx Consortium atlas of genetic regulatory effects across human tissues. BioRxiv2019.