



Supplementary Material

Supplementary Table S1. Demographic and clinical data of study groups.

ALGORITHM TYPE	ALGORITHM	HYPER- PARAMETER	SET OF VALUES
PREPROCESSING	Mode imputation		
	Mean imputation		
	Contant Removal		
	Standardization		
FEATURE	Test-Budgeted	alpha	0.1, 0.01, 0.05
SELECTION	Statistically Equivalent		
	Signature (SES)		
MODELING	LASSO	maxk	3, 2
		penalties	1.25, 2.0, 0.0, 0.25, 1.0, 1.5, 0.5
	Linear Support Vector Machines	costs	0.1, 1.0, 0.001, 100.0, 10.0, 0.01
	Polynomial Support Vector Machines	gammas	1.0, 0.001, 0.1, 0.01, 10.0, 100.0
	RBF Support Vector Machines	costs	0.1, 1.0, 0.001, 100.0, 10.0, 0.01
		degrees	4, 2, 3
	Logistic Regression	gammas	1.0, 0.001, 0.1, 0.01, 10.0, 100.0
		costs	0.1, 1.0, 0.001, 100.0, 10.0, 0.01
	Random Forests	lambdas	1.0, 0.001, 0.01, 100.0, 10.0, 0.1, 1.0E-4
		min leaf sizes	1, 4, 3, 5, 2
	vars to split		0.816 sqrt (nvars), 1.0 sqrt (nvars), 1.291 sqrt (nvars),

			0.577 sqrt (nvars), 1.414 sqrt (nvars), 1.154 sqrt (nvars)
		splits to perform	1.0
		ntrees	1000, 100
	Decision Tree	min leaf sizes	2, 1, 4, 3, 5
		vars to split	nvars // 1.0
		splits to perform	1.0
		alphas	0.1, 0.05, 0.01

Supplementary Table S2. Demographic and clinical data of study groups.

	T2DM	HEALTHY	P-VALUE
	PATIENTS	VOLUNTEERS	
	(N=96)	(N=71)	
GENDER (MALE)	58 (60%)	50 (70%)	0.229
AGE (YEARS)	64 ±8	62 ±10	0.249
BMI (KG/M ²)	30.9 ±4.7	28.4 ±5.2	0.049
SMOKING	16 (17%)	25 (39%)	0.005
GLUCOSE (MG/DL)	138 ±37	85 ±13	0.475
C-PEPTIDE (NG/ML)	4.1 ±3.2	-	
HBA1C (%)	7.2 ±1.1	-	
DIABETES DURATION (YEARS)	14 ±9	-	
DIABETES COMPLICATION (PRESENCE)	25 (26%)	-	

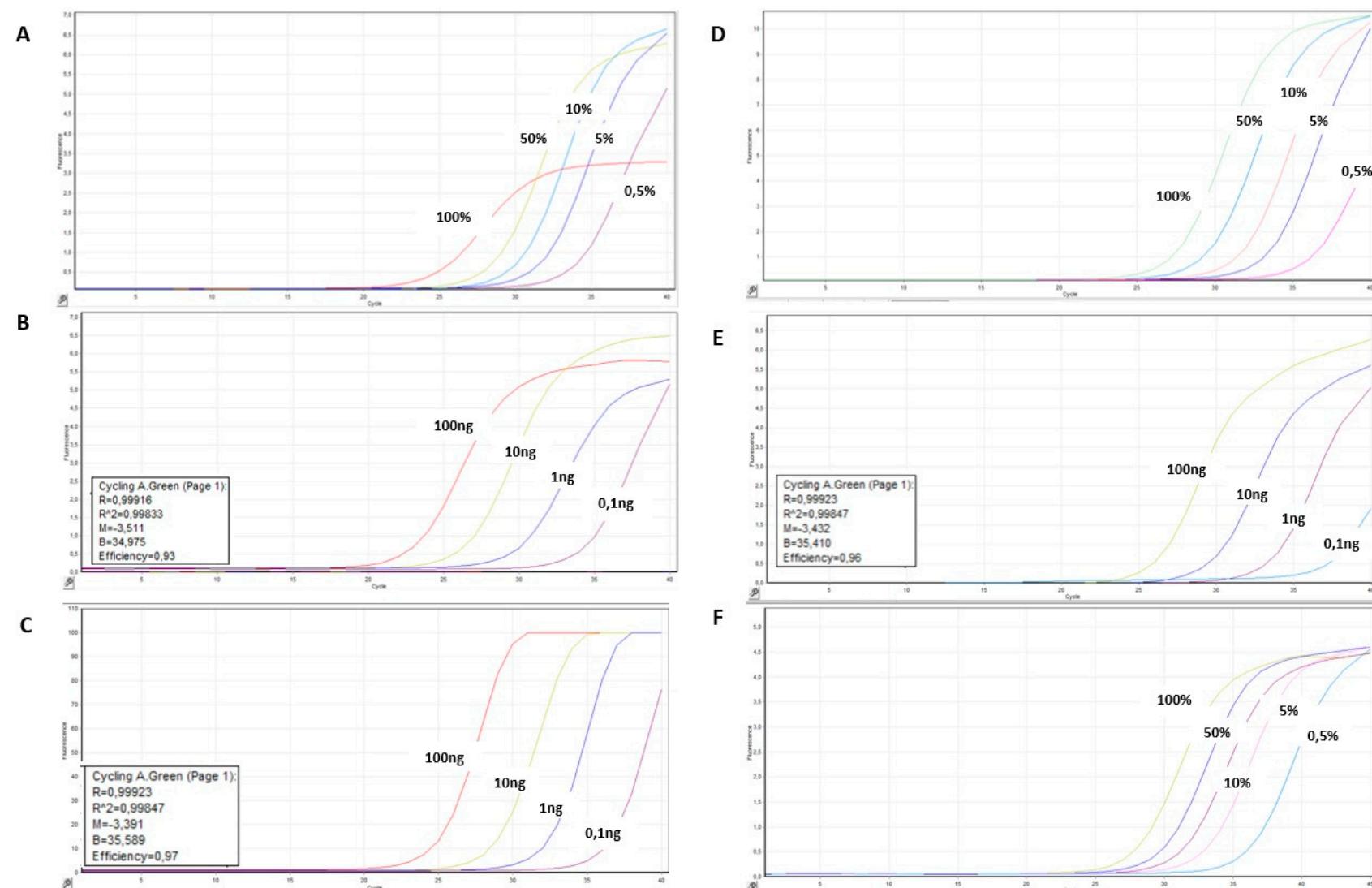
DIABETES THERAPY (YES)	96 (100%)	-
ORAL THERAPY (METFORMIN, ETC.)	96 (100%)	-
INSULIN	42 (44%)	-

Supplementary Table S3. Primer sequences, genomic locations, and related references (where relevant) used for qMSP assays.

PRIMER NAME	PRIMER SEQUENCE (5'- 3')	GENOMIC LOCATION (GRCH38)	REFERENCE
GAPDHF	CCC CAC ACA CAT GCA CTT ACG	12:6,535,875:1	[30]
GAPDHR	CCT AGT CCC AGG GCT TTG ATT	12:6,535,972:1	
ACTBF	TGG TGA TGG AGG AGG TTT AGT AAG T	7:5,558,705:-1	
ACTBR	AAC CAA TAA AAC CTA CTC CTC CC	7:5,558,838:-1	
INSMETHF	CGG AAA TTG TAG TTT TAG TTT TTA GTT ATT TGT C	11:2,159,776:-1	
INSMETHR	CCT AAA AAA CTA AAA ACT ACT AAA CCC CCG	11:2,159,922:-1	
INSUNMETHF	TGG AAA TTG TAG TTT TAG TTT TTA GTT ATT TGT T	11:2,159,776:-1	
INSUNMETHR	CCT AAA AAA CTA AAA ACT ACT AAA CCC CCA	11:2,159,922:-1	
IAPPF	TGT TAT TAG TTA TTA GGT GGA AAA G	12:21,378,228:1	[8]
IAPPMETHR	TAA AAA ATT TAC CAA ACG CTA CG	12:21,378,304:1	
IAPPUNMETHR	TAA AAA ATT TAC CAA ACA CTA CA	12:21,378,304:1	
GCKMETHF	AAT GTC GAG CGG CGT TTG AG	7:44,153,026:-1	[9]
GCKUNMETHF	AGG AAA TGT TGA GTG GTG TTT GAG T	7:44,153,022:-1	

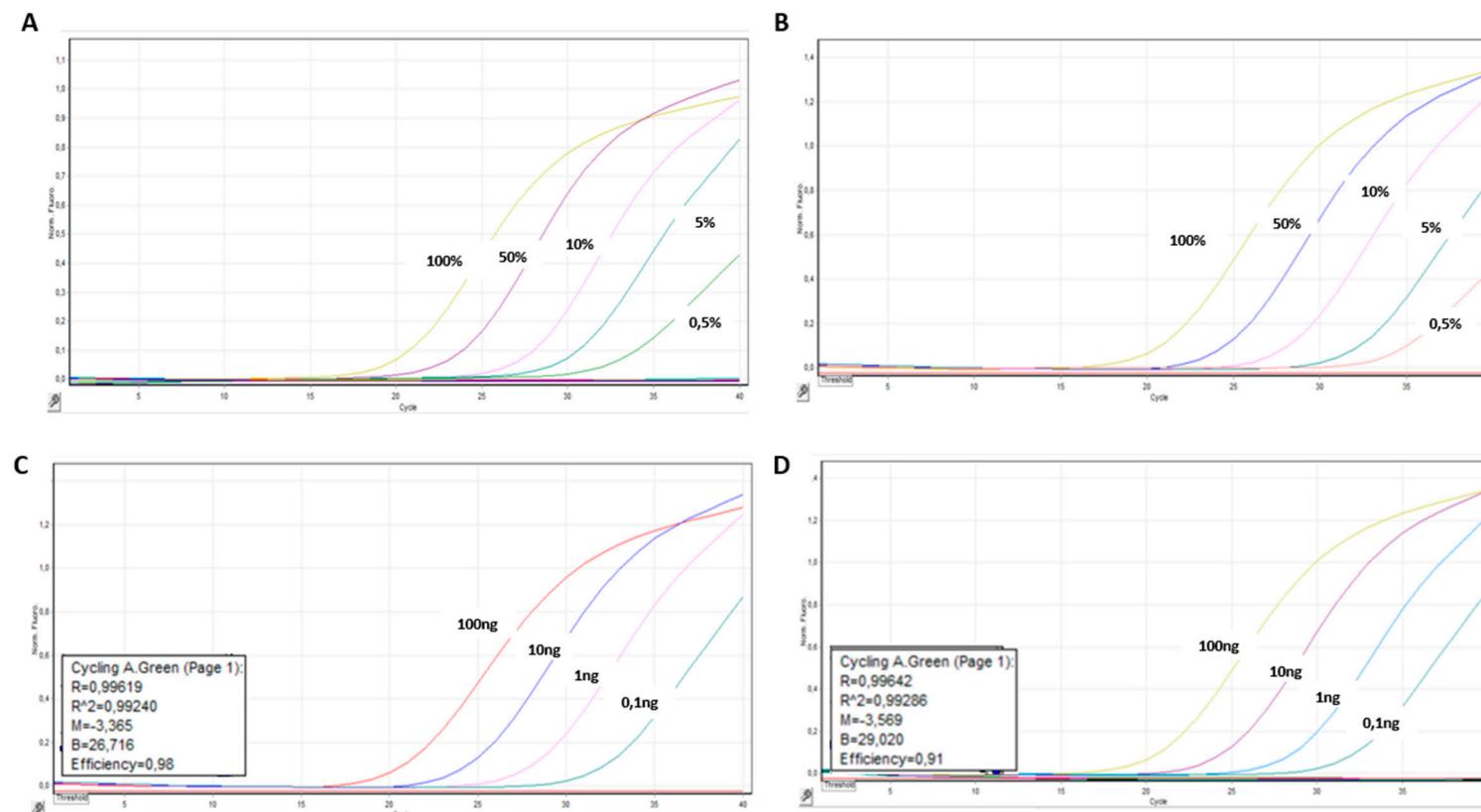
GCKR	ATC CTC TCC CTT CTA TAA CCT AAA AAC AAC	7:44,153,136:-1
KCNJ11METHF	CGG GTT TCG GTT TCG TTC	11:17,389,140:1
KCNJ11METHR	CAC GAA CGA ACA AAC AAA CG	11:17,389,253:1
KCNJ11UNMETHF	TGG GTT TTG GTT TTG TTT GTT GT	11:17,389,140:1
KCNJ11UNMETHR	ACC CAC AAA CAA ACA AAC AAA CA	11:17,389,254:1
ABCC8METHF	TAG GAA GAC GTG CGG TAT TAC	11:17,476,660:1
ABCC8METHR	CTA CGA CAA CGA AAA CCA CT	11:17,476,743:1
ABCC8UNMETHF	GAG TAG GAA GAT GTG TGG TAT TAT	11:17,476,657:1
ABCC8UNMETHR	CTT CTA CAA CAA CAA AAA CCA CT	11:17,476,743:1

F: forward, R: reverse, METH: methylated, UNMETH: unmethylated



Supplementary Figure S1. (A) Specificity of *ABCC8* qMSP assay for the methylated primers set: amplification curves of 100%, 50%, 10%, 5% and 0.5% SB-converted methylated DNA standards. (B) Sensitivity of *KCNJ11* qMSP assay for the unmethylated primers set: amplification curves of 10-fold serially diluted 100% SB-

converted non-methylated DNA standard—efficiency 93%. (C) Sensitivity of *INS* qMSP assay for the unmethylated primers set: amplification curves of 10-fold serially diluted 100% SB-converted non-methylated DNA standard—efficiency 97%. (D) Specificity of *INS* qMSP assay for the methylated primers set: amplification curves of 100%, 50%, 10%, 5% and 0.5% SB-converted methylated DNA standards. (E) Sensitivity of *IAPP* qMSP assay for the unmethylated primers set: amplification curves of 10-fold serially diluted 100% SB-converted non-methylated DNA standard—efficiency 96%. (F) Specificity of *GCK* qMSP assay for the unmethylated primers set: amplification curves of 100%, 50%, 10%, 5% and 0.5% SB-converted non-methylated DNA standards.



Supplementary Figure S2. (A) Specificity of *KCNJ11* qMSP assay for the methylated primers set: amplification curves of 100%, 50%, 10%, 5% and 0.5% SB-converted non-methylated DNA standards. (B) Specificity of *IAPP* qMSP assay for the unmethylated primers set: amplification curves of 100%, 50%, 10%, 5% and 0.5% SB-converted non-methylated DNA standards. (C) Sensitivity of *GCK* qMSP assay for the unmethylated primers set: amplification curves of 10-fold serially diluted 100% SB-converted non-methylated DNA standard—efficiency 98%. (D) Sensitivity of *IAPP* qMSP assay for the methylated primers set: amplification curves of 10-fold serially diluted 100% SB-converted non-methylated DNA standard—efficiency 91%.