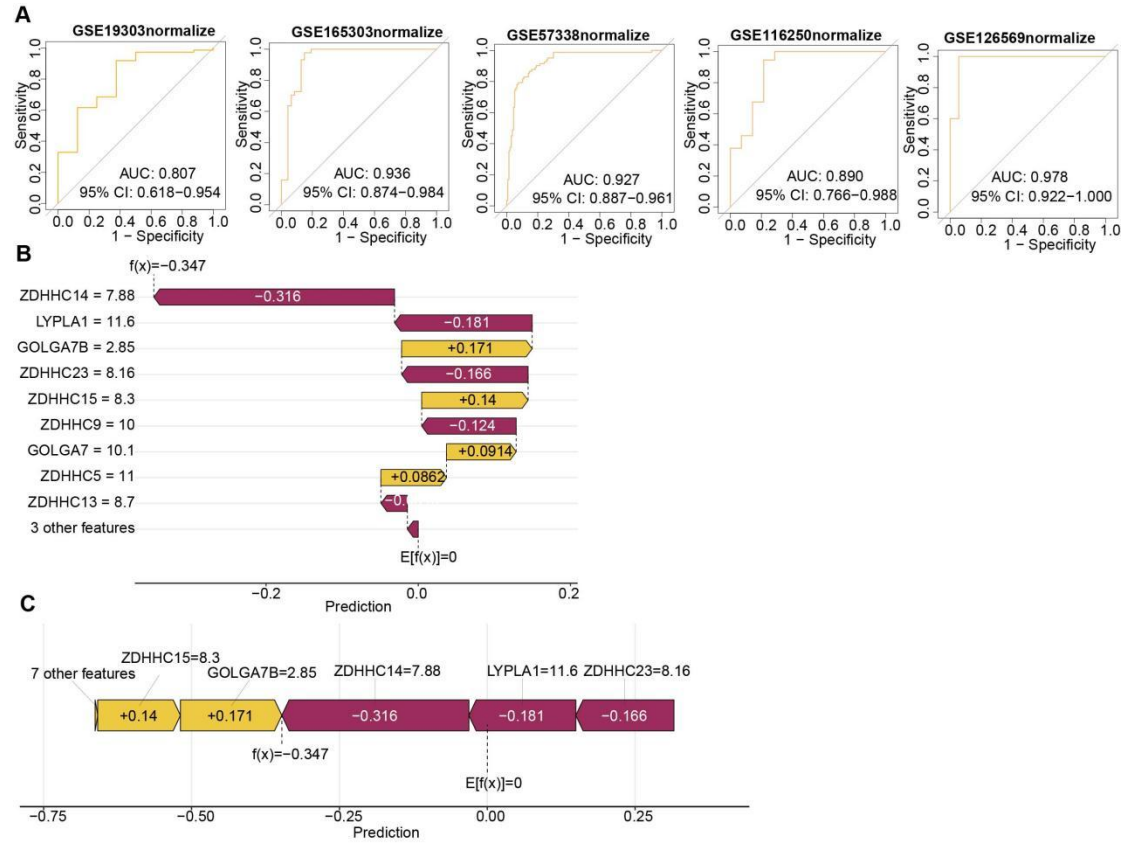
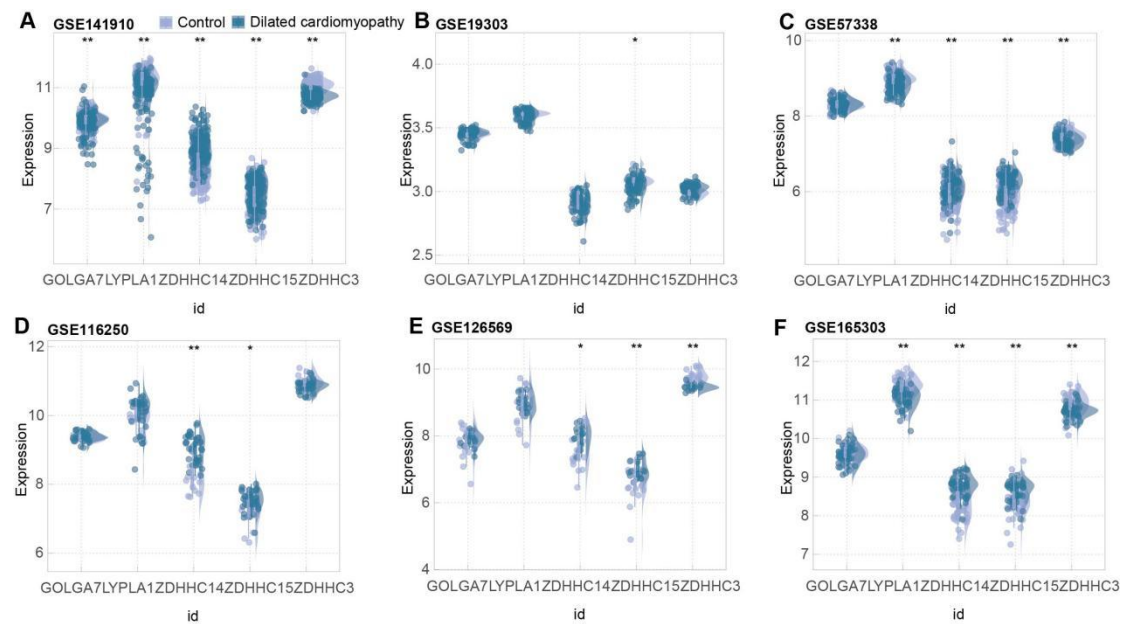


Supplementary Material

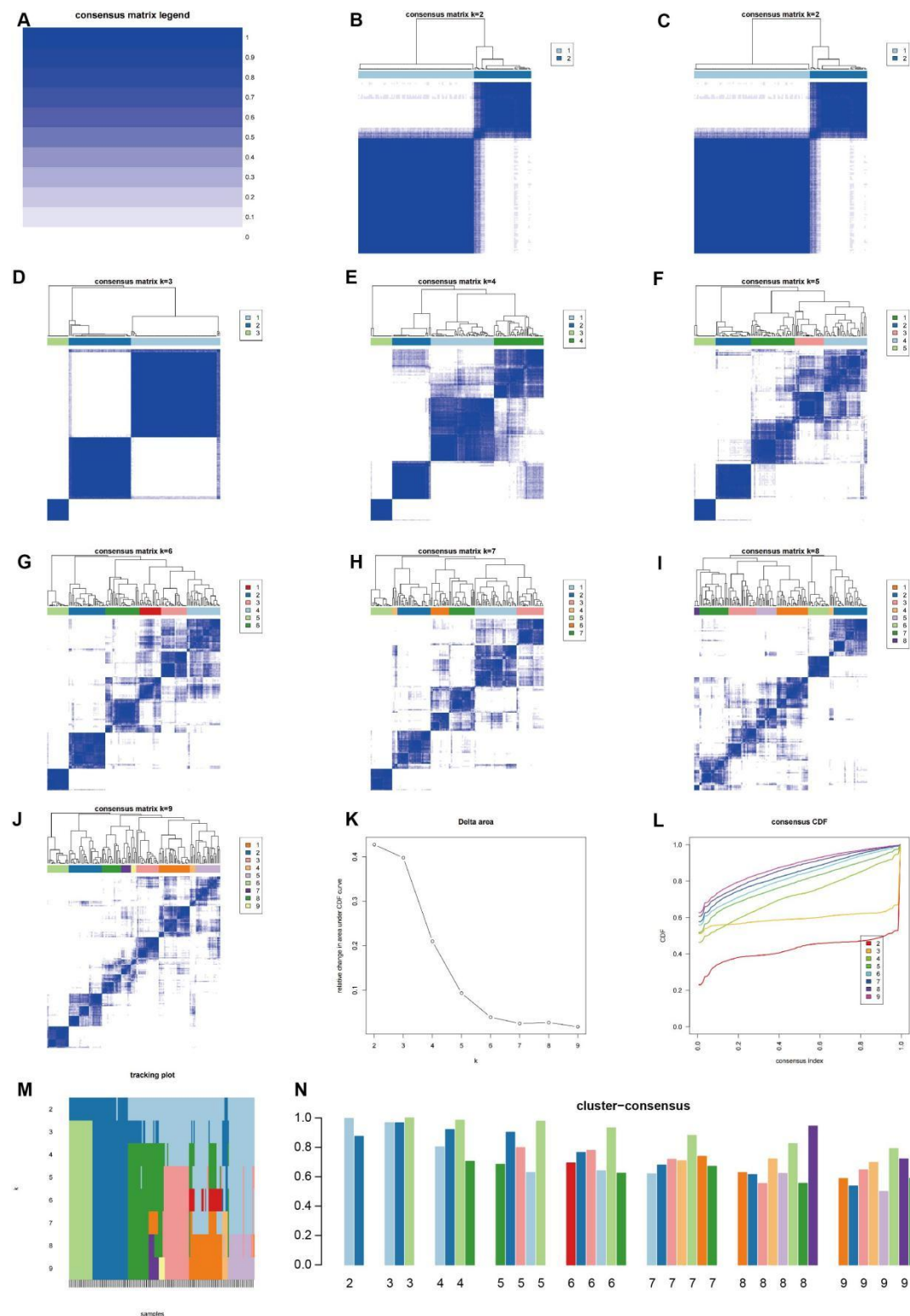
1. Supplementary Figures



Supplementary Figure 1. Model performance in external validation cohorts and individual prediction interpretation. (A) ROC curves and AUC values across validation datasets (GSE19303, GSE165303, GSE57338, GSE116250, and GSE126569). (B) SHAP contribution values of each core gene to the prediction outcome in a single sample. (C) Schematic illustration of the combined effects of core genes in individual predictions.

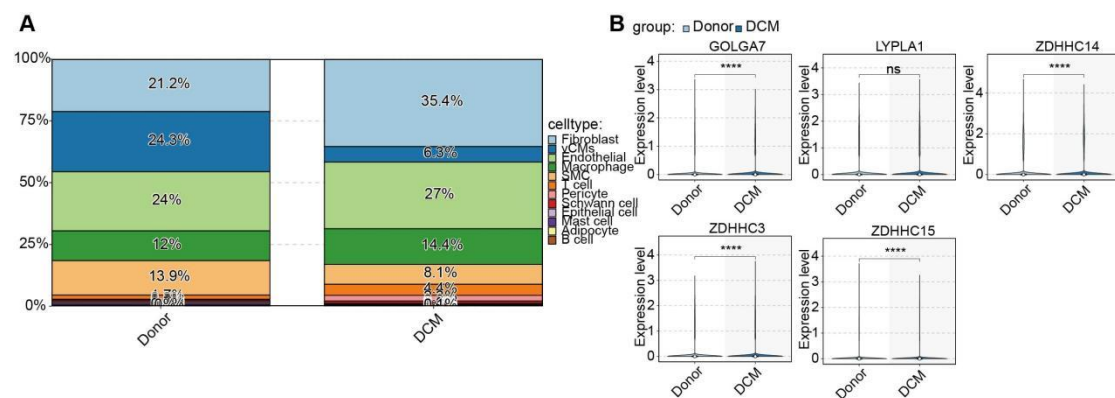


Supplementary Figure 2. Expression validation of core palmitoylation-related genes in training and validation cohorts. (A–F) Differential expression of core genes (GOLGA7, LYPLA1, ZDHHC14, ZDHHC15, and ZDHHC3) across the GSE141910, GSE19303, GSE57338, GSE116250, GSE126569, and GSE165303 datasets. Each point represents an individual sample, and violin plots illustrate the distribution of gene expression, with group comparisons reflecting differences between control and DCM groups. Data are presented as scatter plots combined with violin plots. Group comparisons were performed using an unpaired two-tailed test. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, ns indicates no statistical significance.



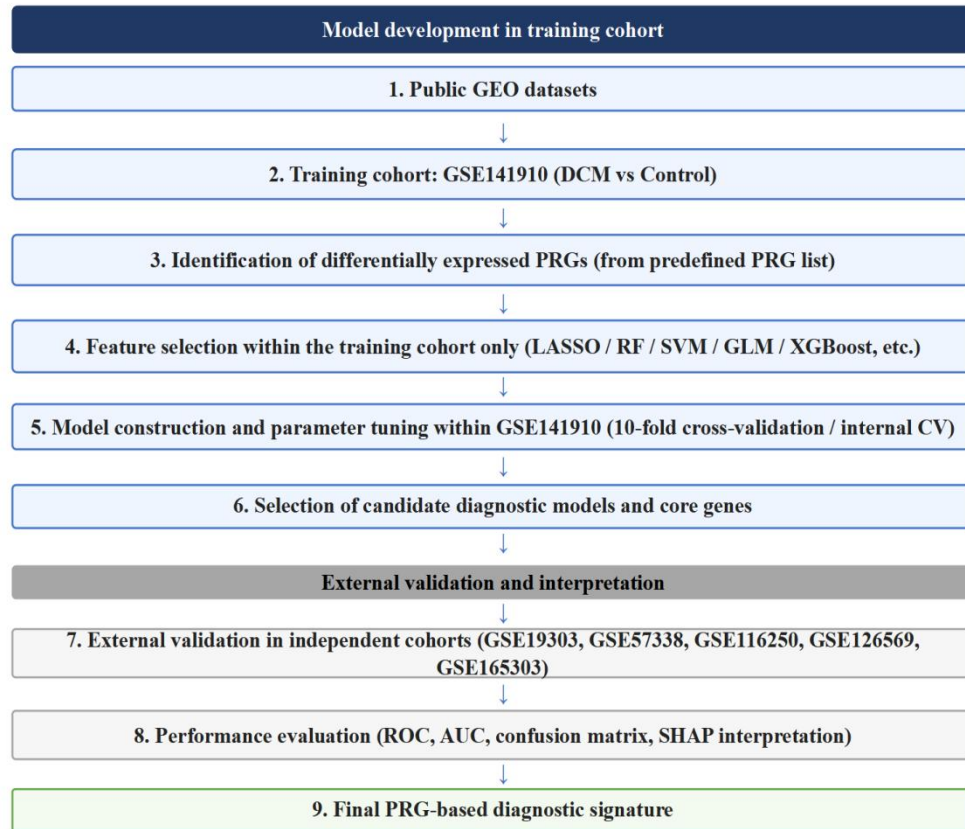
Supplementary Figure 3. Consensus clustering stability analysis. (A) Legend of the consensus matrix. (B–J) Consensus matrices for different cluster numbers ($k = 2-9$). (K) Delta area curve for evaluating changes in clustering stability across different k values. (L) Cumulative distribution function (CDF) curve. (M) Cluster

Supplementary Figure 5. ceRNA regulatory network of core palmitoylation-related genes. The network illustrates predicted regulatory associations among core genes, miRNAs, and lncRNAs based on database-derived interactions. Different node colors represent molecule types: green nodes indicate mRNAs, orange and purple nodes represent miRNAs, and gray nodes denote lncRNAs; edges indicate predicted or potential regulatory associations.



Supplementary Figure 6. Cell composition and PRG expression patterns in single-nucleus data. (A) Stacked bar plot showing the proportions of different cell types in Donor and DCM groups. (B) Violin plots comparing expression levels of core genes (GOLGA7, LYPLA1, ZDHHC3, ZDHHC14, and ZDHHC15) between Donor and DCM groups.

and DCM samples at the single-nucleus level. Data are presented as mean $\pm$ SD. Statistical analysis was performed using the Wilcoxon rank-sum test. ****p < 0.0001, ns: not significant.



Supplementary Figure 7. Machine-learning workflow and external validation design. GSE141910 was used as the training cohort. Differential PRG filtering, feature selection, model fitting, parameter tuning, and internal cross-validation were performed within the training cohort. External validation cohorts were not used for differential expression filtering, feature selection, parameter tuning, internal cross-validation, or model fitting. After model training, candidate models were fixed and applied to GSE19303, GSE57338, GSE116250, GSE126569, and GSE165303 for retrospective performance evaluation.

2. Supplementary Tables

Supplementary Table 1. Molecular docking of binding energy

Compound	Binding energy (kcal/mol)				
	GOLGA 7(9OA6)	LYPLA1 (6QGQ)	ZDHHC3(AF- Q9NYG2-F1)	ZDHHC14(AF- -Q8IZN3-F1)	ZDHHC15(AF- Q96MV8-F1)
Valproic Acid	-5.3	-5.8	-4.8	-4.6	-6.9

Supplementary Table 2. Detailed GSE data for each group

GEO ID	Role	Data type / platform	Samples used	Control / DCM	Tissue/source	Disease/control definition	Preprocessing and batch handling	Purpose
GSE141910	Training cohort	Bulk; GPL16791	322	161 / 161	Human myocardial tissue	Non-failing controls and DCM samples based on GEO annotation	Normalized independently; probes/genes mapped to symbols; duplicated genes averaged; no external validation samples used in model development	Differential PRG screening, feature selection, model training, internal validation
GSE19303	External validation	Bulk; GPL570	82	8/74	Human myocardial biopsy	Based on original GEO annotation	Independently normalized; shared genes retained; no cross-cohort batch correction	External validation
GSE116250	External validation	Bulk; GPL16791	53	15/38	Human myocardial tissue	Based on original GEO annotation	Independently normalized; shared genes retained; no cross-cohort batch correction	External validation

GSE165303	External validation	Bulk; GPL18573/GPL20795	93	48/45	Human heart tissue	Based on original GEO annotation	Platform-specific normalization; shared genes retained; platform heterogeneity acknowledged	External validation
GSE126569	External validation	Bulk; GPL16791/GPL20301	36	18 / 18	Human LV tissue	Healthy adult controls and idiopathic DCM samples based on GEO annotation	Platform-specific normalization; shared genes retained; no cross-cohort batch correction	External validation
GSE57338	External validation	Bulk; GPL11532	231	136 / 95	Human LV tissue	Non-failing and DCM samples based on GEO annotation	Independently normalized; shared genes retained; no cross-cohort batch correction	External validation
GSE183852	snRNA-seq cohort	snRNA-seq; GPL24676	38	25 / 13	Human cardiac nuclei	Donor/non-failing and DCM samples based on GEO annotation	Seurat QC, normalization, clustering, annotation, PRG scoring; not used for ML model training	Cell type-specific PRG analysis

Supplementary Table 3. Curated palmitoylation-related genes used in this study

Gene symbol	Functional category	Evidence/annotation	Source/reference
ZDHHC1	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC2	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC3	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC4	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC5	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC6	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46

ZDHHC7	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC8	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC9	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC11	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC12	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC13	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC14	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC15	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46

ZDHHC16	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC17	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC18	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC19	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC20	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC21	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC22	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46
ZDHHC23	Palmitoyl acyltransferase	ZDHHC-family palmitoylation machinery gene	Refs. 45,46

LYPLA1	Depalmitoylating enzyme	LYPLA-family acyl-protein thioesterase-related gene	Refs. 45,46
LYPLA2P1	Candidate depalmitoylation-associated gene	LYPLA-family pseudogene/candidate gene; not interpreted as a confirmed functional enzyme in this study	Refs. 45,46
PPT1	Depalmitoylating enzyme	Palmitoyl-protein thioesterase-related gene	Refs. 45,46
PPT2	Depalmitoylating enzyme	Palmitoyl-protein thioesterase-related gene	Refs. 45,46
ABHD17A	Depalmitoylating enzyme	ABHD17-family depalmitoylation-associated thioesterase	Refs. 45,46

ABHD17B	Depalmitoylating enzyme	ABHD17-family depalmitoylation-associated thioesterase	Refs. 45,46
ABHD17C	Depalmitoylating enzyme	ABHD17-family depalmitoylation-associated thioesterase	Refs. 45,46
GOLGA7	Accessory regulator	ZDHHC-associated accessory regulator	Refs. 45,46
GOLGA7B	Accessory regulator	GOLGA7-family accessory regulator associated with palmitoylation machinery	Refs. 45,46
SELENOK	Accessory regulator	Palmitoylation machinery-associated regulatory gene	Refs. 45,46

**Supplementary Table 4. Clinical characteristics of the human myocardial tissue
validation cohort**

Variable	Control (n = 4)	DCM (n = 9)	P value
Age, years	45.5 ± 7.8	52.2 ± 7.9	0.202
Sex, male/female	2/2	6/3	1
LVEF, %	61.3 ± 1.7	26.7 ± 4.1	<0.001
NYHA class III/IV	NA	4/5	NA
Disease status / etiology	No documented cardiovascular disease	Dilated cardiomyopathy	NA
Tissue source	Non-failing donor heart	Explanted failing heart	NA
Sampling site	Left ventricle	Left ventricle	NA
Reason for donor heart non-use	Brain death due to non-cardiac cause: 2; severe trauma: 2	NA	NA

Supplementary Table 5. Primer pairs used in this study

Primer Name	Primer Sequence (5'-3')
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GOLGA7-F-Human	GTGTTCAATTCAGCGAGACTACA
GOLGA7-R-Human	CAACCTTCGAGATATGACTGGC
LYPLA1-F-Human	CCTTTGCAGGTATCAGAAGTTCA
LYPLA1-R-Human	GCTGCCTGTTTAATCCCAGAT
ZDHHC3-F-Human	CCACTTCCGAACATTGAGCG
ZDHHC3-R-Human	CCACAGCCGTCACGGATAAA
ZDHHC14-F-Human	TGTGATAACTGCGTAGAACGGT
ZDHHC14-R-Human	CGTGGGTGATAACGAATGCAA
ZDHHC15-F-Human	GGTGCCAGTGCTCGTTATTGT
ZDHHC15-R-Human	AAGACGTAGGCATAGTAGGACC
β -Actin-F-Human	GGCTGTATTCCCCTCCATCG
β -Actin-R-Human	CCAGTTGGTAACAATGCCATGT
GOLGA7-F-Mouse	TGAGGTCCACAATCTTCAGGA
GOLGA7-R-Mouse	CTCTGGCGGGAATTTGGTCT
LYPLA1-F-Mouse	TTTTCCTTCACGGATTGGGAG
LYPLA1-R-Mouse	GGGGACTTTTGATACCTGCAA
ZDHHC3-F-Mouse	ATCCCCACCCATCACTTCC
ZDHHC3-R-Mouse	CTCGGATAAACCACATGGCTC
ZDHHC14-F-Mouse	CACACTCTCAGACATTATGCCC
ZDHHC14-R-Mouse	TGCATGGTACGGCTATGTGC
ZDHHC15-F-Mouse	GGTGCCAGTGCTCGTTATTGT
ZDHHC15-R-Mouse	AACTTTTTCCGCTGGACTCAA
GAPDH-F-Mouse	TGGATTTGGACGCATTGGTC
GAPDH-R-Mouse	TTTGCACTGGTACGTGTTGAT
