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SUPPLEMENTARY DATA

Comprehensive analysis of a NAD+ metabolism-derived gene signature to predict the prognosis and immune landscape in endometrial cancer

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Table S1. Summarization of clinicopathological features of patients in training and validation cohorts

Characteristics	**Overall** N = 540	**Training cohorts** N = 324	**Validation cohorts** N = 216	***P* value**
Year of diagnosis				0.231
1995 - 2007	137 (25.8%)	76 (23.9%)	61 (28.5%)	
2008 - 2010	291 (54.7%)	173 (54.4%)	118 (55.1%)	
2011 - 2013	104 (19.5%)	69 (21.7%)	35 (16.4%)	
Unknown	8	6	2	
Age (years)				0.691
<= 60	208 (38.5%)	127 (39.2%)	81 (37.5%)	
> 60	332 (61.5%)	197 (60.8%)	135 (62.5%)	
Menopause status				0.301
Postmenopausal	442 (86.5%)	259 (84.4%)	183 (89.7%)	
Premenopausal	35 (6.8%)	26 (8.5%)	9 (4.4%)	
Indeterminate	17 (3.3%)	11 (3.6%)	6 (2.9%)	
perinatal period	17 (3.3%)	11 (3.6%)	6 (2.9%)	
Unknown	29	17	12	
Race				0.059
White	369 (68.3%)	209 (64.5%)	160 (74.1%)	
Black	106 (19.6%)	70 (21.6%)	36 (16.7%)	
Others [a]	65 (12.0%)	45 (13.9%)	20 (9.3%)	
Diabetes				0.806
NO	252 (68.3%)	152 (68.8%)	100 (67.6%)	
YES	117 (31.7%)	69 (31.2%)	48 (32.4%)	
Unknown	171	103	68	
Histological type				0.304
Endometrioid adenocarcinoma	404 (74.8%)	236 (72.8%)	168 (77.8%)	
Serous endometrial adenocarcinoma	114 (21.1%)	72 (22.2%)	42 (19.4%)	

Mixed serous and endometrioid	22 (4.1%)	16 (4.9%)	6 (2.8%)	
FIGO stage				0.705
I	337 (62.4%)	199 (61.4%)	138 (63.9%)	
II	51 (9.4%)	34 (10.5%)	17 (7.9%)	
III	123 (22.8%)	75 (23.1%)	48 (22.2%)	
IV	29 (5.4%)	16 (4.9%)	13 (6.0%)	
Grade				0.999
G1	98 (18.1%)	59 (18.2%)	39 (18.1%)	
G2	120 (22.2%)	72 (22.2%)	48 (22.2%)	
G3	322 (59.6%)	193 (59.6%)	129 (59.7%)	
Cancer status				0.273
TUMOR FREE	425 (84.5%)	257 (86.0%)	168 (82.4%)	
WITH TUMOR	78 (15.5%)	42 (14.0%)	36 (17.6%)	
Unknown	37	25	12	
Surgical type				0.192
open	317 (61.3%)	183 (59.0%)	134 (64.7%)	
Minimally Invasive	200 (38.7%)	127 (41.0%)	73 (35.3%)	
Unknown	23	14	9	

Variables are presented as numbers (N) with percent (%) and analyzed with the Pearson's chi-square test. [a] Including American Indian/Alaska native and Asian or pacific islander. FIGO: International Federation of Obstetrics and Gynecology (Federation Internationale de Gynecologie et d'Obstetrique)

Table S2. The list of 42 NMRGs.

BST1	NAMPT	NMNAT3	PARP10	PARP9	SLC5A8	NT5C1A
CD38	NAPRT	NMRK1	PARP14	PTGIS	AOX1	NT5C1B
CYP8B1	NAXD	NMRK2	PARP16	PTGS2	ENPP1	NT5C2
NADK	NAXE	NNMT	PARP4	QPRT	ENPP3	NT5C3A
NADK2	NMNAT1	NT5E	PARP6	RNLS	NNT	NT5M
NADSYN1	NMNAT2	NUDT12	PARP8	SLC22A13	NT5C	PNP

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Table S3. Univariate and multivariate Cox regression analyses of the prognosis-related factors

Variables	Univariate analysis			Multivariate analysis		
	HR	95 % CI	*P* value	HR	95 % CI	*P* value
Train sets						
Age	1.026	0.998-1.055	0.070			
Stage	3.696	2.103-6.496	<0.001	2.870	1.591-5.179	<0.001
Histological_type	2.416	1.372-4.253	0.002	0.620	0.316-1.215	0.164
Grade	3.197	1.724-5.930	<0.001	2.271	1.176-4.386	0.015
Risk score	2.845	1.979-4.091	<0.001	2.534	1.560-4.116	<0.001
validation sets						
Age	1.042	1.010-1.075	0.010	1.045	1.006-1.084	0.020
Stage	4.398	2.273-8.512	<0.001	3.899	1.943-7.824	<0.001
Histological_type	3.842	2.035-7.254	<0.001	2.182	0.983-4.845	0.051
Grade	2.178	1.231-3.856	0.008	1.387	0.741-2.598	0.055
Risk score	1.978	1.216-3.216	0.006	1.355	1.041-1.661	0.044
Entire sets						
Age	1.033	1.012-1.055	0.002	1.023	1.001-1.046	0.043
Stage	3.939	2.579-6.014	<0.001	3.226	2.069-5.028	<0.001
Histological_type	3.307	1.923-5.689	<0.001	1.077	0.642-1.805	0.779
Grade	2.647	1.745-4.013	<0.001	1.676	0.900-3.119	0.103
Risk score	2.465	1.830-3.320	<0.001	1.736	1.167-2.538	0.006

HR: hazard ratio; CI: confidence interval

Table S4. The molecular targets and targeting pathways of drugs in Genomics of Drug Sensitivity in Cancer database

Drugs	**Molecular targets**	**Targeting pathways**
Bleomycin	dsDNA break induction	DNA replication
EHT-1864	RAC1, RAC2, RAC3	Cytoskeleton
Shikonin	not defined	Other
Pazopanib	CSF1R, KIT, PDGFRA, PDGFRB	RTK signaling
Midostaurin	PKC, PPK, FLT1, c-FGR, others	Other
SB 216763	GSK3A, GSK3B	WNT signaling
Nutlin.3a	MDM2	p53 pathway

Roscovitine	CDK2, CDK7, CDK9	Cell cycle
Bexarotene	RXR agonist	Other
PD-0332991	CDK4, CDK6	Cell cycle
Metformin	AMPK	autophagy
AKT inhibitor VIII	AKT1, AKT2, AKT3	PI3K/MTOR signaling

RAC: Ras-related C3 botulinum toxin substrate; CSF1R: Colony stimulating factor 1 receptor; PDGFR: Platelet-derived growth factor receptor; PKC: Protein kinase C; PPK: Polyphosphate kinase; FLT1: Fms related receptor tyrosine kinase 1; GSK3A: Glycogen synthase kinase-3 alpha; GSK3B: Glycogen synthase kinase-3 beta; MDM2: Mouse double minute 2 homolog; CDK: Cyclin-dependent kinase; RXR: Retinioic X receptor.

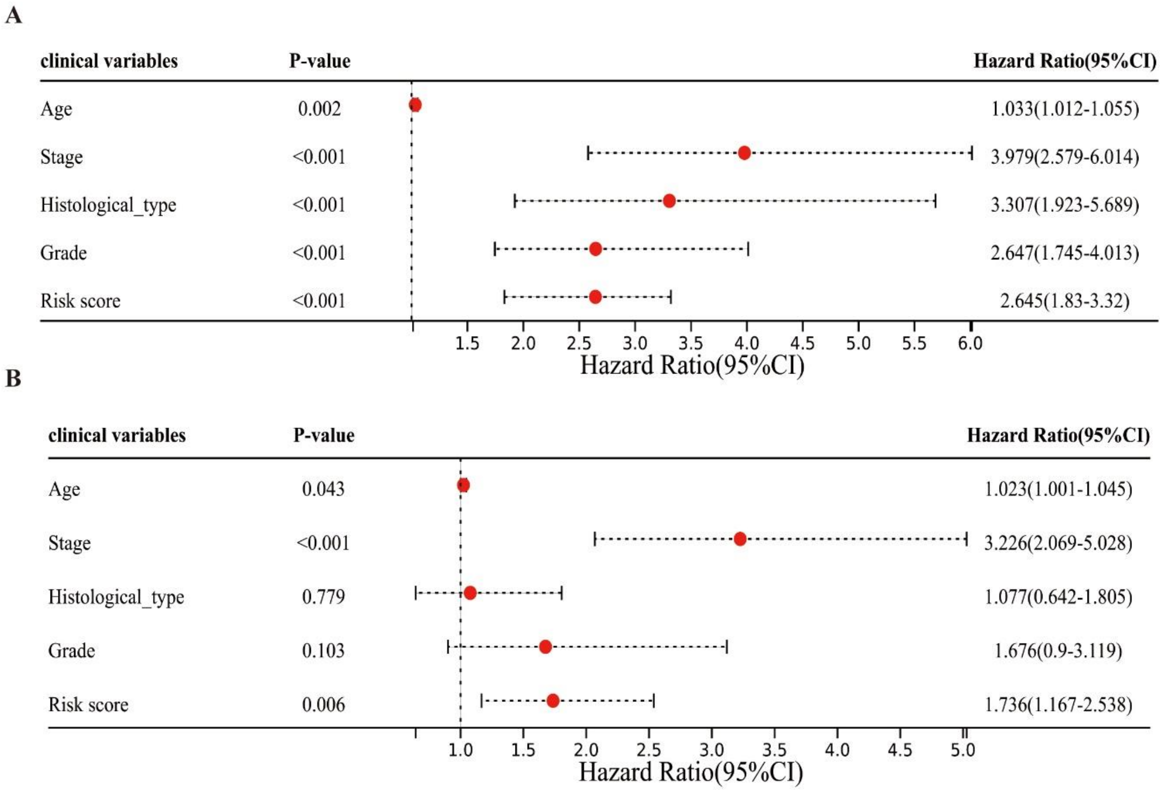

Figure S1. The flowchart of this study.

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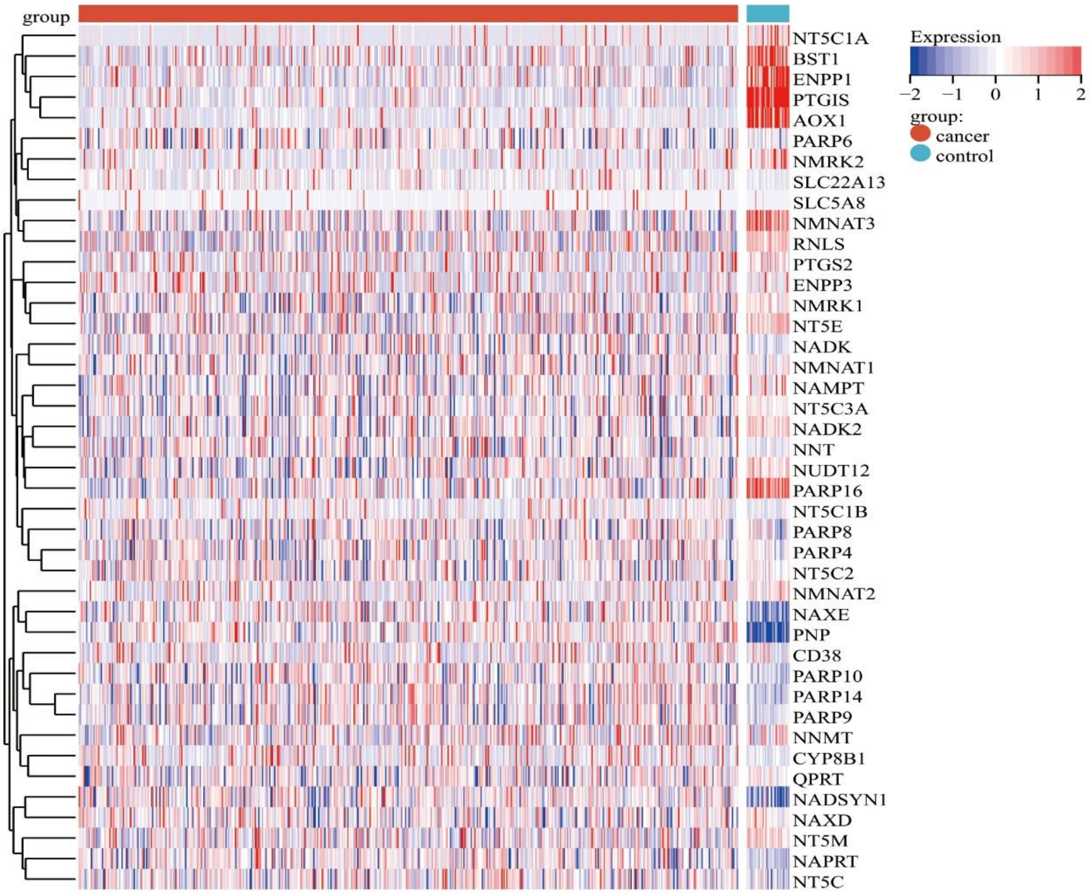

Figure S2. Heatmap of differentially expressed NAD+ metabolism-related genes in endometrial cancer patients from The Cancer Genome Atlas database.

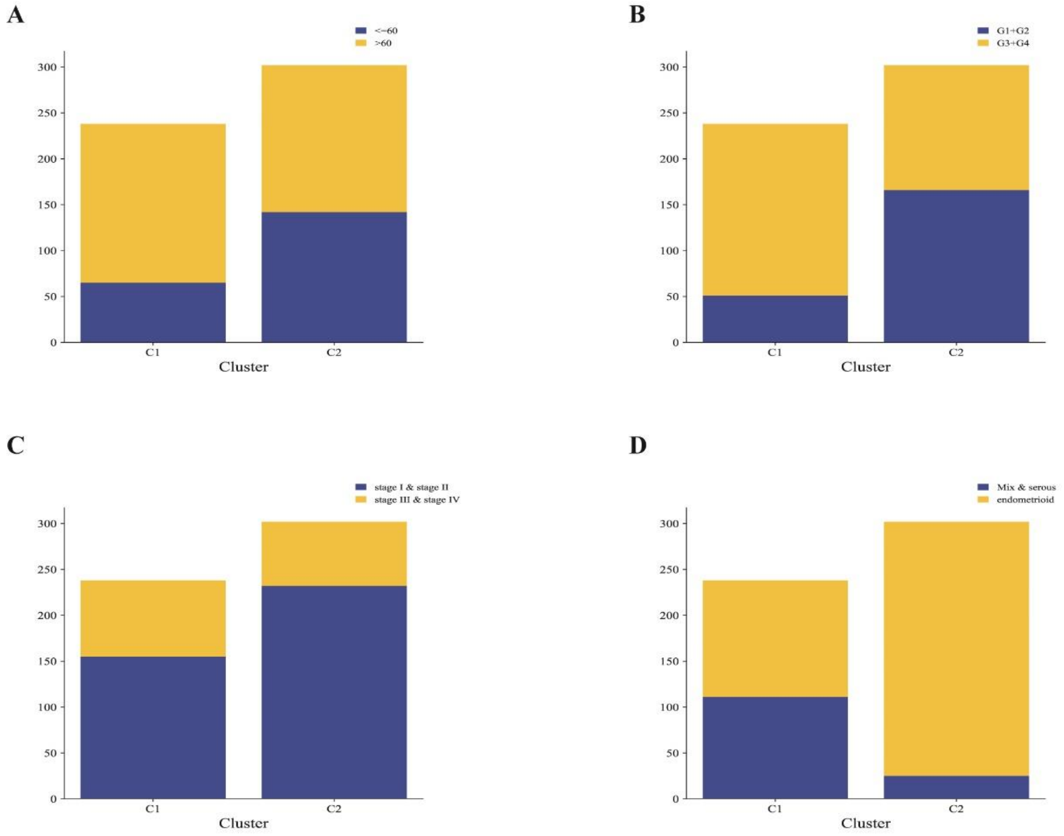

Figure S3. The distribution of clinicopathological variables. A: The distribution of ages between different clusters; B: The distribution of grade between different clusters; C: The distribution of stage between different clusters; D: The distribution of histological type between different clusters.

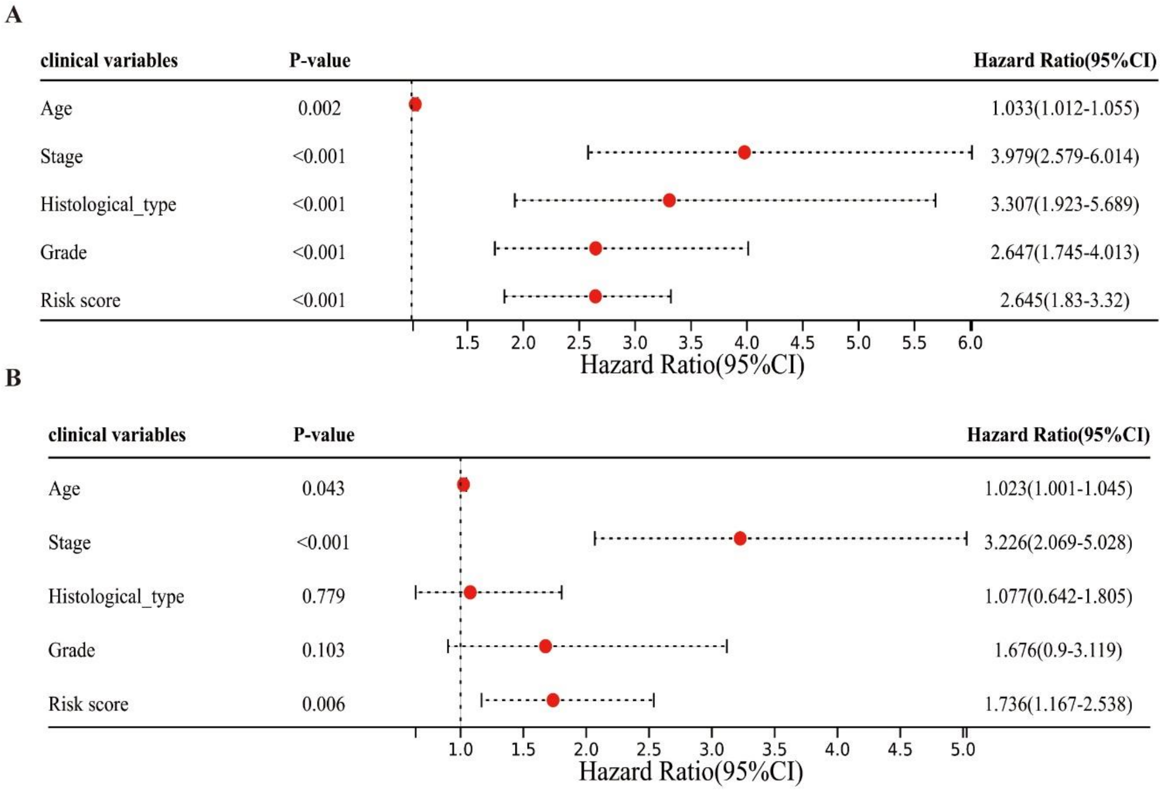

Figure S4. Forrest plot of the univariate and multivariate Cox regression analysis in the entire cohort. A: Forrest plot of the univariate Cox regression analysis in the entire cohort; B: Forrest plot of the multivariate Cox regression analysis in the entire cohort.

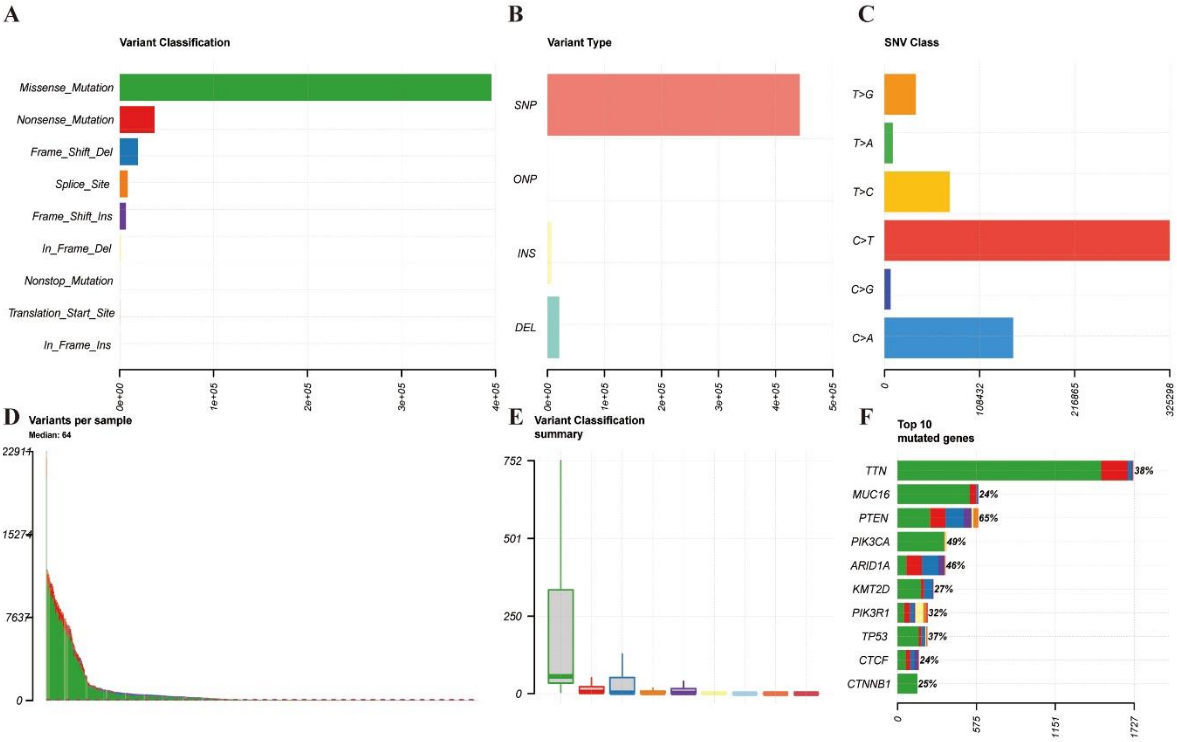

Figure S5. Summary plot of mutation information in all risk groups. A: The distribution of variant classification; B: The distribution of variant types; C: The distribution of single nucleotide variant class; D: The distribution of variants per sample; E: The distribution of variant classification summary; F: The top 10 mutated genes in all risk groups.