

1 **METTL16 enhances proteasome inhibitor resistance**
2 **in multiple myeloma by inhibiting eIF2 α -PERK**
3 **interaction and promoting PSMB5 translation**

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24 **Supplementary Methods**

25 **Cell Culture and Patient Samples:** HEK293T cells were
26 purchased from ATCC. The MM cell lines OCI-MY5, NCI-H929,
27 RPMI-8226, and their respective drug-resistant variants (NCI-
28 H929R, RPMI-8226R5) were sourced from Wen Zhou (Central
29 South University, Changsha, Hunan, China). Cells were
30 maintained in a 37°C incubator with 5% CO₂ and passaged every
31 three days, up to passage 20. MM cell lines were maintained in
32 RPMI 1640 medium (Gibco) supplemented with 1% penicillin-
33 streptomycin (PS) and 10% fetal bovine serum (FBS), while
34 HEK293T cells were grown in DMEM (Gibco) with 10% FBS and
35 1% PS. All cell lines were tested negative for mycoplasma
36 contamination. Bone Marrow Mononuclear Cells (BMMCs) were
37 isolated from bone marrow samples of patients, while peripheral
38 blood mononuclear cells (PBMCs) were separated from the blood
39 of healthy donors using Ficoll-Hypaque density gradient
40 centrifugation. For in vitro studies, biological replicates (n = 3)
41 were chosen according to standard practice in molecular and
42 cellular biology to ensure reproducibility and consistency.
43 Randomization was not applied to in vitro studies because all cell
44 lines were treated identically.

45 **Plasmids and Viral Transduction:** Lentiviral particles were
46 generated by co-transfecting HEK293T cells with psPAX2 and

47 pMD2.G vectors, utilizing Lipofectamine 3000 (Thermo Fisher
48 Scientific) for transfection. After 72 hours, viral supernatants were
49 collected, filtered, and titrated. MM cells were then transduced
50 with the lentivirus and selected for two weeks with 2 µg/mL
51 puromycin.

52 **Cell Cycle Analysis:** MM cells expressing METTL16 shRNA or
53 control shRNA were fixed in 75% ethanol, labeled with propidium
54 iodide (PI)/RNase buffer (BD Biosciences), and analyzed by flow
55 cytometry (FACS Canto II, BD Biosciences).

56 **Apoptosis Analysis:** Apoptosis was assessed using the FITC
57 Annexin V Apoptosis Detection Kit (BD Biosciences) following
58 the manufacturer's instructions. Cells were collected, rinsed with
59 ice-cold PBS, and then resuspended in binding buffer. FITC-
60 conjugated Annexin V and propidium iodide (PI) were applied to
61 the cells, which were subsequently incubated in the dark at room
62 temperature for 15 minutes. Apoptotic cell populations were
63 assessed using flow cytometry (FACS Canto II, BD Biosciences).

64 **Gene Expression Analysis Using Public Data Sets:** Pan-cancer
65 expression profiles were obtained from the Cancer Cell Line
66 Encyclopedia (CCLE; <https://portals.broadinstitute.org/ccle>). GEO
67 datasets (GSE13591, GSE5900, GSE9782, GSE136324, GSE2658,
68 GSE60981) were analyzed for differential expression (LIMMA),
69 correlation (Pearson), survival (Kaplan–Meier, log-rank test), ROC

70 curves (AUC calculation), and GSEA (clusterProfiler). The
71 GSE136324 cohort, including 867 multiple myeloma patients
72 treated under the Total Therapy 3-5 protocols, was used to evaluate
73 overall survival (OS) and progression-free survival (PFS)
74 according to METTL16 expression. Gene essentiality scores were
75 derived from the Cancer Dependency Map. Single-cell
76 transcriptomics was analyzed using datasets from healthy donors
77 (GSE271107) and MM patients (GSE189460). For drug-response
78 correlation, METTL16 expression (TPM) from CCLE was
79 matched with BTZ IC₅₀ values from the Genomics of Drug
80 Sensitivity in Cancer (GDSC). Only overlapping cell lines were
81 analyzed, and Pearson correlation was performed without cross-
82 platform normalization.

83 **Western Blot:** Cells were harvested, lysed in SDS buffer for
84 incubating 30 minutes on ice, and protein concentrations were
85 quantified using the BCA Protein Concentration Measurement Kit
86 (Beyotime, Shanghai, China). Primary antibodies used included
87 METTL16, EIF2S1, Phospho-EIF2S1 (Ser51), PERK, Phospho-
88 PERK/EIF2AK3, LaminB1, α -tubulin, and DYKDDDDK (flag)
89 from Proteintech (Wuhan, China). METTL16 and Puromycin
90 antibodies were obtained from ABclonal (Wuhan, China).

91 **Immunofluorescence:** Cells expressing FLAG-tagged METTL16
92 were fixed with 4% paraformaldehyde, permeabilized with 0.5%

93 Triton X-100, and incubated with 5% BSA for blocking. Primary
94 antibodies targeting DYKDDDDK, eIF2 α , PERK, and METTL16
95 were incubated overnight at 4°C. Afterward, cells were incubated
96 with Alexa Fluor 555- or 488-conjugated secondary antibodies,
97 followed by DAPI staining for nuclear visualization. Images were
98 captured using a confocal laser scanning microscope (Carl Zeiss,
99 Jena, Germany).

100 **Nuclear and Cytoplasmic Protein Extraction:** Nuclear and
101 cytoplasmic proteins were isolated from OCI-MY5 and RPMI-
102 8226 MM cells using the Nucleus and Cytoplasm Extraction Kit,
103 following the manufacturer's instructions. Protein concentrations
104 were quantified using the BCA Protein Assay Kit (Beyotime,
105 Shanghai, China). To standardize protein expression, β -tubulin was
106 used as a marker for the cytoplasm, and LaminB1 as a marker for
107 the nucleus.

108 **Transmission Electron Microscopy (TEM):** Cell pellets were
109 fixed overnight at 4°C in 2.5% glutaraldehyde, followed by post-
110 fixation with 1% osmium tetroxide. After dehydration through an
111 ethanol gradient and treatment with acetone, the samples were
112 embedded, polymerized at 70°C overnight, and sectioned to 70-90
113 nm. The sections were stained with lead citrate and uranyl acetate,
114 then examined under a transmission electron microscope.

115 **SUnSET assay:** Cells were treated with O-propargyl-puromycin

116 (OPP; 10 µg/mL) for 30 min. Cells were washed with cold PBS,
117 lysed in SDS-PAGE buffer, and nascent polypeptide labeling was
118 detected by immunoblotting using an anti-puromycin antibody
119 (validated to recognize OPP-labeled peptides in our system).

120 **RNA Immunoprecipitation (RIP):** FLAG-tagged METTL16-
121 transfected cells were processed for RNA immunoprecipitation
122 (RIP) using the Magna RIP RNA-Binding Protein
123 Immunoprecipitation Kit (Millipore, Billerica, MA, USA). In short,
124 cells were disrupted, and 5 µg of anti-Flag or control IgG
125 antibodies were bound to protein A/G magnetic beads. The
126 immune complexes were incubated overnight at 4°C, followed by
127 washing. RNA was then extracted and analyzed by qRT-PCR.
128 Primers for the target mRNAs are provided in Supplementary
129 Table 1.

130 **LC-MS/MS Analysis:** Proteins were extracted from MM cells and
131 analyzed by liquid chromatography–tandem mass spectrometry
132 (LC-MS/MS). Peptides were detected and quantified using a
133 Thermo Fisher Q Exactive Plus mass spectrometer coupled with an
134 Easy-nLC 1200 system. Raw data were processed with MaxQuant
135 (version 1.6.6.0), and protein identification was filtered at a false
136 discovery rate (FDR) below 1% at both the peptide and protein
137 levels. Label-free quantification (LFQ) was applied to estimate
138 protein abundance, and differential expression analysis was

139 performed using Perseus. Mass spectrometry data are available at
140 <https://figshare.com/s/b37e0ace63a87e4d5cd7>.

141 **Ribo-seq and RNA-seq:** Ribo-seq and RNA-seq libraries were
142 prepared from MM cells using the TruSeq Ribo Profile and TruSeq
143 Stranded mRNA Library Prep Kits (Illumina) following the
144 manufacturer's instructions. Sequencing was performed on an
145 Illumina NovaSeq 6000 platform. Reads were processed using
146 standard quality control and adapter trimming procedures, aligned
147 to the human reference genome (hg38), and quantified at the gene
148 level for downstream differential expression and enrichment
149 analyses. Sequencing data have been deposited in NCBI
150 BioProject under accession PRJNA1390681.

151 **Methylated RNA Immunoprecipitation (MeRIP)-qPCR:**
152 MeRIP-qPCR was performed using the EpiQuik™ MeRIP m6A
153 RNA Enrichment Kit (Epigentek). Total RNA was extracted from
154 MM cell line and treated with DNase I to remove genomic DNA.
155 RNA quality and concentration were assessed using a Nanodrop
156 spectrophotometer. For immunoprecipitation, 5 µg of fragmented
157 RNA was incubated with 2 µg of m6A antibody at room
158 temperature for 1.5 hours, then captured with protein A/G
159 magnetic beads. m6A-enriched RNA was purified, reverse
160 transcribed using the PrimeScript RT Reagent Kit (Takara).
161 Quantitative PCR was performed using TB Green Premix Ex Taq

162 II (Takara). m6A-modified transcripts were normalized to input
 163 RNA using the $\Delta\Delta\text{Ct}$ method. The following primers were used:
 164 PSMB5: Forward: 5'-CACTGAGACTCCCTGGACCT-3'; Reverse:
 165 5'-CGTGTTGGAGAGACCGCTAC-3'
 166 Cyclin D1: Forward: 5'-TCCTCTCCAAAATGCCAGAG-3';
 167 Reverse: 5'-GGCGGATTGGAAATGAACTT-3'
 168 **Immunohistochemistry (IHC):** Paraffin-embedded tissue sections
 169 were cleared in xylene and rehydrated using a graded ethanol
 170 series. Antigen retrieval was carried out by microwaving the slides
 171 in citrate buffer (pH 6.0) for 10 minutes. After blocking with 5%
 172 BSA for 30 minutes, sections were incubated overnight at 4°C with
 173 primary antibodies against METTL16, PSMB5, or p-eIF2 α . The
 174 next day, HRP-conjugated secondary antibodies were incubated for
 175 1 hour at room temperature. Signal detection was achieved with
 176 DAB substrate (ZSGB-BIO, Beijing, China), subsequently
 177 counterstained with hematoxylin. Images were captured using a
 178 Leica light microscope (Leica, Wetzlar, Germany).
 179 **Mitochondrial Membrane Potential Assay:** The mitochondrial
 180 membrane potential ($\Delta\psi\text{m}$) was evaluated with the JC-1
 181 Mitochondrial Membrane Potential Assay Kit (Beyotime, Shanghai,
 182 China). Cells were rinsed with PBS and incubated with JC-1 dye
 183 following the manufacturer's instructions. Flow cytometry was
 184 then employed to evaluate the fluorescence intensity, with a shift in

185 JC-1 fluorescence indicating changes in mitochondrial membrane
186 potential.

187 **Flow cytometry:** Bone marrow mononuclear cells (BMMCs) from
188 multiple myeloma (MM) patients were isolated by Ficoll
189 centrifugation. The 1q21 status was determined clinically by FISH.
190 Plasma cells were identified using PerCP-Cy5.5–conjugated anti-
191 CD138. METTL16 expression was measured by intracellular
192 staining using a primary anti-METTL16 antibody followed by an
193 APC-conjugated secondary antibody after
194 fixation/permeabilization. Mean fluorescence intensity (MFI) was
195 quantified within the live CD138⁺ population.

196 **Cell viability assay:** MM cells were plated in 96-well plates and
197 treated with the specified compounds. Cell viability was
198 subsequently evaluated via a CCK-8 assay (Beyotime, Shanghai,
199 China).

200 **Proteasome 20S Activity Assay:** Proteasome 20S activity in MM
201 cells was measured via the fluorogenic substrate Suc-LLVY-AMC
202 (AAT Bioquest). The cells were lysed and incubated with the
203 substrate at 37°C, and the fluorescence intensity was measured at
204 the appropriate emission wavelengths.

205 **Animal Studies:** Five-week-old male nude mice (BALB/c
206 background) were used in all experiments due to their greater
207 stability in growth and physiological conditions. Mice were

208 purchased from Jiangsu Huachuang Sino Pharma Tech Co., Ltd.
209 (Jiangsu, China). Mice were subcutaneously injected with MM
210 cells (OCI-MY5, 4×10^6 cells or NCI-H929R, 5×10^6 cells)
211 transduced with either METTL16 shRNA or control constructs.
212 After tumor establishment, OCI-MY5-injected mice were
213 randomly divided into four groups: METTL16 knockdown control,
214 METTL16 knockdown treatment, METTL16 empty vector control,
215 and METTL16 empty vector treatment. NCI-H929R-injected mice
216 were assigned to five groups: METTL16 knockdown control,
217 METTL16 knockdown bortezomib monotherapy, METTL16
218 knockdown bortezomib + ISRIB combination therapy, METTL16
219 empty vector control, and METTL16 empty vector bortezomib
220 monotherapy. Tumor growth was monitored using calipers, and
221 treatment groups received bortezomib (1 mg/kg, intraperitoneally,
222 every three days for 12 days) or vehicle control. ISRIB (2.5 mg/kg)
223 was administered every three days for the same duration. Tumor
224 volume was determined using the formula: $\text{length} \times \text{width}^2 / 2$.
225 Sample sizes were selected based on effect sizes observed in
226 preliminary experiments and prior published work in multiple
227 myeloma models. Although a formal power analysis was not
228 conducted, a group size of 5 mice is consistent with established
229 norms in xenograft tumor studies and provides adequate statistical
230 power to detect expected differences in tumor volume. No animals

231 or samples were excluded unless predefined quality-control criteria
232 were not met (e.g., cell viability < 90%, unsuccessful viral
233 transduction, or tumor engraftment failure). All criteria were
234 established prior to data collection. Mice were randomly assigned
235 to treatment groups using a simple randomization approach.
236 Investigators performing tumor measurements were blinded to
237 group allocation. Blinding was not performed in in vitro
238 experiments because measurements were automated and not
239 subjectively assessed.

240 **Code Availability**

241 Analyses were performed using standard software and R (v4.4.2).
242 Custom scripts and parameters used for data processing and
243 visualization are available upon reasonable request.

244 **List of abbreviations**

245 ALL: acute lymphoblastic leukemia; BLCA: bladder urothelial
246 carcinoma; BRCA: breast invasive carcinoma; B-ALL: B-
247 Lymphoblastic Leukemia/Lymphoma; CESC: cervical squamous
248 cell carcinoma & endocervical adenocarcinoma; CLL: chronic
249 lymphocytic leukemia; CML: chronic myelogenous leukemia;
250 COAD_READ: colon & rectal adenocarcinoma; DLBC: diffuse
251 large B-cell lymphoma; ESCA: esophageal carcinoma; GBM:
252 glioblastoma multiforme; HNSC: head & neck squamous cell
253 carcinoma; KIRC: kidney renal clear cell carcinoma; LAML: acute

254 myeloid leukemia; LGG: lower grade glioma; LIHC: liver
255 hepatocellular carcinoma; LUAD: lung adenocarcinoma; LUSC:
256 lung squamous cell carcinoma; MB: medulloblastoma; MESO:
257 mesothelioma; MDS: myelodysplastic syndromes; MPN:
258 Myeloproliferative Neoplasms; NB: neuroblastoma; OV: ovarian
259 serous cystadenocarcinoma; PAAD: pancreatic adenocarcinoma;
260 PRAD: prostate adenocarcinoma; SARC: sarcoma; SKCM: skin
261 cutaneous melanoma; STAD: stomach adenocarcinoma; THCA:
262 thyroid carcinoma; UCEC: uterine corpus endometrial carcinoma;
263 NHL: Non-Hodgkin Lymphoma; HL: Hodgkin Lymphoma.

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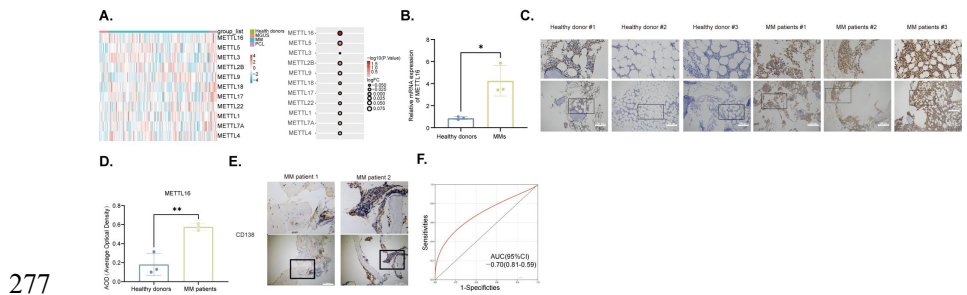
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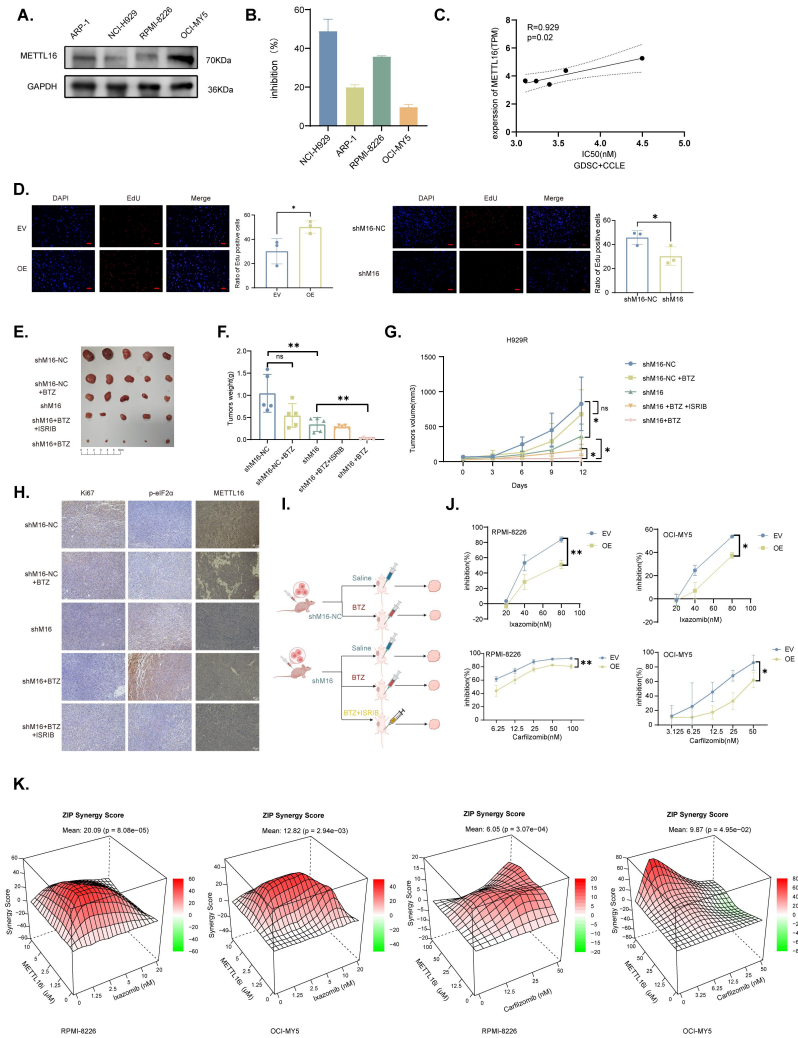
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276 Supplementary Figures



278 **Figure S1. METTL16 Expression and Clinical Relevance in Multiple**
 279 **Myeloma (MM). Related to Figure 1. (A)** Differential expression analysis of
 280 11 METTL genes in the GEO dataset GSE13591, focusing on their expression
 281 profiles in MM. The figure includes a gene expression heatmap and a bubble
 282 plot, representing the fold change and the significance of differences. **(B)** qRT-
 283 PCR analysis the METTL16 mRNA expression levels in BMMCs from MM
 284 patients compared to healthy donors' PBMCs. Data are presented as mean $\pm$ SD,
 285 with statistical significance determined by unpaired t-test. **(C)**
 286 Immunohistochemistry (IHC) staining of tissue samples from MM patients and
 287 healthy donors, assessing METTL16 expression levels (Scale bar = 200 μ m). **(D)**
 288 Bar graph representing the quantitative analysis of the positive staining area or
 289 average optical density (AOD), with data presented as mean $\pm$ SD. Group
 290 comparisons were performed using t-test. $*p < 0.05$; $**p < 0.01$; $***p < 0.001$.
 291 **(E)** Immunohistochemistry (IHC) staining of tissue samples from MM patients,
 292 assessing CD138 expression levels (Scale bar = 200 μ m). **(F)** Receiver operating
 293 characteristic (ROC) curve analysis using the GSE2658 dataset, evaluating the
 294 predictive value of METTL16 expression for survival outcomes. The horizontal
 295 axis represents the false positive rate (1-Specificity), and the vertical axis
 296 represents the true positive rate (Sensitivity). The area under the curve (AUC) is
 297 used to quantify the discriminative ability of the model, with the AUC value
 298 closer to 1 indicating better predictive performance of the model.



300

301 **Figure S2. In Vitro and In Vivo Investigation of METTL16's Role in MM**302 **Proliferation and Drug Resistance. (A)** Representative western blot showing

303 METTL16 protein levels in NCI-H929, ARP-1, RPMI-8226 and OCI-MY5 cells.

304 GAPDH was used as a loading control.(B) Cell viability inhibition (%) at 1.25

305 nM bortezomib measured by CCK-8 after 24 h treatment in the four MM cell

306 lines. (C) Scatter plot showing the correlation between METTL16 expression

307 (CCLE RNA expression; log2 TPM) and bortezomib IC50 values (GDSC data)

308 across five MM cell lines. Pearson correlation coefficient (R) and p-value are

309 shown. Statistical analyses were performed with GraphPad Prism. See Methods

310 for details. (D) EdU assay indicating the EdU-positive cells in MM cells with

311 METTL16 overexpression and knockdown. Representative data and
312 quantification from three independent experiments are presented. (Scale bar =
313 100 μ m) **(E)** Subcutaneous tumor growth in nude mice injected with NCI-
314 H929R cells expressing METTL16 shRNA or control shRNA. Mice were
315 treated with vehicle, bortezomib (1 mg/kg intraperitoneally, every three days), or
316 a combination of bortezomib (1 mg/kg) and ISRIB (an eIF2B activator) (2.5
317 mg/kg) (n = 5 per group). Excised tumors are shown. **(F)** Tumor weight
318 measurements in xenografts. **(G)** Tumor volume growth in xenograft models. **(H)**
319 Immunohistochemical staining of tumors from each treatment group (Scale bar
320 = 50 μ m). **(I)** Schematic of the experimental design. Data are expressed as mean
321 $\pm$ SD from five mice per group. **(J)** METTL16 overexpression reduces
322 sensitivity to carfilzomib and ixazomib in MM cells. Cell viability assays were
323 performed as described. **(K)** Synergistic suppression of MM cell viability by
324 METTL16 inhibitor combined with carfilzomib or ixazomib. ns, $p > 0.05$; $*p <$
325 0.05 ; $**p < 0.01$; $***p < 0.001$.
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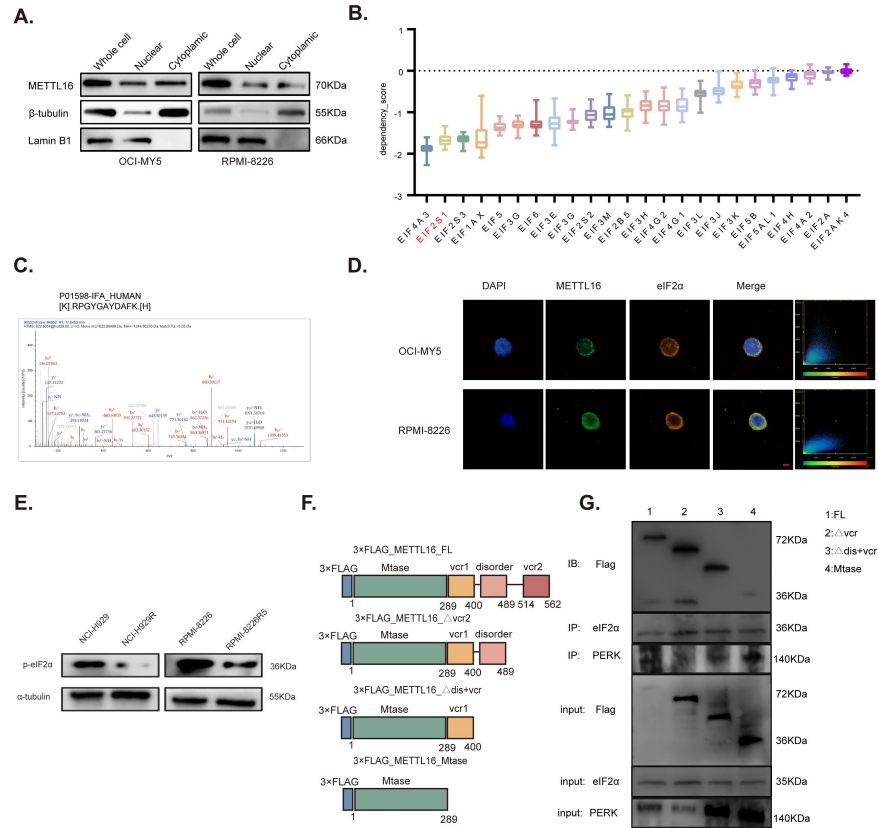


Figure S3. Analysis of EIF Genes and Interaction of METTL16 with eIF2 α in MM Cell Lines.

(A) Nuclear-cytoplasmic fractionation confirming METTL16 localization. Lamin B1 served as a nuclear marker, while β -tubulin functioned as a cytoplasmic marker. (B) Box plot showing the DepMap gene dependency scores of EIF genes across 21 MM cell lines from the CCLE dataset. (C) LC-MS/MS secondary mass spectrometry identifying eIF2 α as a METTL16-interacting protein. (D) Immunofluorescence co-localization of METTL16 (green) and eIF2 α (red) in MM cell lines with DAPI (blue)-stained nuclei. Scale bar = 5 μ m. (E) Western blot comparing p-eIF2 α expression in BTZ-resistant (NCI-H929R, RPMI-8226R5) and BTZ-sensitive (NCI-H929, RPMI-8226) MM cell lines, with α -tubulin as the loading control. (F-G) Schematic representation and co-immunoprecipitation (Co-IP) analysis of full-length METTL16 and its truncated

342 variants to determine the domain involved in the interaction with eIF2 α and
343 PERK.

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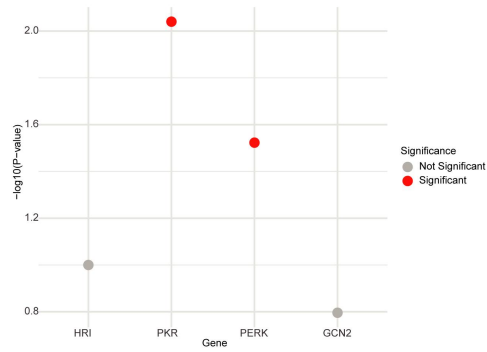
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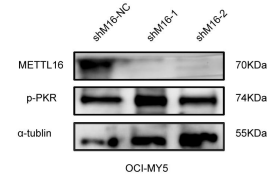
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A.



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361 **Figure S4. Relationship Between METTL16 and Upstream Kinases of**
 362 **eIF2α.**

363 **(A)** Correlation analysis of METTL16 with HRI (EIF2AK1), PKR (EIF2AK2),
 364 PERK (EIF2AK3), and GCN2 (EIF2AK4) based on GEO datasets (GSE5900)
 365 (*: $p < 0.05$, **: $p < 0.01$, ***: $p < 0.001$). **(B)** Western blot analysis of p-PKR
 366 expression in MM cell lines after METTL16 knockdown, with α-tubulin as the
 367 loading control.

372 protein homeostasis, translation regulation, and cell cycle regulation pathways
 373 via Metascape. **(B)** qRT-PCR analysis of CCND1 and CDK4 mRNA abundance
 374 in METTL16-overexpressing cells. Expression was normalized to GAPDH (n =
 375 3; ns, $P > 0.05$). **(C)** Venn diagram showing the overlap of m6A-enriched peaks
 376 identified from two MeRIP-seq comparisons within the GSE182607 dataset **(D)**
 377 Relative m6A enrichment of PSMB5 and CCND1 mRNA in MM cells with or
 378 without METTL16 overexpression was analyzed and normalized to input using
 379 MeRIP-qPCR. **(E)** Schematic of METTL16 constructs (wild-type and
 380 methyltransferase-deficient mutant, P185A/P186A/F187G). Cyclin D1 and
 381 PSMB5 protein levels were assessed by immunoblotting. **(F)** Western blot of c-
 382 Myc and Mcl-1 in control, METTL16-knockdown, and PERKi-treated MM cells;
 383 α -tubulin as loading control. **(G)** Multicolor immunofluorescence of MM bone
 384 marrow biopsies showing METTL16 spatial proximity with PSMB5 and cyclin
 385 D1 in CD138⁺ plasma cells. DAPI (nuclei, blue), METTL16-AF488 (green),
 386 CD138-AF555 (red), PSMB5-Cy5 (far-red), cyclin D1-AF430 (cyan).
 387 Representative confocal images from three patients. Scale bars = 2 μ m.

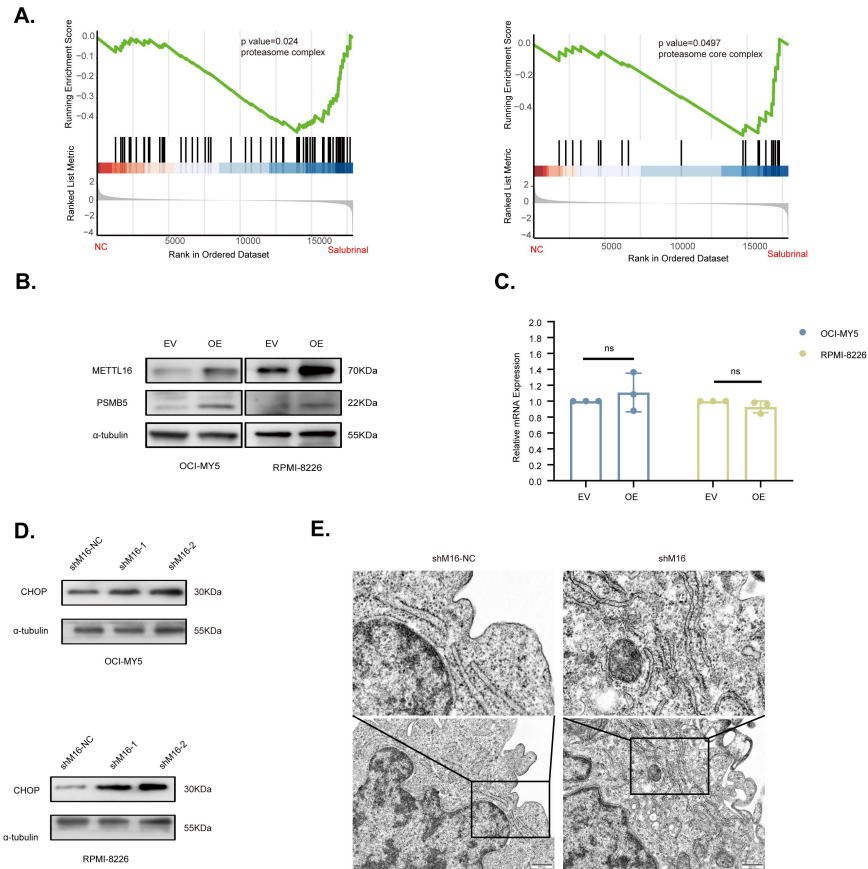


Figure S6. METTL16 is associated with proteasome activity and ER stress in MM cells.

(A) Gene Set Enrichment Analysis (GSEA) plot highlighting the enrichment of proteasome-related pathways in the GSE60981 dataset. (B) Western blot of PSMB5 protein levels in METTL16-overexpressing and control MM cell lines, with α-tubulin as the loading control. (C) qPCR analysis of PSMB5 mRNA expression in METTL16-overexpressing and control MM cells, normalized to GAPDH expression. (n = 3, ns, $p > 0.05$) (D) Western blot analysis showing METTL16 and CHOP protein levels in MM cells, with α-tubulin used as the loading control. (E) Transmission electron microscopy images displaying ER morphology in METTL16-knockdown and control MM cells (Scale bar = 500 nm).

402 **Supplementary Tables**

403 **Supplementary table 1. QPCR primers, shRNA target**
 404 **sequence.**

The sequences of primers used in qRT-PCR	
Gene	Sequences(5'-3')
CCND1	Forward: GATGCCAACCTCCTCAACGA
	Reverse: TGTTTGTTCCTCCGCCTC
CDK4	Forward: GTGGCCCTCAAGAGTGTGAG
	Reverse: CGTCCATCAGCCGGACAAC
CDK6	Forward: TCTGATTACCTGCTCCGCGA
	Reverse: CCTCCTCTTCCTCCTCGAA
PSMB5	Forward: GCCGACCTCACTTCCTTAC
	Reverse: GTTGGCAAGCAGTTTGGAGG
GAPDH	Forward: GGAGCGAGATCCCTCCAAAAT
	Reverse: GGCTGTTGTCATACTTCTCATGG
METTL 16	Forward: AGGGAGTAAACTCACGAAATCCT
	Reverse: AACCCCTTGTATGCGAAGCTC
shM16-1	CCGGGCATAGTCGTTGTACGACATCTCGAGATGTCGTGAC AACGACTATGCTTTTTG
shM16-2	CCGGCCAAAGTAACGTACACTGAATCTCGAGATTCAGTGTA CGTTACTTTGGTTTTTG

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406 **Supplementary table 2. Antibodies**

	SOURCE	IDENTIFIER

METTL16	proteintech	19924-1-AP
METTL16	ABclonal	A15894
PSMB5	proteintech	19178-1-AP
DYKDDDDK	proteintech	66008-4-Ig
Alpha Tubulin	proteintech	66031-1-Ig
GAPDH	proteintech	60004-1-Ig
Puromycin	ABclonal	A23031
PERK/EIF2AK3	proteintech	24390-1-AP
eIF2 α	proteintech	68479-1-Ig
P-eIF2 α (Ser51)	proteintech	28740-1-AP
CHOP	proteintech	15204-1-AP
PKR	proteintech	18244-1-AP
P-PERK	proteintech	29546-1-AP
EIF2AK1	proteintech	81768-1-RR
p-PKR	ABclonal	AP1134
CDK4	CST	12790T
cyclin D1	abcam	ab134175
GCN2	ABclonal	A2307
CDK6	CST	13331T
METTL16	abcam	313743
CD138	biolegend	352309

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