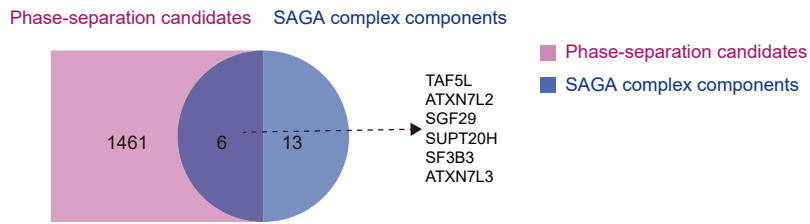
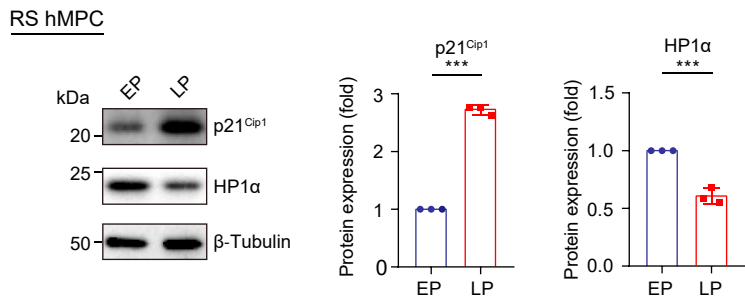


Supplementary Fig. S1

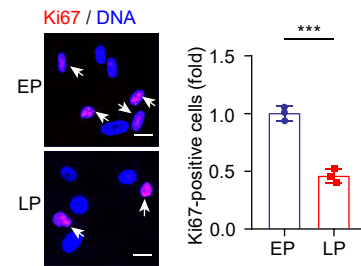
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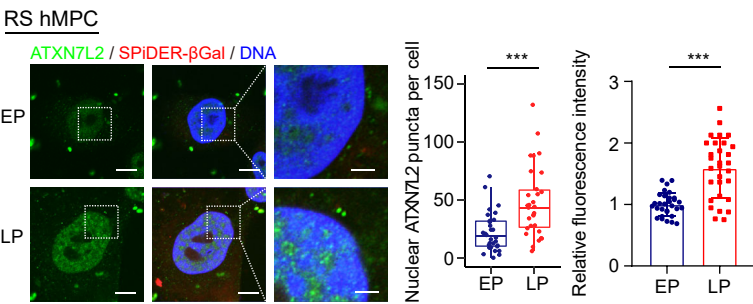
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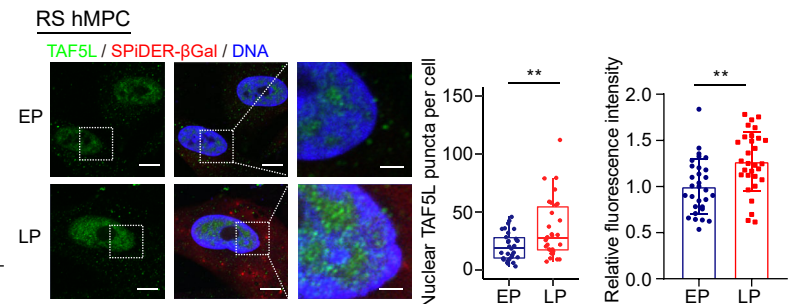
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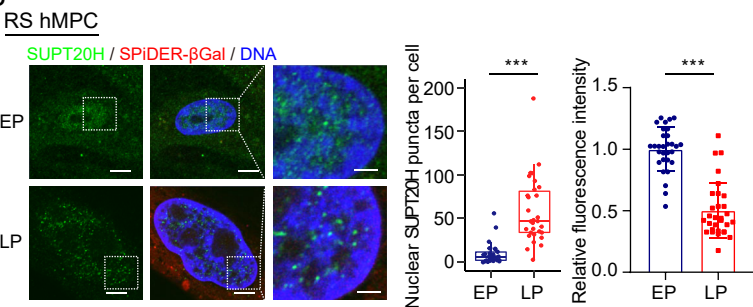
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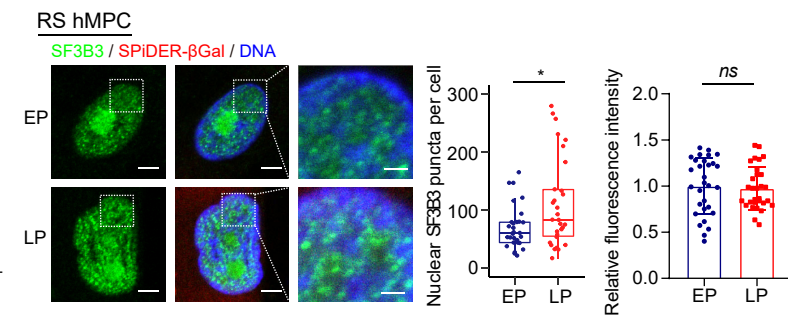
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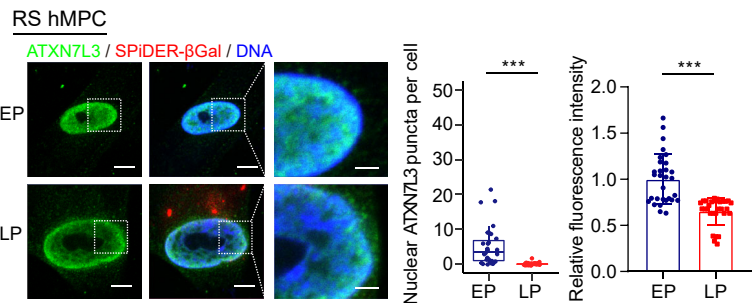
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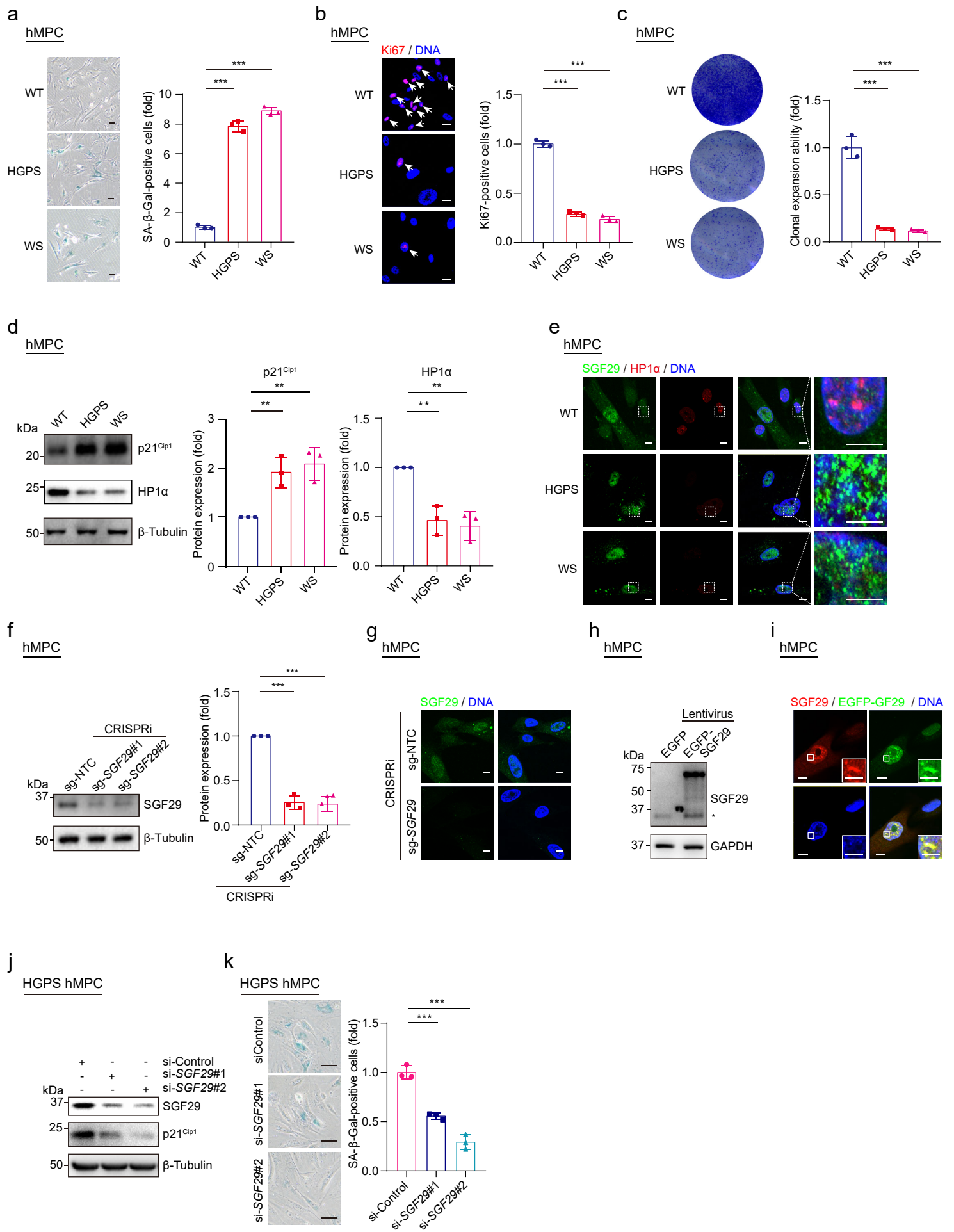


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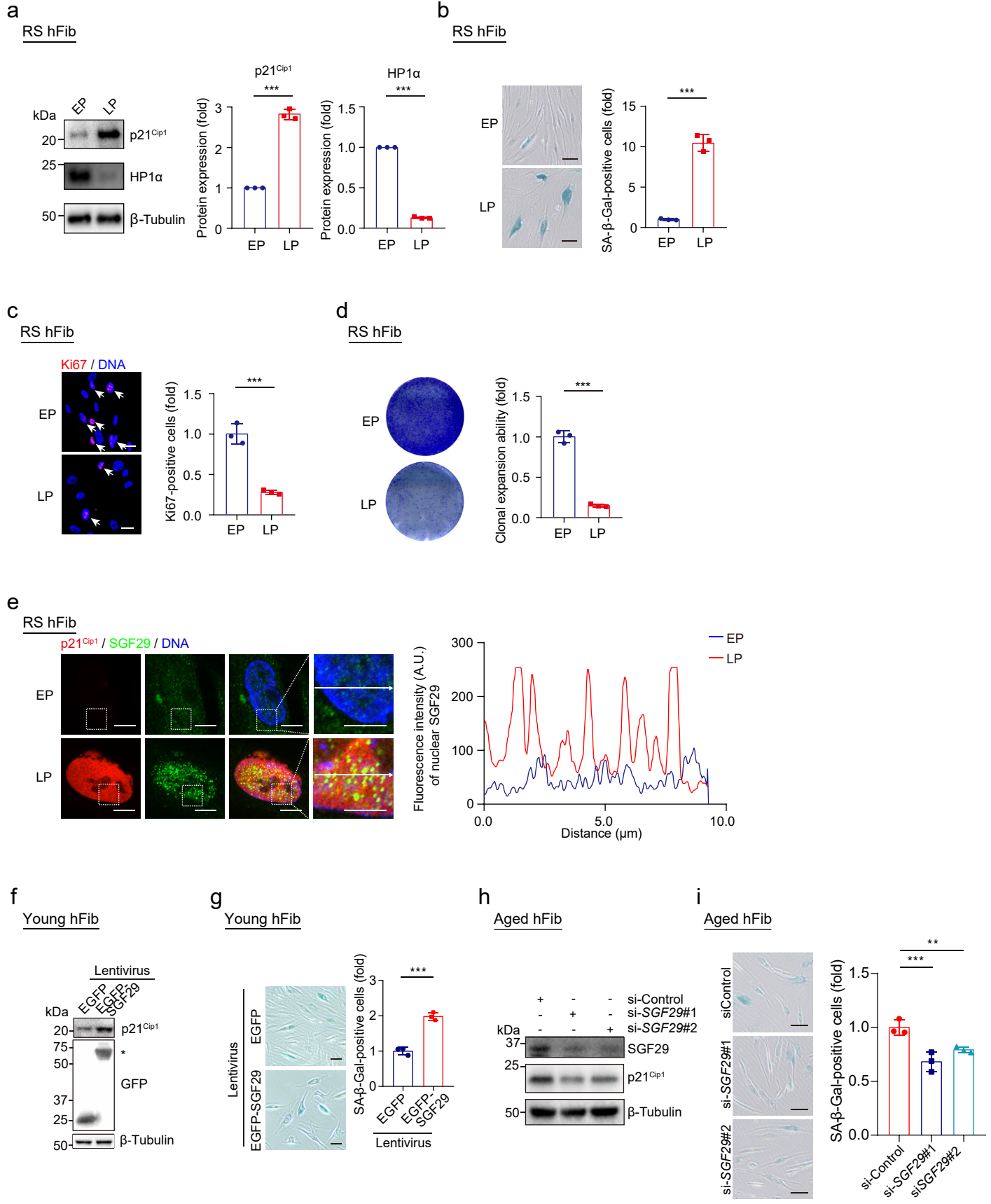


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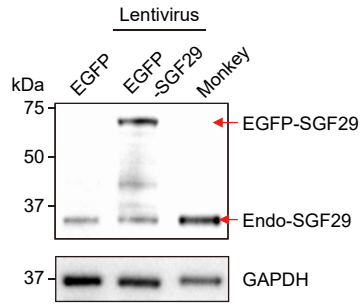


Supplementary Fig. S3



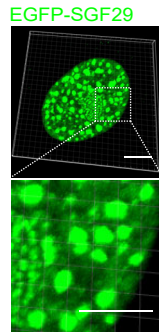
Supplementary Fig. S4

a



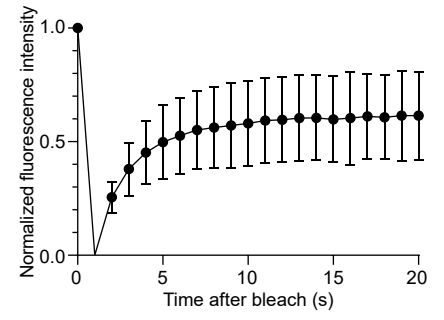
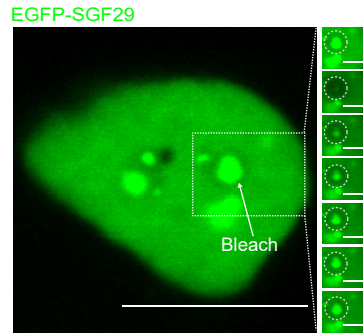
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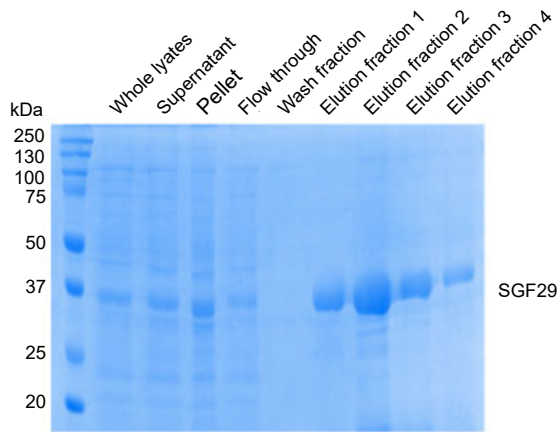


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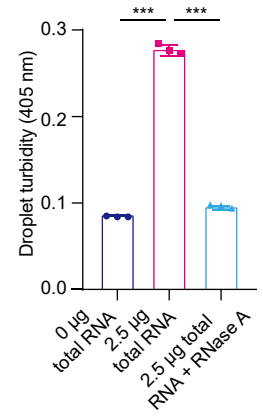
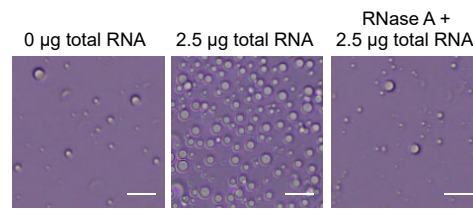
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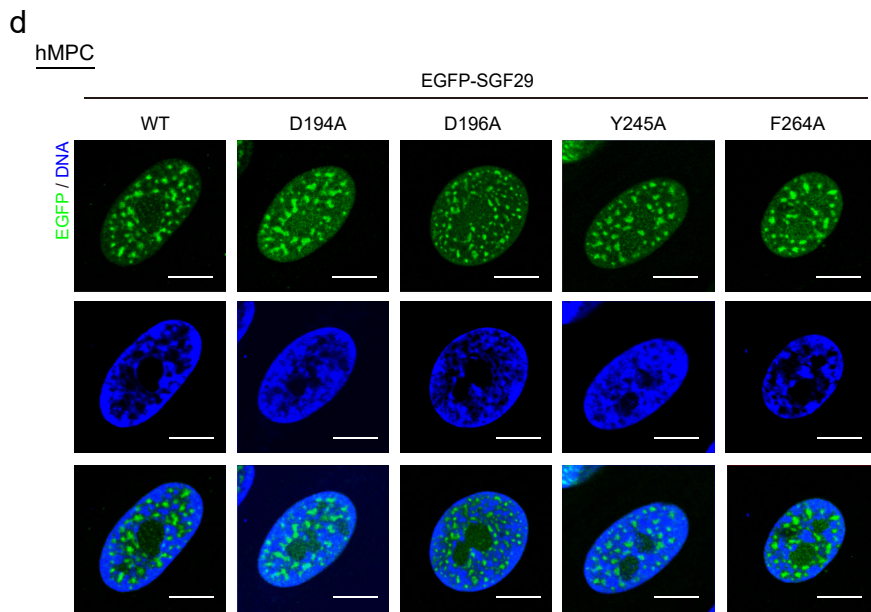
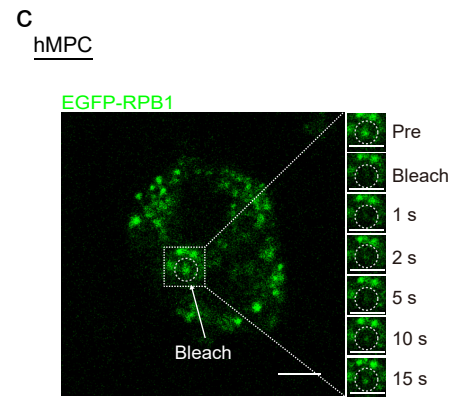
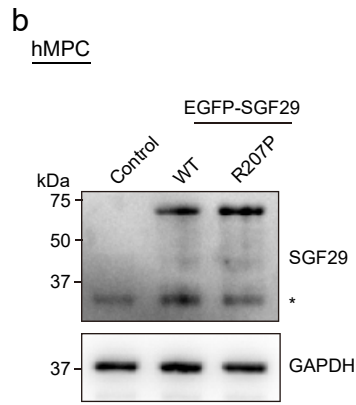
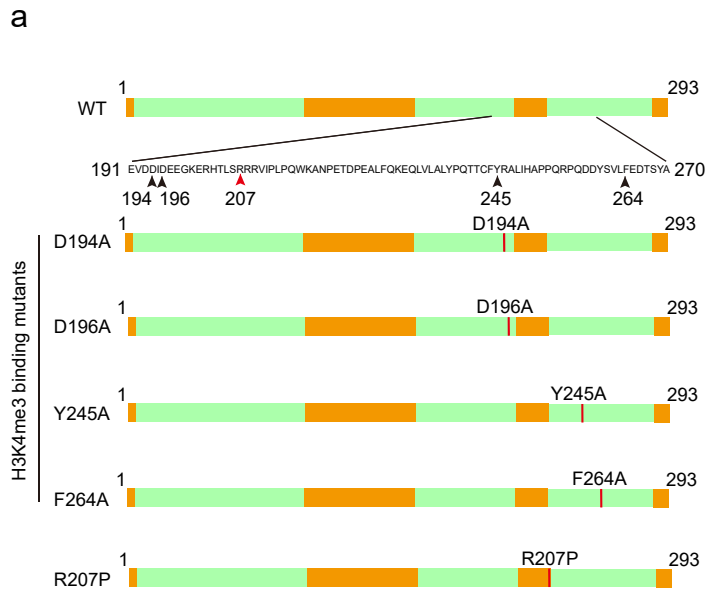
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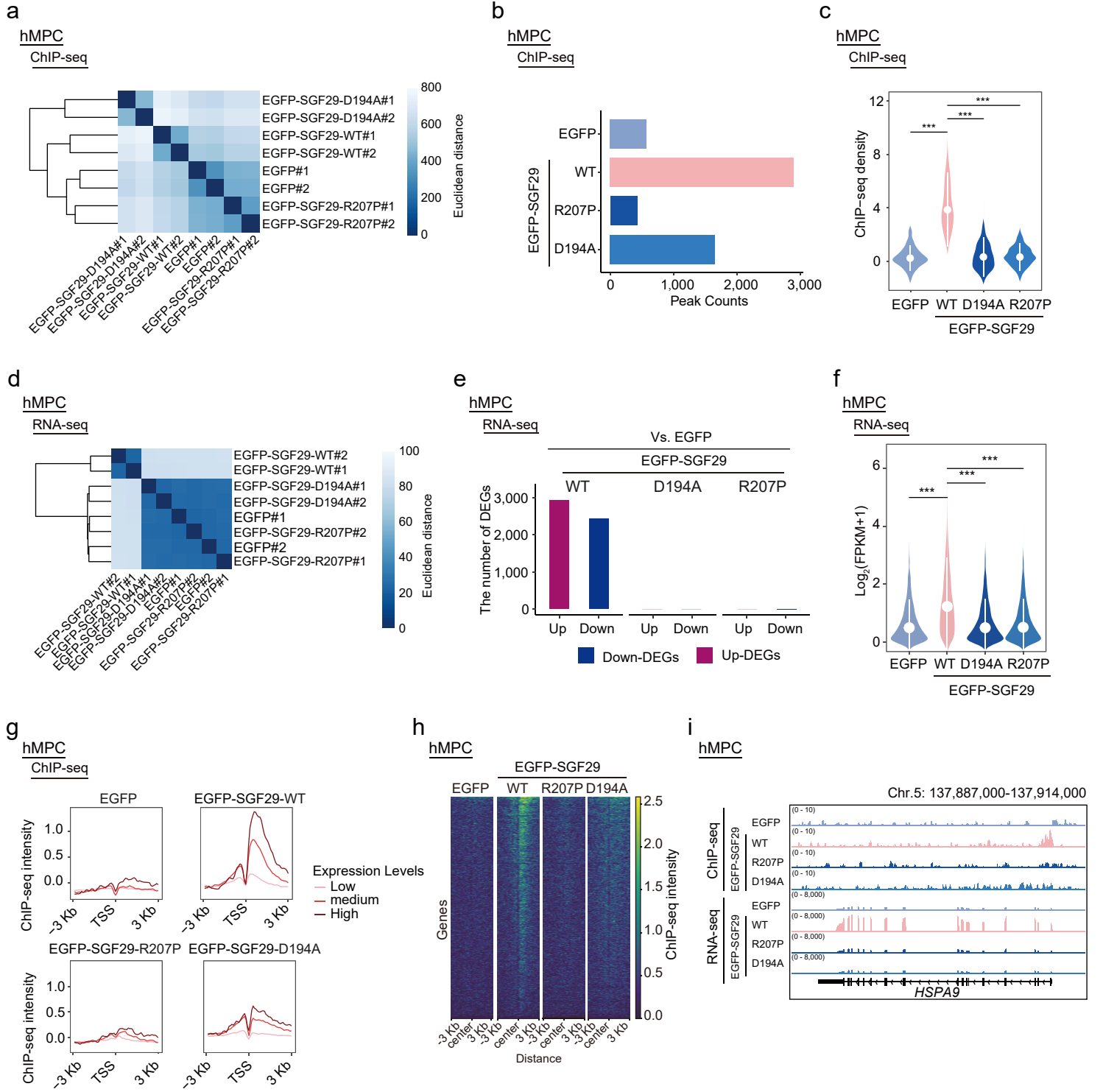
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Supplementary Fig. S5

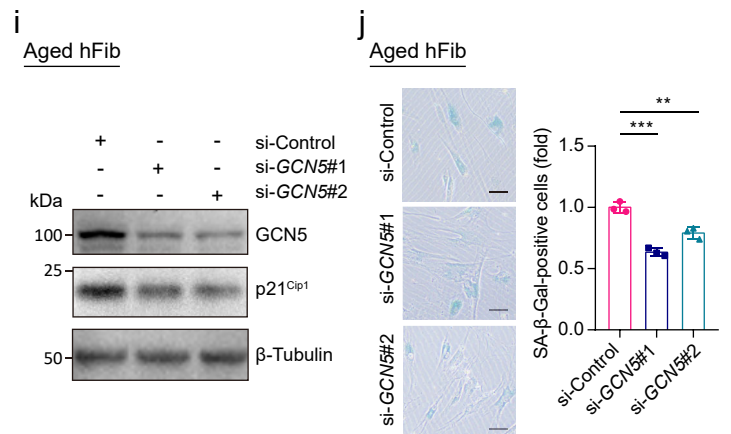
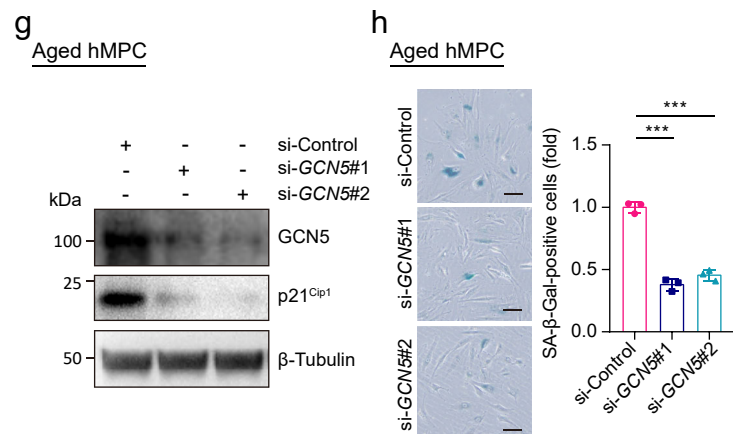
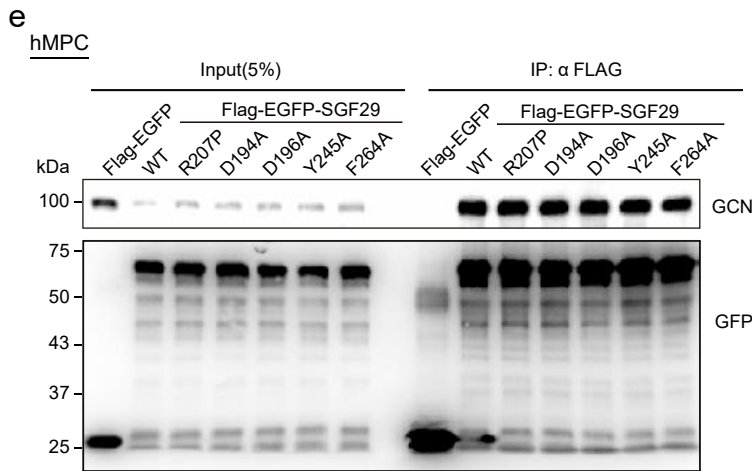
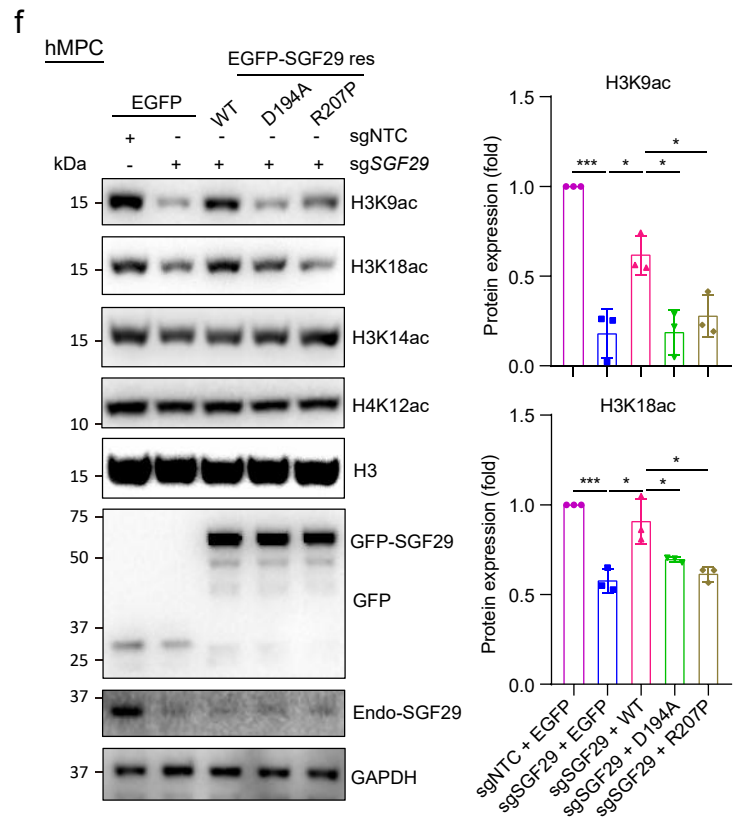
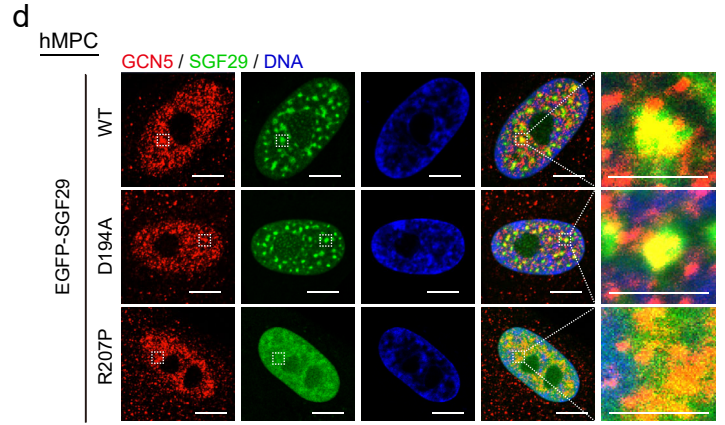
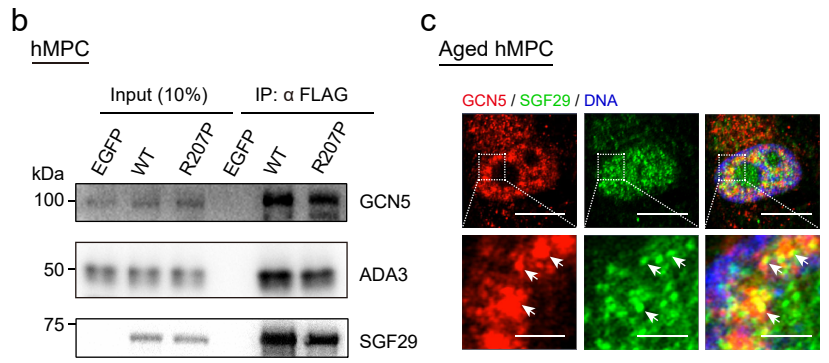


Supplementary Fig. S6



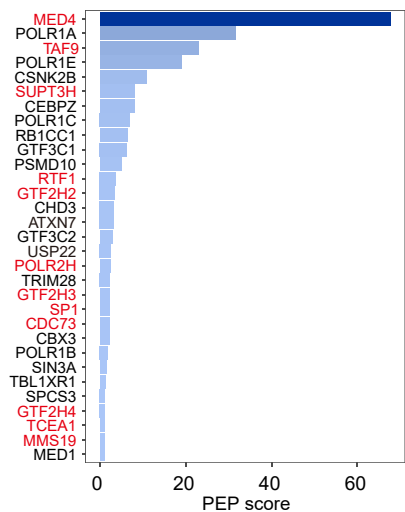
a

| Type | Protein name | Coverage (%) | Unique peptide sequences | | |
|---------------------------------------|--------------|--------------|--|-----|---|
| SGF29 WT and R207P shared interactors | KAT2A | 22% | ELKDPDQLYTTLK EYNPPDSEYCR KLFVADLQR LETPAQFR LFVADLQR LGVFSACK IPYTELSHIKK MDLQQPAANLSELGR NLLAQIK QIPVESVPGIR SCEHPLADHVSHLENVSEDEINR SHPSAWPFMEPVKK SQAEDVATYK TLILTHFPK TLPENLTLEDAKR VIGGICFR YETTHVFGFR | | |
| | | | ADA2A | 15% | KIYDFLIR LGSFSDNPSDKPPCR IVGPVEHDKFIESHAFELR LVPGAYLEYK IYDFLIR TAGITNFC SAR |
| | | | | | ADA3 |
| SGF29 WT specific interactors | MED4 | 53% | | | |
| | | | GTF2H2 | 2% | |
| | | | GTF2H3 | 7% | LAVIASHIQESR |
| | | | GTF2H4 | 9% | LYGHPATCLAVFR |
| | | | SP1 | 1% | FACPECPK |

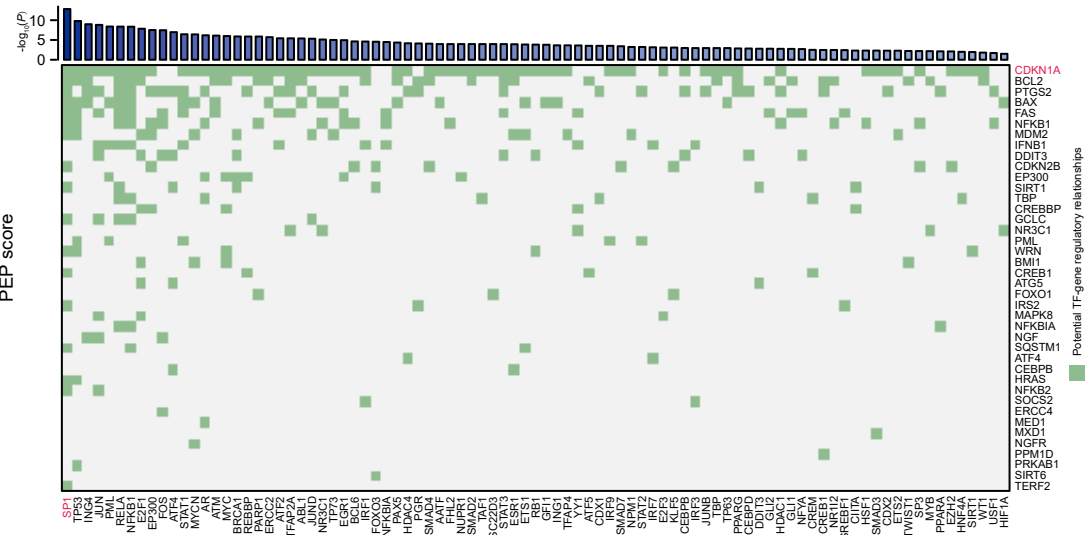


Supplementary Fig. S8

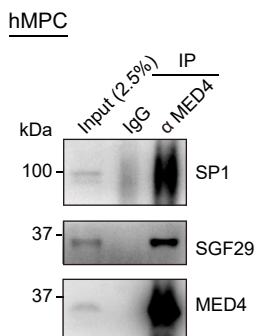
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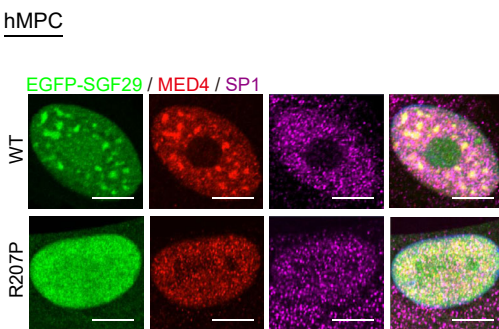
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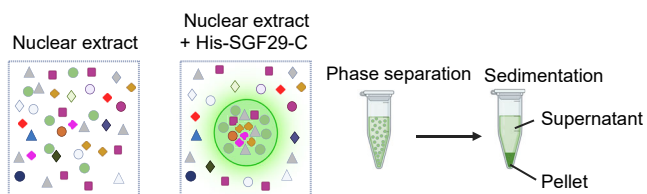
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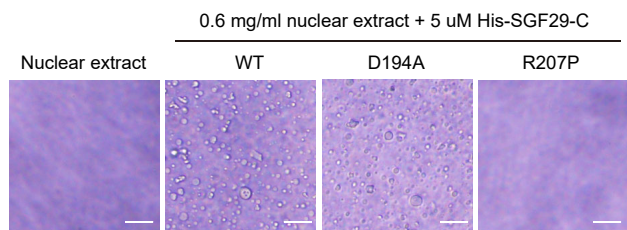
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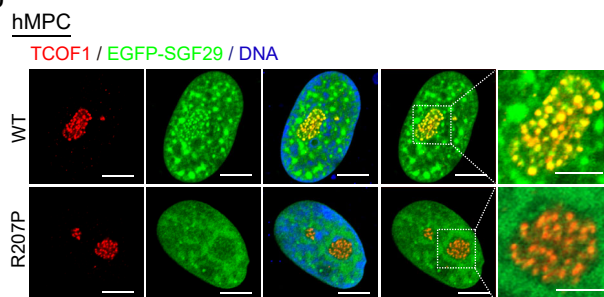
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g



1 **Supplementary Fig. S1. Immunofluorescence staining of SAGA complex members in**
2 **hMPCs at EP (P5) and LP (P16).**

3 (a) Venn diagram showing the members of SAGA complex with potential phase separation
4 capabilities, including TAF5L, SUPT20H, SGF29, ATXN7L2, ATXN7L3, and SF3B3.

5 (b) Western blot analysis of HP1 α , p21^{Cip1} in WT hMPCs at EP (P5) and LP (P16). Left,
6 representative images of western blotting. β -Tubulin was used as the loading control.
7 Right, quantification of the relative protein levels of HP1 α , p21^{Cip1}, and SGF29 proteins.
8 Data are presented as the mean \pm SEM. $n = 3$ biological replicates; *** $p < 0.001$ (t test).

9 (c) Immunofluorescence staining of Ki67 in WT hMPCs at EP (P5) and LP (P16). Left,
10 representative images of Ki67 immunofluorescence. Scale bars, 20 μ m. Right,
11 quantification of the relative percentages of Ki67-positive cells. Data are presented as the
12 mean \pm SEM. $n = 3$ biological replicates. Over 100 cells were quantified in each replicate.
13 *** $p < 0.001$ (t test).

14 (d) Immunofluorescence staining of SPiDER- β Gal and SGF29 in hMPCs at EP (P5) and LP
15 (P16). Left, representative images of SPiDER- β Gal and SGF29 immunofluorescence.
16 Scale bars, 10 μ m and 2.5 μ m (zoomed-in image). Middle, the number of SGF29 puncta
17 in hMPCs at EP (P5) and LP (P16). Right, quantification of the fluorescence intensity of
18 nuclear SGF29 in hMPCs at EP (P5) and LP (P16). $n = 30$ hMPCs. Data are shown as
19 means \pm SEM. *** $p < 0.001$ (t test).

20 (e) Immunofluorescence staining of SPiDER- β Gal and ATXN7L2 in hMPCs at EP (P5) and
21 LP (P16). Left, representative images of SPiDER- β Gal and ATXN7L2
22 immunofluorescence. Scale bars, 10 μ m and 2.5 μ m (zoomed-in image). Middle, the
23 number of ATXN7L2 puncta in hMPCs at EP (P5) and LP (P16). Right, quantification of
24 the fluorescence intensity of nuclear ATXN7L2 in hMPCs at EP (P5) and LP (P16). $n = 30$
25 hMPCs. Data are shown as means \pm SEM. *** $p < 0.001$ (t test).

26 (f) Immunofluorescence staining of SPiDER- β Gal and TAF5L in hMPCs at EP (P5) and LP
27 (P16). Left, representative images of SPiDER- β Gal and TAF5L immunofluorescence.
28 Scale bars, 10 μ m and 2.5 μ m (zoomed-in image). Middle, the number of TAF5L puncta
29 in hMPCs at EP (P5) and LP (P16). Right, quantification of the fluorescence intensity of
30 nuclear TAF5L in hMPCs at EP (P5) and LP (P16). $n = 30$ hMPCs. Data are shown as
31 means \pm SEM. ** $p < 0.01$ (t test).

32 (g) Immunofluorescence staining of SPiDER- β Gal and SUPT20H in hMPCs at EP (P5) and
33 LP (P16). Left, representative images of SPiDER- β Gal and SUPT20H
34 immunofluorescence. Scale bars, 10 μ m and 2.5 μ m (zoomed-in image). Middle, the
35 number of SUPT20H puncta in hMPCs at EP (P5) and LP (P16). Right, quantification of
36 the fluorescence intensity of nuclear SUPT20H in hMPCs at EP (P5) and LP (P16). $n =$
37 30 hMPCs. Data are shown as means \pm SEM. *** $p < 0.001$ (t test).

38 (h) Immunofluorescence staining of SPiDER- β Gal and SF3B3 in hMPCs at EP (P5) and LP
39 (P16). Left, representative images of SPiDER- β Gal and SF3B3 immunofluorescence.
40 Scale bars, 10 μ m and 2.5 μ m (zoomed-in image). Middle, the number of SF3B3 puncta
41 in hMPCs at EP (P5) and LP (P16). Right, quantification of the fluorescence intensity of
42 nuclear SF3B3 in hMPCs at EP (P5) and LP (P16). $n = 30$ hMPCs. Data are shown as
43 means \pm SEM. *ns*, not significant (t test). * $p < 0.05$ (t test).

44 (i) Immunofluorescence staining of SPiDER- β Gal and ATXN7L3 in hMPCs at EP (P5) and
45 LP (P16). Left, representative images of SPiDER- β Gal and ATXN7L3

46 immunofluorescence. Scale bars, 10 μm and 2.5 μm (zoomed-in image). Middle, the
47 number of ATXN7L3 puncta in hMPCs at EP (P5) and LP (P16). Right, quantification of
48 the fluorescence intensity of nuclear ATXN7L3 in hMPCs at EP (P5) and LP (P16). $n = 30$
49 hMPCs. Data are shown as means \pm SEM. *** $p < 0.001$ (t test).

50 **Supplementary Fig. S2. The senescent phenotypes were detected in replicatively**
51 **senescent hMPCs and validation of SGF29 antibody.**

- 52 (a) SA- β -Gal staining of WT, HGPS and WS hMPCs (P7). Left, representative images of
53 SA- β -Gal staining. Scale bars, 20 μm . Right, quantification of the relative percentages of
54 SA- β -Gal-positive cells. Data are presented as the mean \pm SEM. $n = 3$ biological
55 replicates. Over 100 cells were quantified in each replicate. *** $p < 0.001$ (t test).
- 56 (b) Immunofluorescence staining of Ki67 in WT, HGPS and WS hMPCs (P9). Left,
57 representative images of Ki67 immunofluorescence. Scale bars, 20 μm . Right,
58 quantification of the relative percentages of Ki67-positive cells. Data are presented as the
59 mean \pm SEM. $n = 3$ biological replicates. Over 100 cells were quantified in each replicate.
60 *** $p < 0.001$ (t test).
- 61 (c) Clonal expansion assay in WT, HGPS and WS hMPCs (P9). Left, representative images
62 of crystal violet staining. Right, quantification of the relative clonal expansion ability of WT,
63 HGPS and WS hMPCs. Data are presented as the mean \pm SEM. $n = 3$ biological
64 replicates. *** $p < 0.001$ (t test).
- 65 (d) Western blot analysis of HP1 α and p21^{Cip1} in WT, HGPS and WS hMPCs (P9). Left,
66 representative images of western blotting. β -Tubulin was used as the loading control.
67 Right, quantification of the relative protein levels of HP1 α , p21^{Cip1}, and SGF29 proteins.
68 Data are presented as the mean \pm SEM. $n = 3$ biological replicates. ** $p < 0.01$ (t test).
- 69 (e) Immunofluorescence staining of HP1 α and SGF29 in WT, HGPS and WS hMPCs (P9).
70 Scale bars, 10 μm and 5 μm (zoomed-in image).
- 71 (f) Validation of SGF29 antibody by immunoblotting in WT hMPCs transduced with
72 SGF29-targeting sgRNAs at P5 (Passage 3) after transduction. Left, representative
73 images of western blotting. Right, quantification of protein levels of SGF29. Data are
74 presented as the mean \pm SEM. $n = 3$ biological replicates. *** $p < 0.001$ (t test).
- 75 (g) Validation of SGF29 antibody by Immunofluorescence in hMPCs transduced with
76 SGF29-targeting sgRNAs at P5 (Passage 3) after transduction. Scale bars, 10 μm .
- 77 (h) Western blot analysis of SGF29 in hMPCs transduced with lentiviruses expressing EGFP
78 or EGFP-SGF29.
- 79 (i) Immunofluorescence staining of SGF29 in hMPCs transduced with lentiviruses
80 expressing EGFP or EGFP-SGF29. Scale bars, 10 μm and 5 μm (zoomed-in image).
- 81 (j) Western blot analysis of SGF29 in late passage HGPS hMPCs (P9, aged HGPS hMPCs)
82 after treatment with si-Control or si-SGF29. β -Tubulin was used as the loading control.
- 83 (k) SA- β -Gal staining of late passage HGPS hMPCs (P9, aged HGPS hMPCs) after
84 treatment with si-Control or si-SGF29. Scale bars, 50 μm . Left, representative images of
85 SA- β -Gal staining. Right, quantification of the relative percentages of SA- β -Gal-positive
86 cells. Data are presented as the mean \pm SEM. $n = 3$ biological replicates. Over 100 cells
87 were quantified in each replicate; *** $p < 0.001$ (t test).

88 **Supplementary Fig. S3. SGF29 puncta were detected in human fibroblast.**

- 89 (a) Western blot analysis of HP1 α and p21^{Cip1} in human fibroblasts at EP (P13) and LP (P23).
90 Left, representative images of western blotting. β -Tubulin was used as the loading control.
91 Right, quantification of the relative protein levels of HP1 α and p21^{Cip1}. Data are presented
92 as the mean \pm SEM. $n = 3$ biological replicates. *** $p < 0.001$ (t test).
- 93 (b) SA- β -Gal staining of human fibroblasts at EP (P13) and LP (P23). Left, representative
94 images of SA- β -Gal staining. Scale bars, 50 μ m. Right, quantification of the relative
95 percentages of SA- β -Gal-positive cells. Data are presented as the mean \pm SEM. $n = 3$
96 biological replicates. Over 100 cells were quantified in each replicate. *** $p < 0.001$ (t test).
- 97 (c) Immunofluorescence staining of Ki67 in human fibroblasts at EP (P13) and LP (P23).
98 Left, representative images of Ki67 immunofluorescence. Scale bars, 20 μ m. Right,
99 quantification of the relative percentages of Ki67-positive cells. Data are presented as the
100 mean \pm SEM. $n = 3$ biological replicates. Over 100 cells were quantified in each replicate.
101 *** $p < 0.001$ (t test).
- 102 (d) Clonal expansion assay in human fibroblasts at EP (P13) and LP (P23). Left,
103 representative images of crystal violet staining. Right, quantification of the relative clonal
104 expansion ability of EP and LP human fibroblasts. Data are presented as the mean \pm
105 SEM. $n = 3$ biological replicates. *** $p < 0.001$ (t test).
- 106 (e) Immunofluorescence staining of p21^{Cip1} and SGF29 in human fibroblasts at EP (P13) and
107 LP (P23). Left, representative images of p21^{Cip1} and SGF29 staining. Right, quantification
108 of the fluorescence intensity along the line embedded in the zoomed-in images following
109 the arrow direction. Scale bars, 10 μ m and 5 μ m (zoomed-in image).
- 110 (f) Western blot analysis of p21^{Cip1} protein level in early passage human fibroblasts (P13,
111 young human fibroblasts) transduced with lentiviruses expressing either EGFP or
112 EGFP-SGF29. The band of exogenous EGFP-SGF29 protein is marked with *.
- 113 (g) SA- β -Gal staining of early passage human fibroblasts (P13, young human fibroblasts)
114 transduced with lentiviruses expressing either EGFP or EGFP-SGF29. Left,
115 representative images of SA- β -Gal staining. Scale bars, 20 μ m. Right, quantification of
116 the relative percentages of SA- β -Gal-positive cells. Data are presented as the means \pm
117 SEM. $n = 3$ biological replicates; *** $p < 0.001$ (t test).
- 118 (h) Western blot analysis of SGF29 in late passage human fibroblasts (P23, aged human
119 fibroblasts) after treatment with si-Control or si-SGF29. β -Tubulin was used as the
120 loading control.
- 121 (i) SA- β -Gal staining of late passage human fibroblasts (P23, aged human fibroblasts) after
122 treatment with si-Control or si-SGF29. Left, representative images of SA- β -Gal staining.
123 Scale bars, 50 μ m. Right, quantification of the relative percentages of SA- β -Gal-positive
124 cells. Data are presented as the mean \pm SEM. $n = 3$ biological replicates. Over 100 cells
125 were quantified in each replicate; ** $p < 0.01$; *** $p < 0.001$ (t test).

126 **Supplementary Fig. S4. SGF29 condensates exhibit liquid-like properties in cells**

- 127 (a) Western blot analysis of expressed EGFP-SGF29 and endogenous SGF29 protein levels
128 in hMPCs and in cynomolgus monkey testis. Top panel, anti-SGF29 antibody was used.
129 The upper band is the expressed EGFP-SGF29, and the lower bands are endogenous
130 SGF29. Bottom panel, anti-GAPDH antibody was used. GAPDH is used as the internal
131 control.

- 132 (b) 3D-reconstructed representative confocal images of the hMPCs expressing
133 EGFP-SGF29. Scale bars, 10 μm and 5 μm (zoomed-in image).
- 134 (c) Live-cell images of fluorescence recovery after photobleaching (FRAP) experiments in
135 HEK293T cells expressing EGFP-SGF29. Left, representative time-lapse FRAP images
136 of EGFP-SGF29. Scale bars, 10 μm and 2 μm (zoomed-in image). Right, quantification of
137 fluorescence intensity during FRAP assay. Data are presented as mean \pm SEM. $n = 10$
138 HEK293T cells. Photobleaching occurs at $t = 1$ s.
- 139 (d) Purified recombinant His-SGF29 protein were analysed by SDS-PAGE and visualized by
140 coomassie blue staining.
- 141 (e) RNA regulates the phase behavior of SGF29. Left, representative images of purified
142 SGF29 (2.5 μM) in the presence of total RNA, and addition of RNase A to a sample of
143 SGF29 (2.5 μM) solubilized with 2.5 $\mu\text{g/ml}$ of total RNA. Right, quantitative turbidity
144 graphs of droplets. $n = 3$ biological replicates. *** $p < 0.001$ (t test). Scale bars, 50 μm .

145 **Supplementary Fig. S5. Phase separation of SGF29 is not depend on the its H3K4me3**
146 **binding ability**

- 147 (a) Schematic diagram of a series of EGFP-tagged SGF29 H3K4me3 interaction-disrupting
148 truncated mutants and R207P mutant.
- 149 (b) Western blot analysis of SGF29 in hMPCs transduced with lentiviruses expressing either
150 EGFP-SGF29-WT (WT) and EGFP-SGF29-R207P (R207P). GAPDH was used as the
151 internal control. Control (no transfected hMPCs), * band represents endogenous SGF29.
- 152 (c) Representative time-lapse FRAP images of EGFP-RPB1 in hMPCs transduced with
153 lentiviruses expressing EGFP-RPB1. Scale bars, 5 μm and 1 μm (zoomed-in image).
- 154 (d) Immunofluorescence showed the nuclear puncta formation of EGFP-tagged SGF29
155 H3K4me3 interaction-disrupting truncated mutants in hMPC transduced with lentiviruses
156 expressing EGFP-SGF29-WT (WT), EGFP-SGF29-D194A (D194A),
157 EGFP-SGF29-D196A (D196A), EGFP-SGF29-Y245A (Y245A) or EGFP-SGF29-F264A
158 (F264A) variants, respectively.

159 **Supplementary Fig. S6. Condensates formation of SGF29 is necessary for its proper**
160 **promoter binding**

- 161 (a) Euclidean distance heatmap showing sample repeatability of ChIP-seq data in hMPCs
162 (P13) with CRISPR/Cas9-mediated knockdown of endogenous SGF29 followed by
163 overexpression of EGFP, EGFP-SGF29-WT (WT), EGFP-SGF29-D194A (D194A) or
164 EGFP-SGF29-R207P (R207P) variants, respectively. The colour key from dark to light
165 represents relatively near to far Euclidean distance.
- 166 (b) Bar plot showing the number of SGF29 occupancies in hMPCs (P13) with
167 CRISPR/Cas9-mediated knockdown of endogenous SGF29 followed by overexpression
168 of EGFP, EGFP-SGF29-WT (WT), EGFP-SGF29-D194A (D194A) or
169 EGFP-SGF29-R207P (R207P) variants, respectively.
- 170 (c) Boxplot showing the normalized ChIP-seq signals around SGF29-binding TSSs ($n = 439$)
171 in hMPCs (P13) with CRISPR/Cas9-mediated knockdown of endogenous SGF29
172 followed by overexpression of EGFP, EGFP-SGF29-WT (WT), EGFP-SGF29-D194A
173 (D194A) or EGFP-SGF29-R207P (R207P) variants, respectively.

- 174 (d) Euclidean distance heatmap showing sample repeatability of RNA-seq data in hMPCs
 175 (P13) with CRISPR/Cas9-mediated knockdown of endogenous SGF29 followed by
 176 overexpression of EGFP, EGFP-SGF29-WT (WT), EGFP-SGF29-D194A (D194A) or
 177 EGFP-SGF29-R207P (R207P) variants, respectively. The colour key from dark to light
 178 represents relatively near to far Euclidean distance.
- 179 (e) Bar plots showing the number of differentially expressed genes in hMPCs (P13) with
 180 CRISPR/Cas9-mediated knockdown of endogenous SGF29 followed by overexpression
 181 of EGFP-SGF29-WT (WT), EGFP-SGF29-D194A (D194A) or EGFP-SGF29-R207P
 182 (R207P) variants compared to hMPCs with overexpression of EGFP.
- 183 (f) Boxplot showing the expression levels of these genes, which were activated in hMPCs
 184 expressing EGFP-SGF29-WT (WT) but remained silence in hMPCs expressing
 185 EGFP-SGF29-D194A (D194A) or EGFP-SGF29-R207P (R207P) mutants, in all groups.
- 186 (g) Metaplots showing the enriched levels of SGF29 occupancies surrounding the TSS
 187 regions for genes with indicated expression levels in hMPCs (P13) with
 188 CRISPR/Cas9-mediated knockdown of endogenous SGF29 followed by overexpression
 189 of EGFP, EGFP-SGF29-WT (WT), EGFP-SGF29-D194A (D194A) or
 190 EGFP-SGF29-R207P (R207P) variants, respectively.
- 191 (h) Heatmap showing the enriched levels of SGF29 occupancies surrounding the TSS
 192 regions for genes, which were activated in hMPCs expressing EGFP-SGF29-WT (WT)
 193 but remained silence in hMPCs expressing EGFP-SGF29-D194A (D194A) and
 194 EGFP-SGF29-R207P (R207P) variants, in all groups.
- 195 (i) Integrative Genome Viewer tracks of the indicated ChIP-seq and RNA-seq signals at
 196 *HSPA9* locus in hMPCs (P13) with CRISPR/Cas9-mediated knockdown of endogenous
 197 SGF29 followed by overexpression of EGFP, EGFP-SGF29-WT (WT), and
 198 EGFP-SGF29-D194A (D194A) or EGFP-SGF29-R207P (R207P) variants, respectively.

199 **Supplementary Fig. S7. Disruption of SGF29 condensates has no effect on interaction**
 200 **with HAT module but decreased its H3K4me3 promoter binding**

- 201 (a) Detailed information of representative SGF29 interacting candidates identified by mass
 202 spectrometry, including GCN5, ADA2A, ADA3, GTF2H2, GTF2H3, GTF2H4, SP1 and
 203 MED4. The SGF29 interacting candidates identified by mass spectrometry are listed in
 204 the Supplementary Table S2.
- 205 (b) Co-IP analysis showing the interactions between indicated proteins and
 206 EGFP-SGF29-WT (WT) and EGFP-SGF29-R207P (R207P) in hMPCs.
- 207 (c) Immunofluorescence staining of GCN5 and SGF29 in late passage WT hMPCs (P16,
 208 aged hMPCs). The white arrowheads denote colocalization of SGF29 puncta with GCN5.
 209 Scale bars, 10 μ m and 2.5 μ m (zoomed-in image).
- 210 (d) Immunofluorescence staining of GCN5 in hMPCs transduced with lentiviruses expressing
 211 either EGFP-SGF29-WT (WT), and EGFP-SGF29-D194A (D194A) or
 212 EGFP-SGF29-R207P (R207P) variants. Scale bars, 10 μ m and 2.5 μ m (zoomed-in
 213 image).
- 214 (e) Co-IP analysis showing the interactions between GCN5 and EGFP-SGF29-WT (WT),
 215 EGFP-SGF29-R207P (R207P) or EGFP-tagged SGF29 H3K4me3 interaction-disrupting
 216 truncated mutants in hMPCs.

- 217 (f) Global acetylation levels of H3K9, H3K18, H3K14, and H4K12 in hMPCs with
 218 CRISPR/Cas9-mediated knockdown of endogenous SGF29 followed by overexpression
 219 of EGFP, EGFP-SGF29-WT rescue (WT), EGFP-SGF29-D194A rescue (D194A) or
 220 EGFP-SGF29-R207P rescue (R207P) variants, respectively. Left, representative images
 221 of western blotting. GAPDH was used as the loading control. Right, quantification of the
 222 relative acetylation levels of H3K18 and H3K9. *** $p < 0.001$; * $p < 0.05$ (t test).
- 223 (g) Western blot analysis of GCN5 in late passage WT hMPCs (P16, aged hMPCs) after
 224 treatment with si-Control or si-GCN5. β -Tubulin was used as the loading control.
- 225 (h) SA- β -Gal staining of late passage WT hMPCs (P16, aged hMPCs) after treatment with
 226 si-Control or si-GCN5. Left, representative images of SA- β -Gal staining. Scale bars, 50
 227 μ m. Right, quantification of the relative percentages of SA- β -Gal-positive cells. Data are
 228 presented as the mean \pm SEM. $n = 3$ biological replicates. Over 100 cells were quantified
 229 in each replicate; *** $p < 0.001$ (t test).
- 230 (i) Western blot analysis of GCN5 in late passage human fibroblasts (P23, aged human
 231 fibroblasts) after treatment with si-Control or si-GCN5. β -Tubulin was used as the loading
 232 control.
- 233 (j) SA- β -Gal staining of late passage human fibroblasts (P23, aged human fibroblasts) after
 234 treatment with si-Control or si-GCN5. Left, representative images of SA- β -Gal staining.
 235 Scale bars, 50 μ m. Right, quantification of the relative percentages of SA- β -Gal-positive
 236 cells. Data are presented as the mean \pm SEM. $n = 3$ biological replicates. Over 100 cells
 237 were quantified in each replicate; *** $p < 0.001$; ** $p < 0.01$ (t test).

238 **Supplementary Fig. S8. Multivalent interaction of SGF29 is sensitive to condensate**
 239 **perturbation.**

- 240 (a) Bar plot showing the phase-separation-dependent SGF29 interacting proteins related to
 241 RNA polymerase complex. SGF29 interacting proteins were ranked by peptide posterior
 242 error probability (PEP) scores.
- 243 (b) The transcription factor prediction analysis of ageing hotspot genes, which were activated
 244 in hMPCs expressing EGFP-SGF29-WT (WT) but remained silence in hMPCs expressing
 245 EGFP-SGF29-D194A (D194A) and EGFP-SGF29-R207P (R207P) variants.
- 246 (c) Co-IP analysis showing the interactions between endogenous MED4 and SGF29 and
 247 SP1 in hMPCs.
- 248 (d) Immunofluorescence staining of MED4 and SP1 in hMPCs transduced with lentiviruses
 249 expressing either EGFP-SGF29-WT (WT) or EGFP-SGF29-R207P (R207P). Scale bars,
 250 10 μ m.
- 251 (e) Schematic diagram of pelleting experiment.
- 252 (f) Purified recombinant SGF29-C(54-293)-WT and SGF29-C(54-293)-D194A forms
 253 droplets in the nuclear extract. Scale bars, 50 μ m.
- 254 (g) Immunofluorescence staining of TCOF1 in early passage WT hMPCs (P5, young hMPCs)
 255 transduced with lentiviruses expressing either EGFP-SGF29-WT (WT) or
 256 EGFP-SGF29-R207P (R207P). Scale bars, 10 μ m and 5 μ m (zoomed-in image).
 257

258 **Supplementary Video S1.** The fusion of two adjacent EGFP-SGF29 condensates in hMPCs
259 within a 47.5-min duration. Scale bar, 10 μ m.

260 **Supplementary Video S2.** Fluorescence signal recovery of EGFP-SGF29 in hMPCs. A
261 bleaching 488 nm laser pulse was applied. Scale bar, 10 μ m.

262 **Supplementary Video S3.** Fluorescence signal recovery of EGFP-SGF29 in HEK293T cells.
263 A bleaching 488 nm laser pulse was applied. Scale bar, 10 μ m.

264 **Supplementary Video S4.** The fusion of two adjacent SGF29 droplets in vitro. Scale bar, 50
265 μ m.

266

267 **Supplementary Table S1.** IDR Score of SGF29 by PONDR (<http://www.pondr.com/>).

268 **Supplementary Table S2.** Interacting proteins of EGFP, EGFP-SGF29-WT and R207P
269 identified by Co-IP/MS.

270 **Supplementary Table S3.** The sequences of sgRNAs or primers used in this study for gene
271 knockdown, overexpression, DNA FISH, RNA FISH, ChIP-qPCR, and qPCR.

272 **Supplementary Table S4.** The sequencing information of RNA-seq data, differentially
273 expressed genes (DEGs) in hMPCs (P13) with CRISPR/Cas9-mediated knockdown of
274 endogenous SGF29 followed by overexpression of EGFP-SGF29-WT, EGFP-SGF29-D194A
275 (D194A) or EGFP-SGF29-R207P (R207P) variants compared to hMPCs with overexpression
276 of EGFP.

277 **Supplementary Table S5.** The sequencing information of ChIP-seq data, the genomic
278 location of SGF29 peaks identified in hMPCs (P13) with CRISPR/Cas9-mediated knockdown
279 of endogenous SGF29 followed by overexpression of EGFP-SGF29-WT (WT),
280 EGFP-SGF29-D194A (D194A) or EGFP-SGF29-R207P (R207P) variants.

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