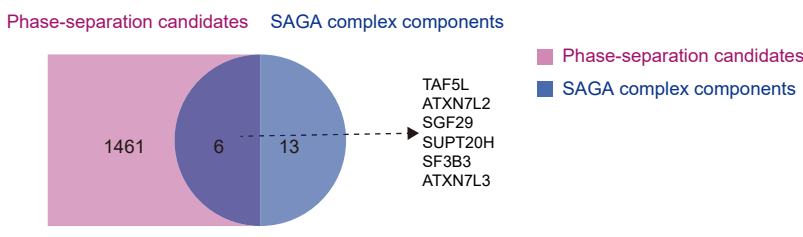
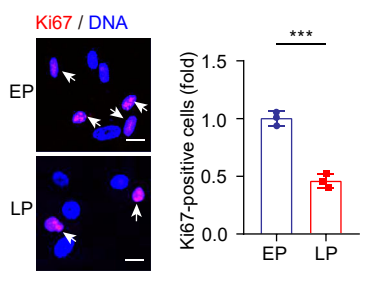


Supplementary Fig. S1

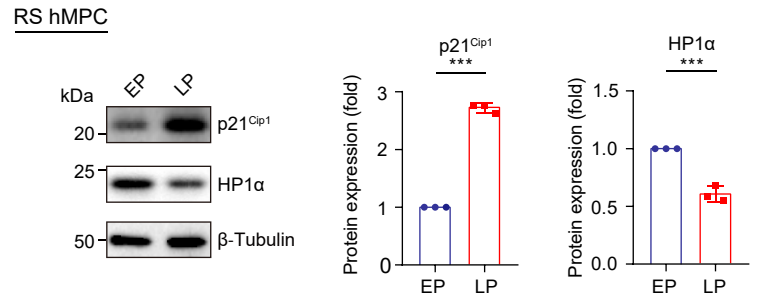
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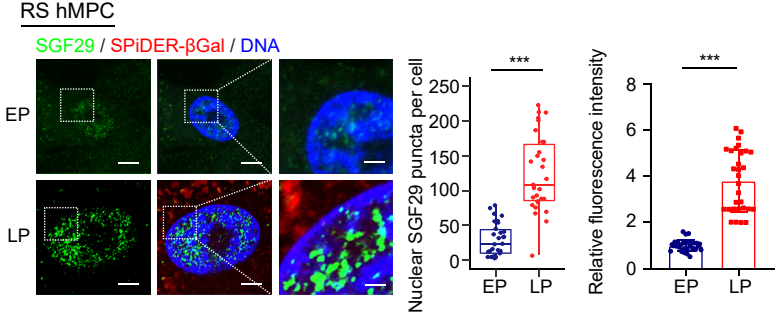
c
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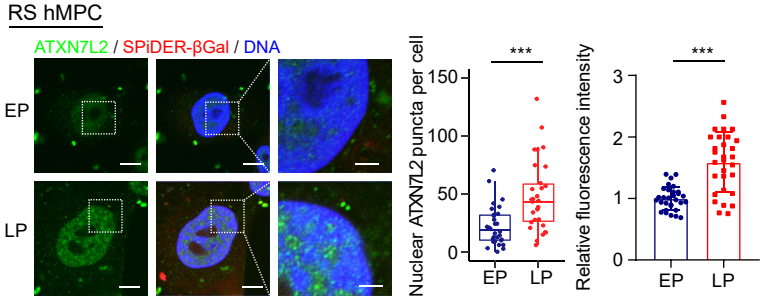
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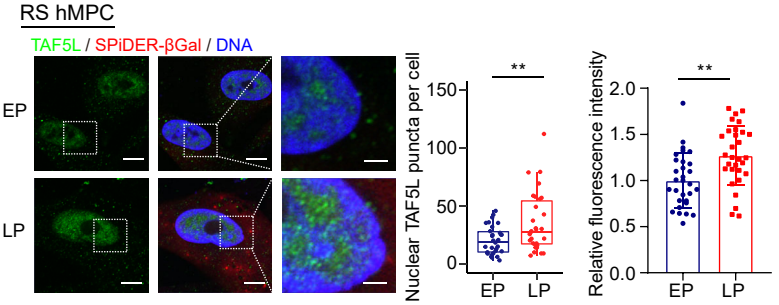
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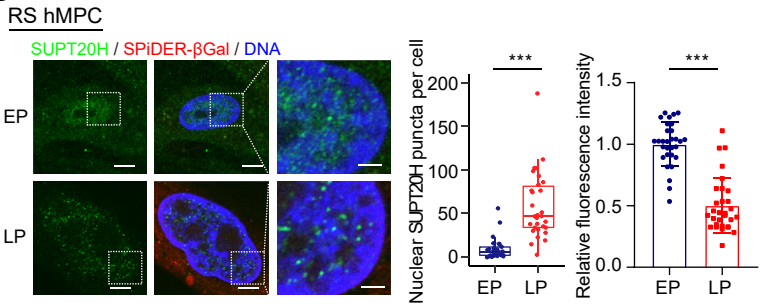
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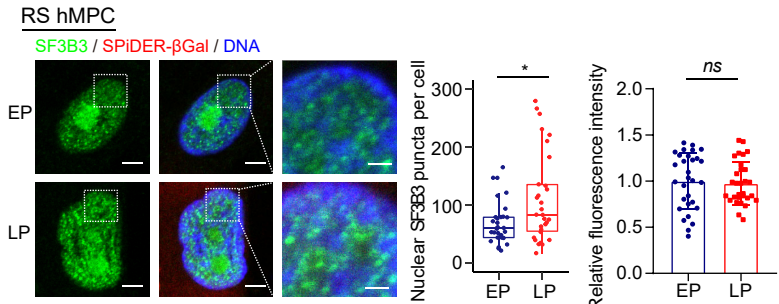
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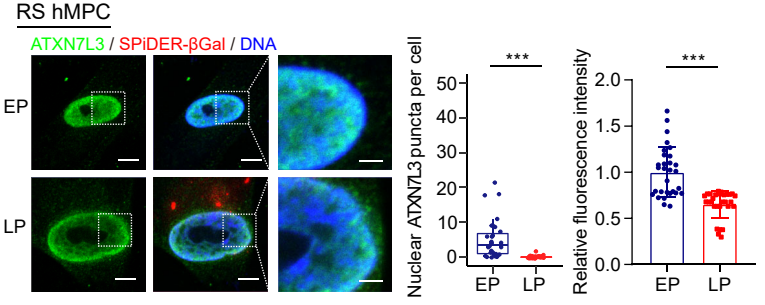
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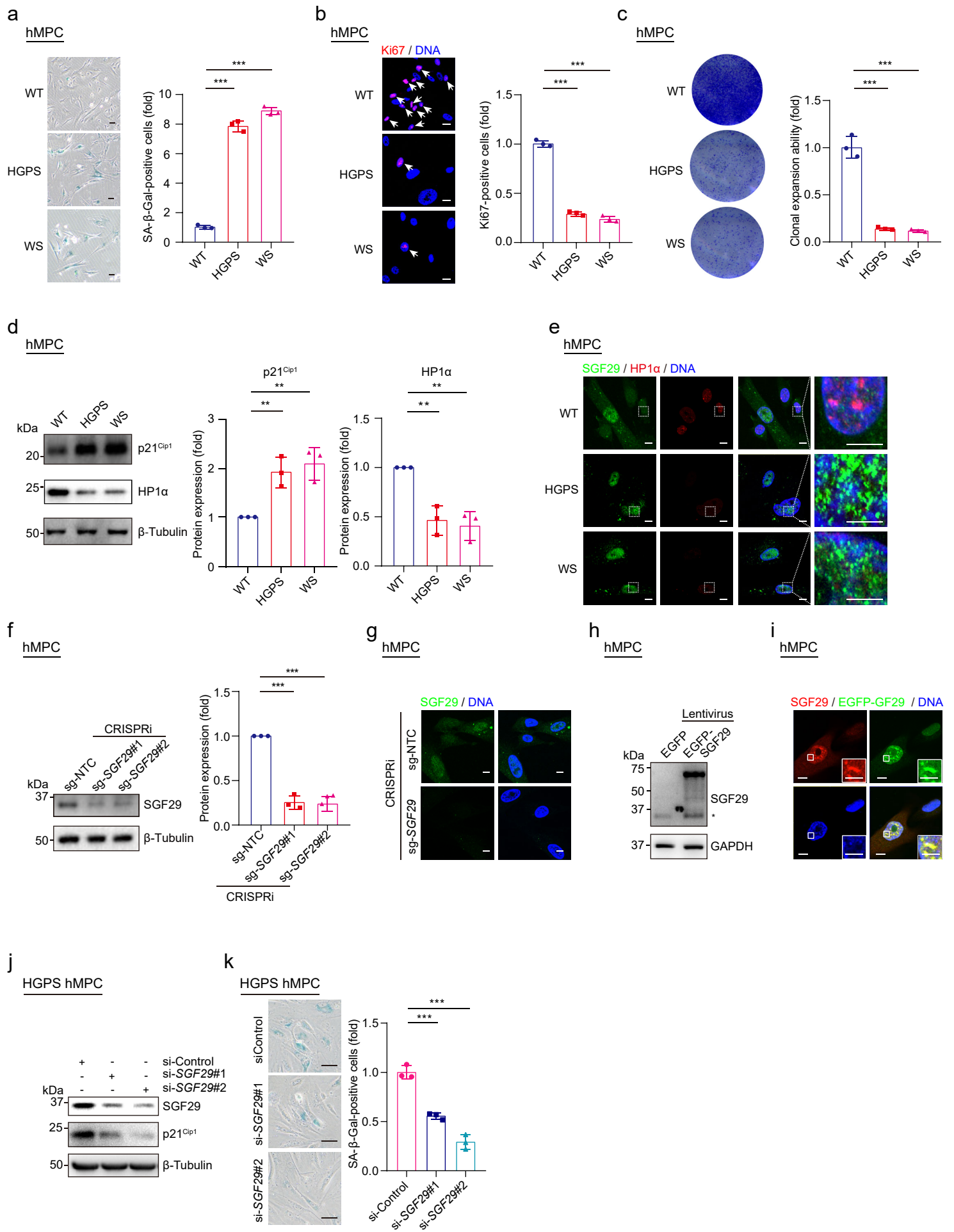


h

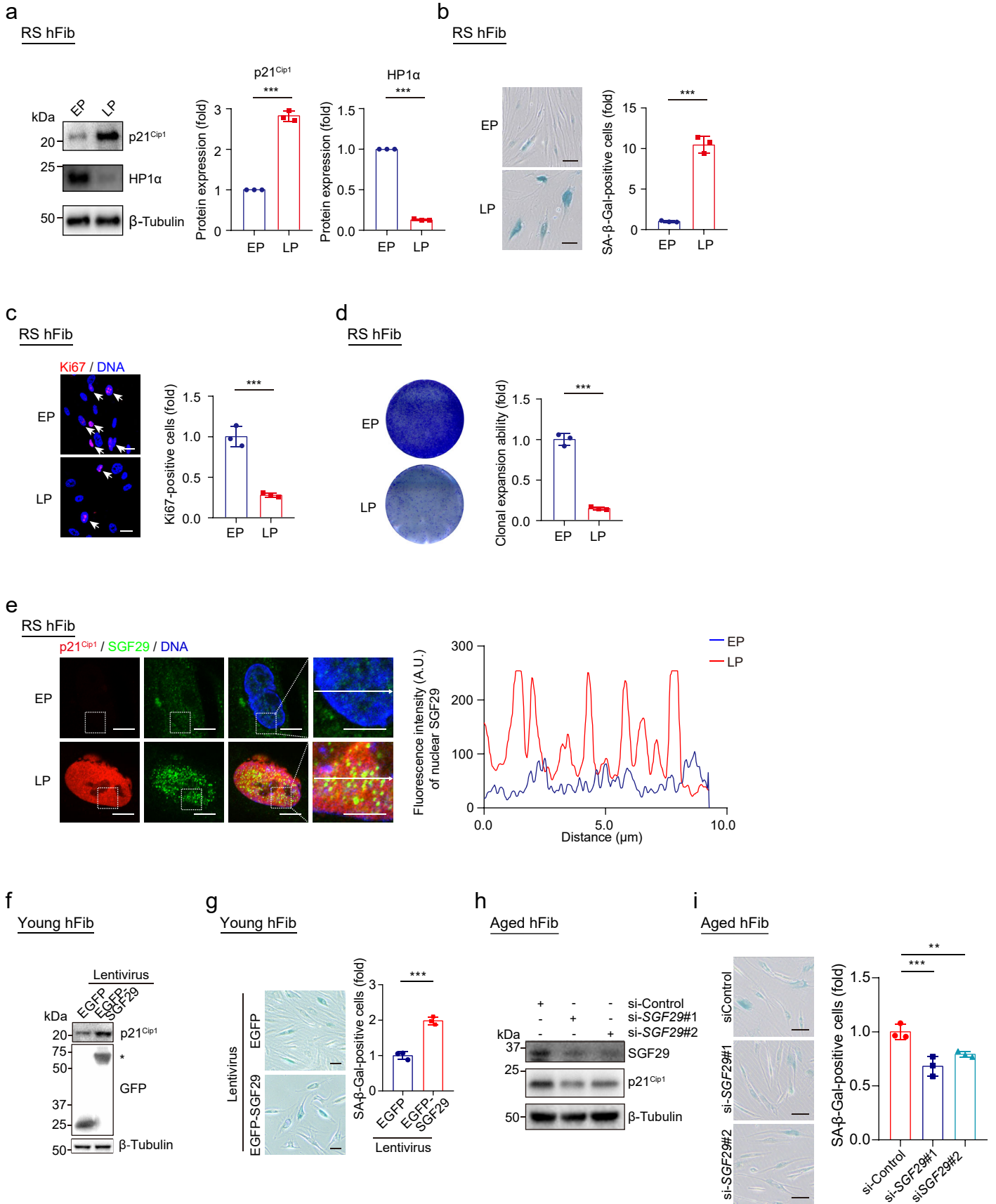


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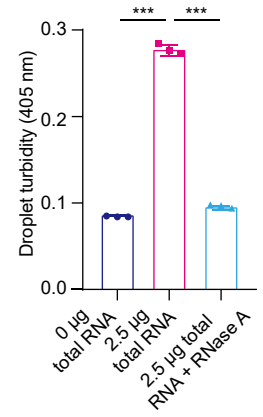
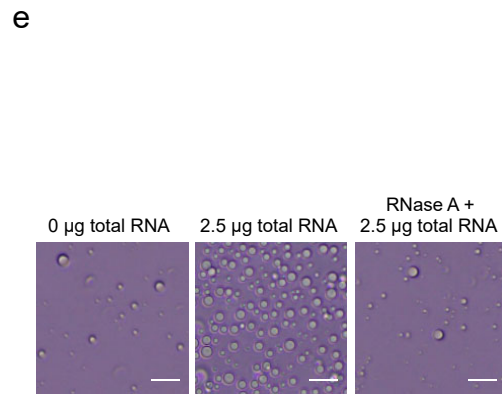
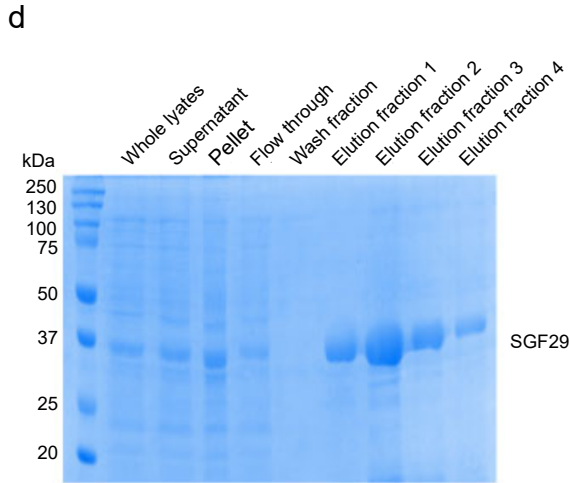
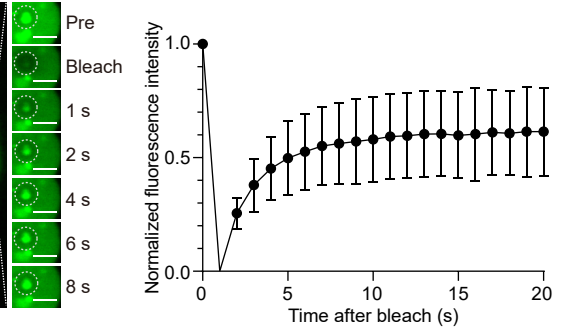
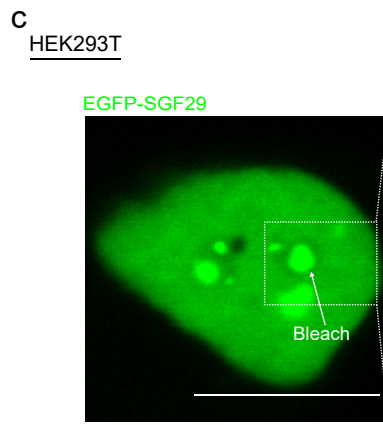
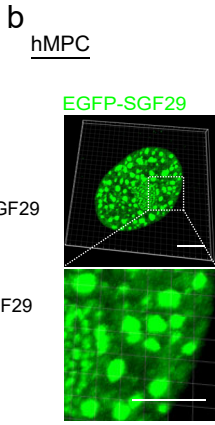
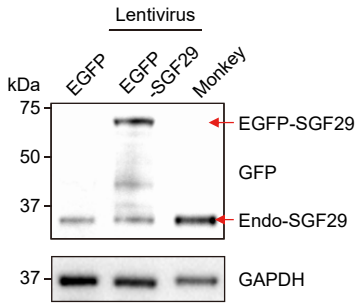


Supplementary Fig. S3

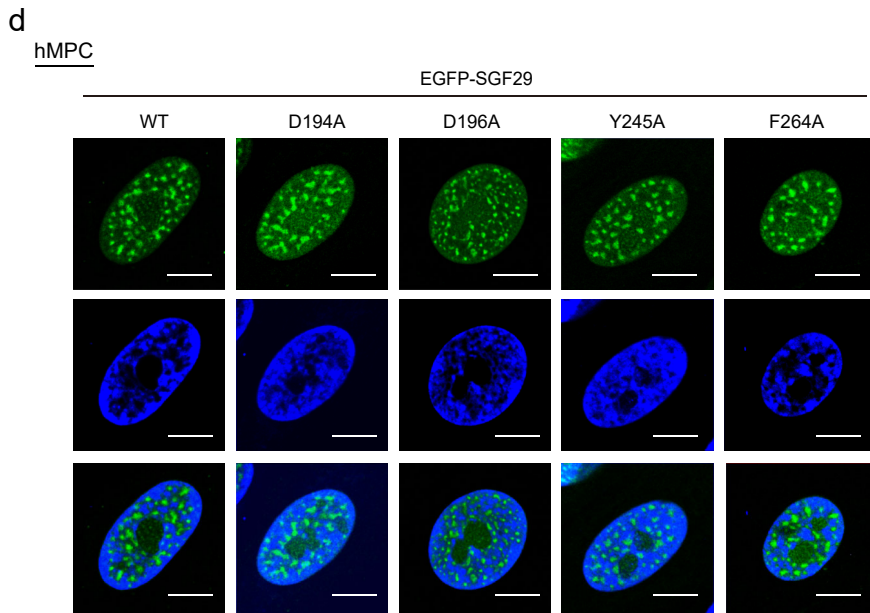
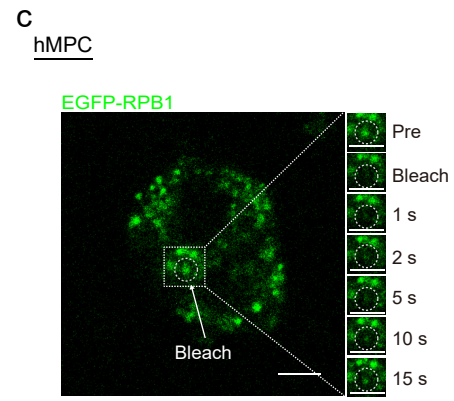
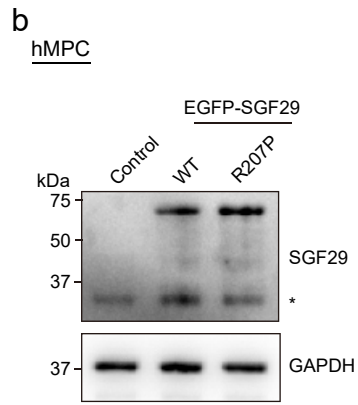
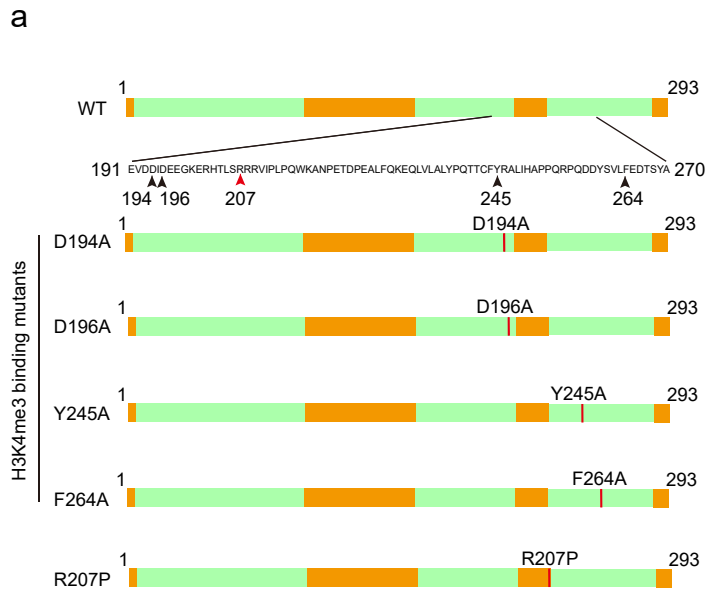


Supplementary Fig. S4

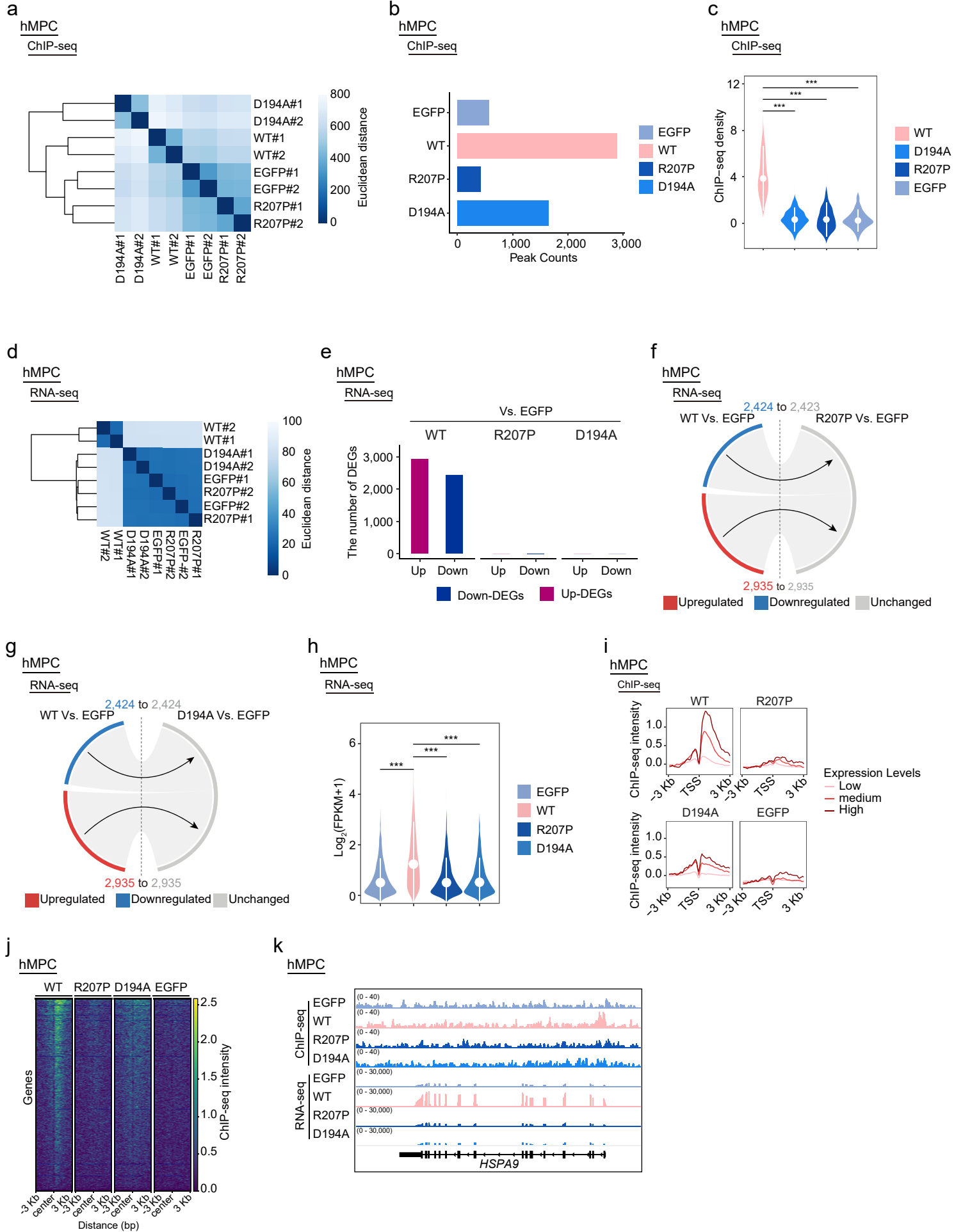
a **b** **c**



Supplementary Fig. S5



Supplementary Fig. S6



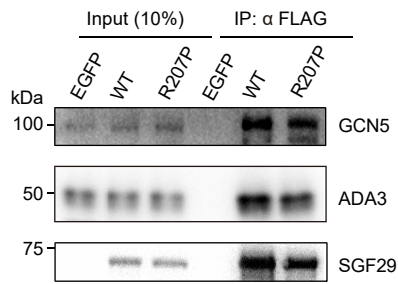
Supplementary Fig. S7

a

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

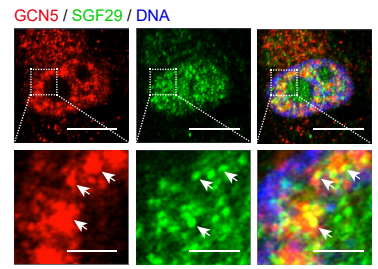
b

WT hMPC



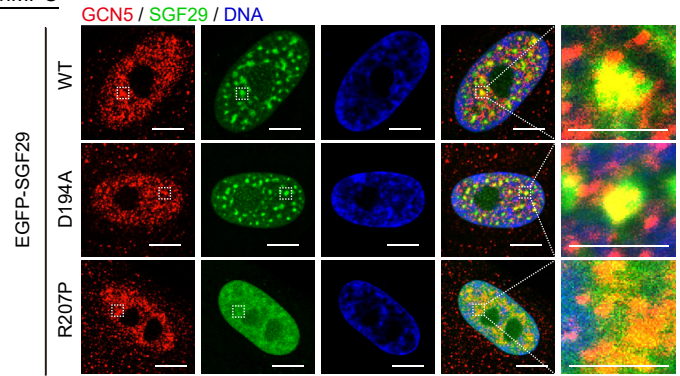
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Aged hMPC



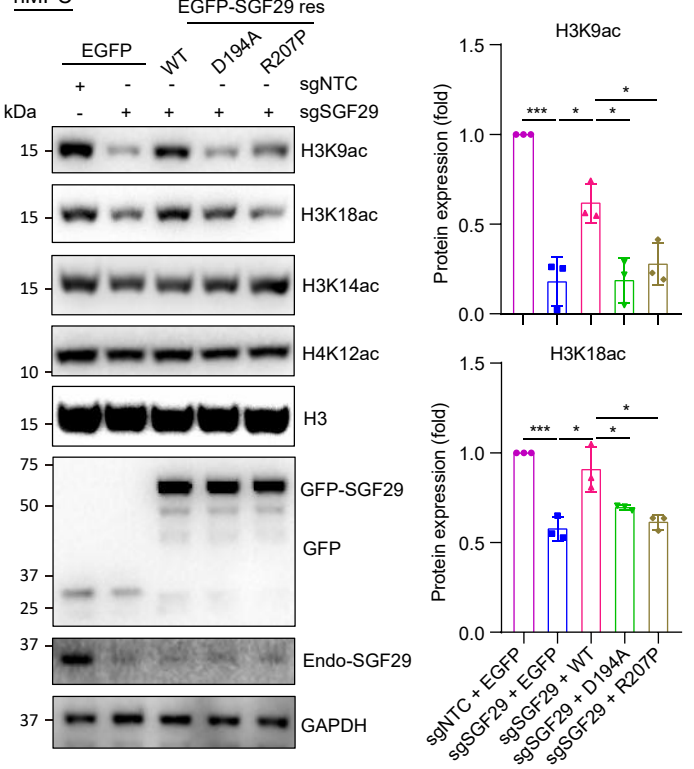
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hMPC



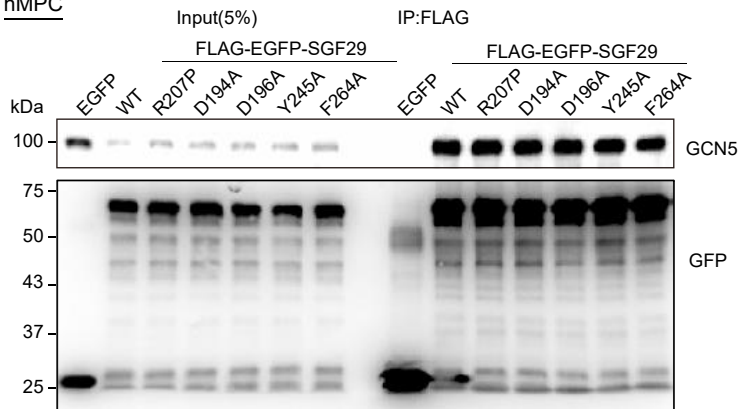
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hMPC



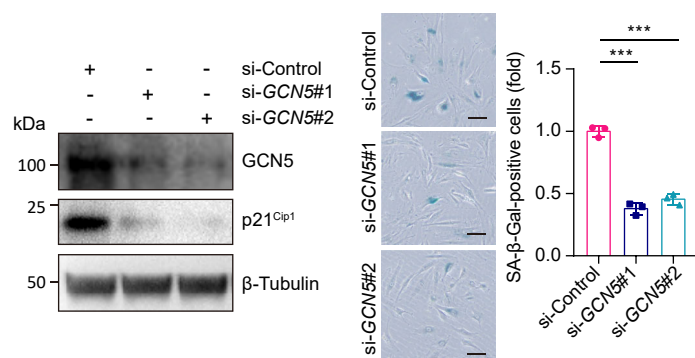
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hMPC



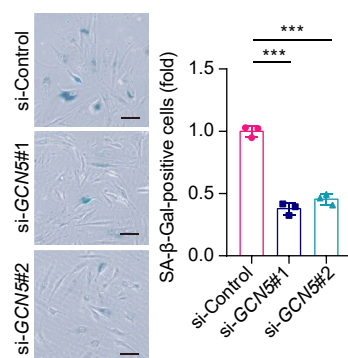
g

Aged hMPC



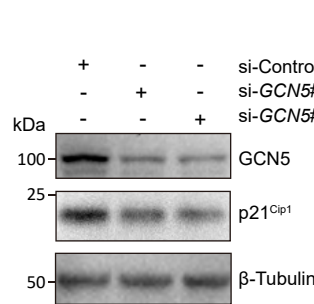
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Aged hMPC



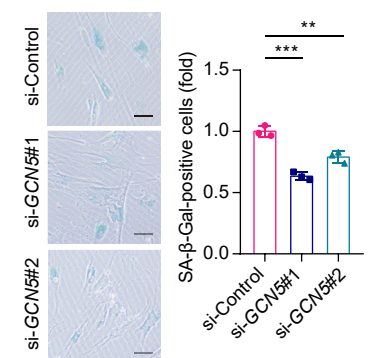
i

Aged hFib



j

Aged hFib



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

3 (a) Venn analysis of SAGA complex and phase separation candidates list and showed that a
4 total of 6 members of SAGA complex including TAF5L, SUPT20H, SGF29, ATXN7L2,
5 ATXN7L3, and SF3B3 had potential phase separation capabilities.

6 (b) Western blotting of HP1 α , p21^{Cip1} in WT hMPCs at EP (P5) and LP (P16). Left,
7 representative western blot images. β -Tubulin was used as a loading control. Right,
8 statistical analysis the relative protein expression of HP1 α , p21^{Cip1}, and SGF29 proteins.
9 Data are presented as the mean \pm SEM. $n = 3$ biological replicates; *ns*, not significant;
10 *** $p < 0.001$ (t test).

11 (c) Immunofluorescence staining of Ki67 in WT hMPCs at EP (P5) and LP (P16). Left,
12 representative images of immunofluorescence staining. Scale bars: 20 μ m. Images were
13 taken with ZEISS confocal LSM900, using a 63 \times HC Plan-Apochromat, NA 1.40
14 oil-immersion objective, and laser wavelengths of 405 nm at 0.6%, 568 nm at 3.3%. Right,
15 statistical analysis of the relative percentages of Ki67-positive cells. Data are presented
16 as the mean \pm SEM. $n = 3$ biological replicates. Over 100 cells were quantified in each
17 replicate. *** $p < 0.001$ (t test).

18 (d) Co-immunostaining of SPIDER- β -gal and SGF29 in hMPCs at EP (P5) and LP (P16). Left:
19 Representative images. Images were taken with ZEISS confocal LSM900, using a 63 \times
20 HC Plan-Apochromat, NA 1.40 oil-immersion objective, and laser wavelengths of 405 nm
21 at 0.6%, 488 nm at 4%, 568 nm at 3.3%. Scale bars: 10 μ m and 2.5 μ m (zoomed-in
22 image). Middle: The number of ATXN7L3 puncta in hMPCs at EP (P5) and LP (P16).
23 Right: Quantification of the fluorescence intensity of nuclear ATXN7L3 in hMPCs at EP
24 (P5) and LP (P16). ($n = 30$ hMPCs). Data are shown as means \pm SEM. *** $p < 0.001$ (t
25 test).

26 (e) Co-immunostaining of SPIDER- β -gal and ATXN7L2 in hMPCs at EP (P5) and LP (P16).
27 Left: Representative images. Images were taken with ZEISS confocal LSM900, using a
28 63 \times HC Plan-Apochromat, NA 1.40 oil-immersion objective, and laser wavelengths of 405
29 nm at 0.6%, 488 nm at 4%, 568 nm at 3.3%. Scale bars: 10 μ m and 2.5 μ m (zoomed-in
30 image). Middle: The number of ATXN7L2 puncta in hMPCs at EP (P5) and LP (P16).
31 Right: Quantification of the fluorescence intensity of nuclear ATXN7L2 in hMPCs at EP
32 (P5) and LP (P16). ($n = 30$ hMPCs). Data are shown as means \pm SEM. *** $p < 0.001$ (t
33 test).

34 (f) Co-immunostaining of SPIDER- β -gal and TAF5L in hMPCs at EP (P5) and LP (P16). Left:
35 Representative images. Images were taken with ZEISS confocal LSM900, using a 63 \times
36 HC Plan-Apochromat, NA 1.40 oil-immersion objective, and laser wavelengths of 405 nm
37 at 0.6%, 488 nm at 4%, 568 nm at 3.3%. Scale bars: 10 μ m and 2.5 μ m (zoomed-in
38 image). Middle: The number of TAF5L puncta in hMPCs at EP (P5) and LP (P16). Right:
39 Quantification of the fluorescence intensity of nuclear TAF5L in hMPCs at EP (P5) and LP
40 (P16). ($n = 30$ hMPCs). Data are shown as means \pm SEM. ** $p < 0.01$ (t test).

41 (g) Co-immunostaining of SPIDER- β -gal and SUPT20H in hMPCs at EP (P5) and LP (P16).
42 Left: Representative images. Images were taken with ZEISS confocal LSM900, using a
43 63 \times HC Plan-Apochromat, NA 1.40 oil-immersion objective, and laser wavelengths of 405
44 nm at 0.6%, 488 nm at 4%, 568 nm at 3.3%. Scale bars: 10 μ m and 2.5 μ m (zoomed-in
45 image). Middle: The number of SUPT20H puncta in hMPCs at EP (P5) and LP (P16).
46 Right: Quantification of the fluorescence intensity of nuclear SUPT20H in hMPCs at EP

47 (P5) and LP (P16). ($n = 30$ hMPCs). Data are shown as means \pm SEM. *** $p < 0.001$ (t
48 test).

49 (h) Co-immunostaining of SPIDER- β -gal and SF3B3 in hMPCs at EP (P5) and LP (P16). Left:
50 Representative images. Images were taken with ZEISS confocal LSM900, using a 63 \times
51 HC Plan-Apochromat, NA 1.40 oil-immersion objective, and laser wavelengths of 405 nm
52 at 0.6%, 488 nm at 4%, 568 nm at 3.3%. Scale bars: 10 μ m and 2.5 μ m (zoomed-in
53 image). Middle: The number of SF3B3 puncta in hMPCs at EP (P5) and LP (P16). Right:
54 Quantification of the fluorescence intensity of nuclear SF3B3 in hMPCs at EP (P5) and
55 LP (P16). ($n = 30$ hMPCs). Data are shown as means \pm SEM. *ns*, not significant (t test). * p
56 < 0.05 (t test).

57 (i) Co-immunostaining of SPIDER- β -gal and ATXN7L3 in hMPCs at EP (P5) and LP (P16).
58 Left: Representative images. Images were taken with ZEISS confocal LSM900, using a
59 63 \times HC Plan-Apochromat, NA 1.40 oil-immersion objective, and laser wavelengths of 405
60 nm at 0.6%, 488 nm at 4%, 568 nm at 3.3%. Scale bars: 10 μ m and 2.5 μ m (zoomed-in
61 image). Middle: The number of ATXN7L3 puncta in hMPCs at EP (P5) and LP (P16).
62 Right: Quantification of the fluorescence intensity of nuclear ATXN7L3 in hMPCs at EP
63 (P5) and LP (P16). ($n = 30$ hMPCs). Data are shown as means \pm SEM. *** $p < 0.001$ (t
64 test).

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

67 (a) SA- β -gal staining of WT, HGPS and WS hMPCs (P7). Scale bars: 20 μ m. Left,
68 representative images of SA- β -gal staining. Right, statistical analysis of the relative
69 percentages of SA- β -gal-positive cells. Data are presented as the mean \pm SEM. $n = 3$
70 biological replicates. Over 100 cells were quantified in each replicate. *** $p < 0.001$ (t test).

71 (b) Immunofluorescence staining of Ki67 in WT, HGPS and WS hMPCs (P7). Left,
72 representative images of immunofluorescence staining. Images were taken with ZEISS
73 confocal LSM900, using a 63 \times HC Plan-Apochromat, NA 1.40 oil-immersion objective,
74 and laser wavelengths of 405 nm at 0.6%, 568 nm at 3.3%. Scale bars: 20 μ m. Right,
75 statistical analysis of the relative percentages of Ki67-positive cells. Data are presented
76 as the mean \pm SEM. $n = 3$ biological replicates. Over 100 cells were quantified in each
77 replicate. *** $p < 0.001$ (t test).

78 (c) Clonal expansion assay in WT, HGPS and WS hMPCs (P7). Left, representative images
79 of crystal violet staining. Right, quantification of the relative clonal expansion ability of WT,
80 HGPS and WS hMPCs. Data are presented as the mean \pm SEM. $n = 3$ biological
81 replicates. *** $p < 0.001$ (t test).

82 (d) Western blotting of HP1 α and p21^{Cip1} in WT, HGPS and WS hMPCs (P7). Left,
83 representative western blot images. β -Tubulin was used as a loading control. Right,
84 statistical analysis of the relative proteins. Data are presented as the mean \pm SEM. $n = 3$
85 biological replicates. ** $p < 0.01$ (t test).

86 (e) Confocal images of HP1 α and SGF29 in WT, HGPS and WS hMPCs (P7). Images were
87 taken with ZEISS confocal LSM900, using a 63 \times HC Plan-Apochromat, NA 1.40
88 oil-immersion objective, and laser wavelengths of 405 nm at 0.6%, 488 nm at 4%, 568 nm
89 at 3.3%. Scale bars: 10 μ m and 5 μ m (zoomed-in image).

90 (f) Validation of SGF29 antibody by immunoblotting in WT hMPCs transduced with
91 SGF29-targeting sgRNAs at P5 (Passage 4) after transduction. Right, statistical analysis

92 of the relative proteins. Data are presented as the mean \pm SEM. $n = 3$ biological
93 replicates. *** $p < 0.001$ (t test).

94 (g) Validation of SGF29 antibody by IF in hMPCs transduced with *SGF29*-targeting sgRNAs
95 at P5 (Passage 4) after transduction. Images were taken with ZEISS confocal LSM900,
96 using a 63 \times HC Plan-Apochromat, NA 1.40 oil-immersion objective, and laser
97 wavelengths of 405 nm at 0.6%, 488 nm at 4%. Scale bars: 10 μ m.

98 (h) Western blot analysis of SGF29 protein level in hMPCs transduced with lentiviruses
99 expressing EGFP or EGFP-SGF29.

100 (i) Immunofluorescence staining of SGF29 in hMPCs transduced with lentiviruses
101 expressing EGFP or EGFP-SGF29. Images were taken with ZEISS confocal LSM900,
102 using a 63 \times HC Plan-Apochromat, NA 1.40 oil-immersion objective, and laser
103 wavelengths of 405 nm at 0.6%, 488 nm at 4%, 568 nm at 3.3%. Scale bars: 10 μ m and 5
104 μ m (zoomed-in image).

105 (j) Western blot analysis of SGF29 in aged HGPS hMPCs after treatment with si-Control or
106 si-SGF29. β -Tubulin was used as the loading control.

107 (k) SA- β -gal staining in aged HGPS hMPCs after treatment with si-Control or si-SGF29.
108 Scale bars: 50 μ m. Quantitative data on the right are presented as the mean \pm SEM. $n = 3$
109 biological replicates. Over 100 cells were quantified in each replicate; *** $p < 0.001$ (t test).

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

111 (a) Western blotting of HP1 α and p21^{Cip1} in human fibroblasts at EP (P13) and LP (P23). Left,
112 representative western blot images. β -Tubulin was used as a loading control. Right,
113 statistical analysis the relative protein expression of HP1 α and p21^{Cip1}. Data are
114 presented as the mean \pm SEM. $n = 3$ biological replicates. *** $p < 0.001$ (t test).

115 (b) SA- β -gal staining of human fibroblasts at EP (P13) and LP (P23). Left, representative
116 images of SA- β -gal staining. Right, statistical analysis of the relative percentages of
117 SA- β -gal-positive cells. Scale bars: 50 μ m. Data are presented as the mean \pm SEM. $n = 3$
118 biological replicates. Over 100 cells were quantified in each replicate. *** $p < 0.001$ (t test).

119 (c) Immunofluorescence staining of Ki67 in human fibroblasts at EP (P13) and LP (P23). Left,
120 representative images of immunofluorescence staining. Images were taken with ZEISS
121 confocal LSM900, using a 63 \times HC Plan-Apochromat, NA 1.40 oil-immersion objective,
122 and laser wavelengths of 405 nm at 0.6%, 568 nm at 3.3%. Scale bars: 20 μ m. Right,
123 statistical analysis of the relative percentages of Ki67-positive cells. Data are presented
124 as the mean \pm SEM. $n = 3$ biological replicates. Over 100 cells were quantified in each
125 replicate. *** $p < 0.001$ (t test).

126 (d) Clonal expansion assay in human fibroblasts at EP (P13) and LP (P23). Left,
127 representative images of crystal violet staining. Right, quantification of the relative clonal
128 expansion ability of EP and LP human fibroblasts. Data are presented as the mean \pm
129 SEM. $n = 3$ biological replicates. *** $p < 0.001$ (t test).

130 (e) Confocal images of p21^{Cip1} and SGF29 in human fibroblasts at EP (P13) and LP (P23).
131 Images were taken with ZEISS confocal LSM900, using a 63 \times HC Plan-Apochromat, NA
132 1.40 oil-immersion objective, and laser wavelengths of 405 nm at 0.6%, 488 nm at 4%,
133 568 nm at 3.3%. Line scans represent fluorescence intensities (FIs) along the inset
134 arrows on the left. Scale bars: 10 μ m and 5 μ m (zoomed-in image).

- 135 (f) Western blot analysis of p21^{Cip1} protein level in young hFibs transduced with lentiviruses
136 expressing either EGFP or EGFP-SGF29. The band of exogenous EGFP-SGF29 protein
137 is marked with *.
- 138 (g) SA- β -gal staining of young hFibs transduced with lentiviruses expressing either EGFP or
139 EGFP-SGF29. Quantitative data on the right are presented as the means \pm SEM. $n = 3$
140 biological replicates; *** $p < 0.001$ (t test).
- 141 (h) Western blot analysis of SGF29 in aged hFibs after treatment with si-Control or si-SGF29.
142 β -Tubulin was used as the loading control.
- 143 (i) SA- β -gal staining in aged hFibs after treatment with si-Control or si-SGF29. Scale bars:
144 50 μ m. Quantitative data on the right are presented as the mean \pm SEM. $n = 3$ biological
145 replicates. Over 100 cells were quantified in each replicate; ** $p < 0.01$; *** $p < 0.001$ (t
146 test). Scale bars: 20 μ m.

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

- 148 (a) Western blot analysis of expressed EGFP-SGF29 and endogenous SGF29 protein levels
149 in hMPCs and in Cynomolgus monkey testis. Top panel, anti-SGF29 antibody is used.
150 The upper band is the expressed EGFP-SGF29, and the lower bands are endogenous
151 SGF29. Bottom panel, anti-GAPDH antibody is used. GAPDH is used as the internal
152 control.
- 153 (b) 3D-reconstructed representative confocal images of the hMPCs expressing
154 EGFP-SGF29. Images were taken with ZEISS confocal LSM900, using a 63 \times HC
155 Plan-Apochromat, NA 1.40 oil-immersion objective, and laser wavelengths of 488 nm at
156 4%. Scale bars: 10 μ m and 5 μ m (zoomed-in image).
- 157 (c) Live-cell images of FRAP experiments with HEK293T cells expressing EGFP-SGF29.
158 Scale bars: 10 μ m and 2 μ m (zoomed-in image). Images were taken with ZEISS confocal
159 LSM900, using a 63 \times HC Plan-Apochromat, NA 1.40 oil-immersion objective, and laser
160 wavelengths of 488 nm at 4%. The curve on the right shows the relative fluorescence
161 intensity quantified during FRAP recovery ($n = 10$ HEK293T cells). Photobleaching
162 occurs at $t = 1$ s. Data are presented as mean \pm SEM.
- 163 (d) SGF29 purified from *E. coli* were analysed by SDS-PAGE and visualized by coomassie
164 blue staining.
- 165 (e) Left, representative images of purified SGF29 (2.5 μ M) in vitro in the presence of total
166 RNA, and addition of RNase A to a sample of SGF29 (2.5 μ M) solubilized with 2.5 μ g/ml
167 of total RNA. Right, quantitative turbidity graphs of phase separation. Scale bars: 50 μ m.

168 **Supplementary Fig. S5. Phase separation of SGF29 is not depend on the its H3K4me3** 169 **binding ability**

- 170 (a) Schematic diagram of a series of EGFP-tagged SGF29 H3K4me3 interaction-disrupting
171 truncated mutants and R207P mutant.
- 172 (b) Western blot analysis of the protein level of expressed either EGFP-SGF29-WT or R207P
173 in hMPCs. GAPDH is used as the internal control. Control (no transfected hMPCs), *
174 band represents endogenous SGF29.

175 (c) Representative time-lapse FRAP images acquired in hMPC transduced with lentiviruses
176 expressing either EGFP-RPB1 with magnified insets showing the pre-bleach and
177 recovery signals of EGFP-RPB1.

178 (d) Immunofluorescence monitored the nuclear puncta formation and the subcellular
179 localization of EGFP-tagged SGF29 H3K4me3 interaction-disrupting truncated mutants in
180 hMPC. Images were taken with ZEISS confocal LSM900, using a 63× HC
181 Plan-Apochromat, NA 1.40 oil-immersion objective, and laser wavelengths of 405 nm at
182 0.6%, 488 nm at 4%. Scale bars: 10 μm.

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

185 (a) Euclidean distance heatmap showing sample repeatability of ChIP-seq data in hMPCs
186 (P8) with SGF29 knockdown using CRISPR/Cas9, followed by expression of
187 EGFP-SGF29-WT, D194A and R207P variants. The colour key from dark to light
188 represents relatively near to far Euclidean distance, respectively.

189 (b) Bar plot showing the number of SGF29 occupancies in hMPCs (P8) with SGF29
190 knockdown using CRISPR/Cas9, followed by expression of EGFP-SGF29-WT, D194A
191 and R207P variants. The SGF29 occupancies in cells expressing EGFP,
192 EGFP-SGF29-D194A or EGFP-SGF29-R207P were considered as sequencing biases
193 unless those co-localized with SGF29 occupancies in cells expressing EGFP-SGF29-WT.

194 (c) Boxplot showing the normalized ChIP-seq signals around SGF29-binding TSSs ($n = 439$)
195 in hMPCs (P8) with SGF29 knockdown using CRISPR/Cas9, followed by expression of
196 EGFP-SGF29-WT, D194A and R207P variants.

197 (d) Euclidean distance heatmap showing sample repeatability of RNA-seq data in hMPCs (P8)
198 with SGF29 knockdown using CRISPR/Cas9, followed by expression of
199 EGFP-SGF29-WT, D194A and R207P variants. The colour key from dark to light
200 represents relatively near to far Euclidean distance, respectively.

201 (e) Bar plots showing the number of differentially expressed genes in hhMPCs (P8) with
202 SGF29 knockdown using CRISPR/Cas9, followed by expression of EGFP-SGF29-WT,
203 D194A and R207P variants.

204 (f) Chord diagram showing the relationship between transcriptional changes in cells
205 expressing EGFP-SGF29-WT compared to cells expressing EGFP and transcriptional
206 changes in cells expressing EGFP-SGF29-R207P compared to cells expressing EGFP.

207 (g) Chord diagram showing the relationship between transcriptional changes in cells
208 expressing EGFP-SGF29-WT compared to cells expressing EGFP and transcriptional
209 changes in cells expressing EGFP-SGF29-D194A compared to cells expressing EGFP.

210 (h) Boxplot showing the expression of these genes, which were activated in cells expressing
211 EGFP-SGF29-WT but remained silence in cells expressing EGFP-SGF29-D194A and
212 EGFP-SGF29-R207P, in all groups.

213 (i) Metaplots showing the enriched levels of SGF29 occupancies surrounding the TSS
214 regions for genes with different indicated expression levels in hMPCs (P8) with SGF29
215 knockdown using CRISPR/Cas9, followed by expression of EGFP-SGF29-WT, D194A
216 and R207P variants.

217 (j) Heatmap showing the enriched levels of SGF29 occupancies surrounding the TSS
218 regions for genes, which were activated in cells expressing EGFP-SGF29-WT but
219 remained silence in hMPCs expressing EGFP-SGF29-D194A and EGFP-SGF29-R207P,
220 in all groups

221 (k) Integrative Genome Viewer tracks of the indicated ChIP-seq and RNA-seq signals at
222 *HSPA9* locus in hMPCs (P8) with SGF29 knockdown using CRISPR/Cas9, followed by
223 expression of EGFP-SGF29-WT, D194A and R207P variants.

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

226 (a) Detailed information illustrated that GCN5, ADA2A, ADA3, GTF2H2, GTF2H3, GTF2H4,
227 SP1 and MED4 were identified as SGF29 interacting candidates by mass spectrometry.
228 The SGF29 interacting candidates identified by mass spectrometry are listed in the
229 Supplementary Table S2.

230 (b) Co-IP analysis of GCN5, ADA3 with exogenous FLAG-tagged and EGFP-tagged
231 SGF29-WT and SGF29-R207P in hMPCs.

232 (c) Co-immunostaining of GCN5 and SGF29 in aged hMPCs at P16. The white arrowheads
233 denote colocalization of SGF29 puncta with GCN5. Images were taken with ZEISS
234 confocal LSM900, using a 63× HC Plan-Apochromat, NA 1.40 oil-immersion objective,
235 and laser wavelengths of 405 nm at 0.6%, 488 nm at 4%, 568 nm at 3.3%. Scale bars: 10
236 μm and 2.5 μm (zoomed-in image).

237 (d) Immunofluorescence staining of GCN5 in hMPCs transduced with lentiviruses expressing
238 either EGFP-SGF29-WT or EGFP-SGF29-R207P, EGFP-SGF29-D194A. Images were
239 taken with ZEISS confocal LSM900, using a 63× HC Plan-Apochromat, NA 1.40
240 oil-immersion objective, and laser wavelengths of 405 nm at 0.6%, 488 nm at 4%, 568 nm
241 at 3.3%. Scale bars, 10 μm and 2.5 μm (zoomed-in image).

242 (e) Co-IP analysis show that EGFP-tagged SGF29-WT, R207P and H3K4me3 binding
243 mutants interact with GCN5 in the hMPCs transduced with lentiviruses expressing either
244 EGFP, EGFP-SGF29-WT, EGFP-SGF29-R207P or EGFP-SGF29-D194A, D196A,
245 Y245A, F264A.

246 (f) Global acetylation levels of H3K9, H3K18, H3K14, and H4K12 in hMPCs infected with
247 sgNTC or sgSGF29 Lentivirus and expressed EGFP-SGF29-WT rescue, D194A and
248 R207P. Quantified values for the H3K18 and H3K9 acetylation levels on the right are
249 present in a bar chart with values as percentage of control (First lane). *** $p < 0.001$; * $p <$
250 0.05 (t test).

251 (g) Western blot analysis of GCN5 in aged hMPCs after treatment with si-Control or si-GCN5.
252 β-Tubulin was used as the loading control.

253 (h) SA-β-gal staining in aged hMPCs after treatment with si-Control or si-GCN5. Scale bars:
254 50 μm. Quantitative data on the right are presented as the mean ± SEM. $n = 3$ biological
255 replicates. Over 100 cells were quantified in each replicate; *** $p < 0.001$ (t test).

256 (i) Western blot analysis of GCN5 in aged hFibs after treatment with si-Control or si-GCN5.
257 β-Tubulin was used as the loading control.

258 (j) SA-β-gal staining in aged hFibs after treatment with si-Control or si-GCN5. Scale bars: 50
259 μm. Quantitative data on the right are presented as the mean ± SEM. $n = 3$ biological

260 replicates. Over 100 cells were quantified in each replicate; *** $p < 0.001$; ** $p < 0.01$ (t
261 test).

262 **Supplementary Fig. S8. Multivalent interaction of SGF29 is sensitive to condensate**
263 **perturbation.**

264 (a) Bar plot showing the phase-separation-dependent potential SGF29 interacting proteins
265 related to RNA polymerase complex. Potential interacting proteins were ranked by PEP
266 scores.

267 (b) The transcription factor prediction analysis of ageing hotspot genes, which were activated
268 in hMPCs expressing EGFP-SGF29-WT but remained silence in hMPCs expressing
269 EGFP-SGF29-D194A and EGFP-SGF29-R207P.

270 (c) Co-IP analysis show that endogenous MED4 interacts with SGF29 and SP1 proteins in
271 hMPCs.

272 (d) Immunofluorescence staining of MED4 and SP1 in hMPCs transduced with lentiviruses
273 expressing either EGFP-SGF29-WT or EGFP-SGF29-R207P. Images were taken with
274 ZEISS confocal LSM900, using a 63× HC Plan-Apochromat, NA 1.40 oil-immersion
275 objective, and laser wavelengths of 405 nm at 0.6%, 488 nm at 4%, 568 nm at 3.3%, and
276 640 nm at 2%. Scale bars: 10 μm .

277 (e) Immunofluorescence staining of TCOF1 in young hMPCs transduced with lentiviruses
278 expressing either EGFP-SGF29-WT or EGFP-SGF29-R207P. Scale bars: 10 μm and 5
279 μm (zoomed-in image).
280

281 **Supplementary Video S1.** The fusion of two adjacent EGFP-SGF29 condensates in hMPCs
282 within a 47.5-min duration. Scale bar, 10 μm .

283 **Supplementary Video S2.** Fluorescence signal recovery of EGFP-tagged SGF29 in hMPCs.
284 A bleaching 488 nm laser pulse was applied. Scale bar, 10 μm .

285 **Supplementary Video S3.** Fluorescence signal recovery of EGFP-tagged SGF29 in
286 HEK293T cells. A bleaching 488 nm laser pulse was applied. Scale bar, 10 μm .

287 **Supplementary Video S4.** The fusion of two adjacent SGF29 droplets in vitro. Scale bar, 50
288 μm .

289

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

291 **Supplementary Table S2.** Interacting proteins of EGFP, EGFP-SGF29-WT and R207P
292 identified by co-IP/MS.

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

295 **Supplementary Table S4.** The sequencing information of RNA-seq data, differentially
296 expressed genes (DEGs) between hMPCs transduced with lentiviruses expressing either
297 EGFP, EGFP-SGF29-WT, or EGFP-SGF29-R207P.

298 **Supplementary Table S5.** The sequencing information of CHIP-seq data, the genomic
299 location of SGF29 peaks identified in hMPCs transduced with lentiviruses expressing either
300 EGFP-SGF29-WT or EGFP-SGF29-R207P.