# Quantitative Mass Spectrometry Reveals that Intact Histone H1 Phosphorylations are Variant Specific and Exhibit Single Molecule Hierarchical Dependence

Yu Chen§II, Michael E. Hoover‡II, Xibei Dang¶, Alan A. Shomo¶, Xiaoyan Guan§, Alan G. Marshall§¶,Michael A. Freitas‡\*,and Nicolas L. Young§\*

	MDA-MB-231			MCF-10A		
Proteoforms	Asyn	S phase	M phase	Asyn	S phase	M phase
H12ac	$16.9 \pm 0.9$	$13.7 \pm 1.0$	$10.5 \pm 1.1$	$4.9 \pm 0.6$	$4.5 \pm 0.2$	$1.2 \pm 0.2$
H12acph	8.1 ± 1.2	$4.3 \pm 0.4$	$6.3 \pm 0.6$	$7.9 \pm 1.1$	$2.3 \pm 0.3$	$2.6 \pm 0.5$
H12SNPac	0	0	0	$4.4 \pm 0.3$	$4.1 \pm 0.3$	$2.2 \pm 0.5$
H12SNPacph	0	0	0	$6.1 \pm 0.7$	$1.8 \pm 0.2$	$2.6 \pm 0.8$
H12SNPacph2	0	0	0	0	0	$2.1 \pm 0.2$
H13ac	0	0	0	$4.6 \pm 0.4$	$2.2 \pm 0.2$	$2.4 \pm 0.3$
H13acph	0	0	0	$1.7 \pm 0.5$	$1.2 \pm 0.2$	$1.1 \pm 0.1$
H14ac	$35.6 \pm 0.8$	$48.2 \pm 1.8$	$27.5 \pm 2.8$	$11.8 \pm 2.4$	38.9 ± 1.4	$10.2 \pm 2.2$
H14ph	$2.3 \pm 0.2$	$2.2 \pm 0.1$	$1.6 \pm 0.2$	$1.8 \pm 0.4$	$3.8 \pm 0.4$	$1.5 \pm 0.4$
H14acph	$24.5 \pm 1.4$	$22.2 \pm 1.0$	$20.1 \pm 0.5$	$26.5 \pm 2.1$	$24.7 \pm 1.7$	$25.6 \pm 2.1$
H14acph2	$11.5 \pm 0.8$	$8.7 \pm 0.9$	$14.7 \pm 2.0$	$22.3 \pm 1.2$	$13.7\pm0.7$	$26.6 \pm 3.5$
H14acph3	$1.0 \pm 0.5$	$0.7 \pm 0.2$	$11.3 \pm 2.4$	8.2 ± 1.9	$2.8 \pm 0.5$	$15.3 \pm 3.7$
H14acph4	0	0	$5.8 \pm 0.7$	0	0	$5.4 \pm 3.4$
H14acph5	0	0	$2.1 \pm 0.2$	0	0	$1.3 \pm 0.2$

Table S1. Relative abundance of proteoforms at different cell cycle stages of two cell lines(%)

	H12ac ( <i>m/z</i> )	H12SNPac (m/z	$\Delta m/z$	Δ mass (Da)
Asyn 1-1	608.86689	609.66750	0.80061	28.02135
Asyn 1-2	608.86739	609.66838	0.80099	28.03465
Asyn 1-3	608.86733	609.66820	0.80087	28.03045
Asyn 2-1	608.86640	609.66762	0.80122	28.04270
Asyn 2-2	608.86673	609.66782	0.80109	28.03815
Asyn 2-3	608.86734	609.66785	0.80051	28.01785
S phase 1-1	608.86597	609.66711	0.80114	28.03990
S phase 1-2	608.86624	609.66726	0.80102	28.03570
S phase 1-3	608.86637	609.66762	0.80125	28.04375
S phase 2-1	608.86607	609.66784	0.80177	28.06195
S phase 2-2	608.86656	609.66796	0.80140	28.04900
S phase 2-3	608.86678	609.66774	0.80096	28.03360
	1 1 2 5 +	1 / . 00.00740	0.01170 0.500	C 1110(1)10 1

Table S2. PTM identification on histone H1.2SNPA18VNα-ac

Note, charge state  $35^+$ , average  $\Delta m/z$  is  $28.03742 \pm 0.01178$ , 0.528  $\sigma$  for H12SNP and dimethylation, and 3.611  $\sigma$  for formylation, given the theoretical mass of H12SNP and dimethylation 28.03132, whereas formylation is 27.9949.

	MDA-MB231		MCF10A	
Proteoforms	ANOVA-test	t-test	ANOVA-test	t-test
H12ac	4.95×10 <sup>-8</sup>	3.72×10 <sup>-4</sup>	8.15×10 <sup>-11</sup>	1.78×10 <sup>-10</sup>
H12acph	3.71×10 <sup>-6</sup>	7.64×10 <sup>-5</sup>	4.64×10 <sup>-10</sup>	0.13
H12SNPac	N/A	N/A	3.70×10 <sup>-8</sup>	6.64×10 <sup>-6</sup>
H12SNPacph	N/A	N/A	1.15×10 <sup>-8</sup>	0.05
H12SNPacph2	N/A	N/A	6.28×10 <sup>-15</sup>	3.48×10 <sup>-10</sup>
H13ac	N/A	N/A	8.30×10 <sup>-10</sup>	0.18
H13acph	N/A	N/A	0.01	0.25
H14ph	8.9×10 <sup>-6</sup>	4.97×10 <sup>-5</sup>	2.03×10 <sup>-7</sup>	2.71×10 <sup>-6</sup>
H14ac	5.92×10 <sup>-11</sup>	3.04×10 <sup>-8</sup>	1.57×10 <sup>-13</sup>	1.22×10 <sup>-10</sup>
H14acph	1.3×10 <sup>-5</sup>	1.15×10 <sup>-3</sup>	0.32	0.47
H14acph2	6.8×10 <sup>-6</sup>	5.92×10 <sup>-5</sup>	1.23×10 <sup>-7</sup>	4.52×10 <sup>-6</sup>
H14acph3	1.5×10 <sup>-9</sup>	9.39×10 <sup>-7</sup>	8.96×10 <sup>-7</sup>	8.86×10 <sup>-6</sup>
H14acph4	1.33×10 <sup>-13</sup>	2.65×10 <sup>-9</sup>	2.92×10 <sup>-4</sup>	3.29×10 <sup>-3</sup>
H14acph5	1.02×10 <sup>-14</sup>	4.81×10 <sup>-10</sup>	1.48×10 <sup>-12</sup>	1.31×10 <sup>-8</sup>

**Table S3.** P-values of ANOVA and t-tests for proteoforms relative abundance at different cell cycle stages

	MDA-MB231		MCF10A	
Proteoforms	ANOVA-test	t-test	ANOVA-test	t-test
H12	2.31×10 <sup>-6</sup>	7.79×10 <sup>-6</sup>	2.26×10 <sup>-15</sup>	1.41×10 <sup>-12</sup>
H13	N/A	N/A	0.02	0.17
H14	7.07×10 <sup>-11</sup>	2.12×10 <sup>-8</sup>	1.49×10 <sup>-13</sup>	5.23×10 <sup>-11</sup>

**Table S4.** P-values of ANOVA and t-tests for histone variants total phosphorylations at different cell cycle stages

**Table S5.** P-values of ANOVA and t-tests for total phosphorylations on different sites at different cell cycle stages

	MDA-MB231		MCF10A	
Proteoforms	ANOVA-test	t-test	ANOVA-test	t-test
H12S173	2.31×10 <sup>-6</sup>	7.79×10 <sup>-6</sup>	2.26×10 <sup>-15</sup>	1.41×10 <sup>-12</sup>
H14S2	1.25×10 <sup>-6</sup>	6.13×10 <sup>-5</sup>	1.94×10 <sup>-6</sup>	2.80×10 <sup>-6</sup>
H14S172	9.10×10 <sup>-11</sup>	2.45×10 <sup>-8</sup>	1.62×10 <sup>-14</sup>	3.72×10 <sup>-11</sup>
H14S187	7.74×10 <sup>-12</sup>	1.03×10 <sup>-8</sup>	7.20×10 <sup>-11</sup>	6.99×10 <sup>-9</sup>
H14T18	1.08×10 <sup>-15</sup>	5.94×10 <sup>-11</sup>	9.01×10 <sup>-6</sup>	7.64×10 <sup>-5</sup>
H14T146	6.48×10 <sup>-14</sup>	1.64×10 <sup>-9</sup>	5.35×10 <sup>-5</sup>	1.13×10 <sup>-3</sup>
H14T153	8.51×10 <sup>-15</sup>	4.26×10 <sup>-10</sup>	2.67×10 <sup>-12</sup>	1.93×10 <sup>-8</sup>

Proteoforms	Asynchronous	S phase	M phase
H12ac	8.01×10 <sup>-11</sup>	5.14×10 <sup>-10</sup>	2.42×10 <sup>-9</sup>
H12acph	0.71	2.58×10 <sup>-6</sup>	5.87×10 <sup>-7</sup>
H12SNPac	5.06×10 <sup>-12</sup>	5.66×10 <sup>-12</sup>	3.49×10 <sup>-7</sup>
H12SNPacph	1.05×10 <sup>-9</sup>	1.80×10 <sup>-9</sup>	1.48×10 <sup>-5</sup>
H12SNPacph2	N/A	N/A	3.48×10 <sup>-10</sup>
H13ac	3.24×10 <sup>-11</sup>	5.18×10 <sup>-11</sup>	6.55×10 <sup>-9</sup>
H13acph	6.48×10 <sup>-6</sup>	4.75×10 <sup>-9</sup>	1.96×10 <sup>-11</sup>
H14ph	0.04	3.23×10 <sup>-6</sup>	0.67
H14ac	5.02×10 <sup>-10</sup>	1.31×10 <sup>-6</sup>	3.39×10 <sup>-7</sup>
H14acph	0.08	0.01	1.14×10 <sup>-4</sup>
H14acph2	6.07×10 <sup>-9</sup>	9.62×10 <sup>-7</sup>	2.84×10 <sup>-5</sup>
H14acph3	4.69×10 <sup>-6</sup>	1.58×10 <sup>-6</sup>	0.05
H14acph4	N/A	N/A	0.77
H14acph5	N/A	N/A	5.99×10 <sup>-5</sup>

Table S6. P-values of t-tests for proteoformrelative abundance between two cell lines

Histone Variants	Asynchronous	S phase	M phase
H12	5.70×10 <sup>-9</sup>	8.35×10 <sup>-8</sup>	7.89×10 <sup>-9</sup>
H13	1.59×10 <sup>-6</sup>	4.70×10 <sup>-9</sup>	1.61×10 <sup>-9</sup>
H14	5.43×10 <sup>-10</sup>	5.99×10 <sup>-8</sup>	3.40×10 <sup>-7</sup>

Table S7. P-values for histone variants total phosphorylations between two cell lines

Table S8. P-values for total phosphorylations on different sites between two cell lines

Proteoforms	Asynchronous	S phase	M phase
H12S173	5.7×10 <sup>-9</sup>	8.35×10 <sup>-8</sup>	7.89×10 <sup>-9</sup>
H14S2	0.19	6.89×10 <sup>-6</sup>	0.51
H14S172	1.15×10 <sup>-10</sup>	8.79×10 <sup>-8</sup>	6.58×10 <sup>-7</sup>
H14S187	1.26×10 <sup>-8</sup>	3.89×10 <sup>-7</sup>	$1.21 \times 10^{-4}$
H14T18	1.22×10 <sup>-5</sup>	1.40×10 <sup>-6</sup>	0.49
H14T146	N/A	N/A	0.29
H14T154	N/A	N/A	3.94×10 <sup>-5</sup>

#### Legends for Supporting Information Figures

**Figure S1.** Broadband ESI positive ion 9.4 T FT-ICR mass spectra of histone H1 from asynchronous, s phase, and m phase cells from cell lines MDA-MB-231 and MCF-10A.

**Figure S2.** ECD fragmentation maps for different histone proteoforms from cell line MDA-MB-231.

Figure S3. ECD fragmentation maps for different proteoforms from cell line MCF-10A.

**Figure S4.** Mass scale-expanded segment of ECD product ion mass spectra of histone H1.2 SNP A18V from asynchronous cells from cell line MCF-10A, showing identification of  $c_{16}^{2+}$ ,  $c_{18}^{2+}$ ,  $c_{19}^{2+}$ ,  $c_{20}^{2+}$ ,  $c_{21}^{2+}$ ,  $c_{22}^{2+}$ , and  $c_{22}^{3+}$  ions.

**Figure S5.** Peak annotations for the ECD product ion mass spectrum of asynchronous histone H1.2 SNP A18V from cell line MCF-10A.

**Figure S6.** Peak annotations for the ECD product ion mass spectrum of S phase histone H1.2 SNP A18V from cell line MCF-10A.

**Figure S7.** Peak annotations for the ECD product ion mass spectrum of asynchronous phosphorylated histone H1.2 SNP A18V from cell line MCF-10A.



# Figure S2

### H12ac\_asyn

ac-S E TÌA P A A P AÌA A P P A E KÌA P V KÌKÌKÌAÌAÌKÌKÌ A GÌGÌT P RÌKÌA SÌG P P VÌSÌEÌL I T KÌAÌVÌAÌAÌSÌK EÌ RÌSÌG V S LÌAÌAÌL KÌKÌAÌL A A A G YÌD VÌEÌKÌNÌNÌS R I KÌL GÌL K S L V S K G T L V QÌT K G T G A S G S F K L N K K A A S GÌE ALK P K V K K A G G TLK P KLK P V G A A KLK P KLKLĂ A G G A T P K K SLĂ K KLT P KLK A K K P A A A TLVLTLKLK V A KLS P KLKLĂLK V ALK PLKL KLĂLĂ KLSLĂLĂLK A VLK P K A ALK PLK V VLK PLKLK ALĂ PLK K K

### H14ph\_asyn

<sup>ph</sup> S E T A P A A P A<sup>1</sup>A P A P A E K<sup>1</sup>T P V K K K A R K S A G A<sup>1</sup>A K R K A S G P P V S<sup>1</sup>E L I T K A V A A S<sup>1</sup>K E<sup>1</sup> R S G V S L<sup>1</sup>A A L K K A L A A A G Y<sup>1</sup>D V E K N N S R I K L G L K S L V S K G T L V Q T K G T G A S G S F K L N K K A A S G E A K P K A K K A G A A K A K K P A G A A K K P K K A T G A A T P K K S A K K T P K K A K K P A A A G A K K K A K S P K K A K A A K P K K A P K S P A K K A K S

#### H12acph asyn

ac-S E TÌA P A A P AÌA A P P A E KÌA P VÌKÌKÌKÌAÌAÌKÌKÌ
AÌGÌGÌT PÌRÌKÌA SÌG P P VÌSÌEÌL I TÌK AÌVÌAÌAÌSÌK EÌ
RÌSÌG VÌSÌLÌAÌAÌL KÌKÌA L A A A G YÌD VÌEÌKÌNÌNÌS R
I KÌL GÌL K SÌL V S K G T L V QÌT K G T G A S G S F
K L N K K A A S GLE ALK P K V K K A G G TLK P KLK P
V GLA A K K P KLKLA A G G ALT P KLKLSLA K K T P KLKL
A KLK P A A ALT VLTLKLK VLA KLS P KLKLALK V ALK PLKL
KLALALKLSLALALK A VLK P K A ALK PLK V VLK PLKLK ALA
PLK K K

#### H14ac\_asyn

\*\*-S E T A P<sup>J</sup>A A P A A P A P A E K<sup>J</sup>T P V K<sup>J</sup>K K<sup>J</sup>A R<sup>J</sup>K S A<sup>J</sup>G<sup>J</sup>A A K R<sup>J</sup>K<sup>J</sup>A S<sup>J</sup>G P P V<sup>J</sup>S<sup>J</sup>E<sup>J</sup>L I T K<sup>J</sup>A<sup>J</sup>V A<sup>J</sup>A<sup>J</sup>S<sup>J</sup>K E<sup>J</sup> R<sup>J</sup>S<sup>J</sup>G<sup>J</sup>V<sup>J</sup>S L<sup>J</sup>A<sup>J</sup>L<sup>J</sup>K<sup>J</sup>K<sup>J</sup>L<sup>J</sup>A A<sup>J</sup>A G<sup>J</sup>Y<sup>J</sup>D V<sup>J</sup>E<sup>J</sup>K<sup>J</sup>N<sup>J</sup>N<sup>J</sup>S<sup>J</sup>R I K<sup>J</sup>L<sup>J</sup>G<sup>J</sup>L K<sup>J</sup>S<sup>J</sup>L<sup>J</sup>V<sup>J</sup>S<sup>J</sup>K G<sup>J</sup>T<sup>J</sup>L V<sup>J</sup>Q<sup>J</sup>T<sup>J</sup>K G T G<sup>J</sup>A S G<sub>L</sub>S<sup>J</sup>F<sup>J</sup> K L N<sup>J</sup>K K A A S G<sup>J</sup>E A<sub>L</sub>K P K<sup>J</sup>A K K A<sub>L</sub>G<sub>L</sub>A A<sub>L</sub>K A K<sub>L</sub>K P A G A<sub>L</sub>A K<sub>L</sub>K P K<sub>L</sub>K<sub>L</sub>A T G A A<sub>L</sub>T P K<sub>L</sub>K<sub>L</sub>S<sub>L</sub>A<sub>L</sub>K<sub>L</sub>K T P<sub>L</sub>K<sub>L</sub>K<sub>L</sub> A K<sub>L</sub>K P A A A<sub>L</sub>A<sub>L</sub>G<sub>L</sub>A<sub>L</sub>K K K K K A<sub>L</sub>K P K T A<sub>L</sub>K P<sub>L</sub>K A A<sub>L</sub> K P<sub>L</sub>K<sub>L</sub>K A<sub>L</sub>A<sub>L</sub>A<sub>L</sub>K K K

### H120acT146ph asyn

ac-S E T<sup>1</sup>A P A A P A<sup>1</sup>A A P P A E K<sup>1</sup>A P V<sup>1</sup>K<sup>1</sup>K<sup>1</sup>K<sup>1</sup>A<sup>1</sup>A<sup>1</sup>K<sup>1</sup>K<sup>1</sup>
A<sup>1</sup>G<sup>1</sup>G<sup>1</sup>T P<sup>1</sup>R<sup>1</sup>K<sup>1</sup>A S<sup>1</sup>G P P V<sup>1</sup>S<sup>1</sup>E<sup>1</sup>L I T<sup>1</sup>K A<sup>1</sup>V<sup>1</sup>A<sup>1</sup>A<sup>1</sup>S<sup>1</sup>K E<sup>1</sup>
R<sup>1</sup>S<sup>1</sup>G V<sup>1</sup>S<sup>1</sup>L<sup>1</sup>A<sup>1</sup>A<sup>1</sup>L K<sup>1</sup>K<sup>1</sup>A L A A A G Y<sup>1</sup>D V<sup>1</sup>E<sup>1</sup>K<sup>1</sup>N<sup>1</sup>N<sup>1</sup>S R
I K<sup>1</sup>L G<sup>1</sup>L K S<sup>1</sup>L V S K G T L V Q<sup>1</sup>T K G T G A S G S F
K L N K K A A S GLE ALK P K V K K A G G TLK P KLK P
V GLA A K K P KLKLA A G G ALT<sup>P<sup>1</sup></sup> P K K S A K K T P K K
A K K P A A A T V T K K V A K S P KLKLALK V ALK PLKL
KLALALKLSLALK A VLK P K A ALK PLK V VLK PLKLK ALA
PLK K K

### H14acph\_asyn

ac-S E<sup>I</sup>T<sup>I</sup>A P A A P A A P A P A P A E K T P V K K K<sup>I</sup>A<sup>I</sup>R K S A G A<sup>I</sup>A K<sup>I</sup>R<sup>I</sup>K<sup>I</sup>A S G P P V S<sup>I</sup>E L I T K A V A<sup>I</sup>A<sup>I</sup>S<sup>I</sup>K E<sup>I</sup> R S G<sup>I</sup>V S<sub>L</sub> A<sup>I</sup>A<sup>I</sup>L K K<sup>I</sup>A<sup>I</sup>L<sup>I</sup>A A A G Y<sup>I</sup>D V E<sup>I</sup>K N<sup>I</sup>N S R I K<sup>I</sup>L<sup>I</sup>G<sup>I</sup>L K S<sup>I</sup>L<sup>I</sup>V S K G T L V<sup>I</sup>Q<sub>L</sub>T<sup>I</sup>K G T G A S G<sup>I</sup>S<sup>I</sup>F<sup>I</sup> K L N<sub>L</sub>K K A A S G<sup>I</sup>E A<sub>L</sub>K P<sub>L</sub>K<sup>I</sup>A K K A<sub>L</sub>G<sup>I</sup>A A<sub>L</sub>K K K P A G<sub>L</sub>A A<sub>L</sub>K<sub>L</sub>K P K<sup>I</sup>K<sub>L</sub>A T<sub>L</sub>G A A<sub>L</sub>T P K<sub>L</sub>K<sub>S</sub>A<sub>L</sub>K K T P K<sub>L</sub>K<sup>I</sup> A K<sub>L</sub>K P<sub>L</sub>A A<sub>L</sub>A<sub>L</sub>G<sub>L</sub>A<sub>L</sub>K K<sub>L</sub>A K<sup>I</sup>S P<sub>L</sub>K<sub>L</sub>K<sub>L</sub>A<sub>L</sub>K<sub>L</sub>A<sub>L</sub>K P K<sub>L</sub>K A A P K S P<sub>L</sub>A<sub>L</sub>K<sub>L</sub>A<sub>L</sub>K A V<sub>L</sub>K P K<sub>L</sub>A A<sub>L</sub>K P K T A<sub>L</sub>K P<sub>L</sub>K A A<sub>L</sub> K P<sub>L</sub>K<sub>L</sub>K A<sub>L</sub>A<sub>L</sub>A<sub>L</sub>K K K

### H14acphx2\_asyn

ac-S E T<sup>I</sup>A P A A P A<sup>I</sup>A P A P A E K<sup>I</sup>T P V K<sup>I</sup>K<sup>I</sup>K R<sup>I</sup>K<sup>I</sup>S
A<sup>I</sup>G<sup>I</sup>A<sup>I</sup>K<sup>I</sup>R<sup>I</sup>K<sup>I</sup>A<sup>I</sup>S<sup>I</sup>G P P V<sup>I</sup>S<sup>I</sup>E<sup>I</sup>L I T<sup>I</sup>K<sup>I</sup>A V<sup>I</sup>A<sup>I</sup>A<sup>I</sup>S<sup>I</sup>K<sup>I</sup>E<sup>I</sup>
R<sup>I</sup>S G V<sup>I</sup>S<sup>I</sup>L<sup>I</sup>A<sup>I</sup>A<sup>I</sup>L<sup>I</sup>K<sup>I</sup>K<sup>I</sup>A<sup>I</sup>L<sup>I</sup>A A A G Y<sup>I</sup>D V<sup>I</sup>E<sup>I</sup>K<sup>I</sup>N<sup>I</sup>N<sup>I</sup>S R
I K<sup>I</sup>L<sup>I</sup>G<sup>I</sup>L K S<sup>I</sup>L<sup>I</sup>V<sup>I</sup>S<sup>I</sup>K G T L V<sup>I</sup>Q<sup>I</sup>T<sup>I</sup>K G T<sub>I</sub>G A S G<sup>I</sup>S F<sup>I</sup>
K L N K K A A S G<sup>I</sup>E A<sup>I</sup>K P<sub>I</sub>K<sup>I</sup>A K K A G<sub>I</sub>A A<sub>I</sub>K A K<sub>I</sub>K P
A G A A K K P K<sup>I</sup>K<sub>I</sub>A T G A A T P K K<sub>I</sub>S A K K T P K<sub>I</sub>K<sub>I</sub>
A K K P A A A<sub>I</sub>A<sub>I</sub>G<sub>I</sub>A<sub>I</sub>K<sub>I</sub>K K K<sup>I</sup>S<sup>I</sup> P<sub>I</sub>K<sub>I</sub>K<sub>I</sub>A<sub>I</sub>K A A<sub>I</sub>K P K K
A P K<sub>I</sub>S<sup>I</sup> P<sub>I</sub>A<sub>I</sub>K<sub>I</sub>K<sub>I</sub>A K V<sub>I</sub>K P<sub>I</sub>K A A<sub>I</sub>K P K T A<sub>I</sub>K P<sub>I</sub>K A A<sub>I</sub>
K P<sub>I</sub>K<sub>I</sub>K A<sub>I</sub>A<sub>I</sub>A<sub>I</sub>K K K

### H12ac\_s phase

ac-S E TÌA P A A P AÌA A P P A E KÌA P VÌKÌKÌKÌAÌAÌKÌKÌ A GÌGÌT PÌRÌKÌAÌSÌG P P VÌSÌEÌL I T KÌAÌVÌAÌAÌSÌK EÌ RÌSÌG VÌSÌLÌAÌAÌLÌKÌKÌAÌL A A A GÌYÌD VÌEÌKÌNÌNÌS R I KÌL GÌL K SÌL V S K G T L VÌQÌTÌK G T G A S GÌS F K L N K K A A S GÌE ALK P K V K K A G G TLK P KLK P V G ALA KLK P KLKLA A G G ALT P K KLSLA K KLT P KLK A KLK P A A A TLVLTLKLK V A KLS P KLKLA K V ALK PLKL KLALA KLSLALALK A VLK P K A ALK PLK V VLK PLKLK ALA PLK K K

### H12acph\_s phase

\*\*\* S E T A P A A P A A A P P A E K<sup>1</sup>A P V K<sup>1</sup>K<sup>1</sup>A<sup>1</sup>A<sup>1</sup>K<sup>1</sup>K<sup>1</sup> A<sup>1</sup>G<sup>1</sup>G<sup>1</sup>T P R<sup>1</sup>K A S<sup>1</sup>G P P V<sup>1</sup>S<sup>1</sup>E<sup>1</sup>L I T<sup>1</sup>K A V<sup>1</sup>A A<sup>1</sup>S<sup>1</sup>K E<sup>1</sup> R<sup>1</sup>S<sup>1</sup>G V<sup>1</sup>S L<sup>1</sup>A<sup>1</sup>A<sup>1</sup>L K<sup>1</sup>K<sup>1</sup>A L A A A G Y<sup>1</sup>D V<sup>1</sup>E<sup>1</sup>K<sup>1</sup>N<sup>1</sup>N<sup>1</sup>S R I K<sup>1</sup>L G L K S L V S K G T L V<sup>1</sup>Q T K G T G A S G S F K L N K K A A S G<sub>1</sub>E A<sub>1</sub>K P K V K K A G G T<sub>1</sub>K P K<sub>1</sub>K P V G A A K K P K<sub>1</sub>K<sub>1</sub>A A G G A T P K K<sub>1</sub>S<sub>1</sub>A K K T P K<sub>1</sub>K A K<sub>1</sub>K P A A A T<sub>1</sub>V<sub>1</sub>T<sub>1</sub>K<sub>1</sub>K V<sub>1</sub>A K<sub>1</sub><sup>S<sup>1</sup></sup> P K<sub>1</sub>K<sub>1</sub>A<sub>1</sub>K V A<sub>1</sub>K P<sub>1</sub>K<sub>1</sub>K K<sub>1</sub>A<sub>1</sub>A K<sub>1</sub>S<sub>1</sub>A<sub>1</sub>A<sub>1</sub>K A V<sub>1</sub>K P K A A<sub>1</sub>K P<sub>1</sub>K V V<sub>1</sub>K P<sub>1</sub>K<sub>1</sub>K A<sub>1</sub>A P<sub>1</sub>K K K

### H12acT146ph s phase

# Figure S2

### Figure S2 H14acph s phase

ac-S ETA PA A PA A PA PA E KT P V K K KA R K S A G A<sup>1</sup>A K<sup>1</sup>R<sup>1</sup>K<sup>1</sup>A S<sup>1</sup>G P P V<sup>1</sup>S<sup>1</sup>E L I T<sup>1</sup>K A V<sup>1</sup>A<sup>1</sup>A<sup>1</sup>S<sup>1</sup>K E<sup>1</sup> RISIGIV S LIAIA L KIKIAILIA A AIG YID VIEIKININISIR I K<sup>1</sup>L<sup>1</sup>G<sup>1</sup>L K S<sup>1</sup>L<sup>1</sup>V<sup>3</sup>S<sup>1</sup>K G T<sup>1</sup>L V<sup>1</sup>Q<sup>1</sup>T<sup>1</sup>K G T G A S G<sup>3</sup>F<sup>1</sup> K L'N K K A A S G E A K P K A K K A G A A K A K K P ALGIALALKIK P KIKLA TIG A ALT P KIKLSIALK K T PIKIKI Α ΚΙΚ Ρ Α Α ΑΙΑΙGΙΑΙΚΙΚΙΑ ΚΙ<sup>S</sup> Ρ ΚΙΚΙΑΙΚΙΑΙΚ Ρ ΚΙΚ ΑΡΚ ΣΡΙΑΙΚΙΑΙΚΑ VΙΚΡΙΚΙΑΑΙΚΡΚΤΑΙΚΡΙΚΑΑΙ Κ Ρ**ι**κ**ι**κ Α**ι**Α**ι**Α κ κ κ

### H14ph s phase

H14ac s phase

ac-SETAPAAPAAPAEKTPVKKKARKS

Alglalalkirikia sig p p visiel I T kiaivialaisikiei

RISIG VISILIAIAILIKIKIAILIA AIA GIYID VIEIKININIS R

I KILIGIL KISILIVISIK G TIL VIQITIK G TIG A S GIS FI

K L N K K A A S G E A K P K A K K A G A A K A K K P

Α G Α Α ΚΙΚ Ρ ΚΙΚΙΑ Τ G ΑΙΑΙΤ Ρ Κ ΚΙ SΙΑΙΚ Κ Τ ΡΙΚΙΚΙ

A KLK P A A ALALGLALKLK ALKLS PLKLKLALKLA ALK P KLK

ΑΡΚSΡΙΑΙΚΑΙΚΑΥΙΚΡΚΑΑΚΡΚΤΑΙΚΡΙΚΑΑΙ

Κ Ρ**ι**κ**ι**κ Α**ι**Α**ι**Ακ κ κ

setapaapaapapaek<sup>1</sup>tpvkkkarks AGAAKIRIKASGPPVISIEILITKAVIAASKEI RSGVSL<sup>1</sup>A<sup>1</sup>A<sup>1</sup>LKKALAAAGY<sup>1</sup>DVE<sup>1</sup>KN<sup>1</sup>N<sup>1</sup>SR I K<sup>1</sup>LGLKS<sup>1</sup>LVS<sup>1</sup>KGTLVO<sup>1</sup>TKGTGASG<sup>1</sup>SF K L N K K A A S G E A K P K A K K A G A A K A K K P A G A A KIK P KIK A TIG A A T P KIKISIA K KIT P KIK Α ΚΙΚ ΡΑΑΑΑ GLA ΚΙΚΑΚΙ ΣΡΙΚΙΚΙΑΙΚΑΑΙΚ ΡΚΙΚ ΑΡΚΙ ΥΡΑΙΚΙΑΙΚΙΑΙ ΥΙΚΡΙΚΑΑΙΚΡΚΤΑΙΚΡΙΚΑΑΙ KPKKAAKKK

**MDA-MB-231** 

H14acph2 s phase

ac-SETAPAAPA ΑΡΑΑΡΑΕΚΊΤΡΥΚΙΚΙΑΙΡΙΚΙSΙ Alglalalklalslg p p visiell i t kla vlalalsikiel RISIG VISILIAIAILIKIKIAILIA A A GIYID VIEIKININIS R I K<sup>1</sup>L<sup>1</sup>G<sup>1</sup>L K S<sup>1</sup>L V<sup>1</sup>S<sup>1</sup>K G T L V<sup>1</sup>Q<sup>1</sup>T<sup>1</sup>K G T<sub>1</sub>G A S G<sup>1</sup>S F<sup>1</sup> KLNKKAASGEAKPKAKKAGAAKAKKP А G A A KIK P KIKIA T G A A T P K KISIAIK KITIPIK K аккрааајај аккјакј <sup>вр</sup> аркі ракачк ркаакритакриаа 

### H12ac m phase

ac-S Ε ΤΑ Ρ Α Α Ρ ΑΑ Α Ρ ΡΑ Ε ΚΑ Ρ ΥΚΙΚΙΚΙΑΑΚΙ Alglglt plrklalslg p p vlslell i tlk Alvlalalslk el RISIG VIS LIAIAILIKIKIAIL A A A G YID VIEIKININIS R I K<sup>1</sup>L G<sup>1</sup>L K S L V S K G T L V O<sup>1</sup>T<sup>1</sup>K G T G A S G S F K L N K K A A S G E A K P K V K K A G G T K P K K P VGALA KLK PKLKLA AGGALT PKKLSLALKKT PKLK A KLK P A A T VLT KLK V A KLS P KLKLA K V ALK PLKL KLALA KLSLALK A VLK P K A ALK PLK V VLK PLKLK ALA ΡͺΚΚΚ

#### H14ph m phase

setapaapa<sup>1</sup>apapaek<sup>1</sup>tpvk<sup>1</sup>kkarks AGAAKR<sup>1</sup>KASGPPVS<sup>1</sup>ELITKAV<sup>1</sup>AAS<sup>1</sup>KE<sup>1</sup> RSGVSL<sup>1</sup>AALKKALAAAGY<sup>1</sup>DVEKNNSR I KLGLKSLVSKGTLVOTKGTGASGSF K L N K K A A S G E A K P K A K K A G A A K A K K P A G A A K K P K K A T G A A T P K K S A K K T P K K A KLK P A A A GLA K K A KLS PLKLKLALKLA ALK P KLK A P KLS PLALKLALKLA VLK PLKLA ALK P K T ALK PLK A AL К Р К К А А А А К К К

### H12acph m phase

ac-SETAPAAPAAAPPAEKAPVKKKAAAAKA Algigit pirikia sig p p visieil iit k aiviaiaisik ei RISIG VIS LIAIAILIKIKIAIL A A A G YID VIEIK NINIS R I K<sup>1</sup>L G<sup>1</sup>L K S L V S K G T L V O<sup>1</sup>T K G T G A S G S F K L N K K A A S G E A K P K V K K A G G T K P K K P ν σ Α Α Κ<u>Ι</u>Κ Ρ ΚΙ<mark>ΚΙ</mark>Α Α G G ΑΙΤ Ρ Κ ΚΙ<mark></mark> SΙΑ Κ Κ Τ Ρ Κ Κ Α ΚΙΚ Ρ Α Α Α ΤΙVΙΤΙΚΙΚ VΙΑ ΚΙ<sup>S</sup> ΡΙΚΙΚΙΑΙΚ V ΑΙΚ ΡΙΚΙ KLALALKISLALALK A VLK P K A ALK PLK V VLK PLKLK ALA РККК

#### H14ac m phase

ac-SETAPAAPAAPAPAEKTPVKKKARKS AIGIA A K RIKIA SIG P P VISIEIL T TIKIA VIAIAISIKIEI RISIGIVISILIAIAILIKIKIAILIA AIA G YID VIEIKININISIR I K<sup>J</sup>L G<sup>J</sup>L K<sup>J</sup>S<sup>J</sup>L<sup>J</sup>V<sup>J</sup>S<sup>J</sup>K<sup>J</sup>G T<sup>J</sup>L V<sup>J</sup>Q<sup>J</sup>T<sup>J</sup>K G T G<sup>J</sup>A S G<sup>J</sup>S<sup>J</sup>F K L N K K A A S G E A K P K A K K A G A A K A K K P ALG A A KLK P KLKLA TLG A ALT P KLKLSLALK K T PLKLK A KLK P ALA ALALGLALKLK ALKLS PLKLKLALKLA ALK P KLK APKSPLALKAVLKPKAAKPKTALKPLKAAL

### H12acT146ph m phase

Figure S2

ас-ЅЕТЪРААРААРРАЕКЪРУЖЖЪЪЪЖЖ Algigit pirikia sig p p visieil iit k aiviaiaisik ei RISIG VIS LIAIAILIKIKIAIL A A A G YID VIEIK NINIS R I K<sup>1</sup>LG<sup>1</sup>LKSLVSKGTLVQ<sup>1</sup>TKGTGASGSF K L N K K A A S G E A K P K V K K A G G T K P K K P VGAAKLKPKLAAGGALTPKKSAKKTPKK ΑΚΚΡΑΑΑΤΥΤΚΚΥΑΚΣΡΙΚΙΑΙΚΥΑΙΚΡΙΚΙ KIAIAIKISIAIAIKA VIK P KA AIK PIK V VIK PIKIKAIA Р∎ККК

#### H14acph m phase

ac-SETAPAAPAAPAPAEKTPVKKKARKA A GIAIAIKIRIKIA SIG P P VISIEIL I TIKIAIVIAIAISIK EI RISIGIVISILIAIAILIKIKIAILIA AIAIGIYID VIEIKININIS R I K<sup>1</sup>L<sup>1</sup>G<sup>1</sup>L K S<sup>1</sup>L<sup>1</sup>V<sup>1</sup>S<sup>1</sup>K G T L V<sup>1</sup>Q<sup>1</sup>T K G T G A S G<sup>3</sup>F<sup>1</sup> K L'N K K A A S G E A K P K A K K A G A A K A K K P A GLA A KLK P K KLA TLG A ALT P KLKLSLALK K T P KLK Α Κ Κ ΡΙΑ Α ΑΙΑΙGΙΑΙΚΙΚΙΑ ΚΙ<sup>S</sup> ΡΙΚΙΚΙΑΙΚΙΑΙΚ ΡΙΚΙΚ A P K S PLALKLALKLA VLK PLKLA ALK P K T ALK PLK A AL K PLKLK ALALAK K K

#### K PLKLK ALALAK K K

# Figure S2

### H14acph2\_m phase

ac-S E TÎA P A A P AÎA PÎA P A EÎKÎT P V KÎKÎKÎAÎRÎKÎSÎ AÎGÎAÎAÎKÎRÎKÎAÎSÎG P P VÎSÎEÎL I TÎKÎAÎVÎAÎAÎSÎK EÎ RÎSÎG VÎSÎLÎAÎAÎLÎKÎKÎAÎLÎA A A GÎYÎD VÎEÎKÎNÎNÎS R I KÎLÎGÎL KÎSÎLÎVÎSÎK G T L VÎQÎTÎK G TLG A S GÎSÎFÎ K LÎNÎK K A A S GÎE AÎK PLKLA K K ALGLA ALK A KLK P A G A A KLK P KÎKLA T G A A T P K KLS A K K T P KLKL A K K P A A ALALGLALK KLA KLÎSÎ P KLKLALK A ALK P K K A P KLÎS PLALKLALK A VLK PLK A ALK P K T ALK PLK A AL K PLKLK ALALALK K K

### H14acph3\_m phase

\*\*-S E TJA P A A P A A P A P A P A E KJT PJV KJKJKJRJKJSJ AJGJAJA KJRJKJA SJG P P VJSJEJL I TJKJA VJAJAJSJK EJ RJSJGJVJSJLJAJAJLJKJKJAJLJA A A G YJD VJEJKJNJNJS R I KJLJGJL K SJLJVJSJK G T L VJQJTJK G T G A S GJSJFJ K L NJK K A A S GJE AJK PJKJA K K A GLA AJK A K K P A G A A KLK P KJKLA T G A A T P KLKJSLALKLKLT P KLKL A K K P ALALAJAJGJALKLKLA KLS PLKLKLALK A AJK PLKLK A P KLS PLAJKLALK A VLK PLK A AJK P K T ALK PLK A AL K PLKLKLALALK K K

### H14acph4 m phase

ac-S E TÌA P A A P A A P A P A P A P A P A'E KIT PÌV KÌKÌKÌAÌRÌKÌSÌ AÌGÌAÌAÌKÌRÌKÌAÌSÌG P P VÌSÌEÌL IÌTÌKÌAÌVÌAÌAÌSÌK EÌ RÌS G VÌSÌLÌAÌAÌLÌKÌKÌAÌLÌA A A G YÌD VÌEÌKÌNÌNÌS R I KÌLÌGÌL K SÌLÌVÌSÌK G T L VÌQÌTÌK G T GÌA S GÌSÌFÌ K L N K K A A S GÌE AÌK P KÌA K K ALGLA ALK A KLK P A G A A KLK P KLKLA T GLA A T P K KLS A K K T P KLKL A KLK P ALALALGLALKLA KLS PLKLKLALKLA ALK PLKL A P KLS PLALKLALKLA VLK PLK A ALK PLK T ALK PLK A AL K PLKLKLALKLA K

### H14acph5\_m phase

### Figure S3

### MCF-10A

### H12 ac\_asyn

ac-s e t a p a a p a a a p p a e k<sup>1</sup>a p v k k<sup>1</sup>k<sup>1</sup>a a<sup>1</sup>k<sup>1</sup>k A<sup>1</sup>G<sup>1</sup>G<sup>1</sup>T p R<sup>1</sup>k a S<sup>1</sup>G p p v<sup>1</sup>S<sup>1</sup>E<sup>1</sup>L I t k a v<sup>1</sup>a<sup>1</sup>S<sup>1</sup>K<sup>2</sup>I R<sup>1</sup>S<sup>1</sup>G v<sup>1</sup>S<sup>1</sup>L<sup>1</sup>A<sup>1</sup>A<sup>1</sup>L k<sup>1</sup>k a L a a a G y<sup>1</sup>D v<sup>1</sup>E<sup>1</sup>k<sup>1</sup>N<sup>1</sup>N<sup>1</sup>S R I k<sup>1</sup>L G L K S L V S K G T L v<sup>1</sup>Q<sup>1</sup>T K G T G A S G S F K L N K K A A S G<sup>1</sup>E A K P K V K K A G G T<sup>1</sup>K P K K P V G A A K<sup>1</sup>K P K K<sup>1</sup>A A G G A<sup>1</sup>T P K K S A K K T P K K A K<sup>1</sup>K P A A T V<sup>1</sup>T<sup>1</sup>K<sup>1</sup>K V A K<sup>1</sup>S P K<sup>1</sup>K<sup>1</sup>A K V A<sup>1</sup>K P K K A A K<sup>1</sup>S<sup>1</sup>A<sup>1</sup>A<sup>1</sup>K A V<sup>1</sup>K P K A A<sup>1</sup>K P K V V K P K K A<sup>1</sup>A

### H12 acph\_asyn

ac-s e tîa p a a p a a a p p a e kîa p vîkîkîkîaîaîkîkî Algîgît pîrîkîa sîg p p vîsîell i tîkîa vîaîaîsîk eî Rîsîg v s lîaîa l kîkîa l a a a g yîd v eîk nîn s r I kîl gîl k s l v s k g t l v qît k g t g a s g s f K l n k k a a s gle alk p k v k k a g g t k p k k k V g a a k k p klkîa a g g a t p k kisîa k kit p kiki a kik p a a alt vitikîk via ki<sup>şî</sup> pikikîaîk v alk p k K la a kisîaîka vik p k a alk pik v vik pikîk ala

### H12SNPac\_asyn

ac-S E TÌA P A A P A A A P P A E KÌV PÌVÌKÌKÌKÌAÌAÌKÌKÌ A GÌGÌT P RÌK AÌSÌG P P VÌSÌEÌL I TÌK A VÌA AÌSÌKÌEÌ RÌSÌG VÌSÌLÌAÌAÌLÌKÌKÌAÌL A A A G YÌD VÌEÌKÌNÌNÌS R I KÌLÌGÌL KÌSÌL VÌSÌK G T L VÌQÌT K G T G A S GÌS FÌ K L N K K A A S GLE ALK PÌK V K K A G G TLK P KLK P V G A A KLK P KLKLA A G G ALT P K KLS A K K T P K K A K K P A A A TLVLTLKLK V A KLS P KLK A K V A K PLK K A A KLSLALALK A VLK P K A ALK PLK V VLK P K K ALA PLK K K

### H12SNPacph\_asyn

### H13 ac\_asyn

### H14ac asyn

ac-S E T A P A A P A A P A P A P A E K<sup>1</sup>T P V K<sup>1</sup>K<sup>1</sup>K<sup>1</sup>A<sup>1</sup>R<sup>1</sup>K<sup>1</sup>S<sup>1</sup> A<sup>1</sup>G<sup>1</sup>A<sup>1</sup>K<sup>1</sup>R<sup>1</sup>K<sup>1</sup>A<sup>1</sup>S<sup>1</sup>G P P V<sup>1</sup>S<sup>1</sup>E<sup>1</sup>L I T K<sup>1</sup>A V<sup>1</sup>A<sup>1</sup>S<sup>1</sup>K<sup>2</sup>I<sup>1</sup> R<sup>1</sup>S<sup>1</sup>G<sup>1</sup>V<sup>1</sup>S<sup>1</sup>L<sup>1</sup>A<sup>1</sup>A<sup>1</sup>L<sup>1</sup>K<sup>1</sup>K<sup>1</sup>A<sup>1</sup>L<sup>1</sup>A A<sup>1</sup>A G<sup>1</sup>Y<sup>1</sup>D V<sup>1</sup>E<sup>1</sup>K<sup>1</sup>N<sup>1</sup>N<sup>1</sup>S R I K<sup>1</sup>L<sup>1</sup>G<sup>1</sup>L K S<sup>1</sup>L<sup>1</sup>V<sup>1</sup>S<sup>1</sup>K G T L V<sup>1</sup>Q<sup>1</sup>T<sup>1</sup>K G T G A S G<sup>1</sup>S<sup>1</sup>F K L N K K A A S G<sup>1</sup>E A K P KLA K K ALGLA ALK A KLK P A G A A KLK P KLKLA T G A ALT P KLKLSLA K K T P KLK A KLK P A A ALALGLALK K A KLS PLKLKLAKLA ALK P KLK A P KLS PLALKLALK A VLK P K A ALK P K T ALK PLK A AL K PLKLK ALALK K K

### MCF-10A

### H14acph\_asyn

ac-s e tîa p a a p aîa pîa pîaîe kît p v kîkîkîaîrîkîsî Algîaîaîkîrîkîaîsîg p p vîsîell lîtîkîaîvîaîaîsîkê Rîsîgîvîsîlîaîaîlîkîkîaîlîa a a gîyîd vîeîkînînîs r I kîlîgîl k sîlîvîsîk g t l vîqîtîk g t g a s gîs fî K l n k k a a s gîe aîk pikia k k aigîa aik a kik p A g a a kik p kikia t g a alt p kikisia k k t p kiki A k k p ala alagîalk kia ki<sup>s</sup> p kikiaikala k p k k A p k s piaikîaîk a vik p k a alk p k t alk pik a al K pikik alaşîk k k

#### H14acph2\_asyn

ac-S E TÌA P A A P AÌA P A PÌA E KÌT P V KÌKÌKÌAÌRÌKÌSÌ AÌGÌAÌAÌKÌRÌKÌAÌSÌG P P VÌSÌEÌL IÌTÌKÌAÌVÌAÌAÌSÌKÌEÌ RÌS G VÌSÌLÌAÌAÌLÌKÌKÌAÌLÌA A A GÌYÌD VÌEÌKÌNÌNÌS R I KÌLÌGÌL K SÌL VÌS K G T L VÌQÌTÌK G TLG A S GÌSÌF K L N K K A A S GÌE A K P K A K K A GLA ALK A K K P A G A A KLK P KLKLĂ T G A ALT P K KLS A KÌKLT P K KL A KLK P A A ALALGLALKLK A KLS P KLKLALK A ALK P K K A P KLS PLALKLALK A VLK PLK A ALK P K T ALK PLK A AL K PLKLK ALALALK K K

### Figure S3 H14acph3 asyn

ac-s e tî a p a a p a a p a p a p î a e kîtî p v kîkîk a rîkîs aîgî a a kîrîk a sîg p p vîsîeîl i t k a vîaîaîs k eî Rîs g vîs lîaîaîl kîkî a l a a a g yîd vîeîkînînîs r i kîl gîl k s l v sîk g t l vîq t k g t g a s g s f k l n k k a a s gîe a k p k a k k a g a a k a k k p a g a a k k p k kla t g a a t p k kls a k k t p k k a k k p a a alalgî a k kla kl<sup>î</sup>sî p klkîalk a alk p k k a p kl<sup>î</sup>s plalkî k k

### MCF-10A s phase

#### H12ac\_s phase

\*\*-S E T A P A A P A A A P P A E K<sup>1</sup>A P V<sup>1</sup>K K<sup>1</sup>K<sup>1</sup>A<sup>1</sup>A<sup>1</sup>K<sup>1</sup>K<sup>1</sup>A<sup>1</sup>G<sup>1</sup>G<sup>1</sup>T P R<sup>1</sup>K A S<sup>1</sup>G P P V<sup>1</sup>S<sup>1</sup>E<sup>1</sup>L I T<sup>1</sup>K<sup>1</sup>A<sup>1</sup>V<sup>1</sup>A<sup>1</sup>S<sup>1</sup>K<sup>2</sup>F<sup>1</sup> R<sup>1</sup>S<sup>1</sup>G V<sup>1</sup>S<sup>1</sup>L<sup>1</sup>A<sup>1</sup>L<sup>1</sup>K<sup>1</sup>K<sup>1</sup>A<sup>1</sup>L A A A G<sup>1</sup>Y<sup>1</sup>D V<sup>1</sup>E<sup>1</sup>K<sup>1</sup>N<sup>1</sup>N<sup>1</sup>S R I K<sup>1</sup>L<sup>1</sup>G<sup>1</sup>L K S<sup>1</sup>L<sup>1</sup>V S<sup>1</sup>K G T L V<sup>1</sup>Q<sup>1</sup>T<sup>1</sup>K G T G A S G<sup>1</sup>S F K L N K K A A S G<sup>1</sup>E A K P K V K K A G G T<sub>1</sub>K P K<sub>1</sub>K P V G A A K<sub>1</sub>K P K K<sub>1</sub>A A G G A<sub>1</sub>T P K<sub>1</sub>K<sub>1</sub>S A K K T P K<sub>1</sub>K A K K P A A A T V<sub>1</sub>T<sub>1</sub>K<sub>1</sub>K V A K<sub>1</sub>S P K<sub>1</sub>K<sub>1</sub>A K V A<sub>1</sub>K P<sub>1</sub>K<sub>1</sub> K<sub>1</sub>A A K<sub>1</sub>S<sub>1</sub>A<sub>1</sub>A<sub>1</sub>K A V<sub>1</sub>K P K A A<sub>1</sub>K P<sub>1</sub>K V V<sub>1</sub>K P<sub>1</sub>K<sub>1</sub>K A<sub>1</sub>A

#### H12acph\_s phase

ac-S E T A P A A P A A A P P A E K<sup>1</sup>A P V K K<sup>1</sup>K<sup>1</sup>A A<sup>1</sup>K<sup>1</sup>A A G<sup>1</sup>G<sup>1</sup>T P R K A S<sup>1</sup>G P P V<sup>1</sup>S<sup>1</sup>E<sup>1</sup>L I T K A V<sup>1</sup>A A S<sup>1</sup>K E<sup>1</sup> R S G V S L<sup>1</sup>A<sup>1</sup>A L K<sup>1</sup>K A L A A A G Y<sup>1</sup>D V E K N N S R I K L G L K S L V S K G T L V Q<sup>1</sup>T K G T G A S G S F K L N K K A A S G<sub>1</sub>E A K P K V K K A G G T K P K K P V G A A K K P K K A A G G A T P K K<sup>1</sup>S A K K T P K K A K K P A A A T<sup>1</sup>V<sup>1</sup>T<sup>1</sup>K K V<sup>1</sup>A K<sup>1</sup>S P K<sup>1</sup>K<sup>1</sup>A<sup>1</sup>K V A<sup>1</sup>K P K K A A K<sup>1</sup>S<sup>1</sup>A<sup>1</sup>K A V<sup>1</sup>K P K A A<sup>1</sup>K P K V V<sup>1</sup>K P K K A<sup>1</sup>A P<sup>1</sup>K K K

#### H12SNPac\_s phase

ac-S E TÌA P A A P A A P P A EÌKÌV PÌVÌKÌKÌKÌAÌAÌKÌK A GÌGÌT P RÌKÌA SÌG P P VÌSÌEÌL I TÌKÌA VÌAÌAÌSÌKÌEÌ RÌSÌG VÌSÌLÌAÌAÌLÌKÌKÌAÌL A A A G YÌD VÌEÌKÌNÌNÌS R I KÌLÌGÌL KÌSÌLÌVÌSÌK G T L VÌQÌT K G T G A S GÌS FÌ K L N K K A A S GÌE ALK PÌK V K K A G G TLK P KLK P V GLALA KLK P KLKLA A G G ALT P K K S A K K T P KLK A K K P A A A TLVLTLKLK V A KLS P KLKLALK V A K PLK KLA A KLSLALALK A VLK P K A ALK PLK V VLK PLK K ALA PLK K K

PLKKK

### MCF-10A H13ac\_s phase

ac-S E TÎA PÎL A P T I P A P A E KÎT P V KÎKÎKÎAÎKÎK A
GÎAÎTÎAÎGÎKÎRÎK A S G P P VÎSÎEÎL I TÎKÎA VÎA AÎSÎK
EÎRÎSÎG V SÎLÎAÎAÎL KÎKÎAÎL A A A G YÎD VÎEÎKÎNÎNÎS
R I KÎLÎGÎL K S L VÎS K G T L VÎQÎTÎK G T G A S GÎS
FÎK L N K K A A S GÎE GÎK P K<sub>L</sub>A K K A G A A K P R K
P A G A A K K P K<sub>L</sub>K V A G A A T P K K<sub>L</sub>S I K K T P K<sub>L</sub>
K V K K P A T<sub>L</sub>A A<sub>L</sub>G<sub>L</sub>T<sub>K</sub><sub>L</sub>K V A K<sub>L</sub>S<sub>L</sub>A<sub>L</sub>K<sub>L</sub>K<sub>L</sub>V K<sub>L</sub>T P<sub>L</sub>Q P
K<sub>L</sub>K<sub>L</sub>A<sub>L</sub>A K<sub>L</sub>S P A<sub>L</sub>K<sub>L</sub>A K A P<sub>L</sub>K K K

#### H14ac\_s phase

ac-S E TÌA PÌA A P AÌA PÌA P A E KÌT P V KÌKÌKÌAÌRÌKÌSÌ AÌGÌAÌAÌKÌRÌKÌAÌSÌG P P VÌSÌEÌL IÌTÌKÌAÌVÌAÌAÌSÌKÌEÌ RÌSÌG VÌSÌLÌAÌAÌLÌKÌKÌAÌLÌA A A GÌYÌD VÌEÌKÌNÌNÌS R I KÌLÌGÌL K SÌLÌVÌSÌK G TÌL VÌQÌTÌK G T G A S GÌS FÌ K L N K K A A S GÌE ALK PLKLA K K ALGÌA ALK A KLK P A G A A KLK P KLKLA TLG A ALT P KLKLSLA K KLT PLKLK A KLK P A A ALALGLALKLK A KLS PLKLKLALKLA ALK P K K A P K S PLALKLA K A VLK P K A ALK P K T ALK PLK A AL K PLKLK ALALALK K K

### Figure S3 H14acph\_s phase

\*\*\*-S E TJA P A A P AJA P A P A E KJT P V KJKJKJAJRJKJSJ AJGJAJAJKJRJKJAJSJG P P VJSJEJL IJTJKJAJVJAJAJSJKJEJ RJSJG VJSJLJAJAJLJKJKJAJLJA A A GJYJD VJEJKJNJNJS R I KJLJGJL K SJL V SJK G T L VJQJT K G T G A S GJS F K L N K K A A S GJE ALK PLKLA K K ALGLA ALK A KLK P A G A A KLK P KLKLA T G A A T P K KLS A K K T P KLK A K K P A A ALALGLALK KLA KLS P KLKLALKLA ALK P KLK A P K S PLALKLALK A VLK P K A A K P K T ALK PLK A AL K PLKLK ALALALK K K

### H14acph2\_s phase

ac-S E TÎA P A A P AÎA P A P A E KÎT P V KÎKÎKÎAÎRÎKÎSÎ AÎGÎAÎAÎKÎRÎKÎAÎSÎG P P VÎSÎEÎL I TÎKÎAÎVÎAÎAÎSÎKÎEÎ RÎSÎGÎV SÎLÎAÎAÎLÎKÎKÎAÎLÎA A A GÎYÎD VÎEÎKÎNÎNÎS R I KÎLÎGÎL K SÎLÎVÎSÎK G T L VÎQÎTÎK G TLG A S GÎS FÎ K L NÎK K A A S GÎE AÎK P K A K K A GÎA ALK A K K P A G A A K K P KLKLA T G A A T P K KLS A K K T P KLKL A K K P ALA ALALGLALK KLA KL<sup>S</sup> P KLKLALK A ALK P K K A P KL<sup>S</sup> PLALKLA K A VLK PLK A ALK P K T ALK PLK A AL K PLKLK ALALALK K K

# Figure S3

## MCF-10A m phase H14ac\_m phase

ac-S E T A P A A P A A P A P A P A E K<sup>1</sup>T P V K<sup>1</sup>K<sup>1</sup>A<sup>1</sup>R<sup>1</sup>K<sup>1</sup>S
A<sup>1</sup>G<sup>1</sup>A<sup>1</sup>A K<sup>1</sup>R<sup>1</sup>K<sup>1</sup>A S<sup>1</sup>G P P V<sup>1</sup>S<sup>1</sup>E<sup>1</sup>L I T K<sup>1</sup>A V A<sup>1</sup>A<sup>1</sup>S K E<sup>1</sup>
R S G V S L<sup>1</sup>A A L K K A L A A A G Y<sup>1</sup>D V E K N N S R
I K L G L K S L V S K G T L V Q T K G T G A S G S F
K L N K K A A S G<sub>1</sub>E A K P K A K K A G A A K A K K P
A G A A K K P K K<sub>1</sub>A T G A A T P K K S A K K T P K K
A K K P A A A A G A<sub>1</sub>K K A K<sub>1</sub>S P<sub>1</sub>K<sub>1</sub>K<sub>1</sub>A<sub>1</sub>K A A<sub>1</sub>K P K K
A P K S P A<sub>1</sub>K<sub>1</sub>A K A V<sub>1</sub>K P K A A<sub>1</sub>K P K T A<sub>1</sub>K P K A A<sub>1</sub>

### H14acph3 \_m phase

ac-S E T A P A A P A A P A P A P A P A E K T P V K K K A R K S
A G A A K R K A S G P P V S E L I T K A V A A S K E
R S G V S L A A L K K A L A A G Y D V E K N N S R
I K L G L K S L V S K G T L V Q T K G T G A S G S F
K L N K K A A S G E A K P K A K K A G A A K K K P
A G A A K K P K K A T G A A T P K K S A K K T P K K
A K K P A A A A A G A K K P K K K S P K K K S P K K K P K K K
A P K S P A K K K K

### H14acph \_m phase

ac-S E T A P A A P A A P A A P A E K T P V K K K A R K S A G A A K R K A S G P P V S E L I T K A V A A S K E R S G V S L A A L K K A L A A A G Y D V E K N N S R I K L G L K S L V S K G T L V Q T K G T G A S G S F K L N K K A A S G E A K P K A K K A G A A K A K K P A G A A K K P K K A T G A A T P K K S A K K T P K K A K K P A A A A A A A A S P K A K K S P K K A K K P K K A P K S P A K A A V K P K A A K P K T A K P K A A K P K K A A A K K

### H14acph2 \_m phase

ac-S E TÌA P A A P A A P A P A P A E KÌT P V KÌKÌKÌAÌRÌKÌSÌ AÌGÌAÌAÌKÌRÌKÌA SÌG P P VÌSÌEÌL I T KÌA VÌA AÌSÌK EÌ RÌS G V S LÌAÌA L KÌKÌA L A A A G YÌD VÌE KÌNÌN S R I KÌL G L K SÌL V S K G T L V QÌT K G T G A S G S F K L N K K A A S GLE A K P K A K K A G A A K A K K P A G A A K K P K KLA T G A A T P K K S A K K T P K K A K K P A A ALALGLA K KLA KLS P KLKLALK A ALK P K K A P KLS PLALKLA K A VLK P K A ALK P K T ALK PLK A AL K PLKLK ALALALK K K

### H14acph4 \_m phase

ac-S E T A P A A P A A P A P A P A E KIT P V KIKIK A RIKIS AIGIAIA KIRIKIA SIG P P VISIEIL I T KIA VIA AIS K EI RIS G VIS LIAIA L KIKIAIL A A A G YID VIEIKININIS R I KIL GIL K SILIV S K G T L VIQITIK G T G A S GIS FI K L N K K A A S GJE A K P K A K K A GLA A K A K K P A G A A K K P KLK A T G A A T P K KLS A K K T P KLKL A K K P A A ALALGLALK K K K S P KLKLALK A ALK P K K A P KLS PLALKLALK A VLK P K A ALK P K T ALK PLK A AL K PLKLK ALALALK K

### H14acph5 \_m phase

ac-S E T A P A A P A A P A P A P A E K T P V K K A R K S A G A A K R K A S G P P V S E L I T K A V A A S K E R S G V S L A A L K K A L A A A G Y D V E K N N S R I K L G L K S L V S K G T L V Q T K G T G A S G S F K L N K K A A S G E A K P K A K K A G A A K A K K P A G A A K K P K K A T G A A T P K K S A K K T P K K A K K P A A A A G A K K A K F K K A K K P K K S A K K T P K K A P K S P A A A A K K K







