iClust 1: N = 140 iClust 2: N = 72 ESR1|ILMN\_1678535 (ER binding) ESR1|ILMN\_1678535 (ER binding) [<=60] p = 0.15156Age-dependent trend: [<=60] p = 0.05226No detectable trend: 16 16 [>60] p = 0.34446|FC|>2 and adjPval<0.01 [>60] p = 0.0027928 |FC|<2 or adjPval>0.01 [AII] p = 1.1559e - 07[AII] p = 0.000176624 4 Raw Expression (4, 16) Raw Expression (4, 16) 12 12 10 10  $\infty$  $\infty$ 9 9 20 40 60 80 100 20 40 60 80 100 Age at diagnosis Age at diagnosis iClust 3: N = 294 iClust 4: N = 344 ESR1|ILMN\_1678535 (ER binding) ESR1|ILMN\_1678535 (ER binding) [<=60] p = 0.024605Age-dependent trend: [<=60] p = 0.11736Age-dependent trend: 16 16 [>60] p = 0.96886[>60] p = 0.094183|FC|>2 and adjPval<0.01 |FC|>2 and adjPval<0.01 [AII] p = 2.8642e - 09[AII] p = 5.0115e-074 4 Raw Expression (4, 16) Raw Expression (4, 16) 12 12 19 10 ω  $\infty$ 9 9 20 40 60 80 100 20 40 60 80 100

Age at diagnosis

Age at diagnosis

iClust 5: N = 191 iClust 6: N = 86 ESR1|ILMN\_1678535 (ER binding) ESR1|ILMN\_1678535 (ER binding) [<=60] p = 0.043985Age-dependent trend: [<=60] p = 0.20513No detectable trend: 16 16 [>60] p = 0.14922 [>60] p = 0.94638|FC|>2 and adjPval<0.01 |FC|<2 or adjPval>0.01 [AII] p = 5.2381e-09[AII] p = 5.6912e - 064 4 Raw Expression (4, 16) Raw Expression (4, 16) 12 12 10 10  $\infty$  $\infty$ 9 9 20 40 60 80 100 20 40 60 80 100 Age at diagnosis Age at diagnosis iClust 7: N = 193 iClust 8: N = 300 ESR1|ILMN\_1678535 (ER binding) ESR1|ILMN\_1678535 (ER binding) [<=60] p = 0.0022747[<=60] p = 0.00018364No detectable trend: Age-dependent trend: 16 16 [>60] p = 0.93143|FC|<2 or adjPval>0.01 [>60] p = 0.04451|FC|>2 and adjPval<0.01 [AII] p = 5.1103e-05[All] p = 1.2983e-114 4 Raw Expression (4, 16) Raw Expression (4, 16) 12 12 10 10 ω  $\infty$ 9 9 20 40 60 80 100 20 40 60 80 100 Age at diagnosis Age at diagnosis

iClust 9: N = 146 ESR1|ILMN\_1678535 (ER binding)

iClust 10: N = 226 ESR1|ILMN\_1678535 (ER binding)

