Supplement Figure legends

sFig. 1. A. WikiPathway of the down-regulated genes in the iAs-induced CSCs. B. Down-regulation of genes for the respiratory chain of mitochondria in the iAs-induced CSCs. The minus numbers indicate fold decrease relative to the non-CSCs of these individual genes.

sFig. 2. Screening of Nrf2 knockout (KO) cells from the BEAS-2B cells subjected to CRISPR-Cas9 gene editing using sgRNA1 and sgRNA2 as indicated, respectively. The successful Nrf2 knockout rates are 15% for sgRNA1 and 60% for sgRNA2, respectively.

sFig. 3. Nrf2 element(s) on the glycolytic genes as exampled for ENO1, GPI and GAPDH.

sFig. 4. Identification of a conserved known Nrf2 element at the 32.5 kb upstream of the transcription stat site of HIF1α gene.

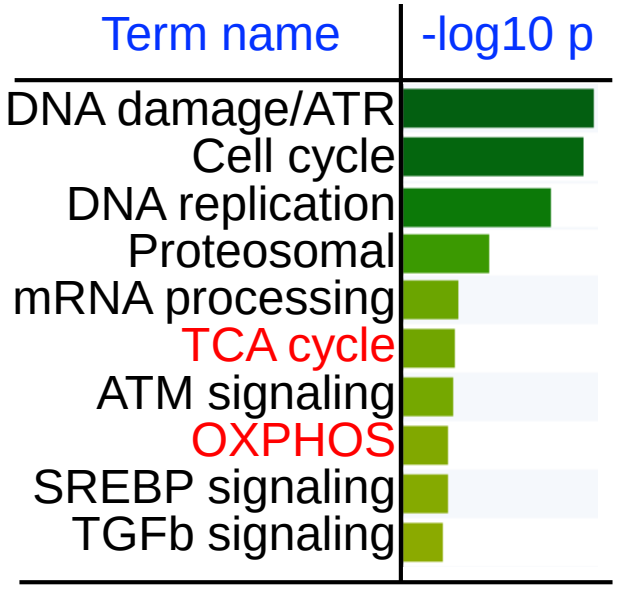
sFig. 5. Multiple Nrf2 elements identified at the upstream of the ZEB1 gene.

sFig. 6. Known and de novo Nrf2 binding motifs in the gene loci of BACH1, Hes1 and TBC1D7. Red arrows indicate the iAs-induced HIF1α binding.

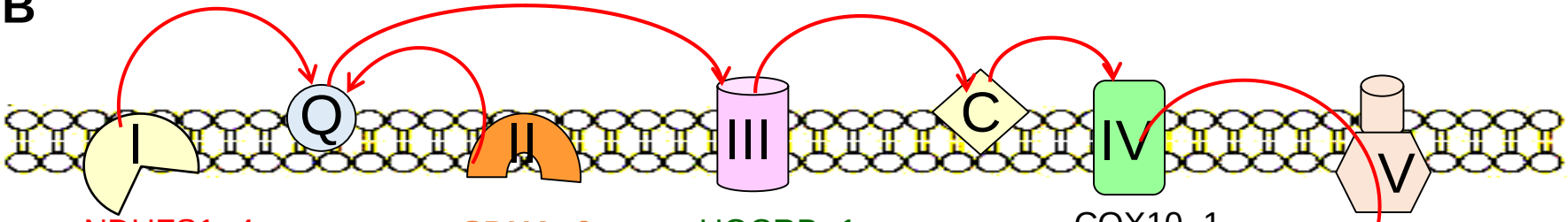
sFig. 7. Cooperative regulation of Nrf2 and HIF1α on NAMPT, CD44 and EGFR. Known and/or de novo Nrf2 motifs were indicated. Red arrows indicate the iAs-induced HIF1α binding.

sFig.1 **A**

WikiPathway of the down-regulated genes in CSCs



B



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NDUFS2 -2
NDUFS3 -4
NDUFS4 -1
NDUFS5 -30
NDUFS7 2
NDUFV3 -5
NDUFB4 -4
NDUFB5 -37
NDUFB11 -2
NDUFC2 -41

SDHA -6
SDHB -16
SDHC -2

UQCRB -1
UQCRC2 -13
UQCRQ -21

COX10 -1
COX15 -4
COX16 -21
SCO1 -3
COX5A -2
COX5B -6
COX6A1 -40
COX6C -10
COX7A2 -4
COX7B -26
COX7C -14

ATP5C1 -17
ATP6V0C -2
ATP5J2 -11
ATP5L -7
ATP5O -7
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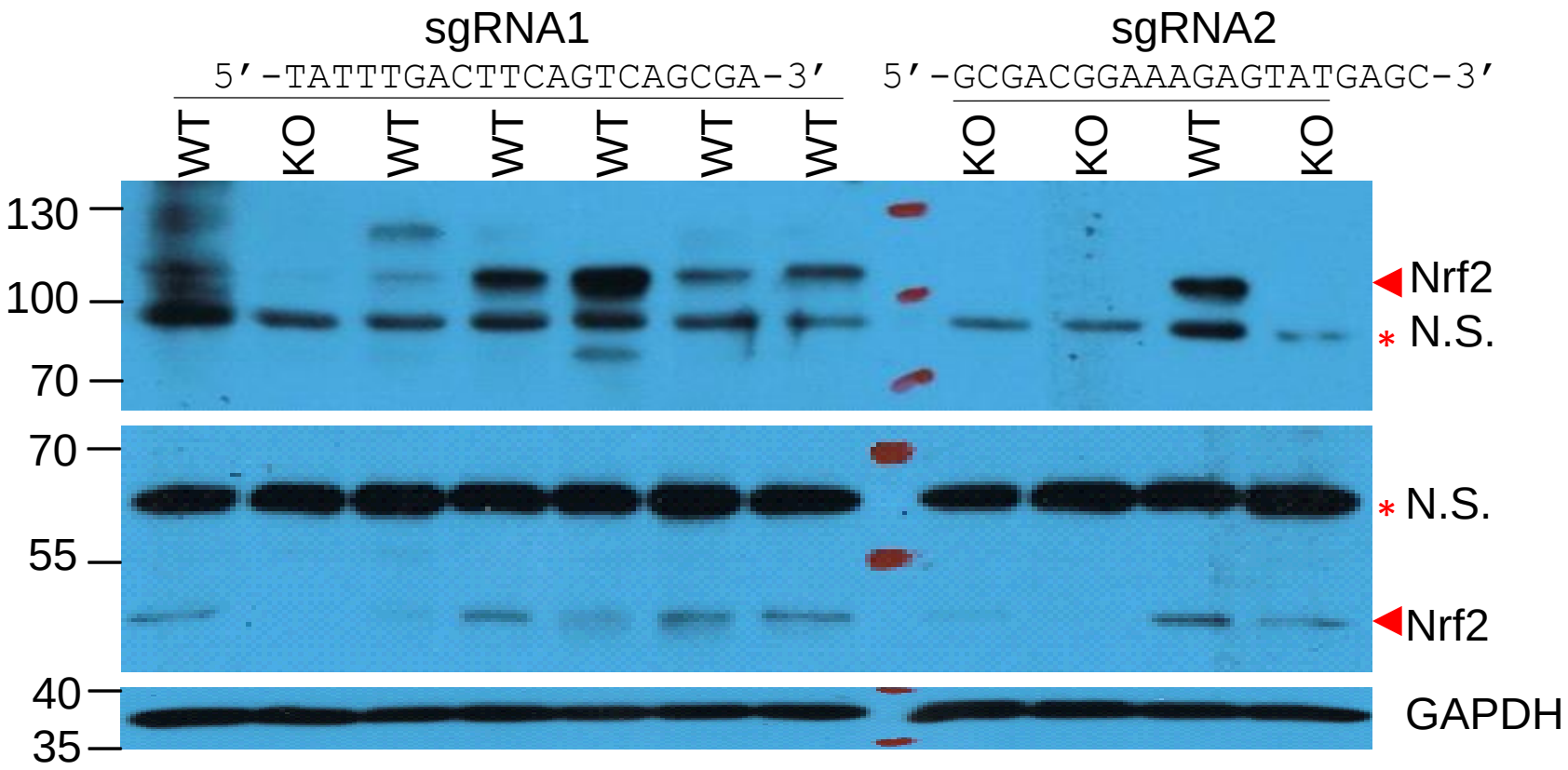
ATP6V0E1 -25
ATP5F1 -2

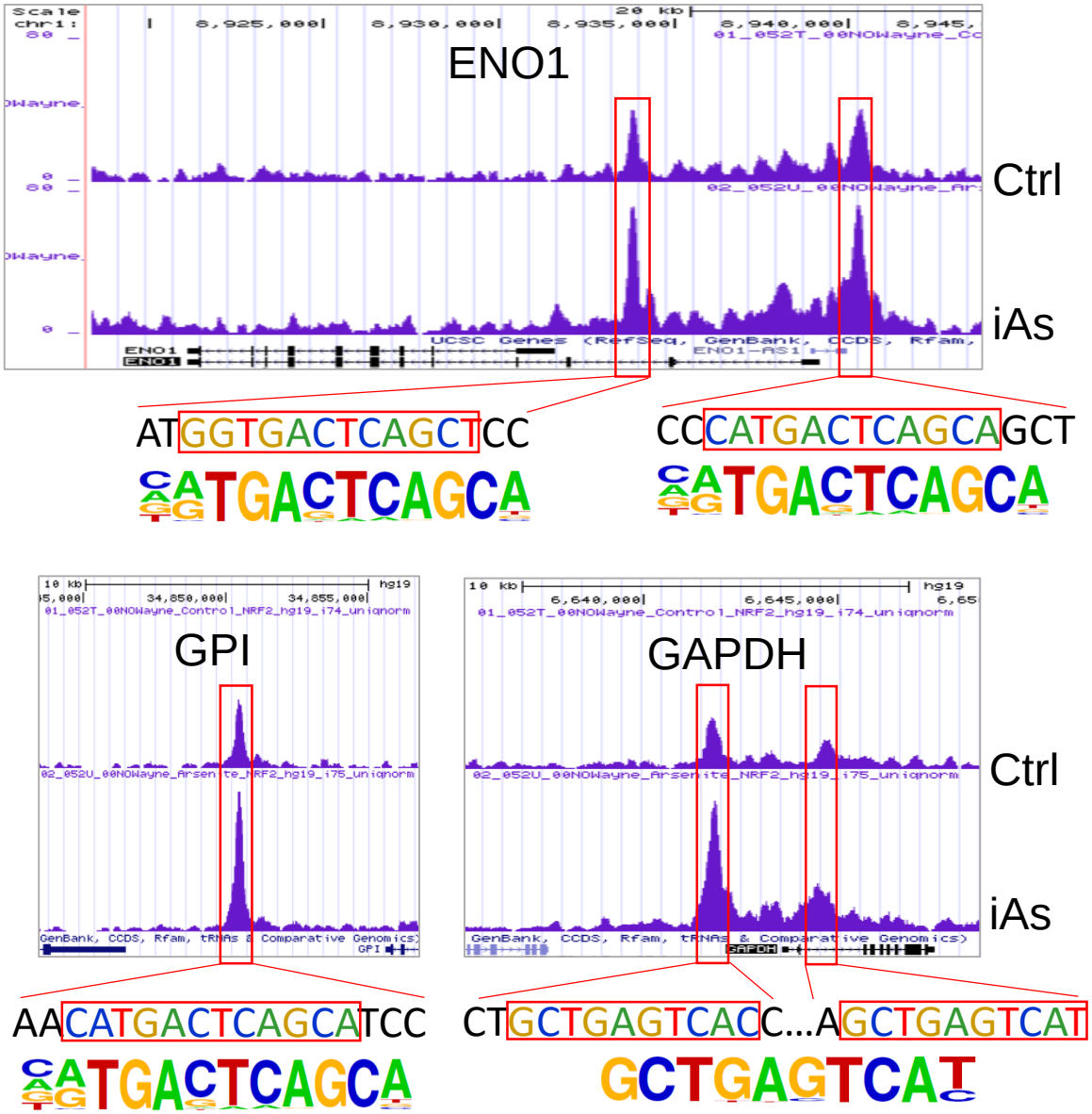
sFig. 2



Sources of Nrf2 antibodies for screening:

Upper panel: 12721 Cell Signaling D1Z9C XP Rabbit mAb
Lower panel: sc-365949 A-10 Mouse mAb

sFig.3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GPI
GAPDH
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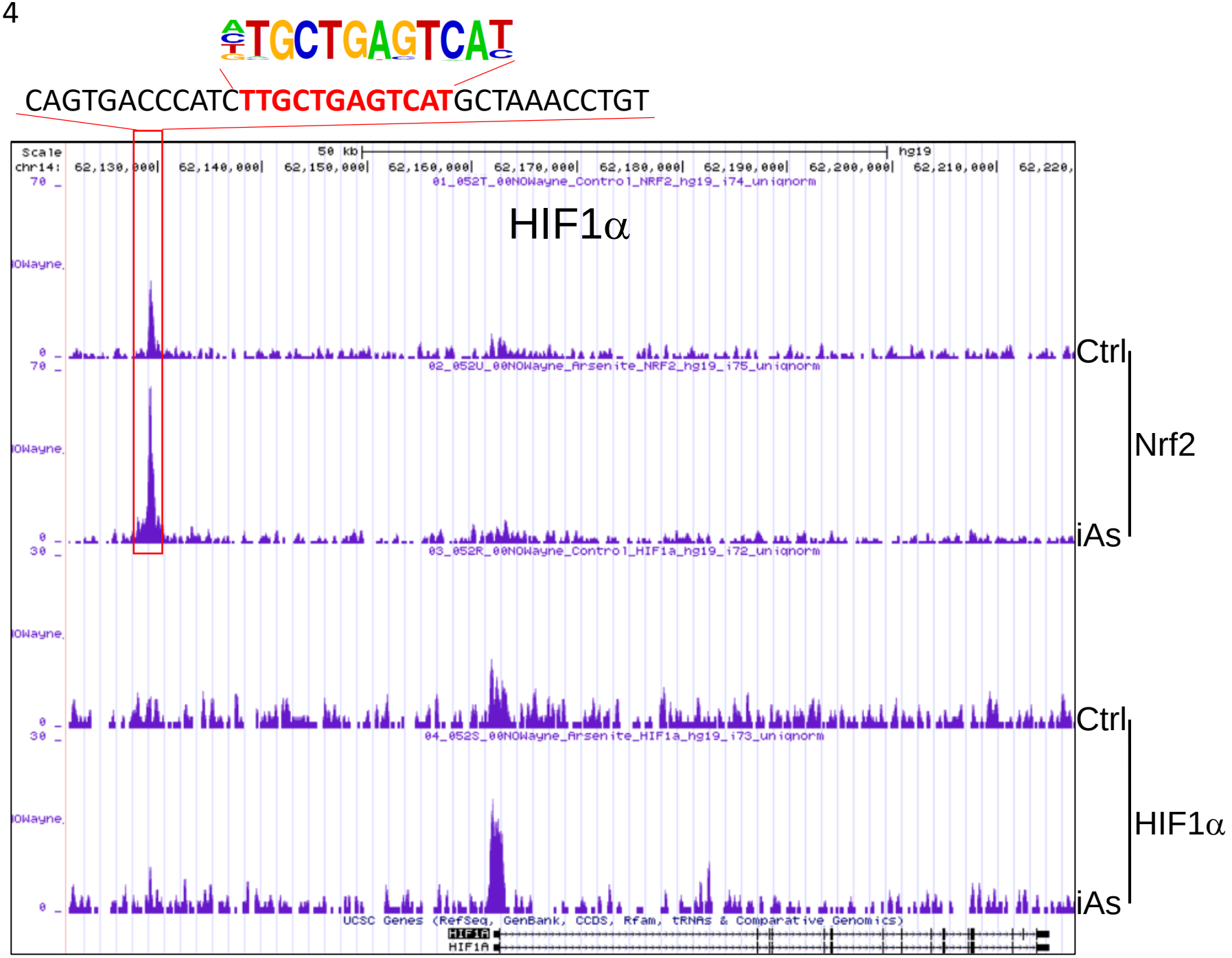
sFig. 4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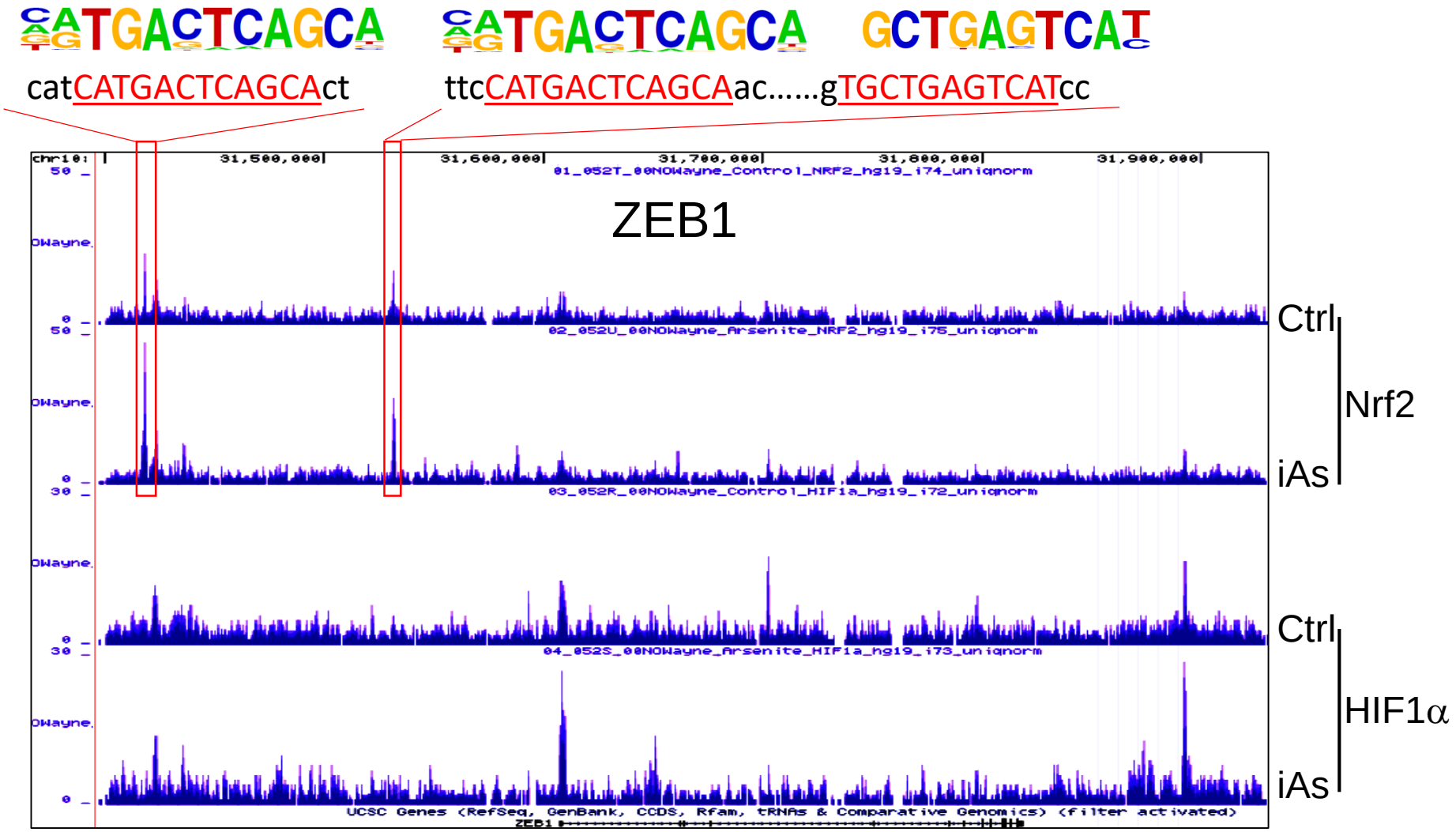
Nrf2
iAs
Ctrl
HIF1α
iAs

sFig. 5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chr10:
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31,600,000
31,700,000
31,800,000
31,900,000
01_052T_00NOWayne_Control_NRF2_hg19_i74_uniqnorm
02_052U_00NOWayne_Arsenite_NRF2_hg19_i75_uniqnorm
03_052R_00NOWayne_Control_HIF1a_hg19_i72_uniqnorm
04_052S_00NOWayne_Arsenite_HIF1a_hg19_i73_uniqnorm
UCSC Genes (RefSeq, GenBank, CCDS, Rfam, tRNAs & Comparative Genomics) (filter activated)
ZEB1
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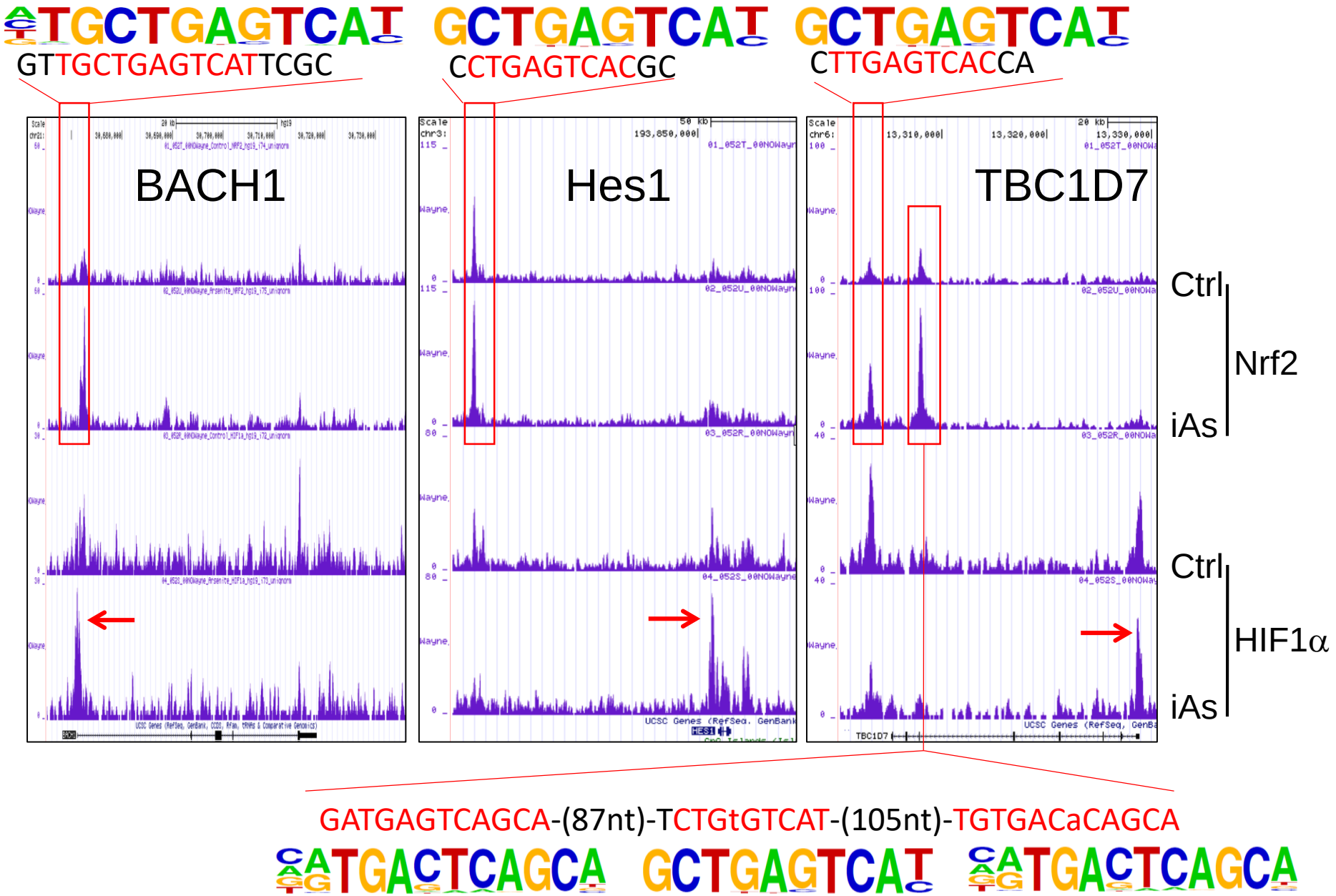
iAs
Nrf2
Ctrl
iAs
HIF1α

sFig. 6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CCTGAGTCACGC
CTTGAGTCACCA
BACH1
Hes1
TBC1D7
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Nrf2
iAs
Ctrl
HIF1α
iAs
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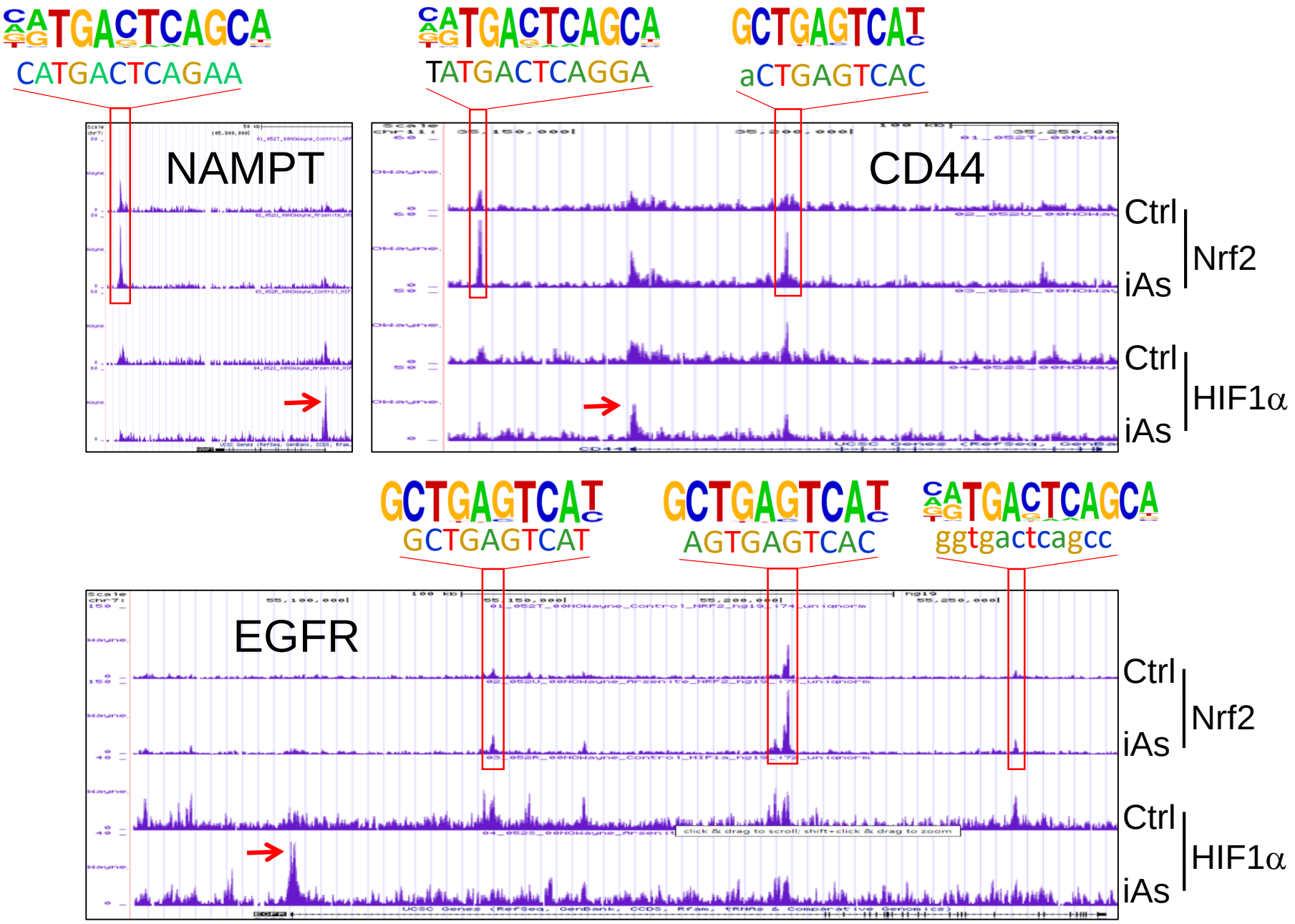
sFig. 7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ggtgactcagcc
EGFR
Ctrl
iAs
Nrf2
Ctrl
iAs
HIF1α