Fig.S1

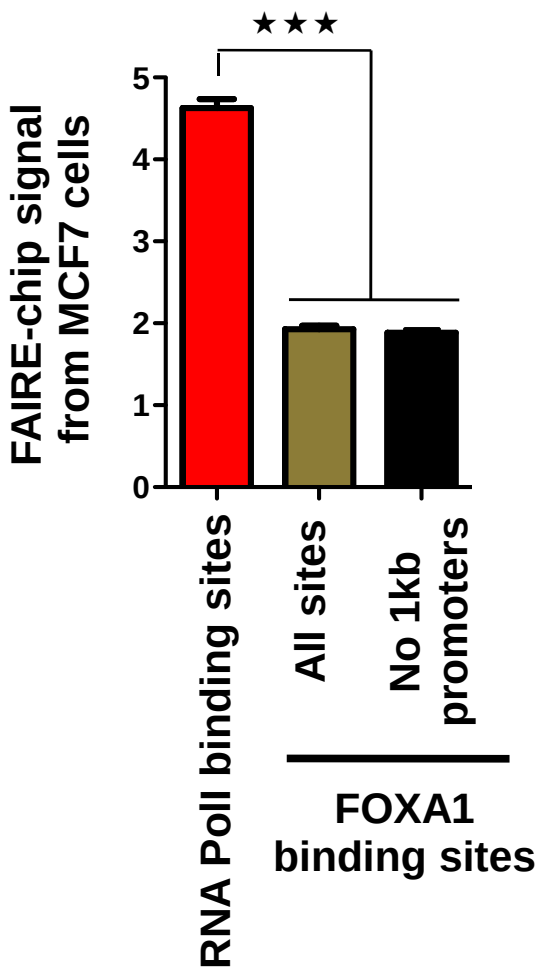

★★★
FAIRE-chip signal from MCF7 cells
5
4
3
2
1
0
RNA PolII binding sites
All sites
No 1kb promoters
FOXA1 binding sites

Fig.S2

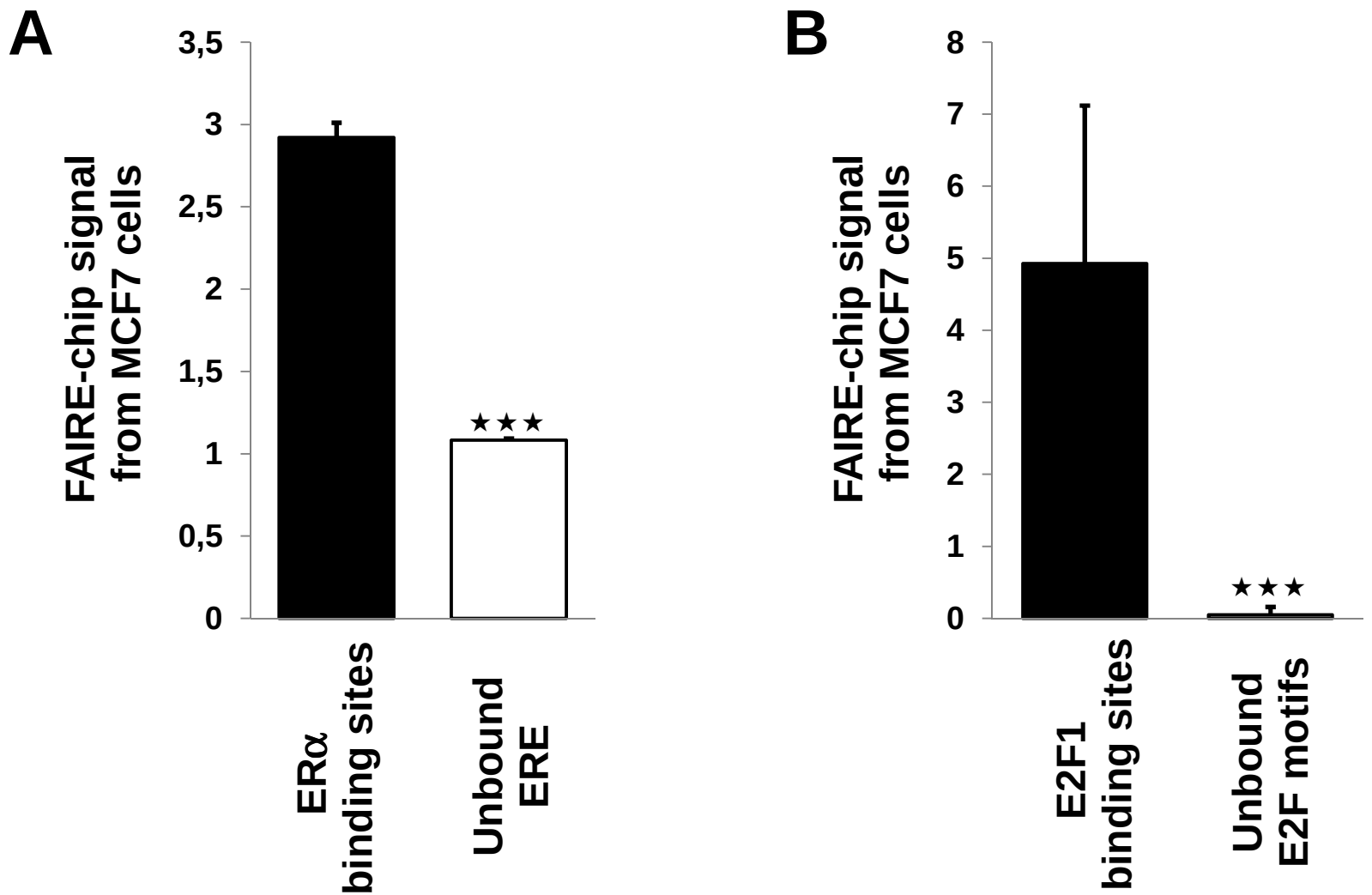

A
FAIRE-chip signal from MCF7 cells
3,5
3
2,5
2
1,5
1
0,5
0
★★★
ERα binding sites
Unbound ERE
B
FAIRE-chip signal from MCF7 cells
8
7
6
5
4
3
2
1
0
★★★
E2F1 binding sites
Unbound E2F motifs

Fig.S3

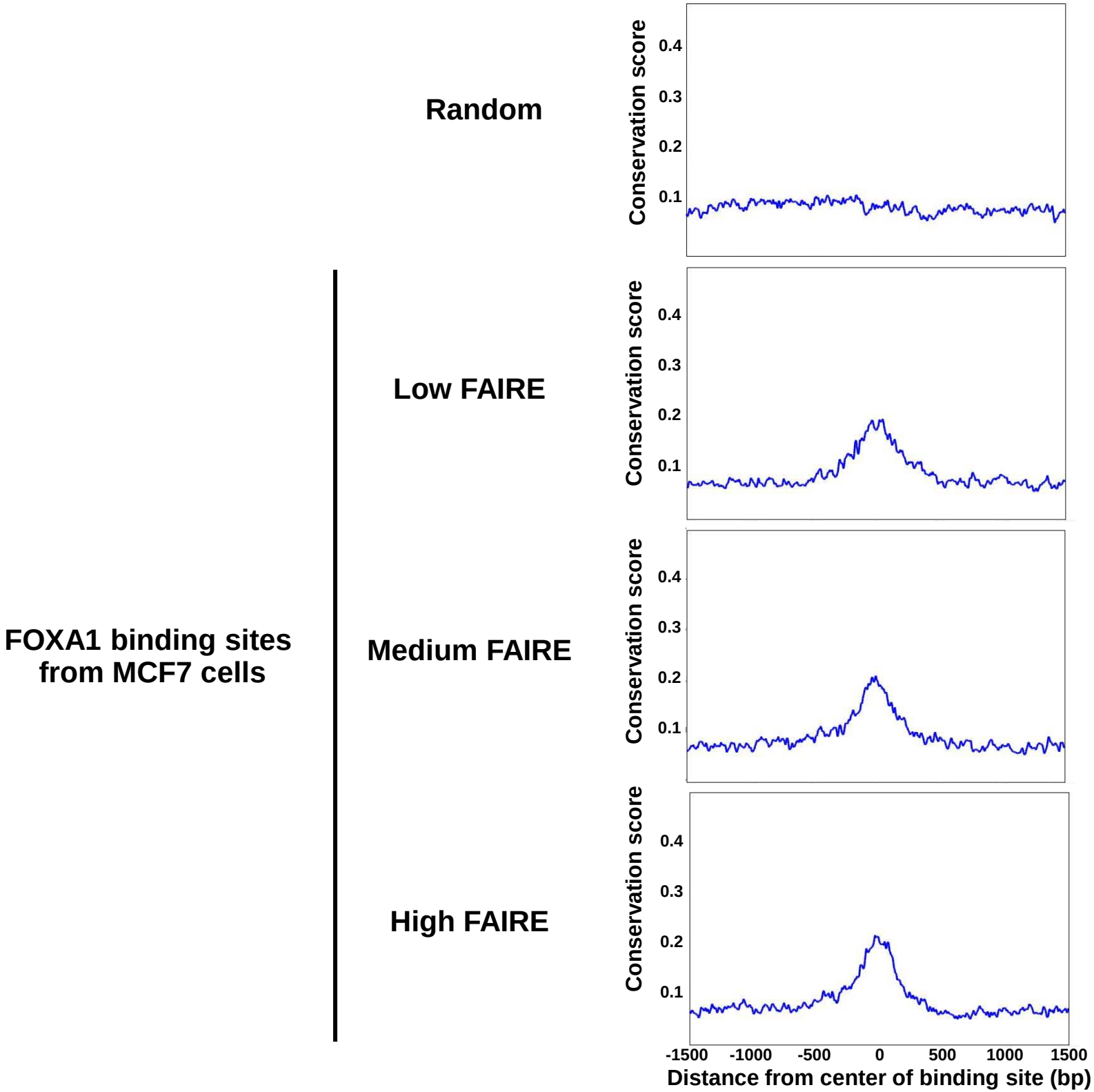

FOXA1 binding sites from MCF7 cells
Random
Low FAIRE
Medium FAIRE
High FAIRE
Conservation score
0.4
0.3
0.2
0.1
-1500
-1000
-500
0
500
1000
1500
Distance from center of binding site (bp)

Fig.S4

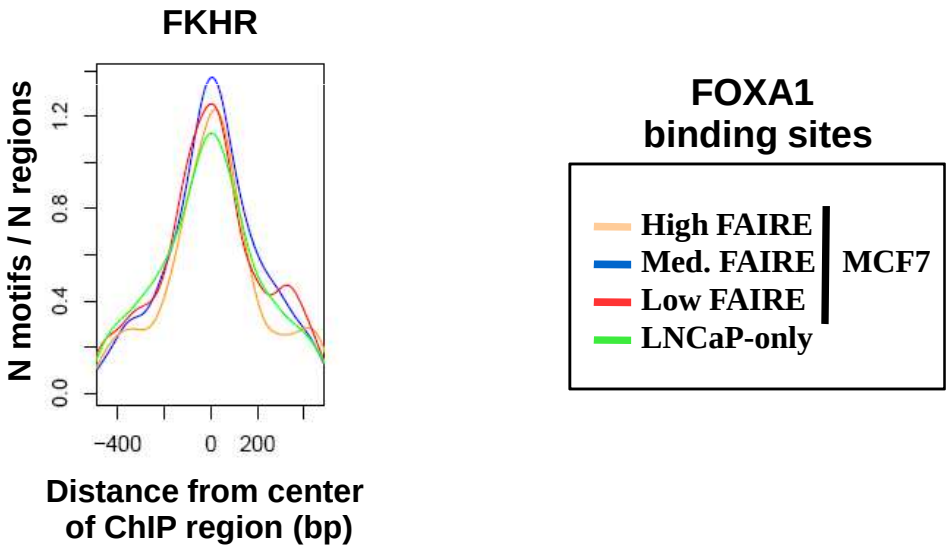

FKHR
N motifs / N regions
0.0
0.4
0.8
1.2
−400
0
200
Distance from center
of ChIP region (bp)
FOXA1
binding sites
High FAIRE
Med. FAIRE
Low FAIRE
LNCaP-only
MCF7

Fig.S5

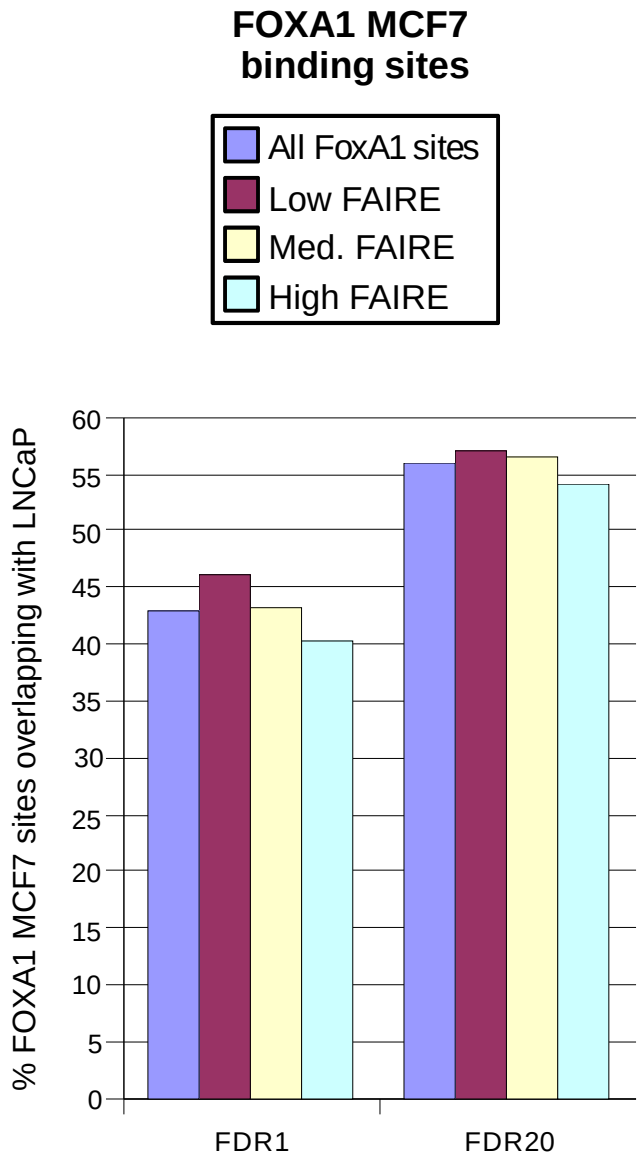

FOXA1 MCF7
binding sites
All FoxA1 sites
Low FAIRE
Med. FAIRE
High FAIRE
% FOXA1 MCF7 sites overlapping with LNCaP
60
55
50
45
40
35
30
25
20
15
10
5
0
FDR1
FDR20

Fig.S6

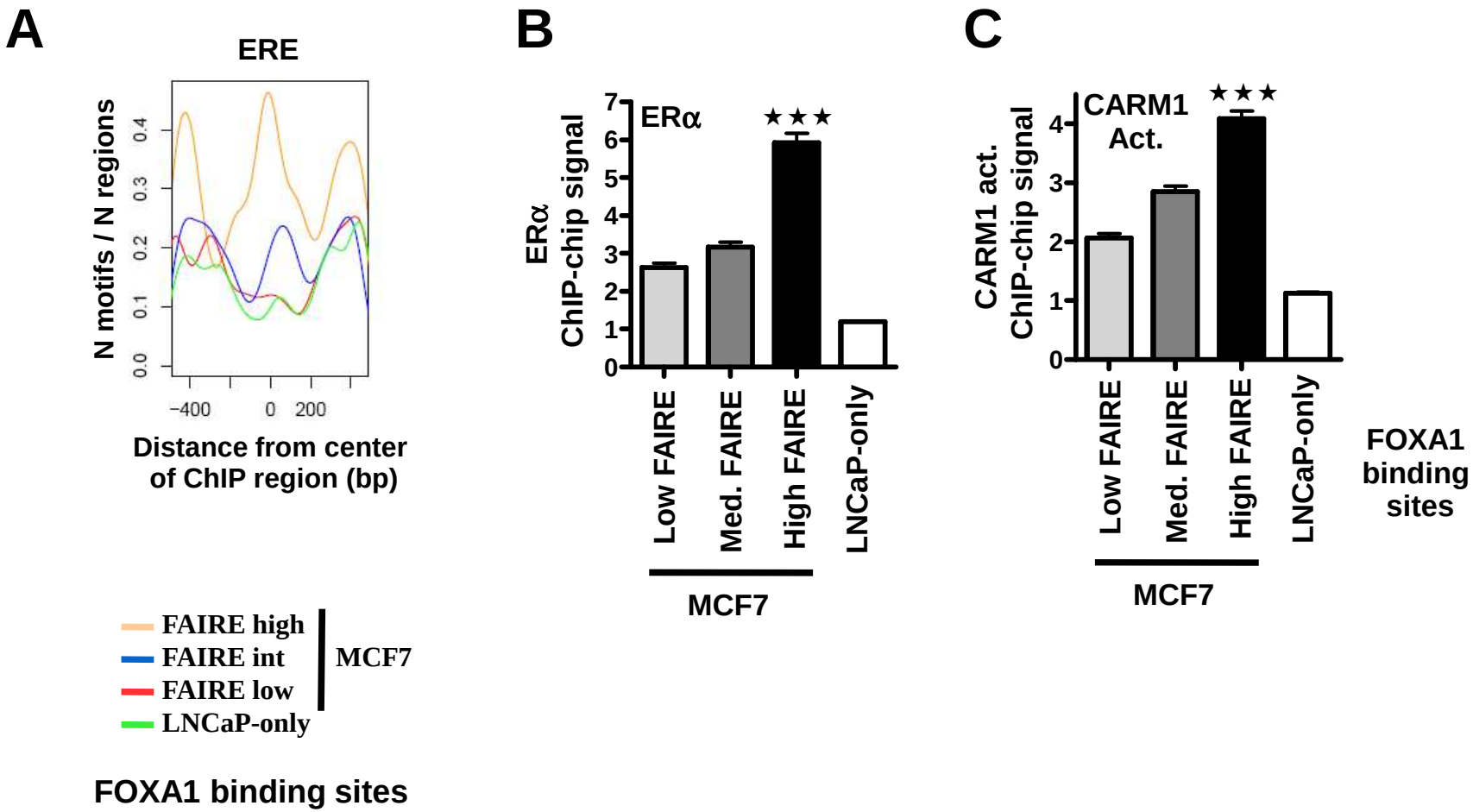

A
ERE
N motifs / N regions
0.0
0.1
0.2
0.3
0.4
−400
0
200
Distance from center of ChIP region (bp)
FAIRE high
FAIRE int
FAIRE low
LNCaP-only
MCF7
FOXA1 binding sites
B
ERα
ERα ChIP-chip signal
0
1
2
3
4
5
6
7
★★★
Low FAIRE
Med. FAIRE
High FAIRE
LNCaP-only
MCF7
C
CARM1 Act.
CARM1 act. ChIP-chip signal
0
1
2
3
4
★★★
Low FAIRE
Med. FAIRE
High FAIRE
LNCaP-only
MCF7
FOXA1 binding sites

Fig.S7

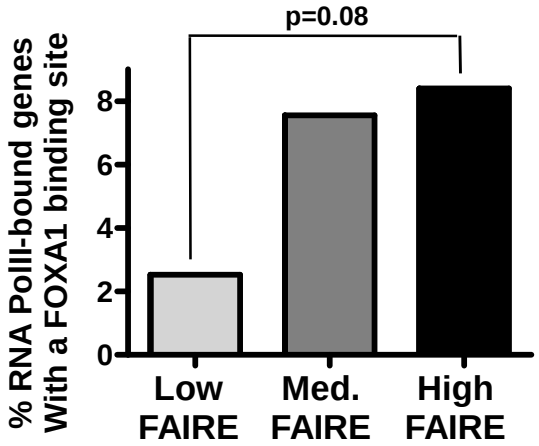

p=0.08
% RNA PolII-bound genes
With a FOXA1 binding site
0
2
4
6
8
Low
FAIRE
Med.
FAIRE
High
FAIRE

Fig.S8

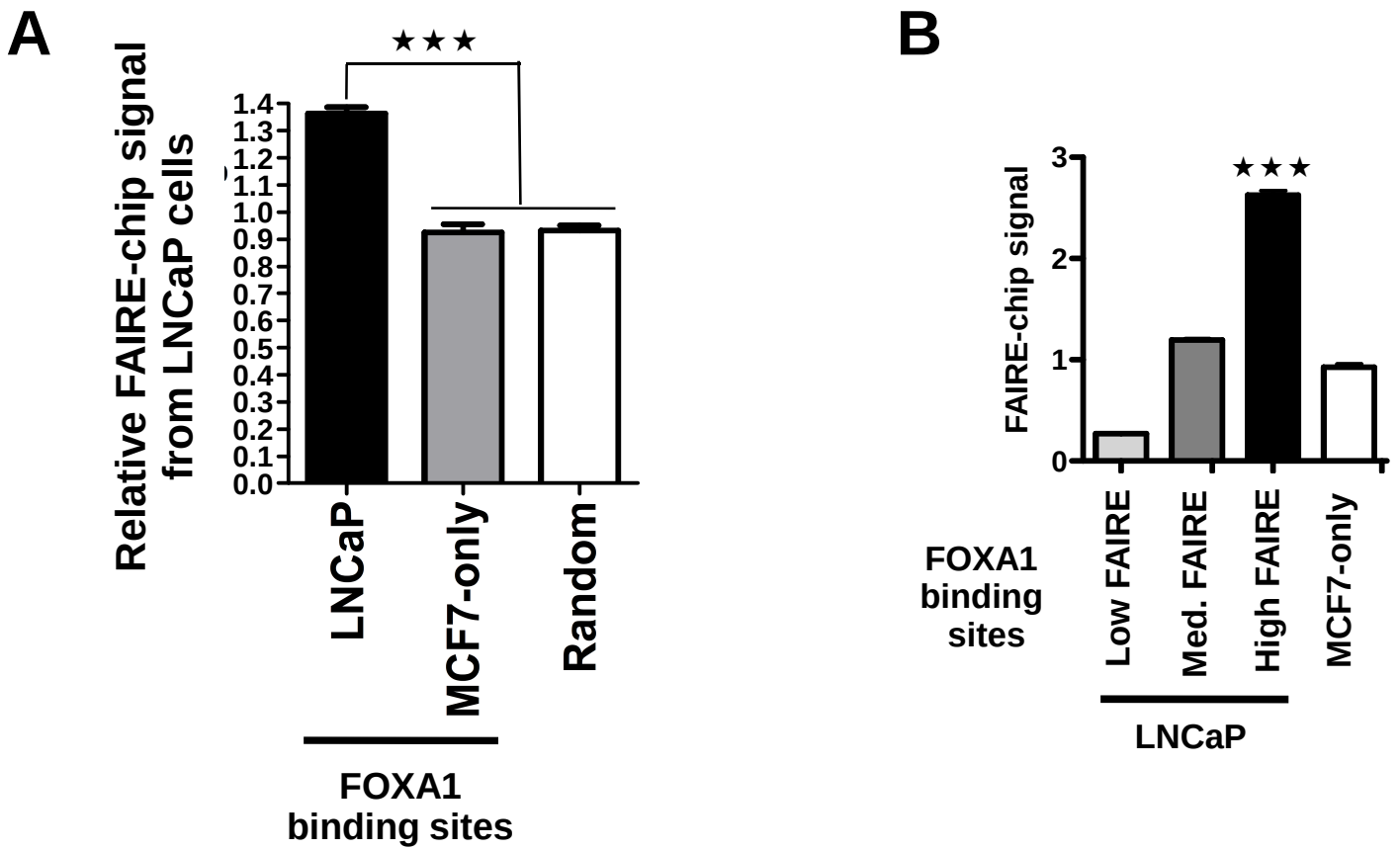

A
Relative FAIRE-chip signal from LNCaP cells
★★★
1.4
1.3
1.2
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0.0
LNCaP
MCF7-only
Random
FOXA1 binding sites
B
FAIRE-chip signal
★★★
3
2
1
0
Low FAIRE
Med. FAIRE
High FAIRE
MCF7-only
FOXA1 binding sites
LNCaP

Fig.S9

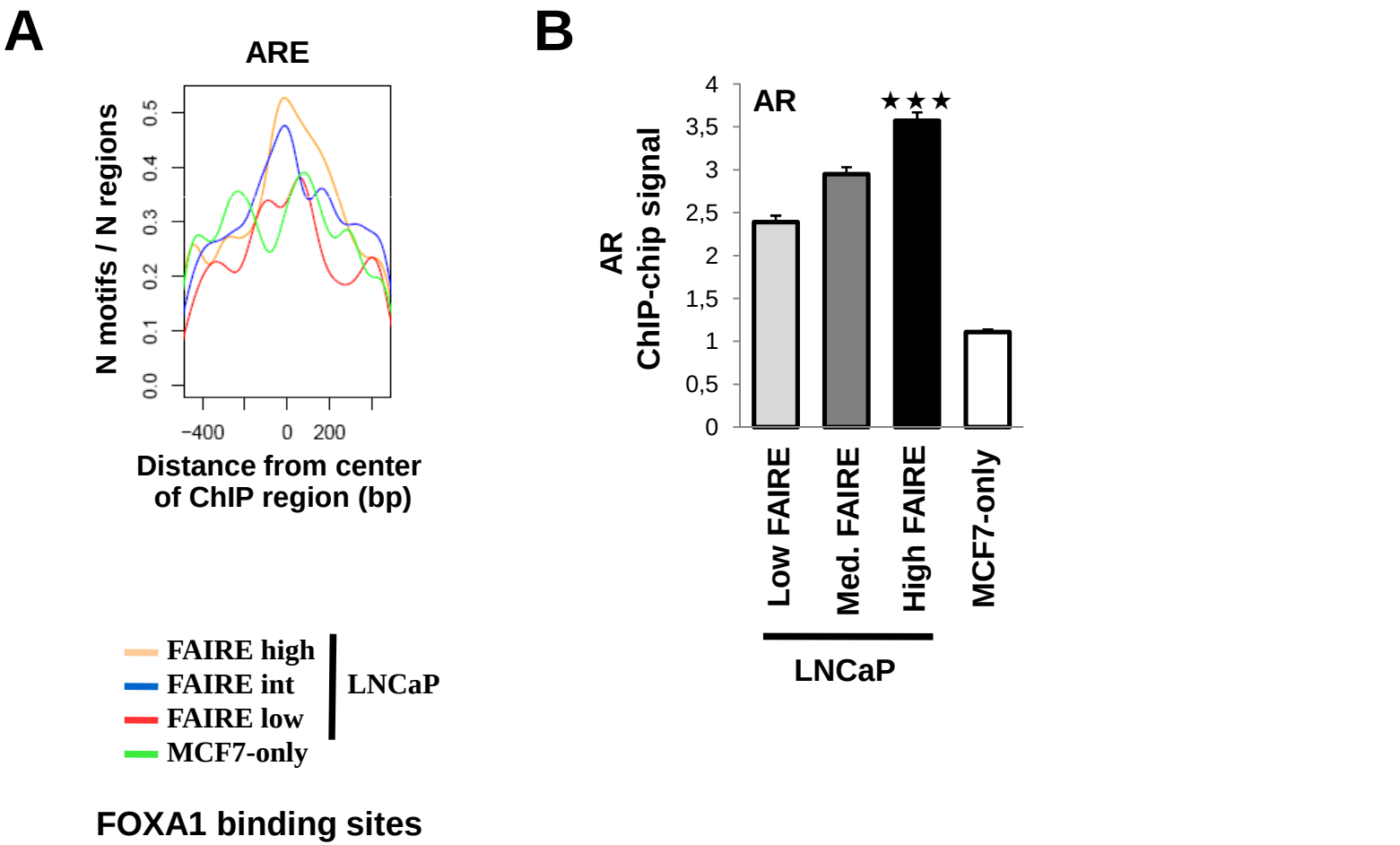

A
ARE
N motifs / N regions
0.0
0.1
0.2
0.3
0.4
0.5
−400
0
200
Distance from center
of ChIP region (bp)
FAIRE high
FAIRE int
FAIRE low
MCF7-only
LNCaP
FOXA1 binding sites
B
AR
AR
ChIP-chip signal
4
3,5
3
2,5
2
1,5
1
0,5
0
★★★
Low FAIRE
Med. FAIRE
High FAIRE
MCF7-only
LNCaP

Fig.S10

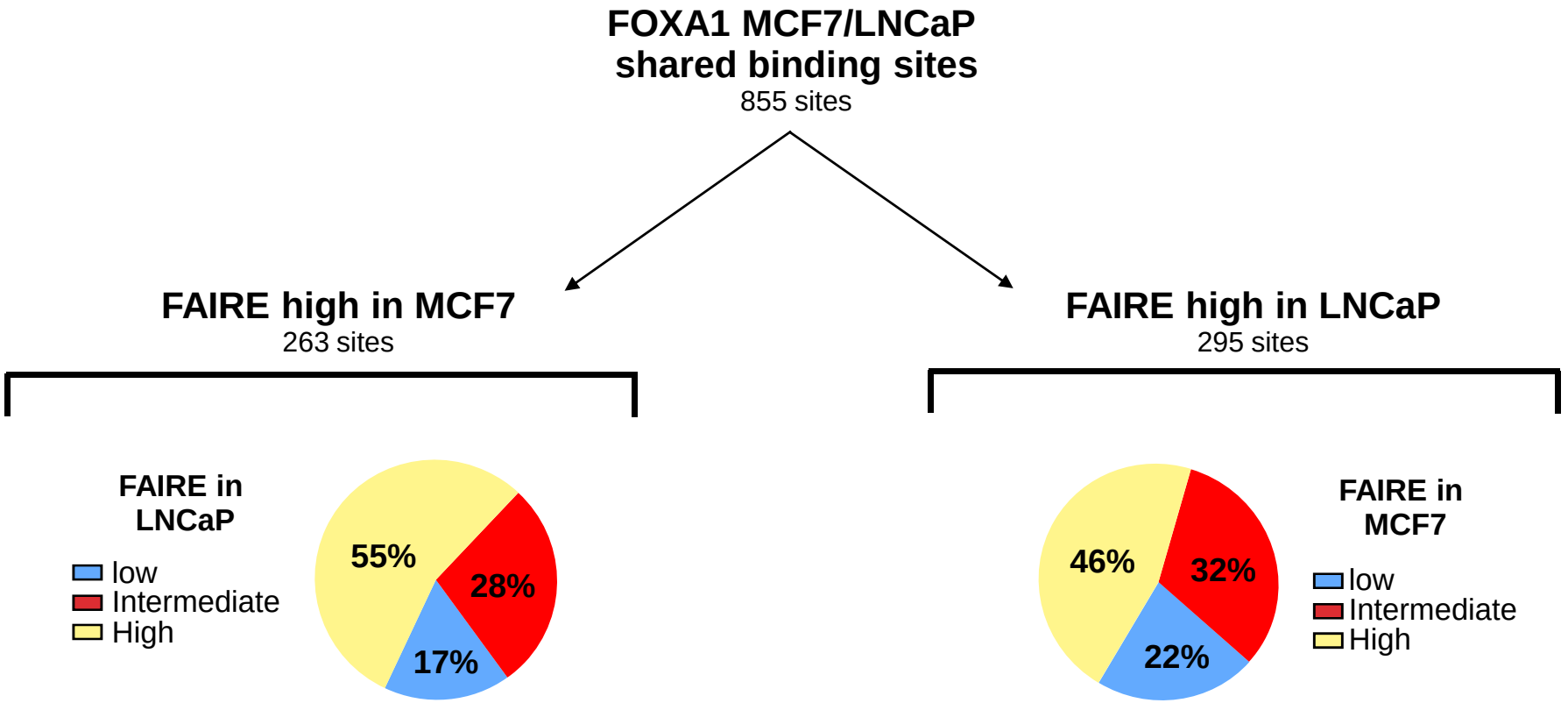
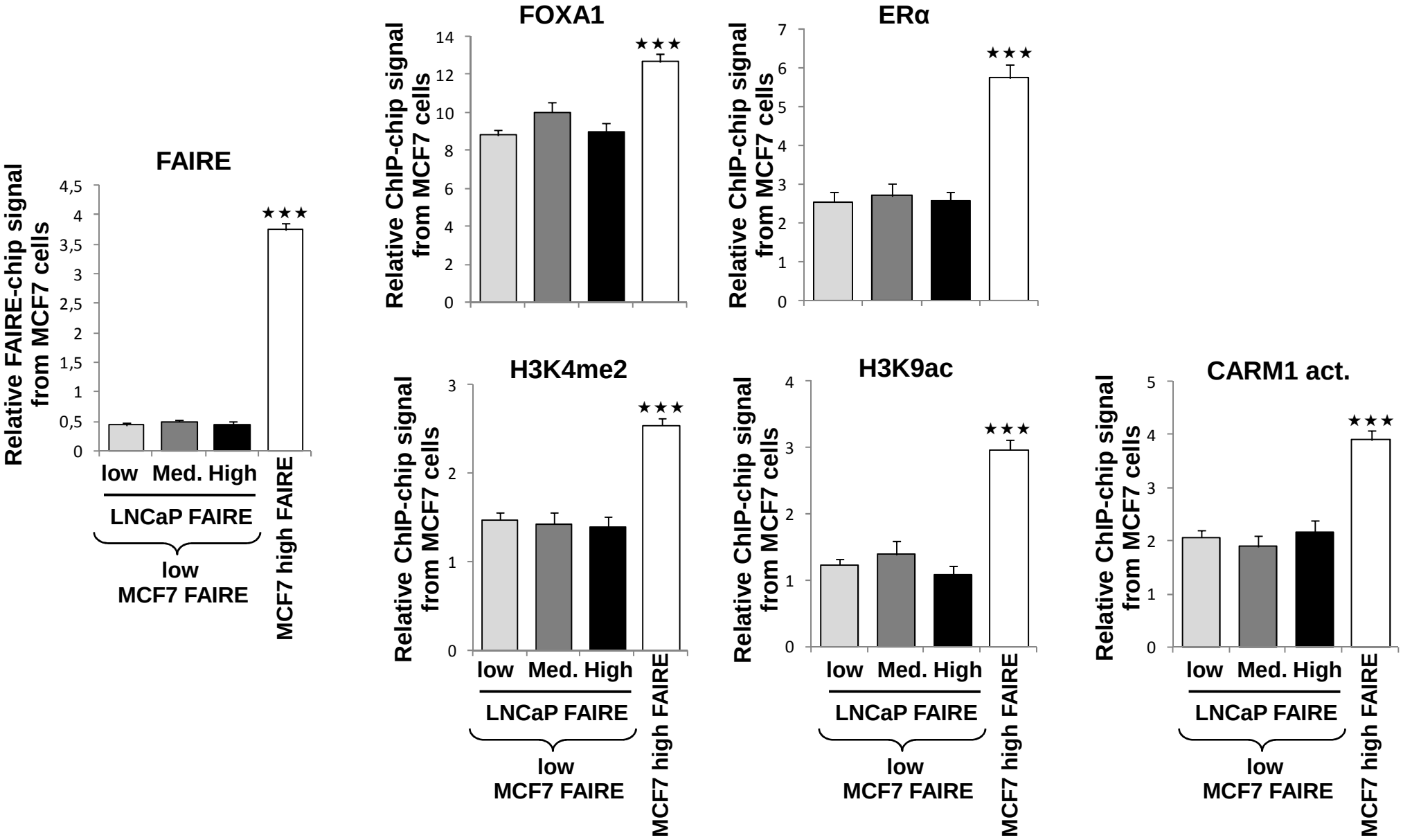

FOXA1 MCF7/LNCaP
shared binding sites
855 sites
FAIRE high in MCF7
263 sites
FAIRE high in LNCaP
295 sites
FAIRE in
LNCaP
low
Intermediate
High
55%
28%
17%
46%
32%
22%
FAIRE in
MCF7
low
Intermediate
High

Fig.S11


FAIRE
Relative FAIRE-chip signal from MCF7 cells
4,5
4
3,5
3
2,5
2
1,5
1
0,5
0
★★★
low
Med.
High
LNCaP FAIRE
low MCF7 FAIRE
MCF7 high FAIRE
FOXA1
Relative ChIP-chip signal from MCF7 cells
14
12
10
8
6
4
2
0
★★★
ERα
Relative ChIP-chip signal from MCF7 cells
7
6
5
4
3
2
1
0
★★★
H3K4me2
Relative ChIP-chip signal from MCF7 cells
3
2
1
0
★★★
low
Med.
High
LNCaP FAIRE
low MCF7 FAIRE
MCF7 high FAIRE
H3K9ac
Relative ChIP-chip signal from MCF7 cells
4
3
2
1
0
★★★
low
Med.
High
LNCaP FAIRE
low MCF7 FAIRE
MCF7 high FAIRE
CARM1 act.
Relative ChIP-chip signal from MCF7 cells
5
4
3
2
1
0
★★★
low
Med.
High
LNCaP FAIRE
low MCF7 FAIRE
MCF7 high FAIRE

FAIRE-qPCR

Fig.S12

LNCaP

MCF7

Ratios

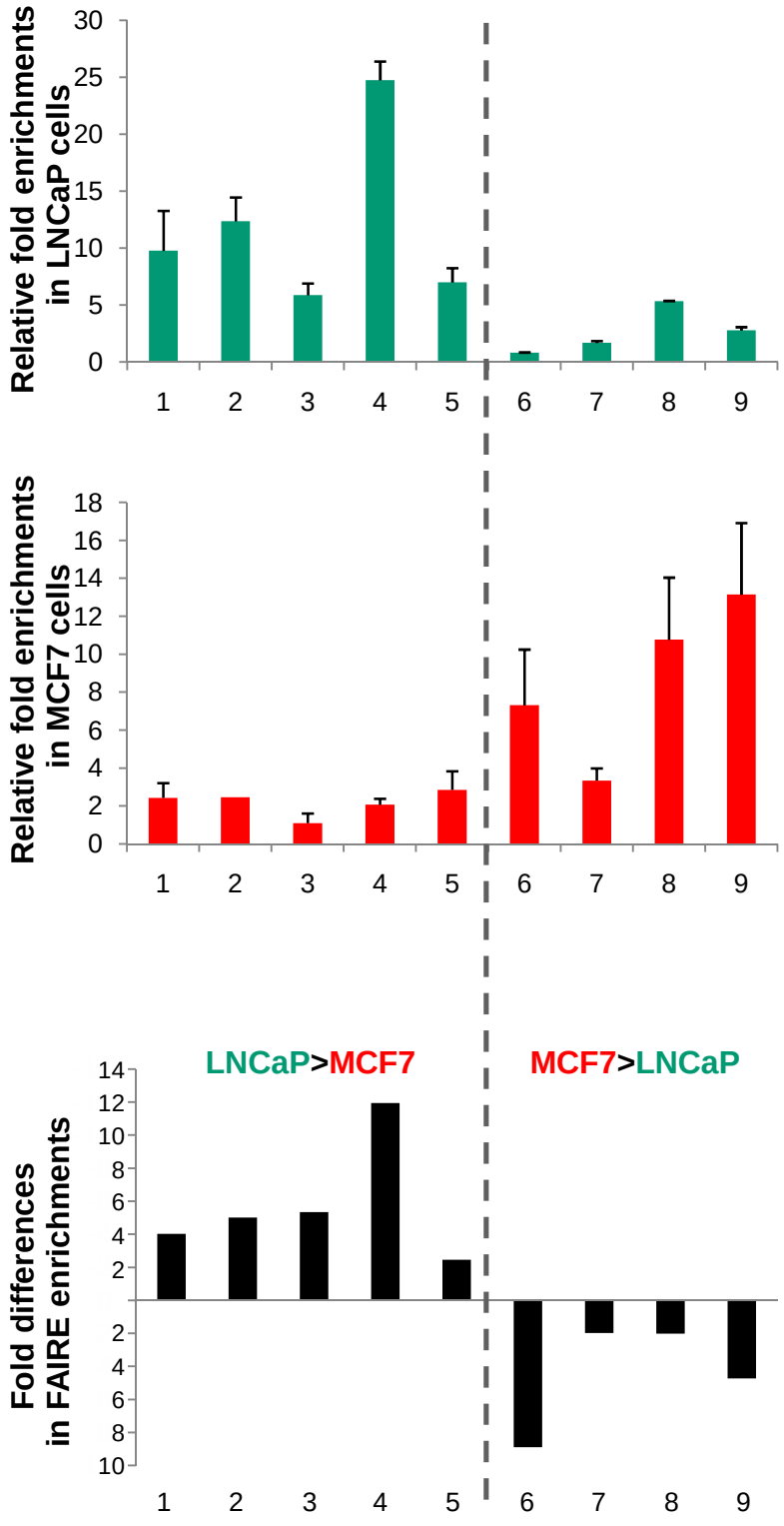


Fig.S13

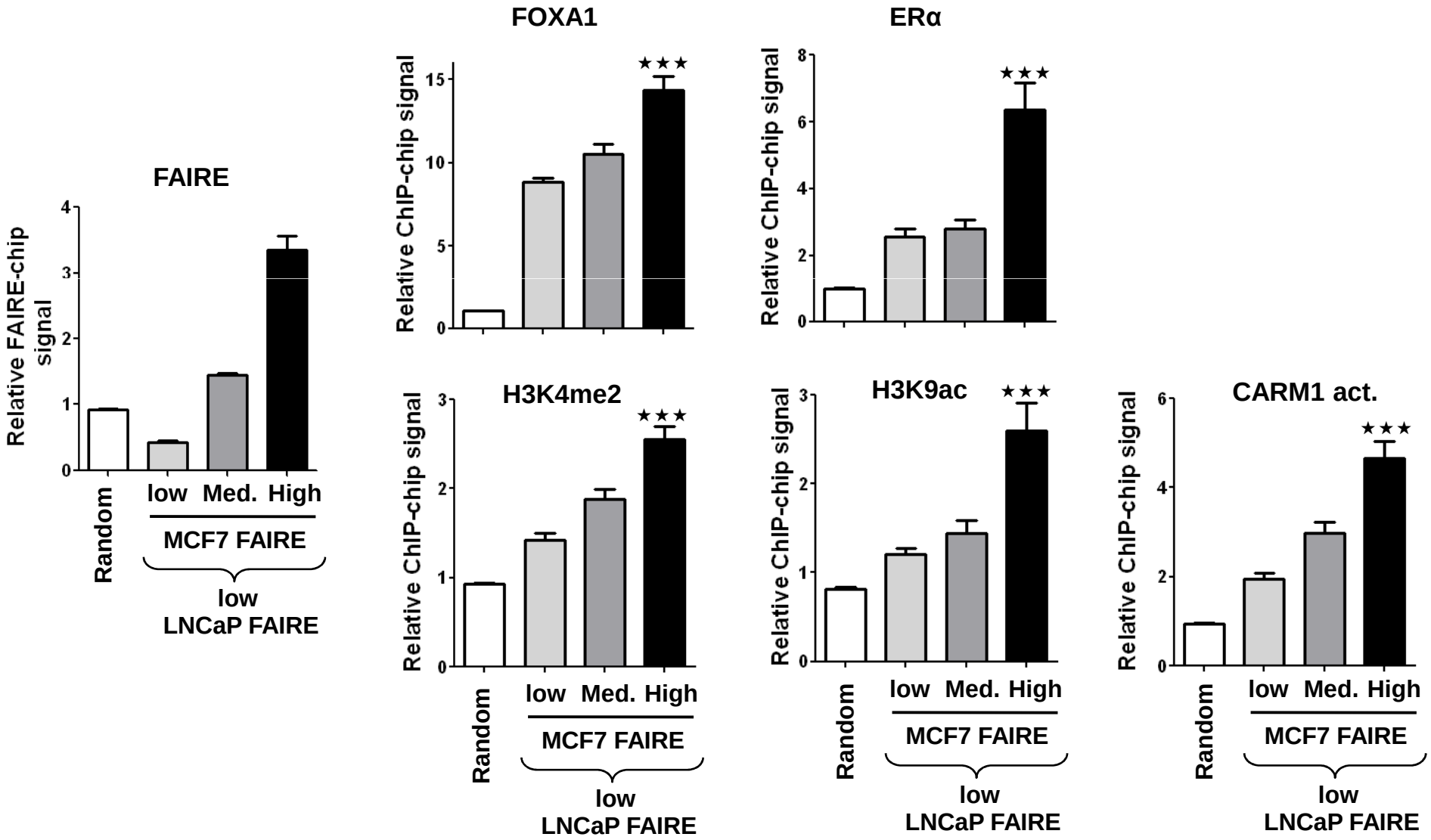

FAIRE
Relative FAIRE-chip signal
0
1
2
3
4
Random
low
Med.
High
MCF7 FAIRE
low
LNCaP FAIRE
FOXA1
Relative ChIP-chip signal
0
5
10
15
★★★
ERα
Relative ChIP-chip signal
0
2
4
6
8
★★★
H3K4me2
Relative ChIP-chip signal
0
1
2
3
★★★
Random
low
Med.
High
MCF7 FAIRE
low
LNCaP FAIRE
H3K9ac
Relative ChIP-chip signal
0
1
2
3
★★★
Random
low
Med.
High
MCF7 FAIRE
low
LNCaP FAIRE
CARM1 act.
Relative ChIP-chip signal
0
2
4
6
★★★
Random
low
Med.
High
MCF7 FAIRE
low
LNCaP FAIRE

Fig.S14

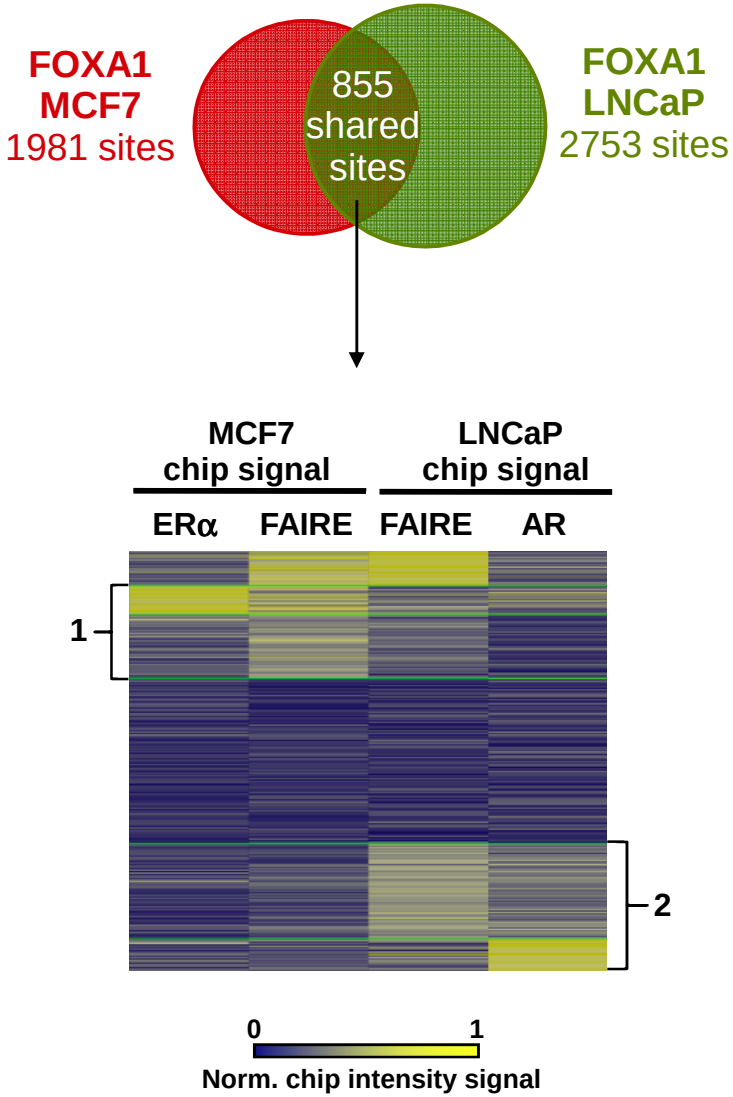

FOXA1
MCF7
1981 sites
855
shared
sites
FOXA1
LNCaP
2753 sites
MCF7
chip signal
LNCaP
chip signal
ERα
FAIRE
FAIRE
AR
1
2
0
1
Norm. chip intensity signal

Fig.S15

A

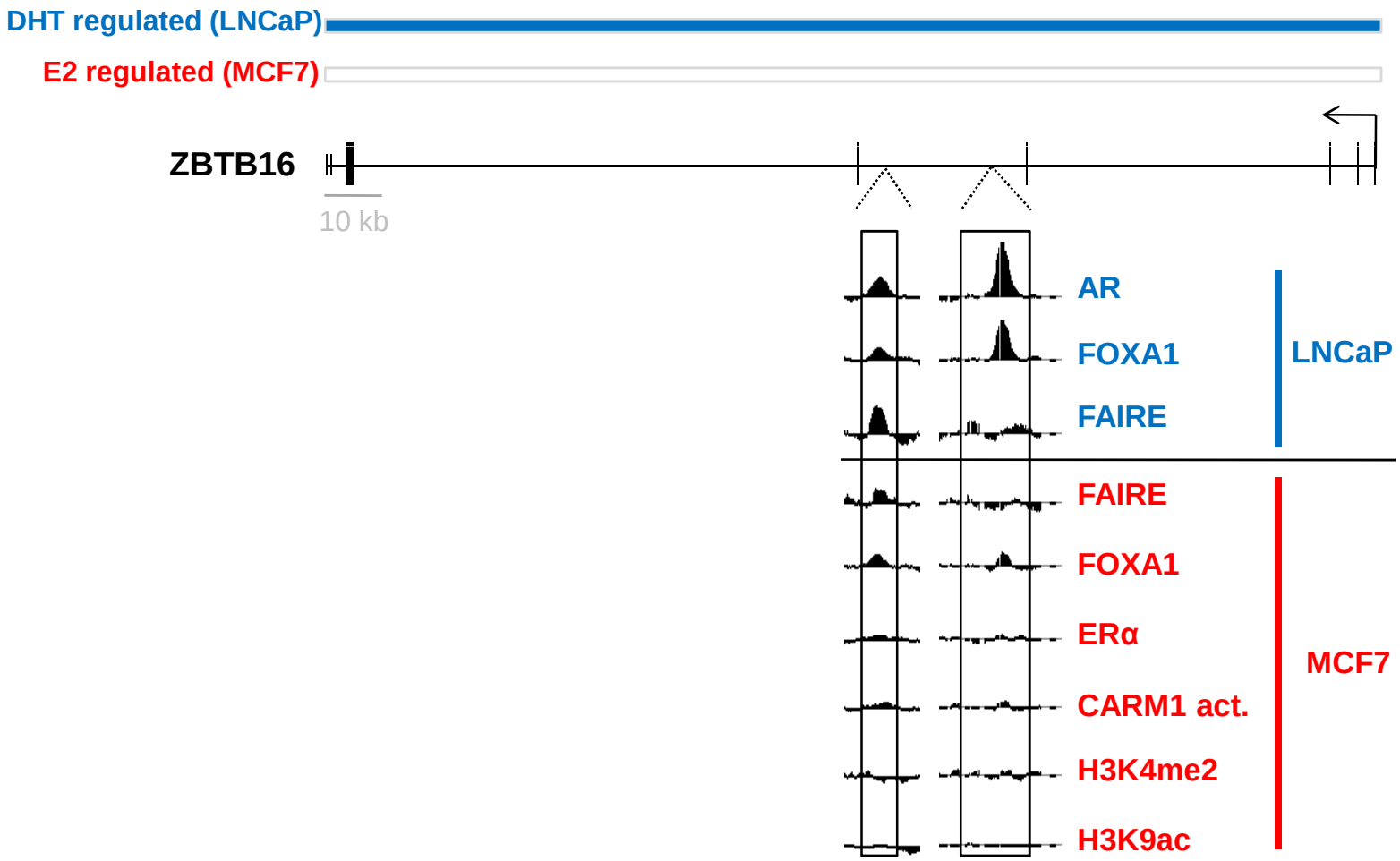

DHT regulated (LNCaP)
E2 regulated (MCF7)
ZBTB16
10 kb
AR
FOXA1
FAIRE
LNCaP
FAIRE
FOXA1
ERα
CARM1 act.
H3K4me2
H3K9ac
MCF7

Fig.S15
(continued)

B

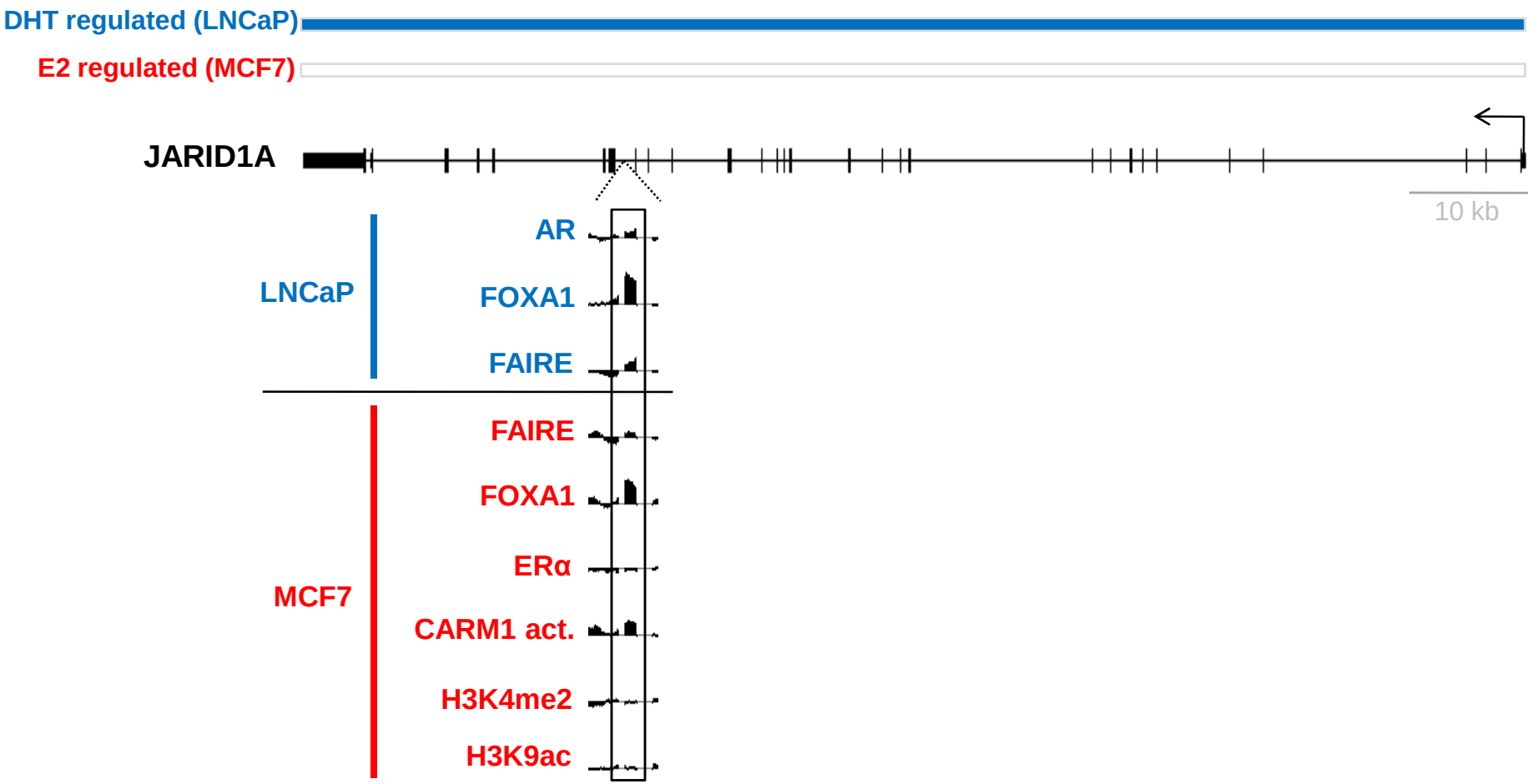
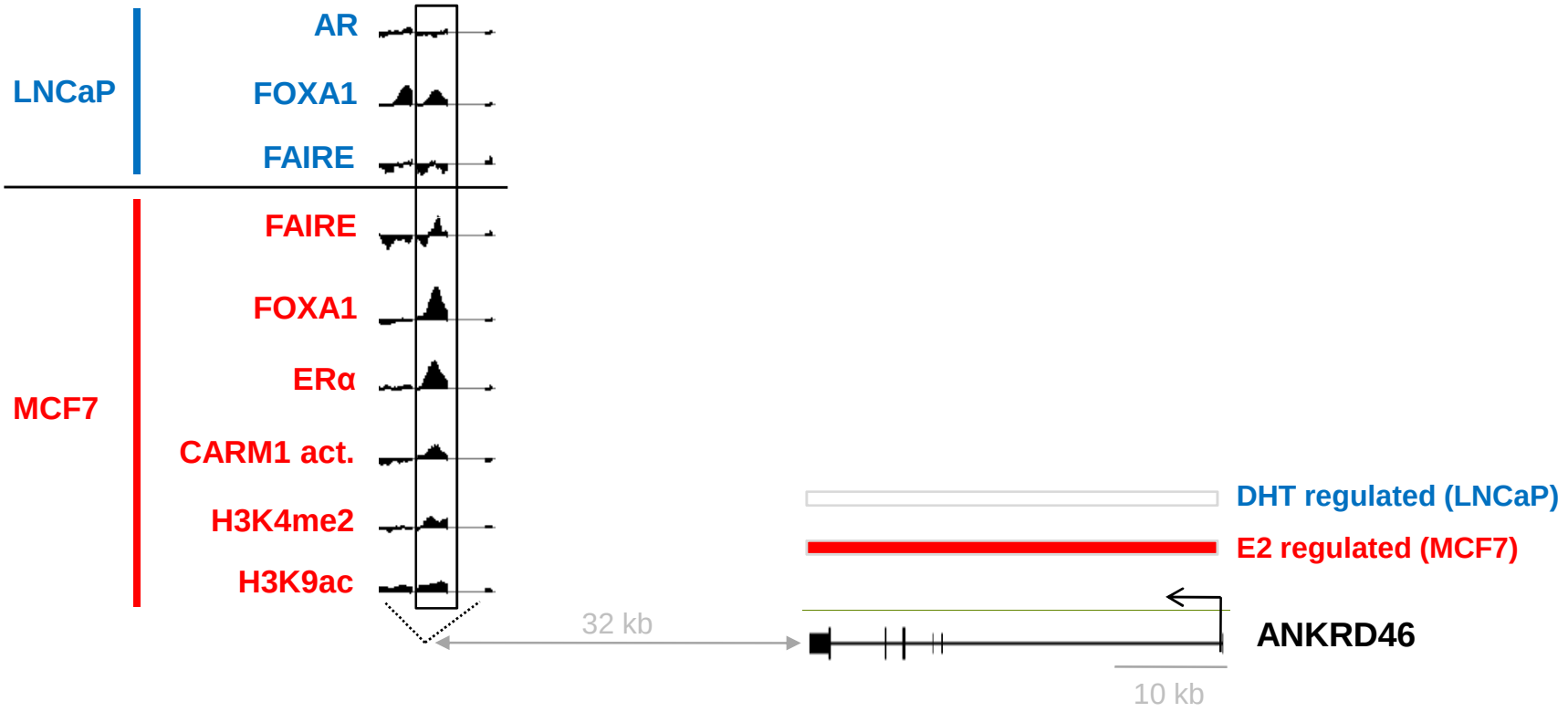


Fig.S15
(continued)

C



D

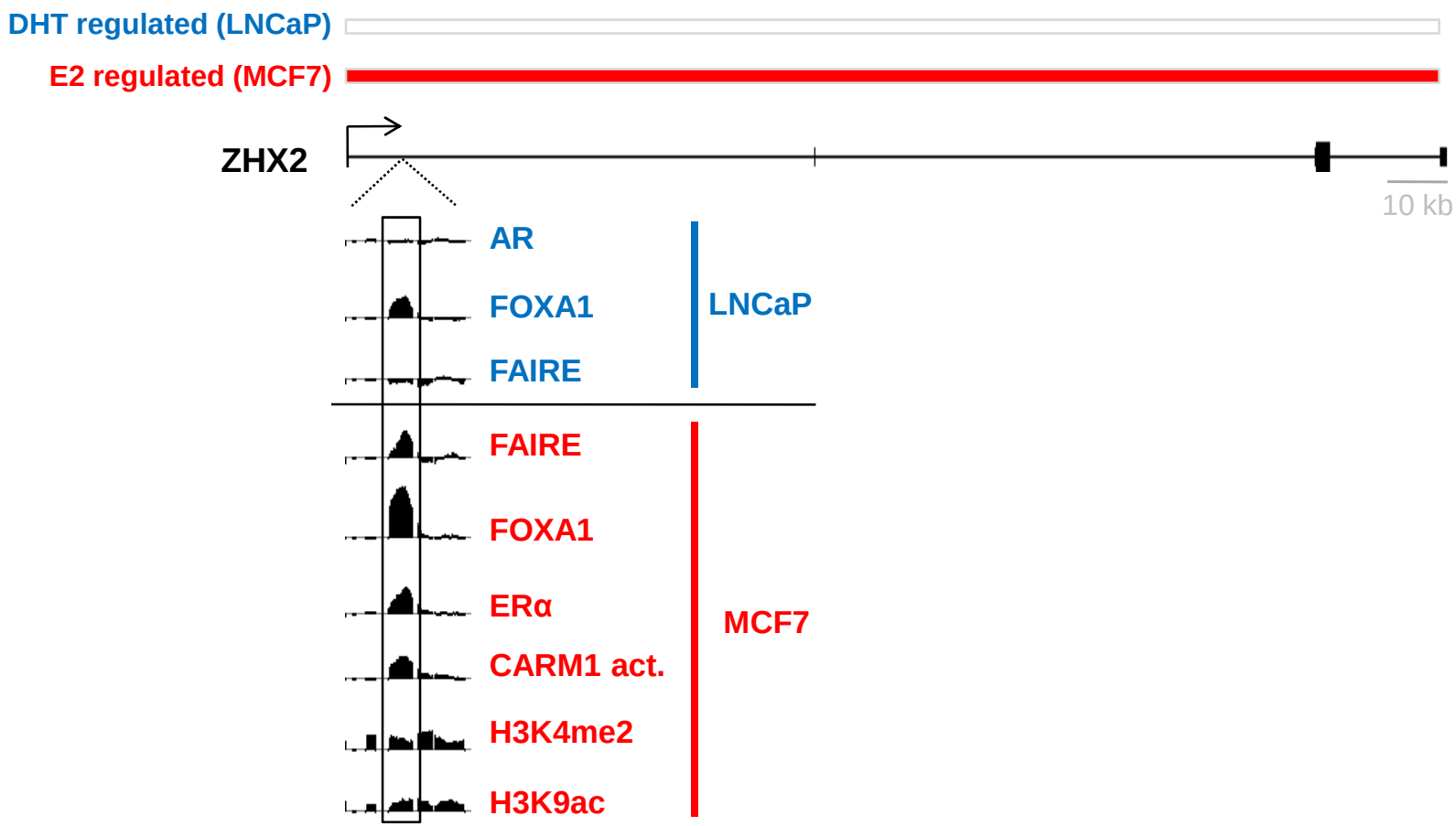
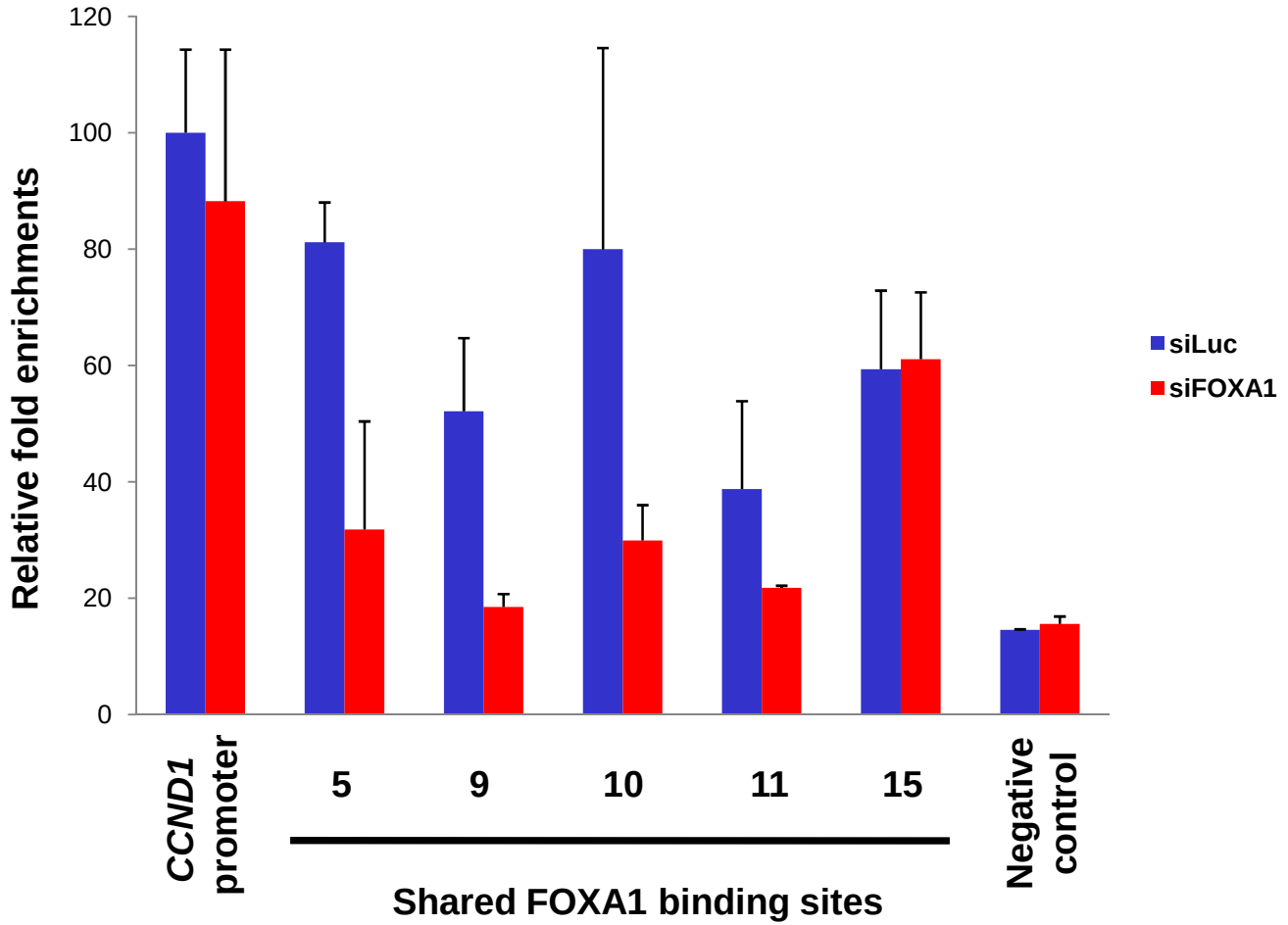

DHT regulated (LNCaP)
E2 regulated (MCF7)
ZHX2
10 kb
AR
FOXA1
FAIRE
LNCaP
FAIRE
FOXA1
ERα
CARM1 act.
H3K4me2
H3K9ac
MCF7

Fig.S16


Relative fold enrichments
120
100
80
60
40
20
0
siLuc
siFOXA1
CCND1 promoter
5
9
10
11
15
Negative control
Shared FOXA1 binding sites

LEGENDS TO SUPPLEMENTARY FIGURES

Fig.S1 FAIRE-chip signal at RNA PolII and FOXA1 recruitment sites from MCF7 cells.

FAIRE-chip signal from MCF7 cells within high confidence RNA PolII and FOXA1 recruitment sites from MCF7 cells. All FOXA1 binding sites or only those lying outside of 1 kb promoters were analyzed. Data represent means ± SEM of signals derived from MAT analysis of FAIRE-chip data. *** indicates statistically significant differences ($p<0.001$).

Fig.S2 FAIRE-chip signal from MCF7 cells at ERα and E2F1 bound and unbound sites.

FAIRE-chip signal from MCF7 cells within high confidence ERα (A) or E2F1 (B) recruitment sites in MCF7 cells was compared to signals obtained at unbound recognition motifs (ERE and E2F motifs, respectively). ERα binding sites were from Carroll et al. (Carroll et al. 2006) while E2F1 recruitment sites were from Bieda et al. (Bieda et al. 2006). Since E2F1 data were obtained using arrays covering the ENCODE regions, only E2F motifs that are common to these regions and the arrays used for FAIRE-chip in our study were considered. Data represent means ± SEM of signals derived from MAT analysis of FAIRE-chip data. *** indicates statistically significant differences with FAIRE-chip signals at bound sites ($p<0.001$).

Fig.S3 Evolutionary conservation of FOXA1 recruitment sites with different FAIRE enrichments.

Cis-regulatory element annotation system (CEAS) (Ji et al. 2006) was used to determine evolutionary conservation levels of FOXA1 binding sites with low, medium or high FAIRE enrichments, as indicated. An equivalent number of randomly selected 1 kb regions were also analyzed (Random). As expected, the conservation score was higher towards the center of the identified FOXA1 binding sites. Importantly, the conservation score was similar for FOXA1 recruitment sites with different FAIRE

enrichments.

Fig.S4 FKHR motif enrichment within FOXA1 binding sites with low, medium or high FAIRE signals in MCF7 cells

Presence of the Forkhead motif (FKHR) was monitored within FOXA1 binding sites from MCF7 with low, medium or high FAIRE enrichments as well as in FOXA1 sites specific to LNCaP cells (LNCaP-only). The occurrence of the motifs (N motifs) was normalized to the number of sites in each subset (N binding sites).

Fig.S5 FOXA1 binding sites with low, medium or high FAIRE enrichments in MCF7 cells have an equivalent chance of being independently identified in another cell-type.

Histogram showing the percentage of FOXA1 recruitment sites from MCF7 cells with different FAIRE enrichments that also bind FOXA1 in LNCaP cells, as determined by ChIP-chip. High confidence FOXA1 sites from MCF7 cells (FDR1) and FOXA1 binding sites identified at FDR1 or 20 in LNCaP cells were used for these analyses, as indicated.

Fig.S6 High FAIRE enrichments at FOXA1 binding sites correlate with stronger ERα recruitment and CARM1 activity in MCF7 cells.

A) Presence of Estrogen Response Elements (ERE) was monitored within FOXA1 binding sites from MCF7 with low, medium or high FAIRE enrichments as well as in FOXA1 sites specific to LNCaP cells (LNCaP-only). The occurrence of the motifs (N motifs) was normalized to the number of sites in each subset (N binding sites). ERα (**B**) and CARM1 activity (**C**)(including notably H3R17me2) ChIP-chip signals at FOXA1 binding sites from MCF7 or specific to LNCaP cells were analyzed. Data represent means ± SEM of signals derived from MAT analysis of the ChIP-chip data. *** indicates a statistically significant difference ($p<0.001$) between FOXA1 sites from MCF7 with high FAIRE

versus low FAIRE enrichments.

Fig.S7 High FAIRE enrichments at FOXA1 binding sites correlate with RNA PolII-bound genes in MCF7 cells.

Genes whose TSS ± 1 kb was bound by RNA PolII in MCF7 cells were selected and the proportion of these genes with a FOXA1 binding site within 20 kb of the TSS is indicated. FOXA1 recruitment sites belonging to the three categories of FAIRE enrichments were analyzed. Similar results were obtained using RNA PolII ChIP-chip data generated in the absence or presence of estradiol (not shown).

Fig.S8 FAIRE-chip in LNCaP cells.

A) FAIRE-chip signal from LNCaP cells within high confidence FOXA1 recruitment sites from LNCaP cells or specific to MCF7 as well as randomly selected regions was analyzed. Data represent means ± SEM of signals derived from MAT analysis of FAIRE-chip data. *** indicates statistically significant differences ($p<0.001$). **B**) FOXA1 binding sites from LNCaP cells were divided into tertiles and the average FAIRE-chip signal (based on MAT scores, see Materials and Methods) for each subset of sites (low, medium and high FAIRE) was calculated. Each subset comprised 918 sites. FAIRE-chip enrichments at FOXA1 MCF7-specific sites were also analyzed. Data represent means ± SEM of signals derived from MAT analysis of FAIRE-chip data. *** indicates statistically significant differences ($p<0.001$).

Fig.S9 High FAIRE enrichments at FOXA1 binding sites correlate with stronger AR recruitment in LNCaP cells.

A) Presence of Androgen Response Elements (ARE) was monitored within FOXA1 binding sites from LNCaP with low, medium or high FAIRE enrichments as well as in FOXA1 sites specific to MCF7

cells (MCF7-only). The occurrence of the motifs (N motifs) was normalized to the number of sites in each subset (N binding sites). **B**) AR ChIP-chip signals at FOXA1 binding sites from LNCaP or specific to MCF7 cells were analyzed. Data represent means ± SEM of signals derived from MAT analysis of the ChIP-chip data. *** indicates a statistically significant difference ($p<0.001$) between FOXA1 sites from LNCaP with high FAIRE *versus* low FAIRE enrichments.

Fig.S10 Differential FAIRE enrichments of common FOXA1 sites.

FOXA1 binding sites shared between MCF7 and LNCaP (Lupien et al. 2008) and harboring high FAIRE enrichments in MCF7 or LNCaP cells were selected. These sites were then classified relative to their FAIRE enrichment levels (low, medium or high) in the other cell-type.

Fig.S11 Levels of histone post-translational modifications, CARM1 activity and ERα recruitment in breast cells at FOXA1 sites with low FAIRE signals in both MCF7 and LNCaP cells.

FAIRE-chip and ChIP-chip signals for the indicated histone marks or factors were monitored within MCF7/LNCaP shared FOXA1 binding sites with low FAIRE enrichments in MCF7 cells and low, medium or high FAIRE signals in LNCaP cells, as indicated. Data represent means ± SEM of signals derived from MAT analysis of FAIRE-chip or ChIP-chip data. *** indicates a statistically significant difference ($p<0.001$) between FOXA1 sites with high FAIRE enrichments compared to those with low FAIRE enrichments in MCF7. Note that sites with selectively low FAIRE in MCF7 cells have significantly lower levels of active histone marks as well as FOXA1 and ERα binding compared to sites with high FAIRE in these breast cells. Therefore, those sites do not represent regions that would be high FAIRE in both cell-types but falsely detected as low FAIRE in MCF7 cells.

Fig.S12 FAIRE-qPCR validation of differential FAIRE enrichments at FOXA1 binding sites shared between MCF7 and LNCaP cells.

A few common FOXA1 binding sites with differential FAIRE-chip enrichments in LNCaP and MCF7 cells were analyzed by FAIRE-qPCR: 5 sites with high FAIRE in LNCaP but low FAIRE in MCF7 (1-5) and 4 sites with high FAIRE in MCF7 but low FAIRE in LNCaP (6-9). FAIRE enrichments within each cell-line as determined using qPCR are shown. Data represent means ± SD from 2-3 independent experiments. The bottom panel shows the ratios between enrichments in the two cell-types.

Fig.S13 Cell-specific activity of FOXA1 binding sites conserved between breast and prostatic cells correlates with active histone marks, CARM1 activity and ERα recruitment in breast cells.

FAIRE-chip and ChIP-chip signals for the indicated histone marks or factors were monitored within MCF7 /LNCaP shared FOXA1 binding sites with low FAIRE enrichments in LNCaP cells and low, medium or high FAIRE signals in MCF7 cells as well as within sites from MCF7 with high FAIRE signals. Data represent means ± SEM of signals derived from MAT analysis of FAIRE-chip or ChIP-chip data. *** indicates a statistically significant difference ($p<0.001$) between FOXA1 sites with high FAIRE enrichments in MCF7 compared to those with low FAIRE enrichments in both MCF7 and LNCaP cells.

Fig.S14 Differential FAIRE enrichments at shared FOXA1 binding sites correlate with alternate co-recruitment of ERα and AR in breast and prostate cells, respectively.

Cluster analysis of the relative distribution of FAIRE-chip, ER and AR signals from MCF7 or LNCaP cells performed as described in Materials and Methods. FOXA1 binding sites shared between MCF7 and LNCaP cells were included in this analysis. Clusters including sites with differential FAIRE enrichments between MCF7 and LNCaP cells are highlighted. These clusters also show sites with ERα (1) or AR (2) recruitment.

Fig.S15 Correlation between selective activity of common FOXA1 binding sites and cell type-specific gene regulation.

Examples of genes associated with FOXA1 binding sites common to MCF7 and LNCaP cells but regulated in a cell type-specific manner. Individual probe level signal for FAIRE-chip and ChIP-chip of the indicated factors or histone marks within the FOXA1 binding sites is shown. Transcriptional regulation by estradiol (E2) in MCF7 cells (Carroll et al. 2006) or by dihydrotestosterone (DHT) in LNCaP cells (Wang et al. 2007) was determined using a *t* test ($p<5.10^{-3}$). **A-B**) Examples of genes regulated by DHT in LNCaP but not by E2 in MCF7. **C-D**) Examples of genes regulated by E2 in MCF7 but not by DHT in LNCaP. Note that shared FOXA1 binding sites with selective activities are often associated with cell type-specific ones in the vicinity of target genes. This is consistent with the clustering of transcription factor recruitment regions nearby regulated genes (Krum et al. 2008; Chan and Song 2008).

Fig.S16 Effect of FOXA1 silencing on FAIRE enrichments at common chromatin-bound regions selectively open in DLD1 cells.

DLD1 cells were transfected using siRNA directed against FOXA1 (siFOXA1) or luciferase (siLuc), as a control. FAIRE-qPCR experiments were then performed to monitor the effect of FOXA1 silencing on chromatin structure at sites identified as selectively open in this cell-type in Fig.7 (sites # 16-20). Data represent means ± SD from two independent experiments.