FIGURE LEGENDS

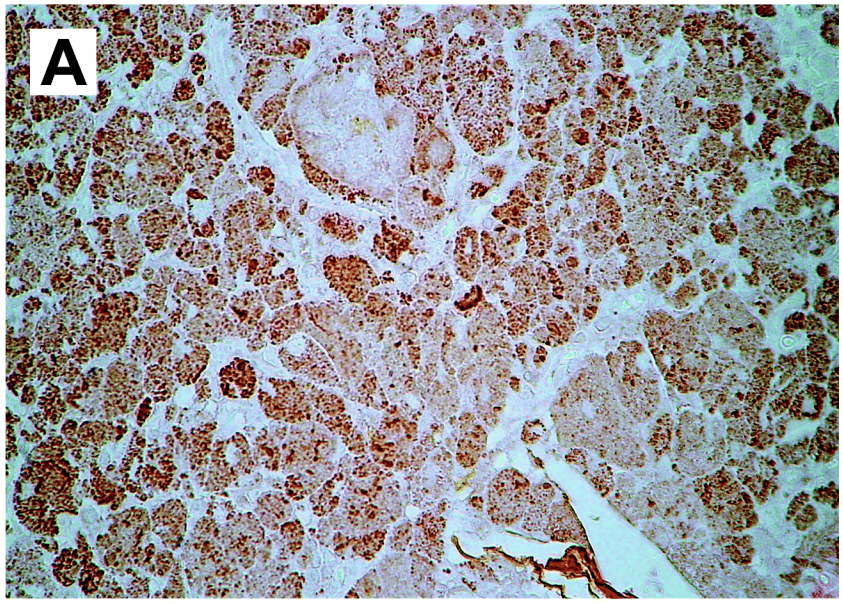
Fig. 1. Semi-quantitative immunohistochemical analyses of CTSD, Ki-67, and PCNA expression. Shown to the left are representative photomicrographs of primary chemosensitive (*A*) and primary chemoresistant (*B*) ovarian cancers immunostained for CTSD at 40X magnification. To the right are results of immunohistochemical scoring for CTSD (*C*), Ki-67 (*D*), and PCNA (*E*). Histograms represent mean score and error bars represent standard deviation.

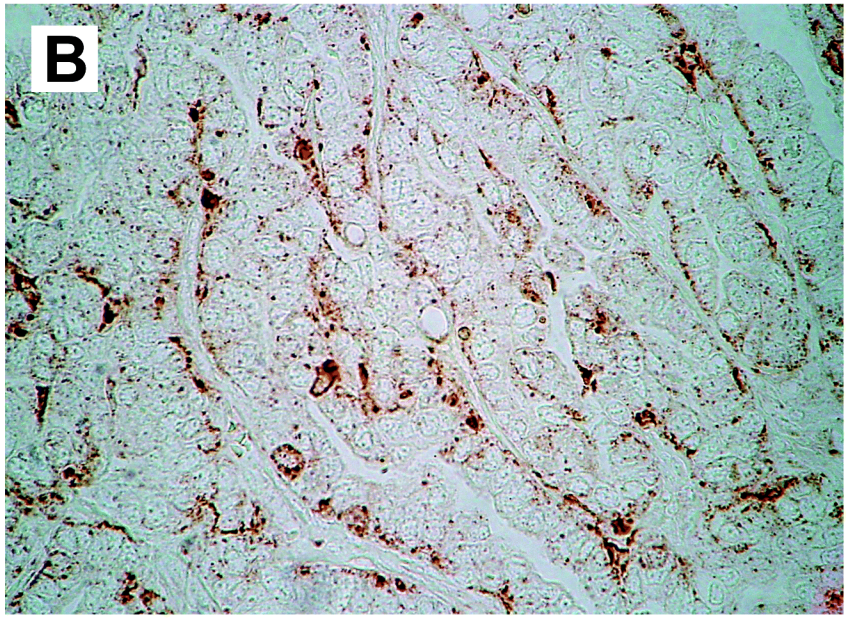
Fig. 2. Gene expression differences between post-chemo and primary chemosensitive or primary chemoresistant tumors. *A*, An overview of the number of differentially expressed genes ($P < 0.001$) , with the top circle representing post-chemo vs. primary chemosensitive samples, the bottom circle representing post-chemo vs. primary chemoresistant samples, and the overlap region representing genes differentially expressed between post-chemo samples and primary tumors irrespective of intrinsic chemosensitivity. *B*, Changes in the magnitude and direction of the 178 genes that discriminated the post-chemo samples from all primary tumors ($P < 0.001$). For each gene, the fold-difference between the post-chemo and the primary chemoresistant tumors (x-axis), is plotted against the fold-difference between the post-chemo and primary chemosensitive tumors (y-axis). Values less than 1.0 reflect higher expression in the primary tumors. r, Pearson correlation coefficient.

Fig. 3. Specific genes with statistically significant differential expression between post-chemo and primary tumors ($P < 0.001$). The corresponding expression values from normal postmenopausal ovaries are shown for comparison. *A*, Genes that were differentially expressed between the post-chemo tumors and both groups of primary tumors. The top 50 genes are shown; the full list may be found in supplemental data. *B*, Genes that were differentially higher expressed by two-fold or greater ($n = 41$) in the post-chemo compared to primary

chemosensitive tumors. Genes encoding extracellular matrix-related proteins are shown in bold type. *C*, Genes that were differentially higher expressed by two-fold or greater (n = 10) in primary chemosensitive compared to post-chemo tumors. *D*, Genes differentially expressed between the post-chemo tumors and the primary chemoresistant tumors.

Fig. 4. Diagrammatic depiction of chemoresistance in primary and post-chemo samples. Smaller differences in gene expression observed between primary chemosensitive and chemoresistant tumors are likely the result of low relative abundance of intrinsically chemoresistant clones as predicted by the Goldie-Coleman hypothesis. Chemotherapy results in a reduction in the number of chemosensitive and an enrichment of chemoresistant clones in the post-chemo samples. In addition, chemotherapy is likely to induce additional genetic changes contributing to acquired chemoresistance. The combination of these effects is likely to be responsible for the robust differences in gene expression observed between the primary and post-chemo samples.


A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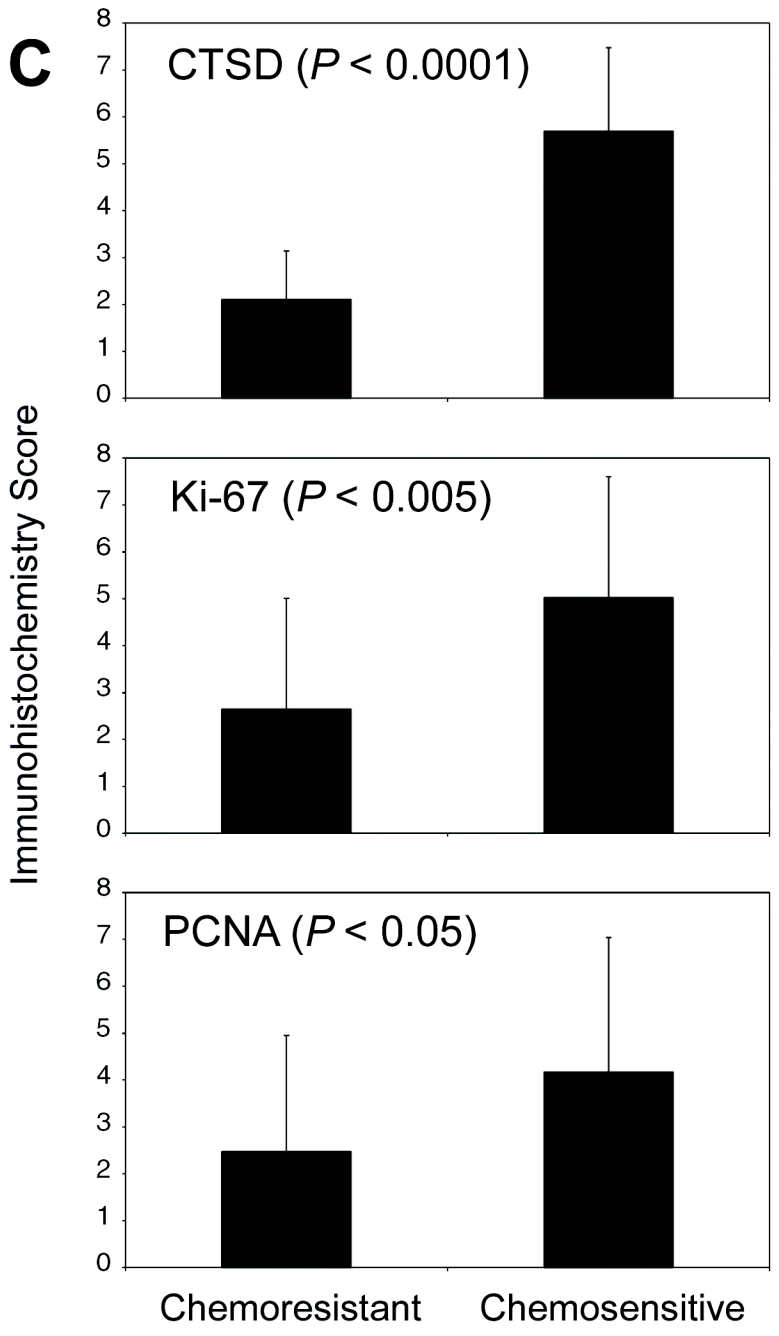
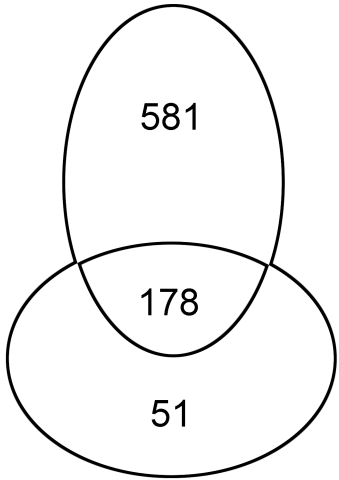

C
CTSD (P < 0.0001)
Ki-67 (P < 0.005)
PCNA (P < 0.05)
Immunohistochemistry Score
0
1
2
3
4
5
6
7
8
Chemoresistant
Chemosensitive

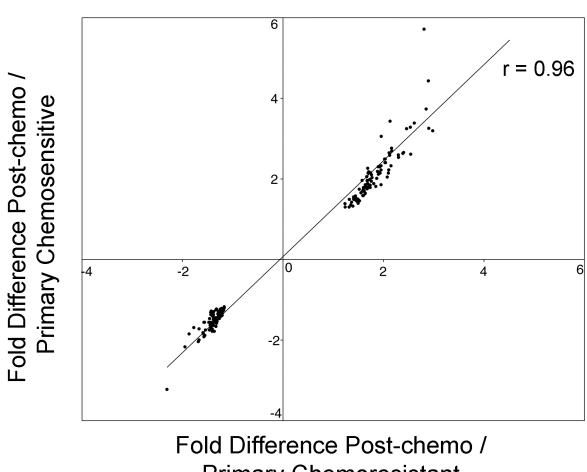
A

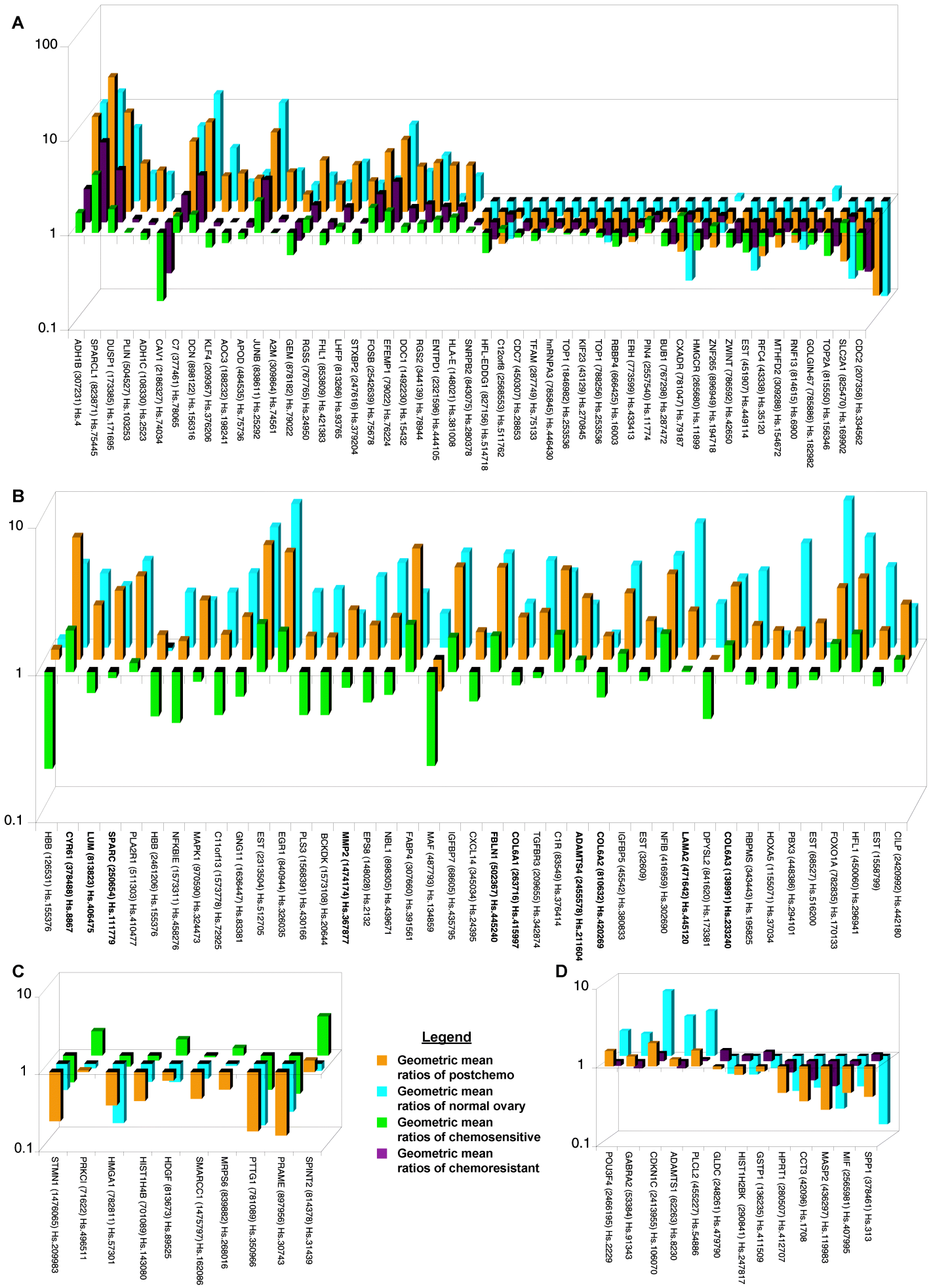
Primary chemosensitive
vs.
Post-chemo samples

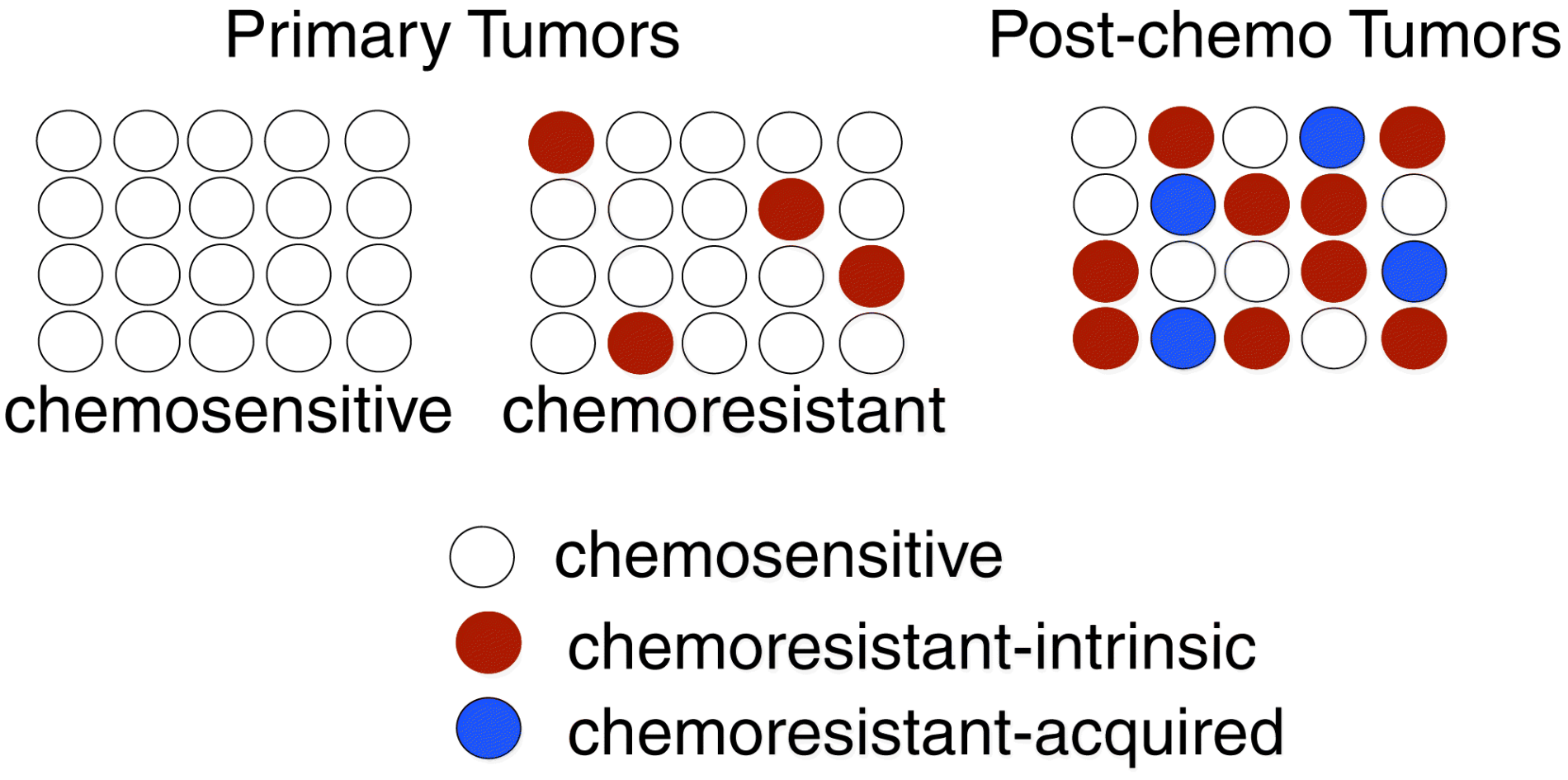
Primary chemoresistant
vs.
Post-chemo samples



B




A
100
10
1
0.1
ADH1B (307231) Hs.4
SPARCL1 (823871) Hs.75445
DUSP1 (173385) Hs.171695
PLIN (504527) Hs.103253
ADH1C (108330) Hs.2523
CAV1 (2186327) Hs.74034
C7 (377461) Hs.78065
DCN (898122) Hs.156316
KLF4 (209367) Hs.376206
AOC3 (188232) Hs.198241
APOD (484535) Hs.75736
JUNB (838611) Hs.25292
A2M (309864) Hs.74561
GEM (878182) Hs.79022
RGS5 (767765) Hs.24950
FHL1 (853809) Hs.421383
LHFP (813266) Hs.93765
STXBP2 (247616) Hs.379204
FOSB (2542639) Hs.75678
EFEMP1 (79022) Hs.76224
DOC1 (1492230) Hs.15432
RGS2 (344139) Hs.78944
ENTPD1 (2321596) Hs.444105
HLA-E (148021) Hs.381008
SNRPB2 (843075) Hs.280378
HFL-EDDG1 (827156) Hs.514718
C12orf8 (2568553) Hs.511762
CDC7 (450307) Hs.28883
TFAM (287749) Hs.75133
hnRNPA3 (785845) Hs.446430
TOP1 (1846982) Hs.253536
KIF23 (43129) Hs.270845
TOP1 (788256) Hs.253536
RBBP4 (666425) Hs.16003
ERH (773599) Hs.433413
PIN4 (2557540) Hs.11774
BUB1 (767298) Hs.287472
CXADR (781047) Hs.79187
HMGCR (265680) Hs.11899
ZNF265 (696949) Hs.194718
ZWINT (786592) Hs.42650
EST (451907) Hs.449114
RFC4 (43338) Hs.35120
MTHFD2 (309288) Hs.154672
RNF13 (814615) Hs.6900
GOLGIN-67 (785886) Hs.182982
TOP2A (815550) Hs.156346
SLC2A1 (825470) Hs.169902
CDC2 (207358) Hs.334562
B
10
1
0.1
HBB (126531) Hs.155376
CYR61 (378488) Hs.8867
LUM (813823) Hs.406475
SPARC (250654) Hs.111779
PLA2R1 (511303) Hs.410477
HBB (2461206) Hs.155376
NFKBIE (1573311) Hs.458276
MAPK1 (970590) Hs.324473
C11orf13 (1573778) Hs.72925
GNG11 (1636447) Hs.83381
EST (2313504) Hs.512705
EGR1 (840944) Hs.326035
PLS3 (1568391) Hs.430166
BCKDK (1573108) Hs.20644
MMP2 (1474174) Hs.367877
EPS8 (148028) Hs.2132
NBL1 (898305) Hs.439671
FABP4 (307660) Hs.391561
MAF (487793) Hs.134659
IGFBP7 (68605) Hs.435795
CXCL14 (345034) Hs.24395
FBLN1 (502367) Hs.445240
COL6A1 (263716) Hs.415997
TGFBR3 (209655) Hs.342874
C1R (83549) Hs.376414
ADAMTS4 (2455578) Hs.211604
COL6A2 (810632) Hs.420269
IGFBP5 (45542) Hs.380833
EST (32609)
NFIB (416959) Hs.302690
LAMA2 (471642) Hs.445120
DPYSL2 (841620) Hs.173381
COL6A3 (138991) Hs.233240
RBPMS (343443) Hs.195825
HOXA5 (1155071) Hs.37034
PBX3 (448386) Hs.294101
EST (68527) Hs.516200
FOXO1A (782835) Hs.170133
HFL1 (450060) Hs.296941
EST (1558799)
CILP (2420992) Hs.442180
C
10
1
0.1
STMN1 (1476065) Hs.209983
PRKCI (71622) Hs.496511
HMGA1 (782811) Hs.57301
HIST1H4B (701089) Hs.143080
HDGF (813673) Hs.89525
SMARCC1 (1475797) Hs.162086
MRPS6 (839882) Hs.268016
PTTG1 (781089) Hs.350966
PRAME (897956) Hs.30743
SPINT2 (814378) Hs.31439
Legend
Geometric mean ratios of postchemo
Geometric mean ratios of normal ovary
Geometric mean ratios of chemosensitive
Geometric mean ratios of chemoresistant
D
10
1
0.1
POU3F4 (2466195) Hs.2229
GABRA2 (53384) Hs.91343
CDKN1C (2413955) Hs.106070
ADAMTS1 (62263) Hs.8230
PLCL2 (455227) Hs.54886
GLDC (248261) Hs.479790
HIST1H2BK (290841) Hs.247817
GSTP1 (136235) Hs.411509
HPRT1 (280507) Hs.412707
CCT3 (420096) Hs.1708
MASP2 (436297) Hs.119983
MIF (2565981) Hs.407995
SPP1 (378461) Hs.313


Primary Tumors
Post-chemo Tumors
chemosensitive
chemoresistant
chemosensitive
chemoresistant-intrinsic
chemoresistant-acquired