FIG. 1A

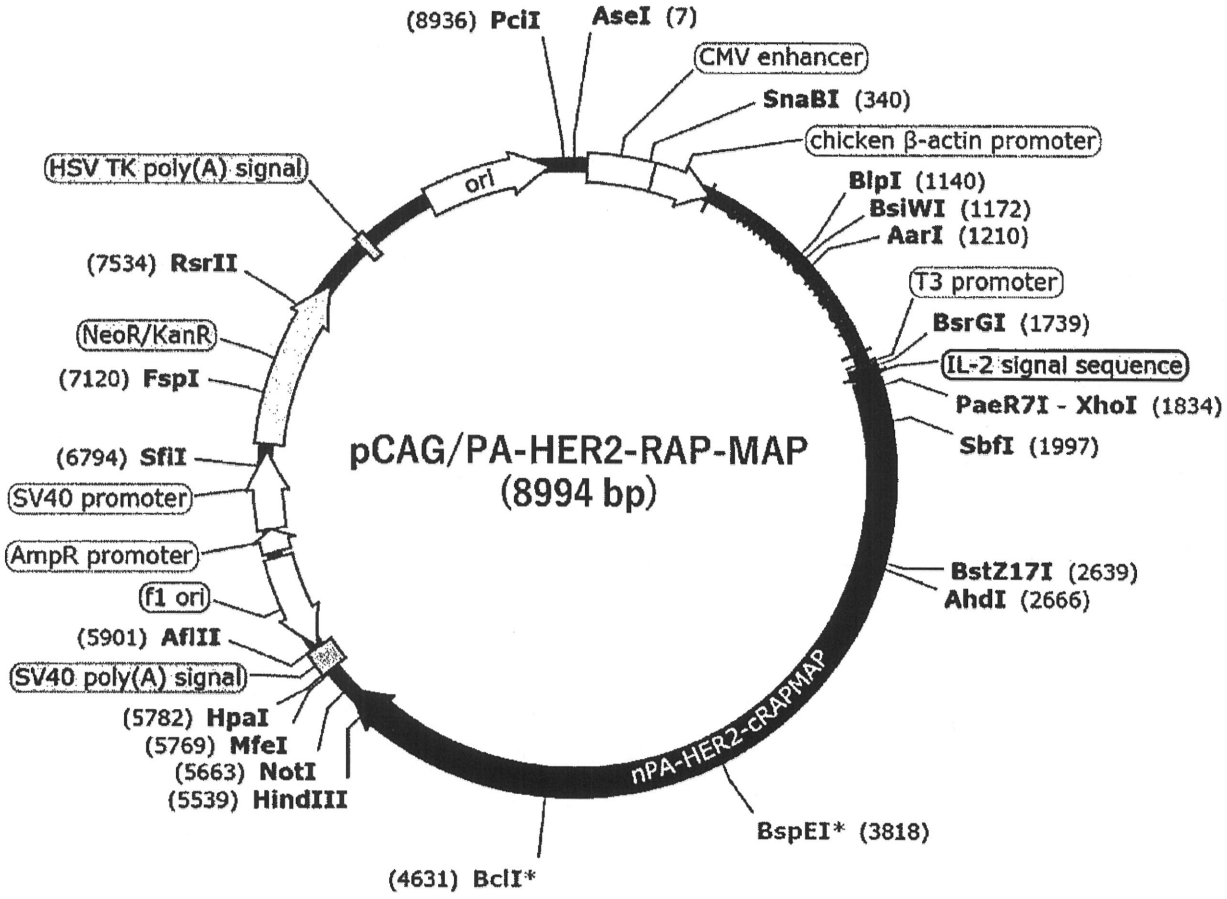

pCAG/PA-HER2-RAP-MAP
(8994 bp)
(8936) PciI
AseI (7)
CMV enhancer
SnaBI (340)
chicken β-actin promoter
BlpI (1140)
BsiWI (1172)
AarI (1210)
T3 promoter
BsrGI (1739)
IL-2 signal sequence
PaeR7I - XhoI (1834)
SbfI (1997)
BstZ17I (2639)
AhdI (2666)
BspEI* (3818)
(4631) BclI*
HindIII (5539)
NotI (5663)
MfeI (5769)
HpaI (5782)
SV40 poly(A) signal
AflII (5901)
f1 ori
AmpR promoter
SV40 promoter
SfiI (6794)
FspI (7120)
NeoR/KanR
RsrII (7534)
HSV TK poly(A) signal
ori
nPA-HER2-cRAPMAP

FIG. 1B

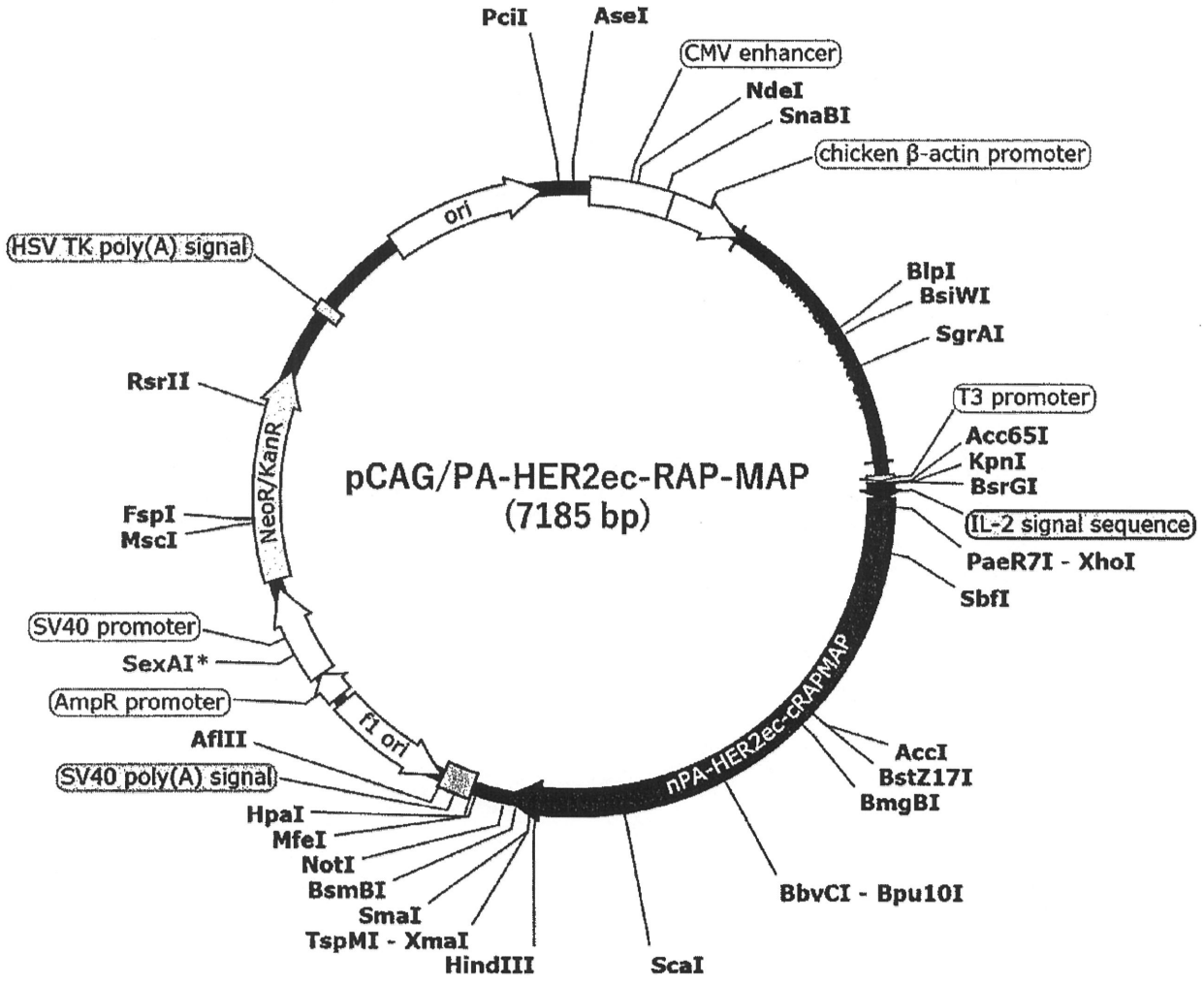

pCAG/PA-HER2ec-RAP-MAP
(7185 bp)
PciI
AseI
CMV enhancer
NdeI
SnaBI
chicken β-actin promoter
BlpI
BsiWI
SgrAI
T3 promoter
Acc65I
KpnI
BsrGI
IL-2 signal sequence
PaeR7I - XhoI
SbfI
nPA-HER2ec-cRAPMAP
AccI
BstZ17I
BmgBI
BbvCI - Bpu10I
ScaI
HindIII
TspMI - XmaI
SmaI
BsmBI
NotI
MfeI
HpaI
SV40 poly(A) signal
AflII
f1 ori
AmpR promoter
SexAI*
SV40 promoter
FspI
MscI
NeoR/KanR
RsrII
HSV TK poly(A) signal
ori

FIG. 2

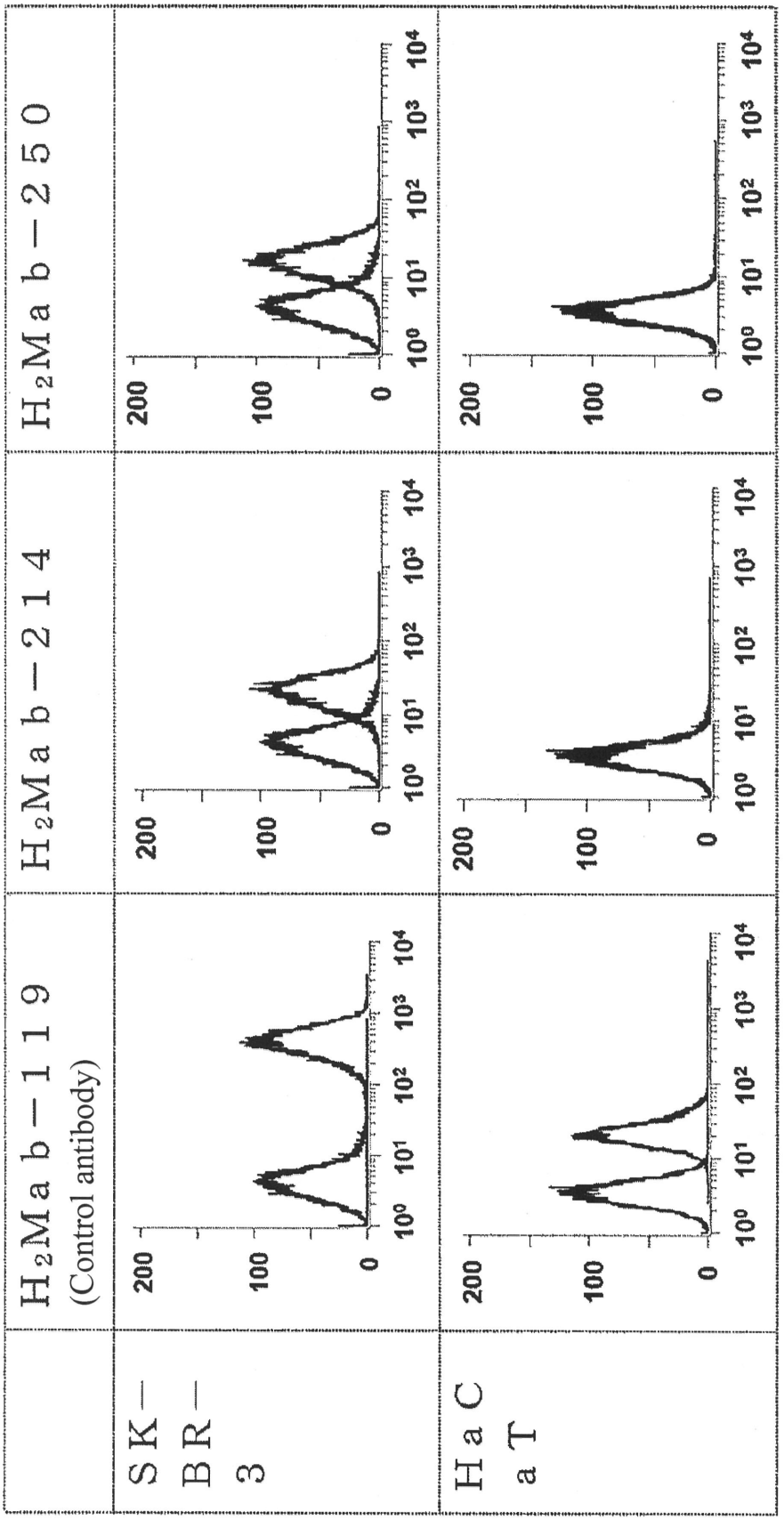

H2Mab-119
(Control antibody)
H2Mab-214
H2Mab-250
SK-BR-3
HaCaT
200
100
0
10^0 10^1 10^2 10^3 10^4

FIG. 3

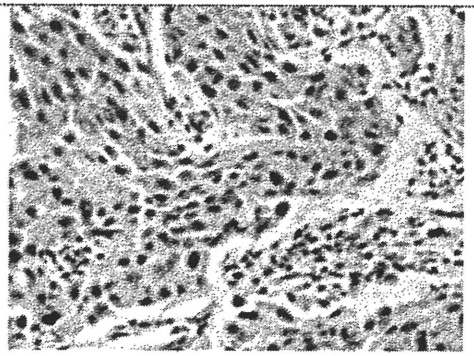
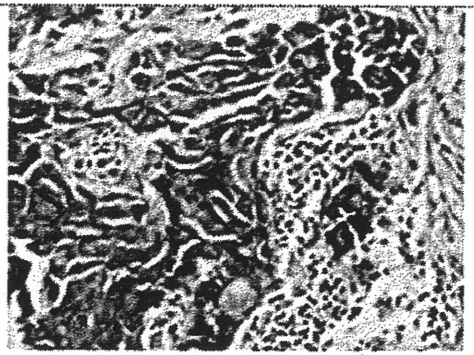
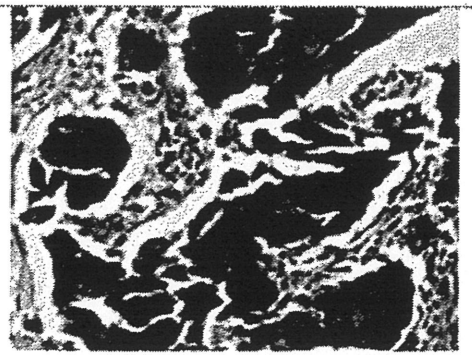
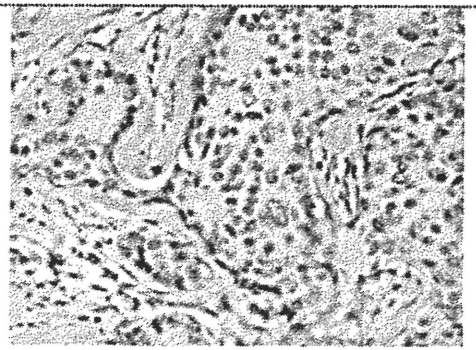
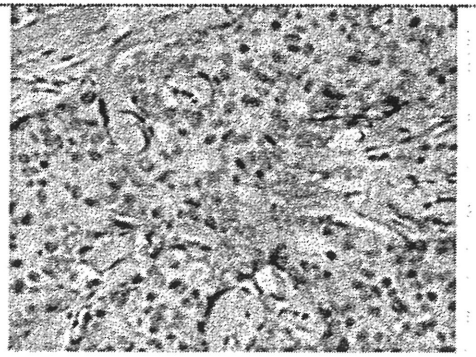
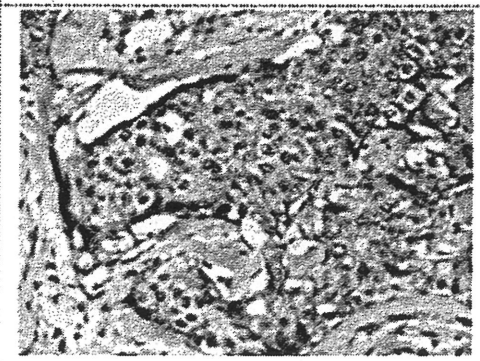
HER2-negative breast cancer	$H_2Mab-119$ (Control antibody)	$H_2Mab-214$	$H_2Mab-250$
TMA Core F 10	 HER2 Negative	 HER2 2+	 HER2 3+
TMA Core F 11	 HER2 Negative	 HER2 1+	 HER2 1+

FIG. 4

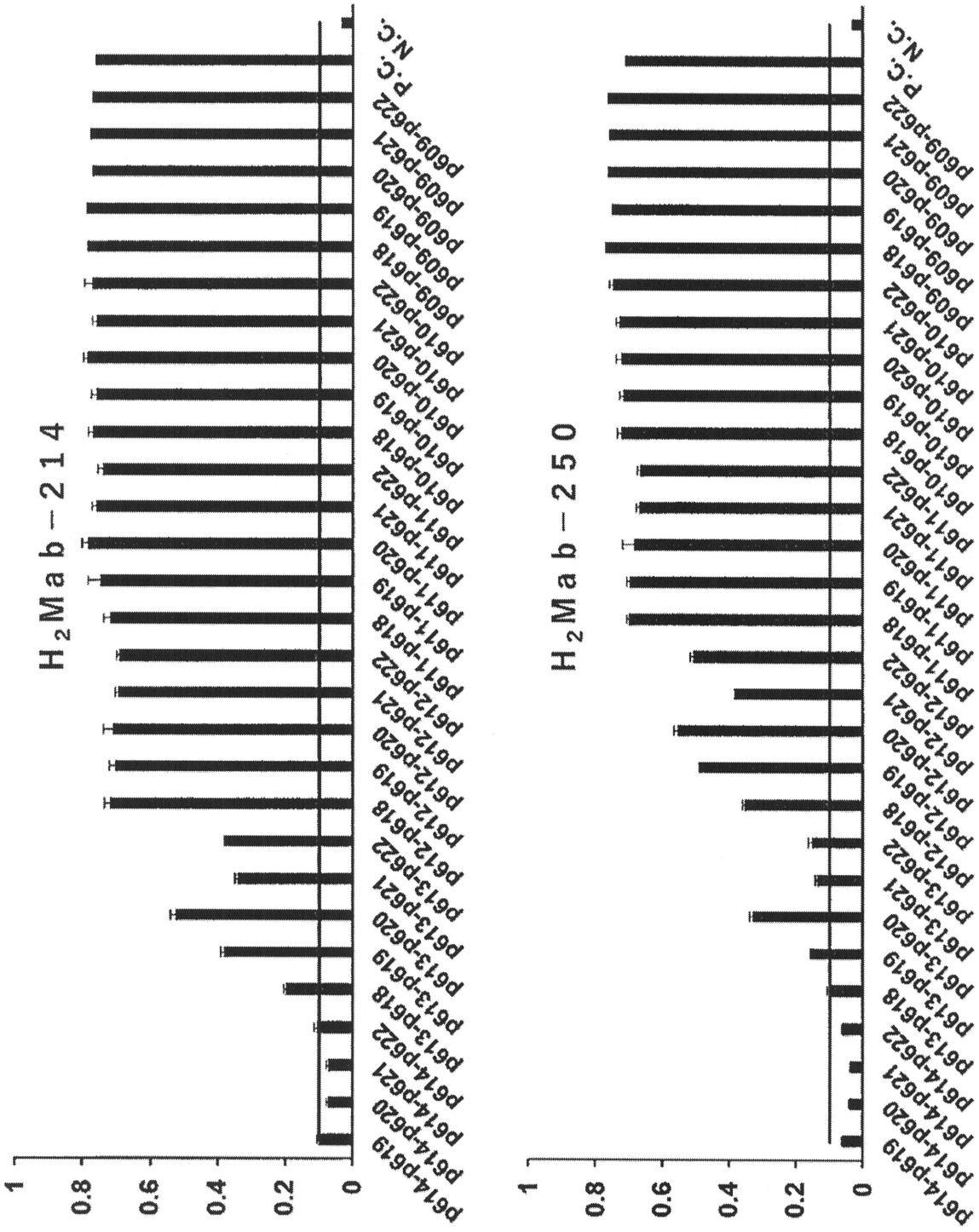

H2Mab-214
H2Mab-250
1
0.8
0.6
0.4
0.2
0
p614-p619
p614-p620
p614-p621
p614-p622
p613-p618
p613-p619
p613-p620
p613-p621
p613-p622
p612-p618
p612-p619
p612-p620
p612-p621
p612-p622
p611-p618
p611-p619
p611-p620
p611-p621
p611-p622
p610-p618
p610-p619
p610-p620
p610-p621
p610-p622
p609-p618
p609-p619
p609-p620
p609-p621
p609-p622
P.C.
N.C.

FIG. 5

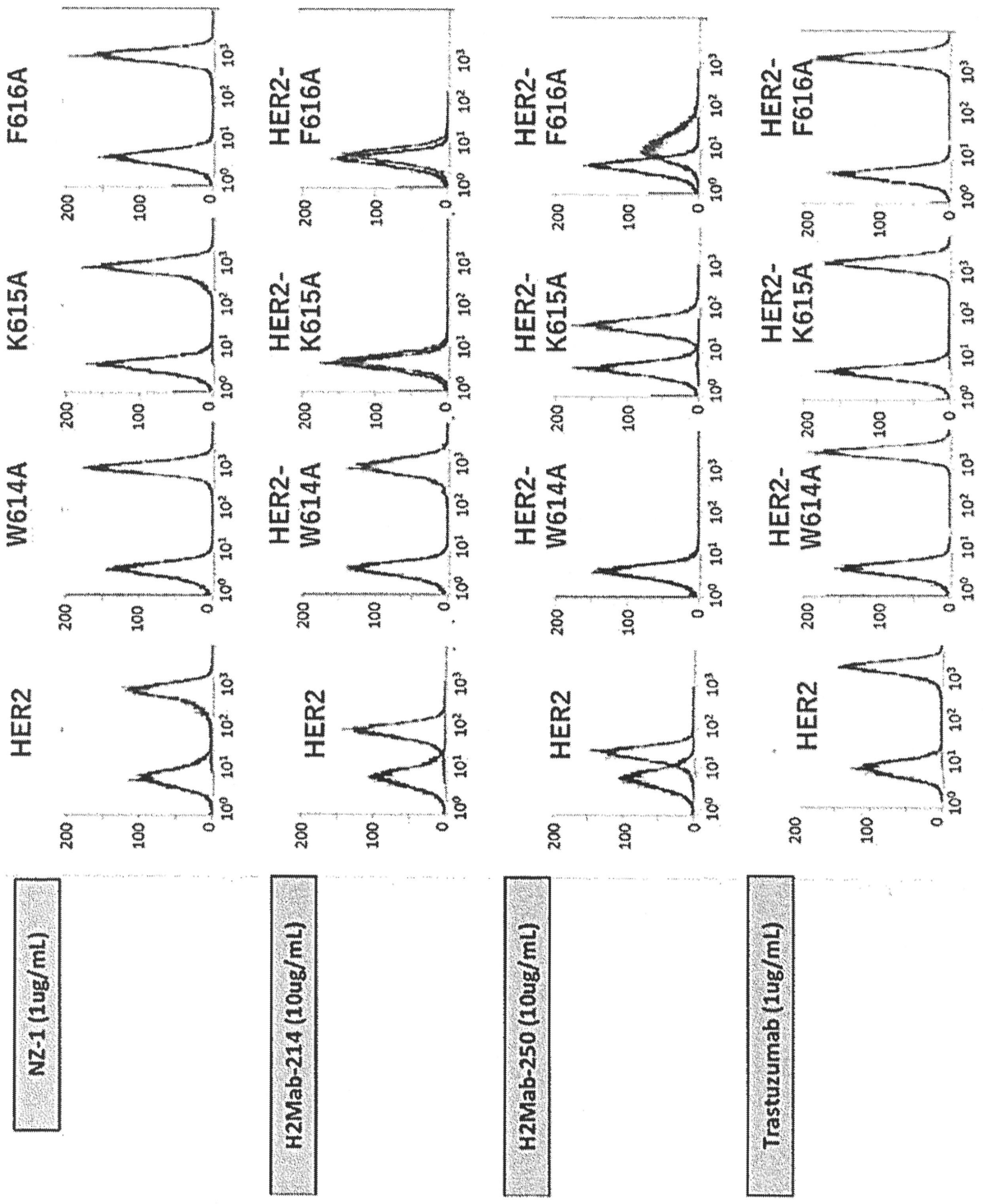
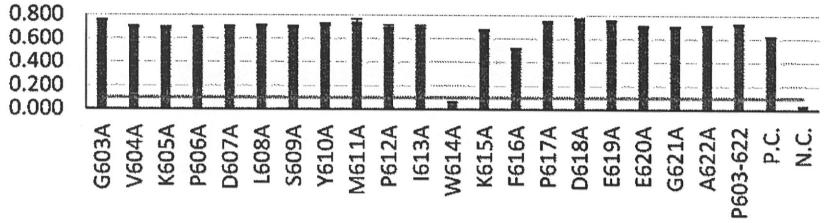

HER2
HER2-W614A
HER2-K615A
HER2-F616A
NZ-1 (1ug/mL)
H2Mab-214 (10ug/mL)
H2Mab-250 (10ug/mL)
Trastuzumab (1ug/mL)

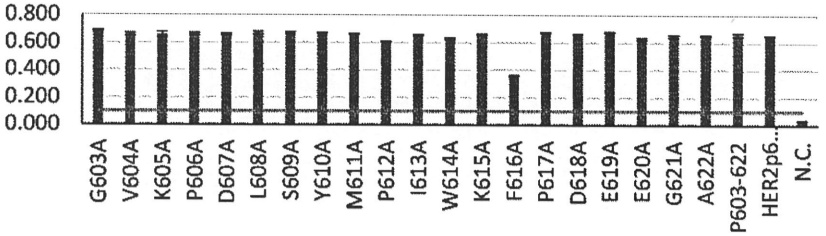
FIG. 6A

Results of epitope mapping

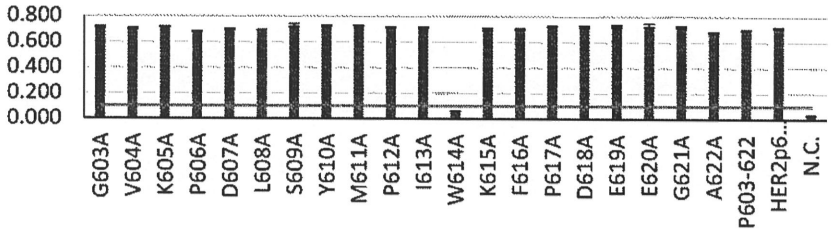
H_2Mab-250 Estimated epitope : **GVKPDLSYMPIWKFPDEEGA**



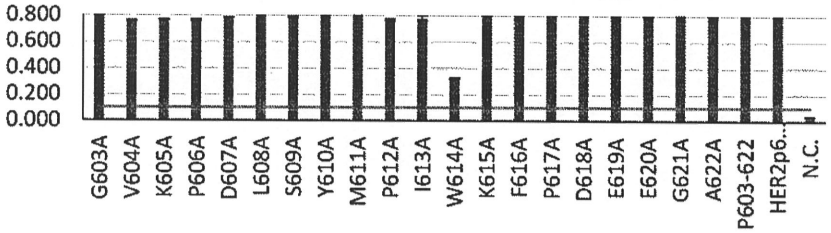
H_2Mab-279 Estimated epitope : **GVKPDLSYMPIWKFPDEEGA**



H_2Mab-280 Estimated epitope : **GVKPDLSYMPIWKFPDEEGA**



H_2Mab-281 Estimated epitope : **GVKPDLSYMPIWKFPDEEGA**



H_2Mab-282 Estimated epitope : **GVKPDLSYMPIWKFPDEEGA**

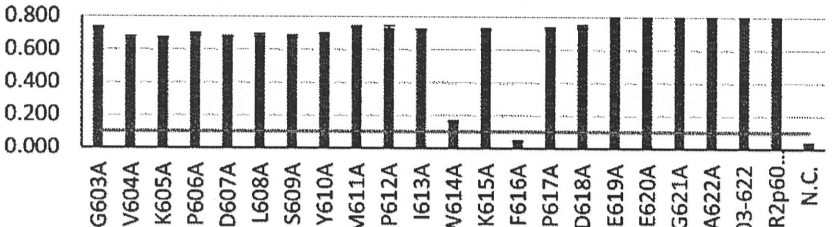
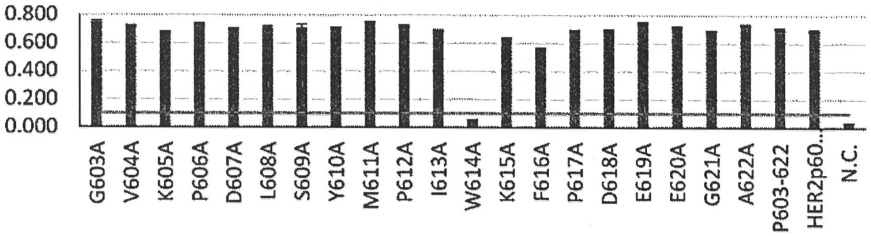


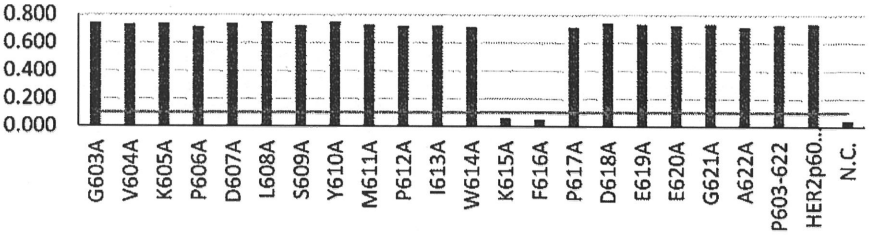
FIG. 6B

Results of epitope mapping

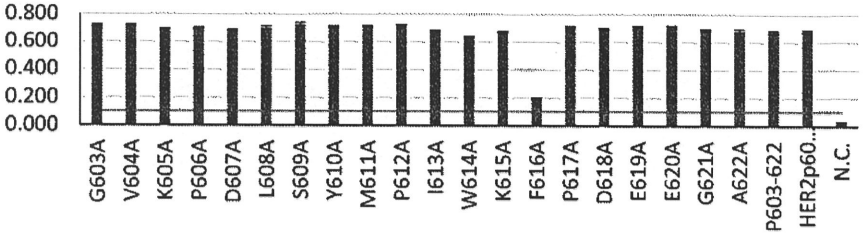
H_2Mab-283 Estimated epitope : **GVKPDLSYMPIWKFPDEEGA**



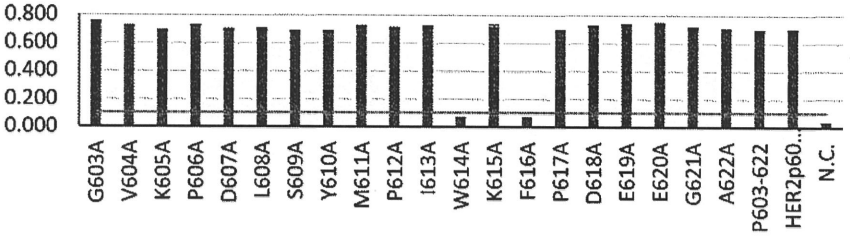
H_2Mab-284 Estimated epitope : **GVKPDLSYMPIWKFPDEEGA**



H_2Mab-285 Estimated epitope : **GVKPDLSYMPIWKFPDEEGA**



H_2Mab-286 Estimated epitope : **GVKPDLSYMPIWKFPDEEGA**



H_2Mab-287 Estimated epitope : **GVKPDLSYMPIWKFPDEEGA**

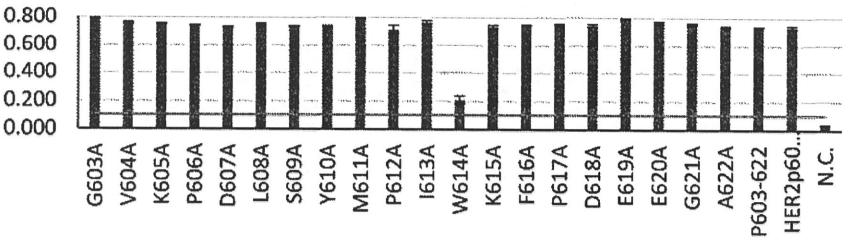


FIG. 6C

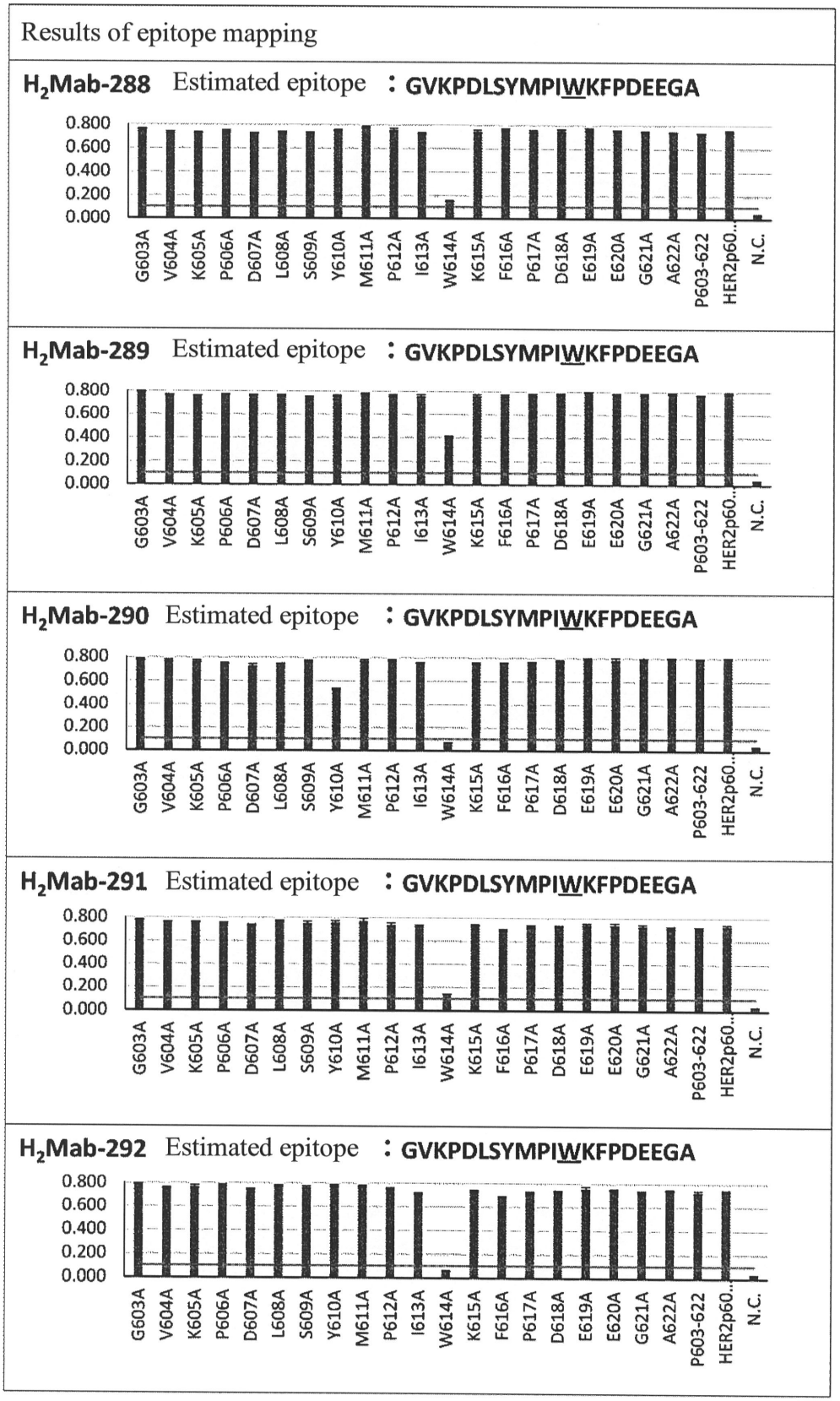

Results of epitope mapping
H2Mab-288 Estimated epitope : GVKPDLSYMPIWKFPDEEGA
H2Mab-289 Estimated epitope : GVKPDLSYMPIWKFPDEEGA
H2Mab-290 Estimated epitope : GVKPDLSYMPIWKFPDEEGA
H2Mab-291 Estimated epitope : GVKPDLSYMPIWKFPDEEGA
H2Mab-292 Estimated epitope : GVKPDLSYMPIWKFPDEEGA
0.800
0.600
0.400
0.200
0.000
G603A V604A K605A P606A D607A L608A S609A Y610A M611A P612A I613A W614A K615A F616A P617A D618A E619A E620A G621A A622A P603-622 HER2p60... N.C.

FIG. 6D

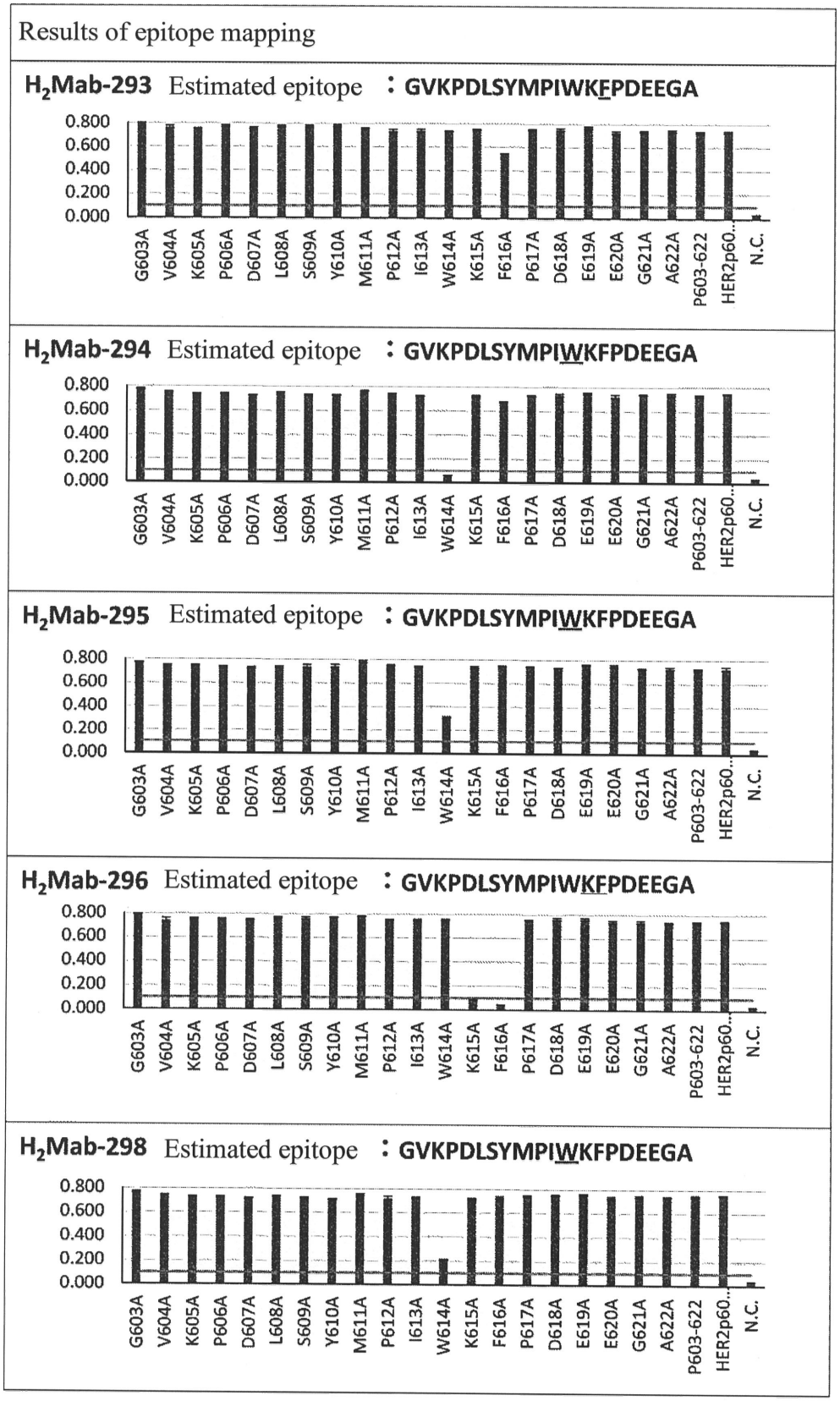

Results of epitope mapping
H2Mab-293 Estimated epitope : GVKPDLSYMPIWKFPDEEGA
H2Mab-294 Estimated epitope : GVKPDLSYMPIWKFPDEEGA
H2Mab-295 Estimated epitope : GVKPDLSYMPIWKFPDEEGA
H2Mab-296 Estimated epitope : GVKPDLSYMPIWKFPDEEGA
H2Mab-298 Estimated epitope : GVKPDLSYMPIWKFPDEEGA
0.800
0.600
0.400
0.200
0.000
G603A
V604A
K605A
P606A
D607A
L608A
S609A
Y610A
M611A
P612A
I613A
W614A
K615A
F616A
P617A
D618A
E619A
E620A
G621A
A622A
P603-622
HER2p60...
N.C.

FIG. 6E

Results of epitope mapping

H_2Mab-299 Estimated epitope : **GVKPDLSYMPIWKFPDEEGA**

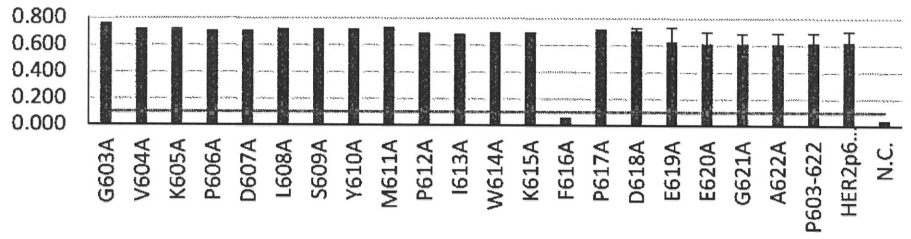


FIG. 7A

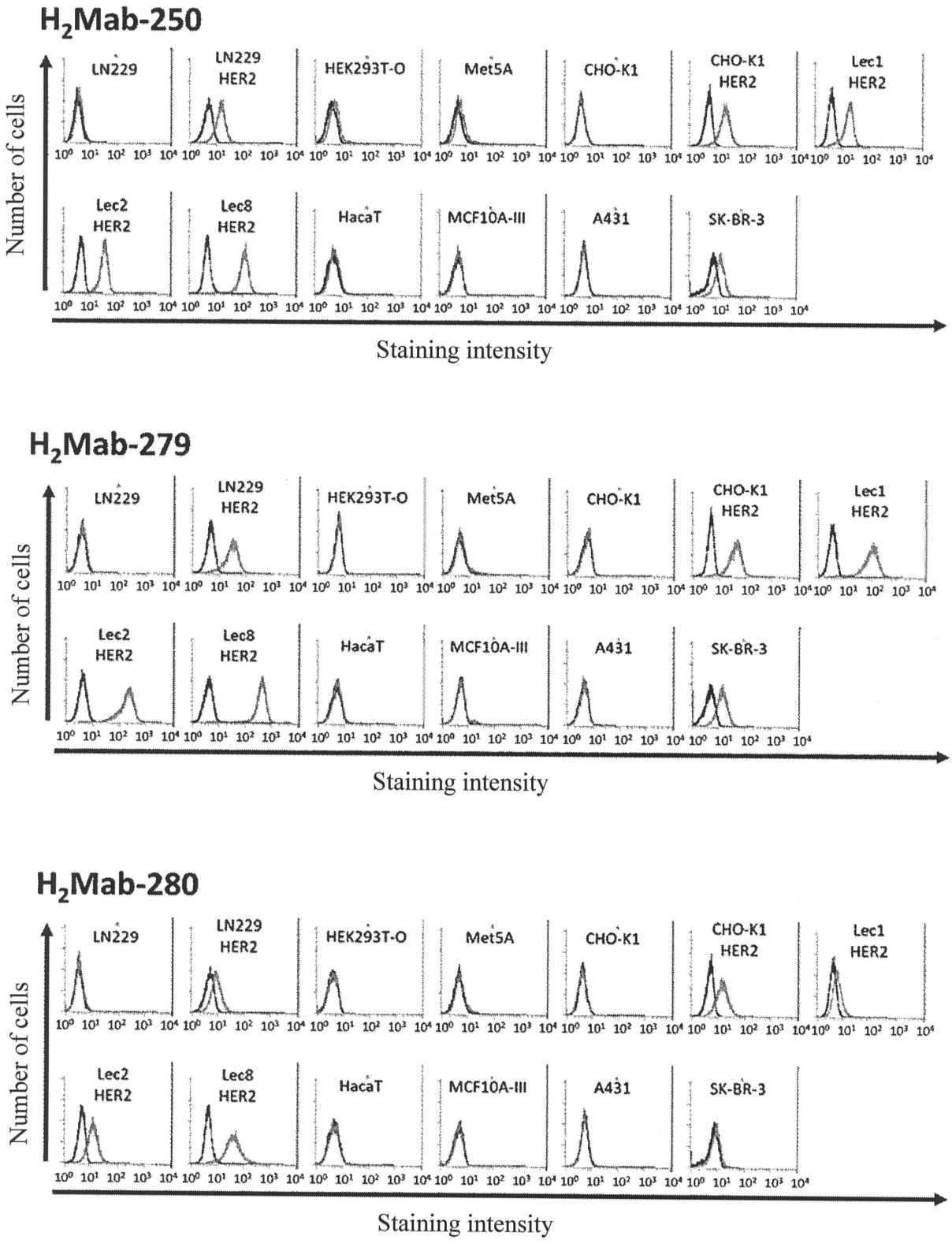

H2Mab-250
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HacaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-279
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HacaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-280
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HacaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity

FIG. 7B

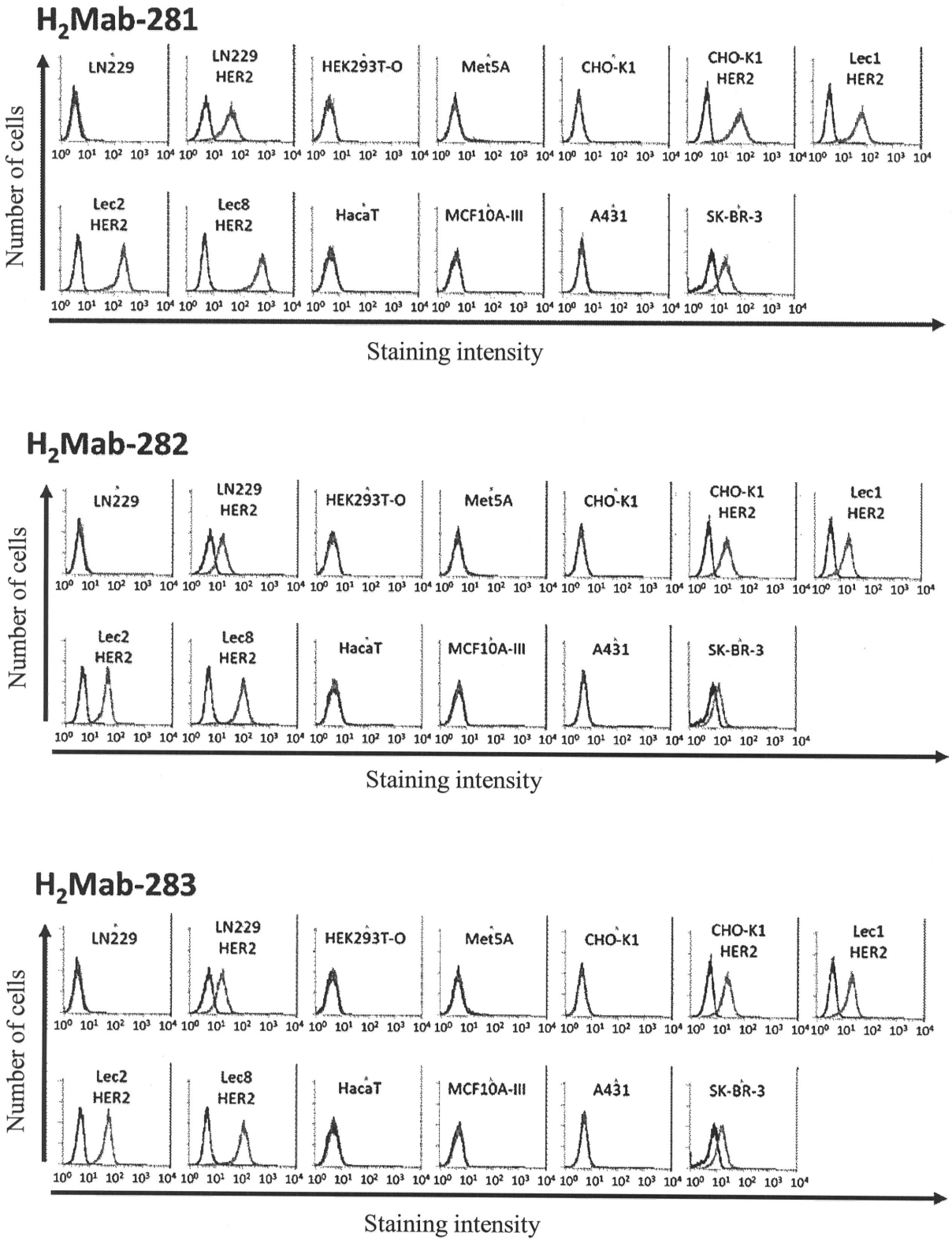

H2Mab-281
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HaCaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-282
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HaCaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-283
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HaCaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity

FIG. 7C

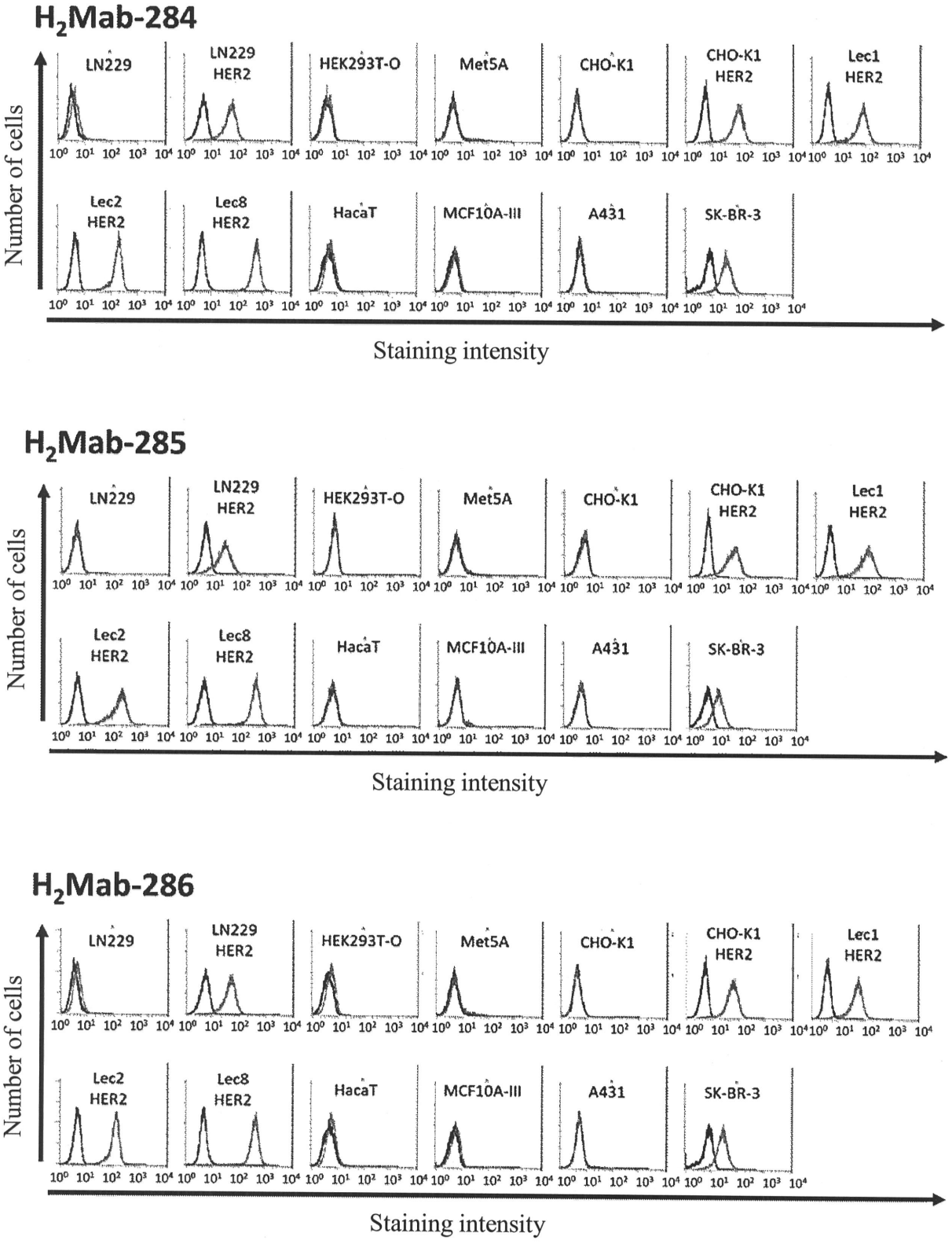

H2Mab-284
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HacaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-285
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HacaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-286
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HacaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity

FIG. 7D

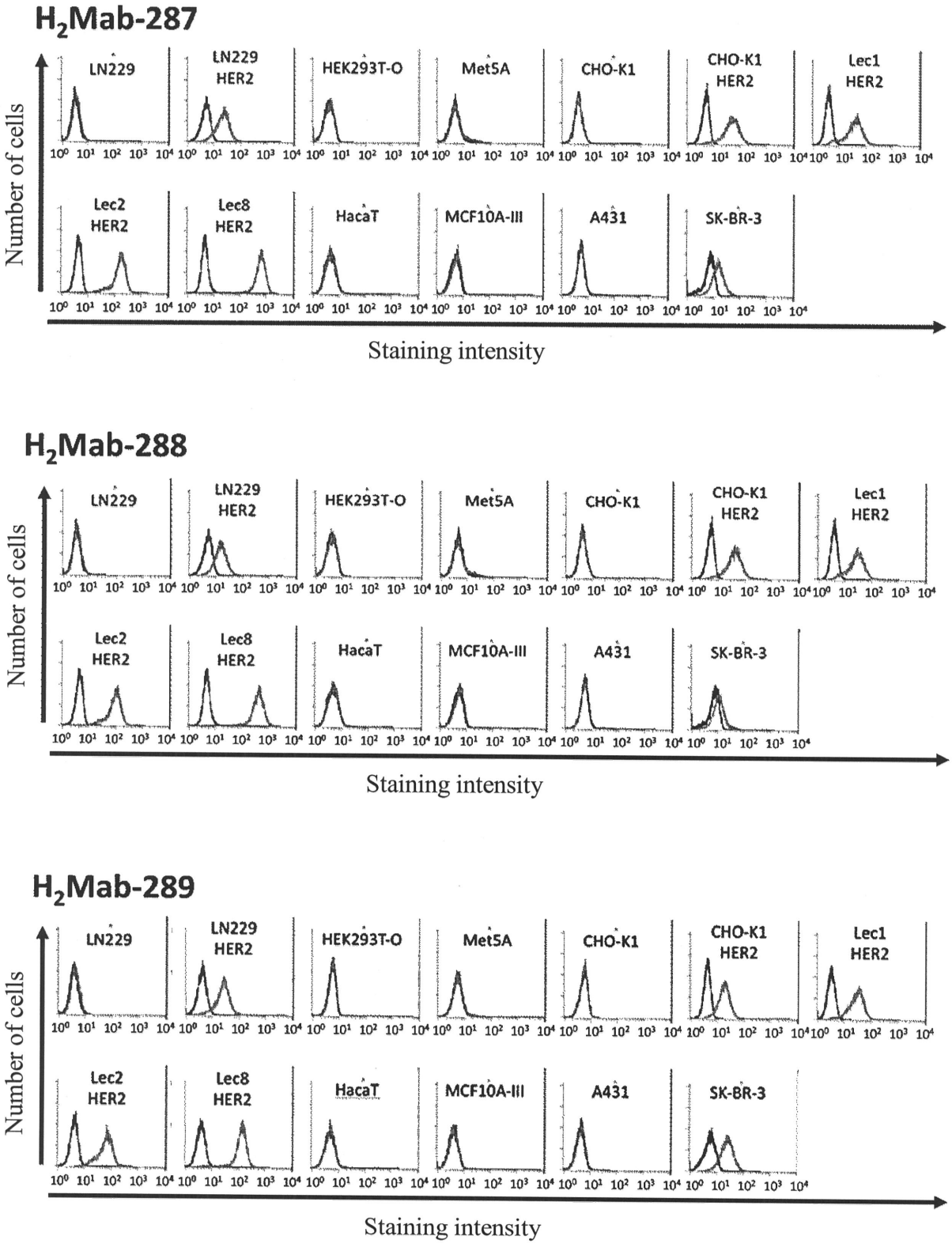

H2Mab-287
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HaCaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-288
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HaCaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-289
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HaCaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity

FIG. 7E

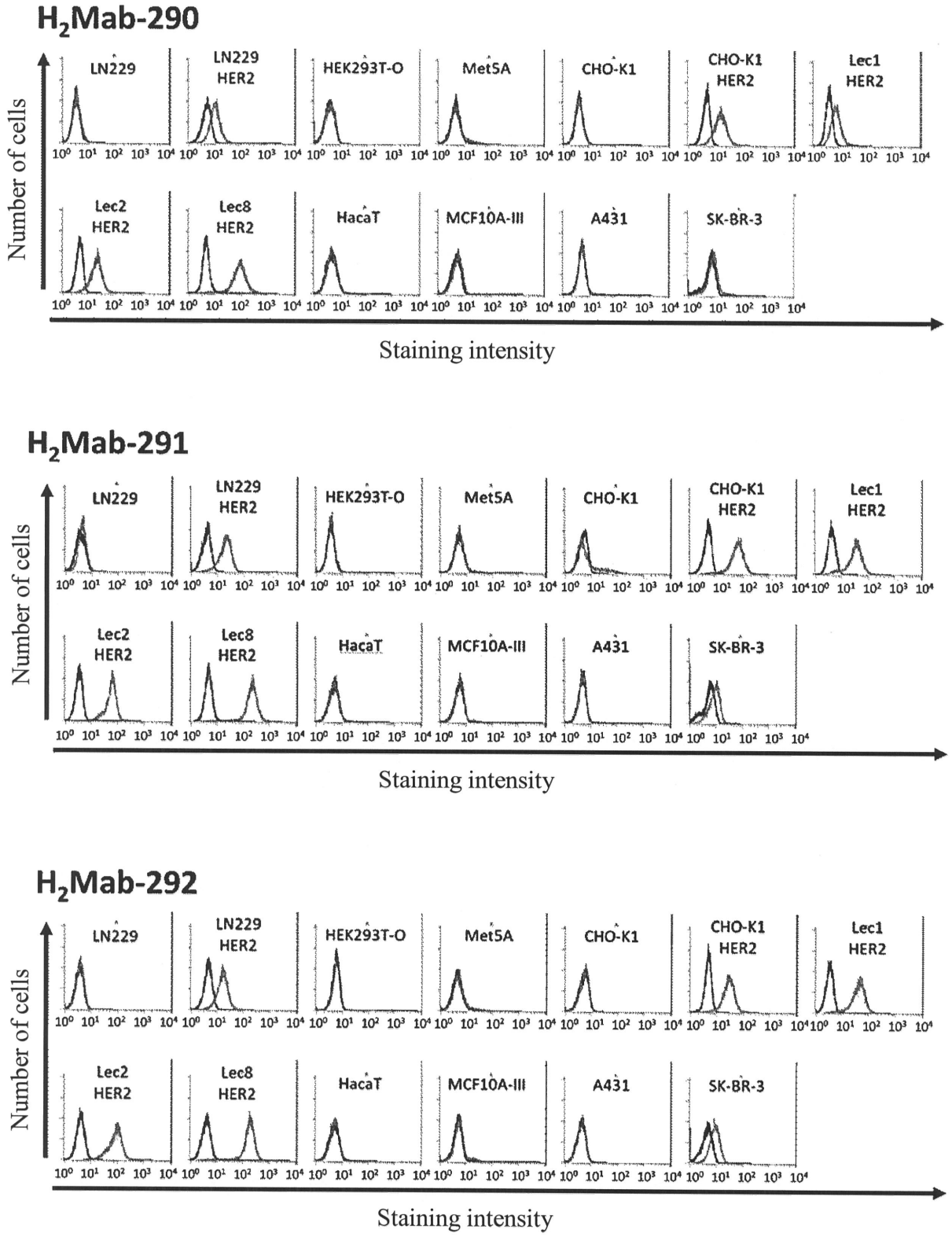

H2Mab-290
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HaCaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-291
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HaCaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-292
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HaCaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity

FIG. 7F

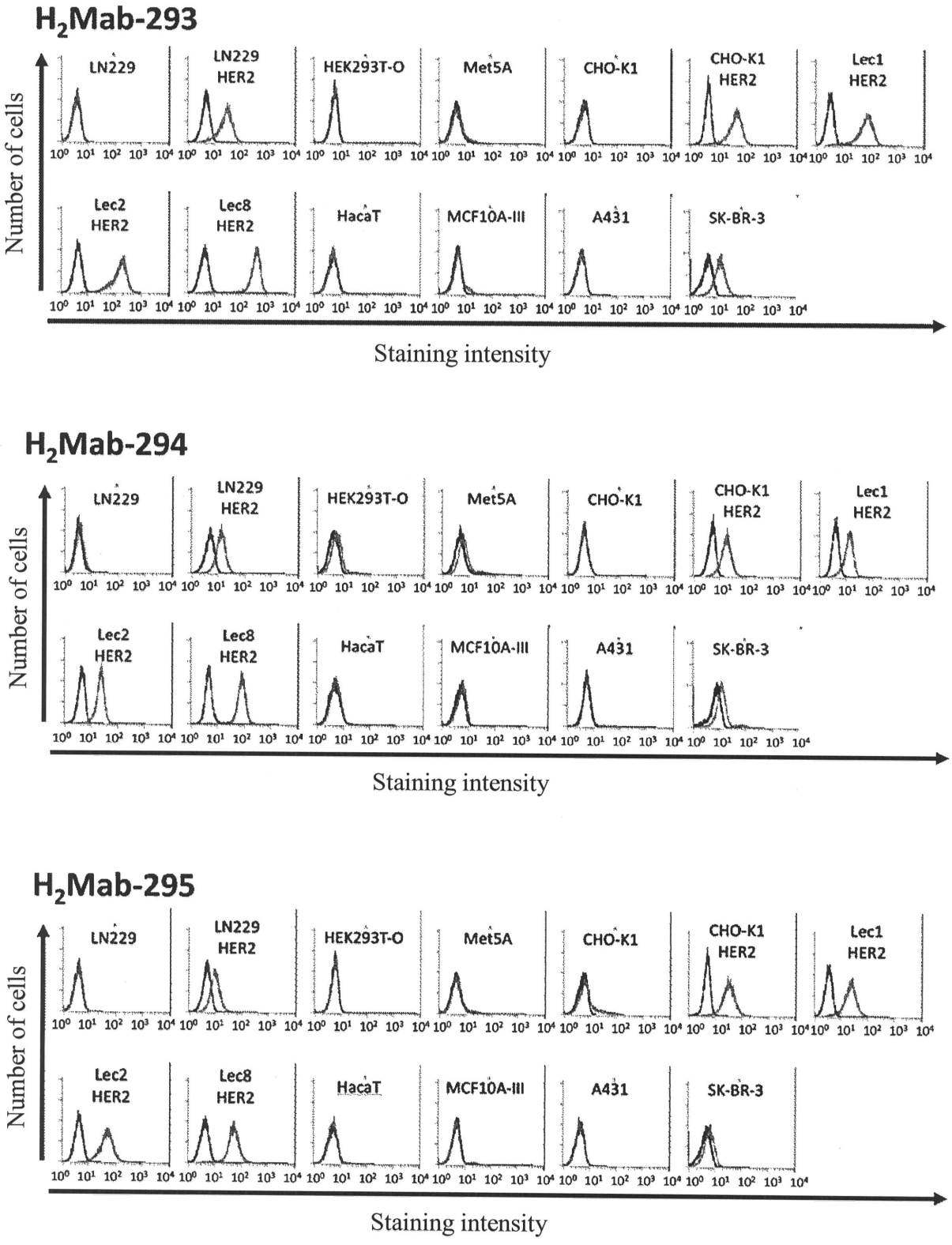

H2Mab-293
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HacaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-294
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HacaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-295
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HacaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity

FIG. 7G

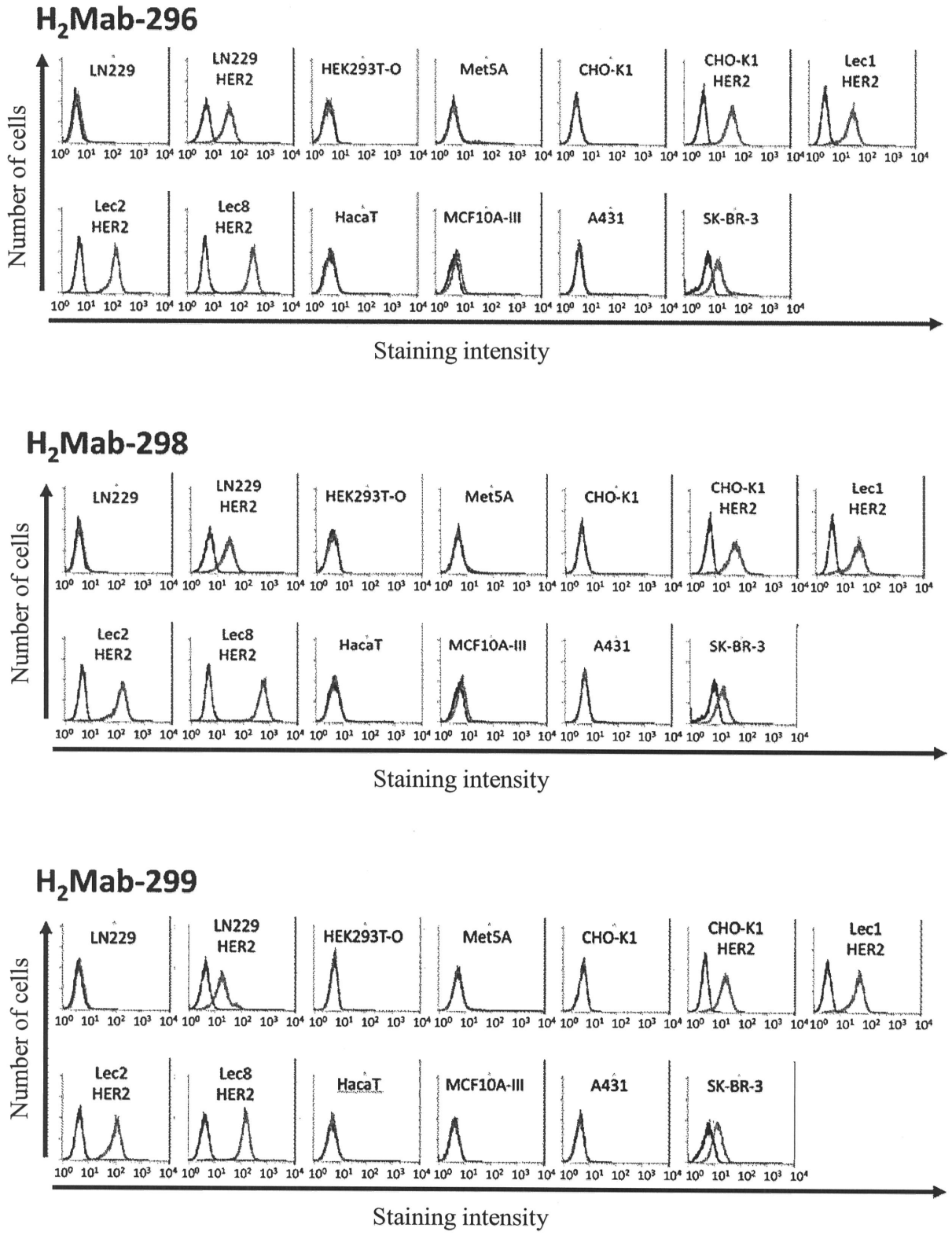
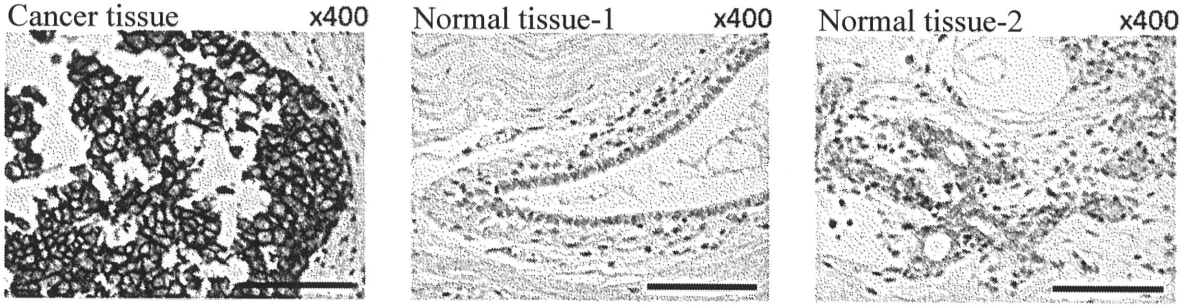

H2Mab-296
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HacaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-298
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HacaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity
H2Mab-299
LN229
LN229 HER2
HEK293T-O
Met5A
CHO-K1
CHO-K1 HER2
Lec1 HER2
Lec2 HER2
Lec8 HER2
HacaT
MCF10A-III
A431
SK-BR-3
Number of cells
Staining intensity

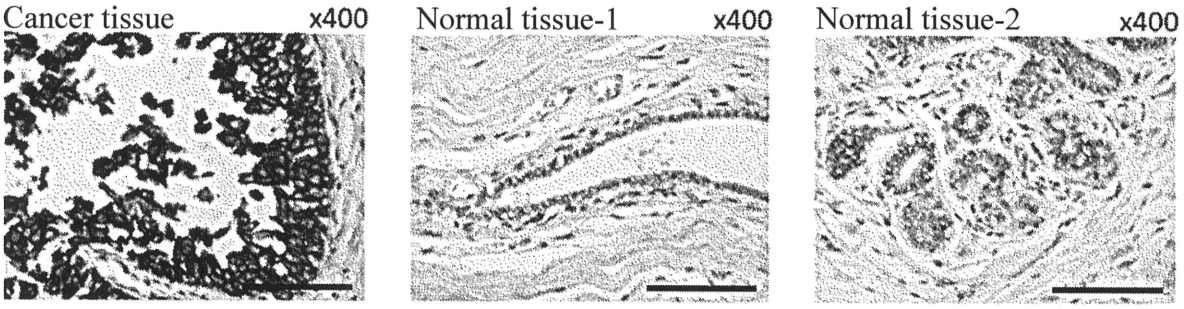
FIG. 8A

H_2Mab-250



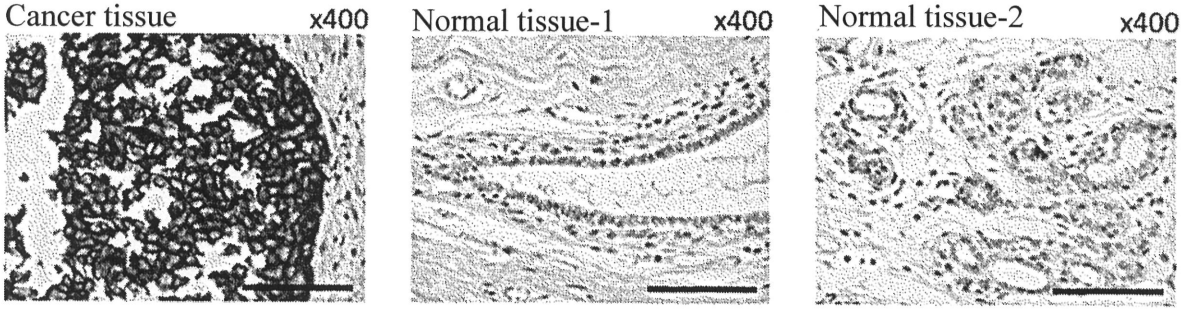
Scale bar: 100 μm

H_2Mab-279



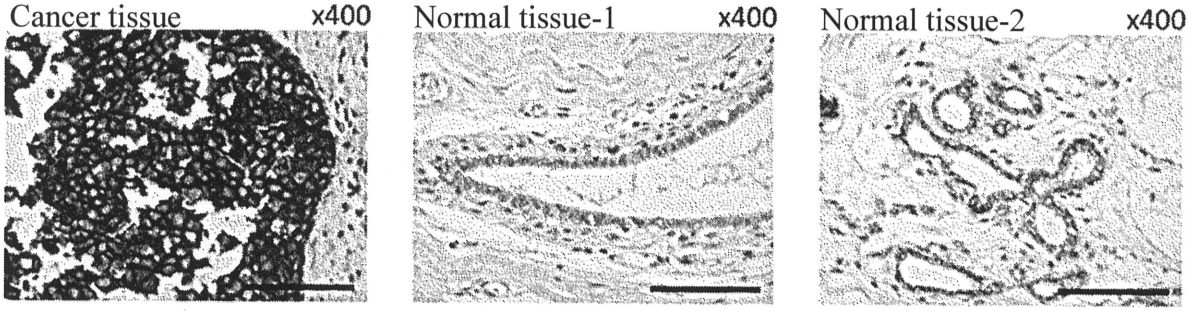
Scale bar: 100 μm

H_2Mab-280



Scale bar: 100 μm

H_2Mab-281



Scale bar: 100 μm

FIG. 8B

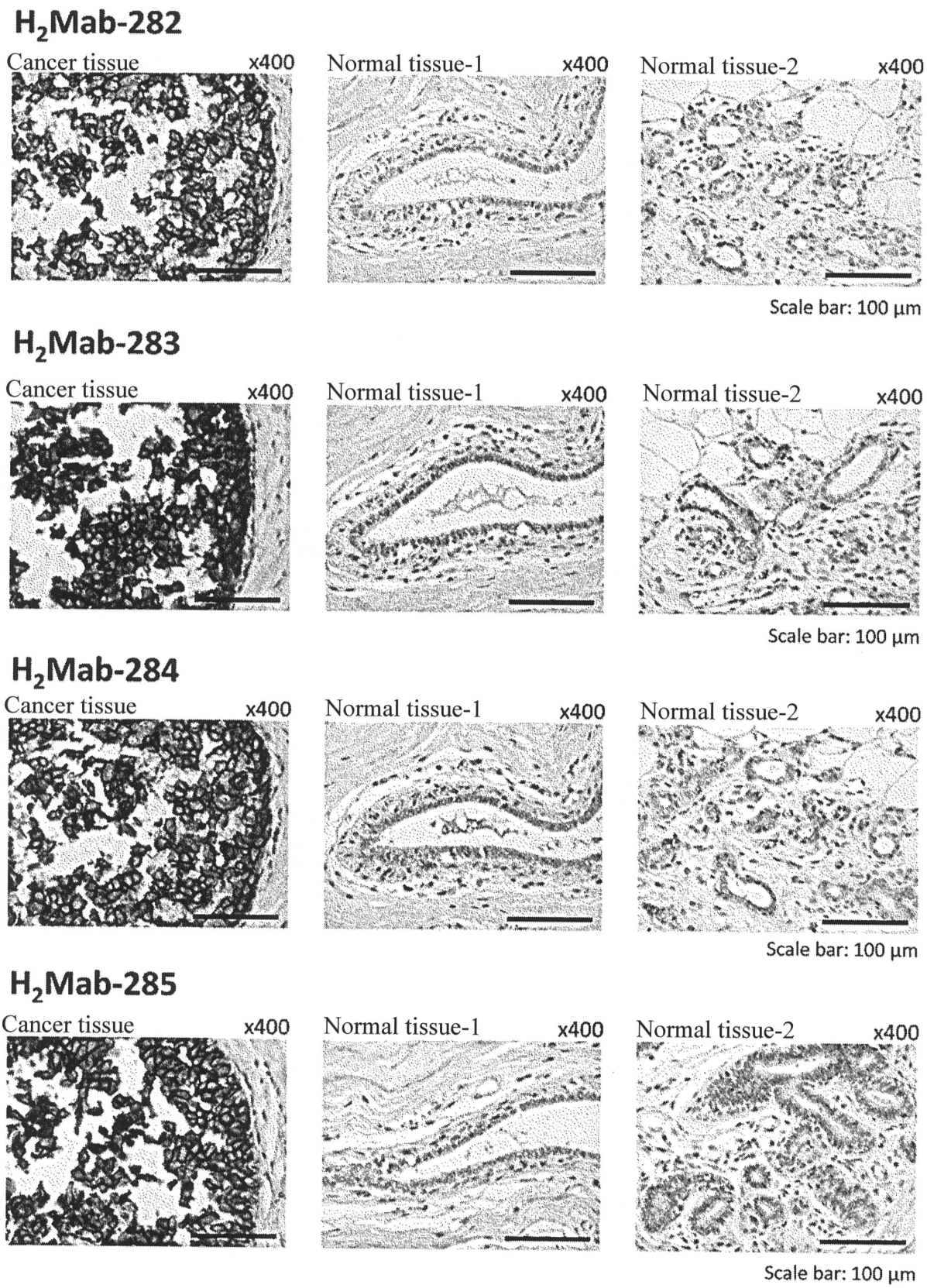
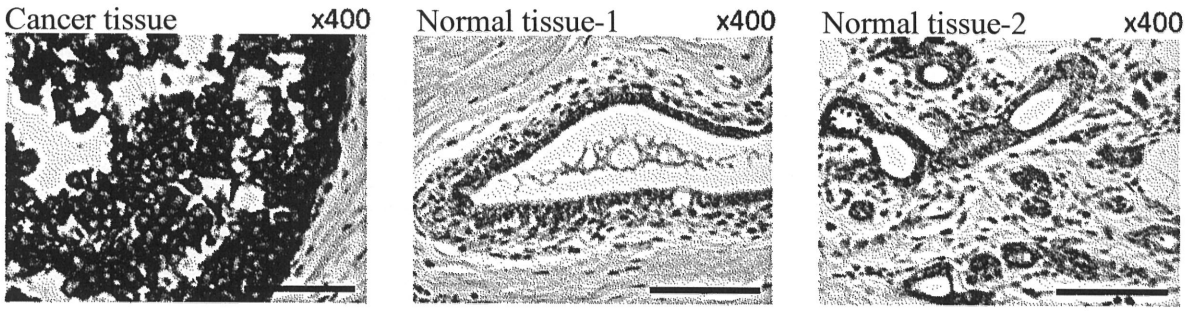

H2Mab-282
Cancer tissue x400
Normal tissue-1 x400
Normal tissue-2 x400
Scale bar: 100 μm
H2Mab-283
Cancer tissue x400
Normal tissue-1 x400
Normal tissue-2 x400
Scale bar: 100 μm
H2Mab-284
Cancer tissue x400
Normal tissue-1 x400
Normal tissue-2 x400
Scale bar: 100 μm
H2Mab-285
Cancer tissue x400
Normal tissue-1 x400
Normal tissue-2 x400
Scale bar: 100 μm

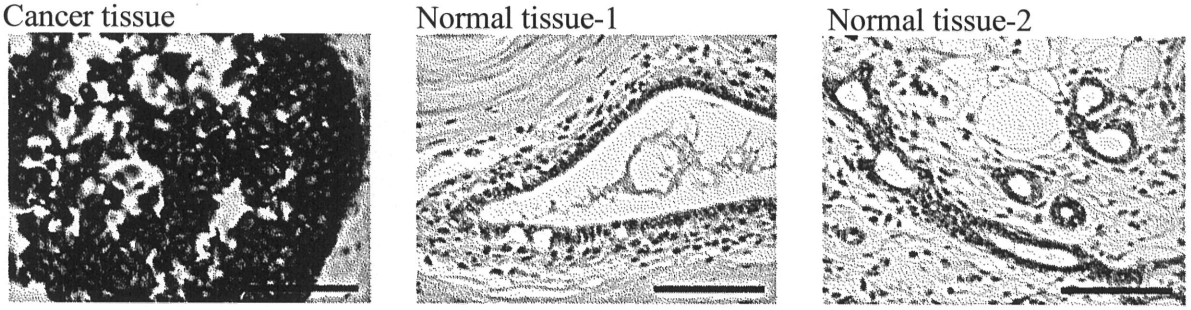
FIG. 8C

H_2Mab-286



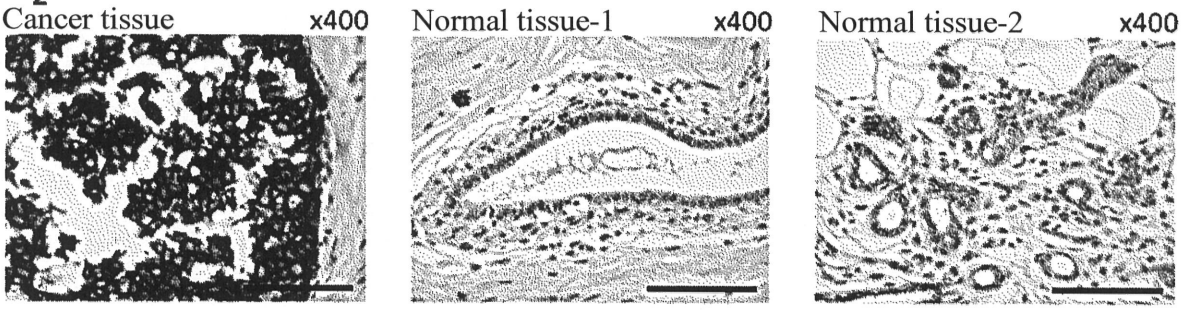
Scale bar: 100 μm

H_2Mab-287



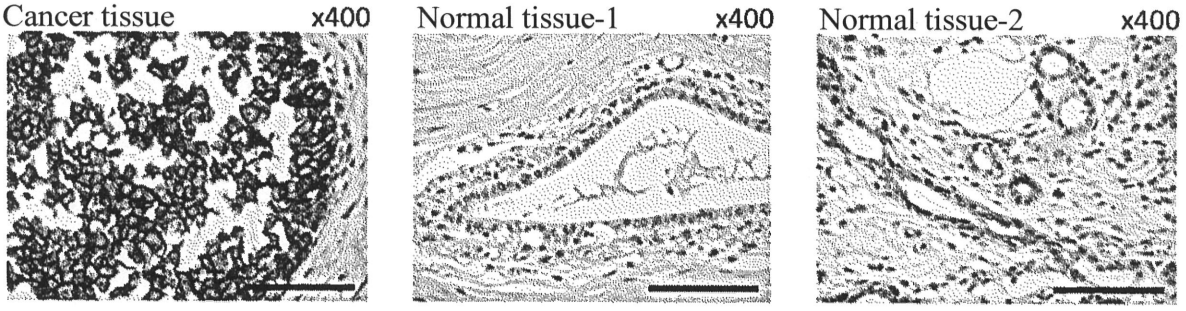
Scale bar: 100 μm

H_2Mab-288



Scale bar: 100 μm

H_2Mab-289



Scale bar: 100 μm

FIG. 8D

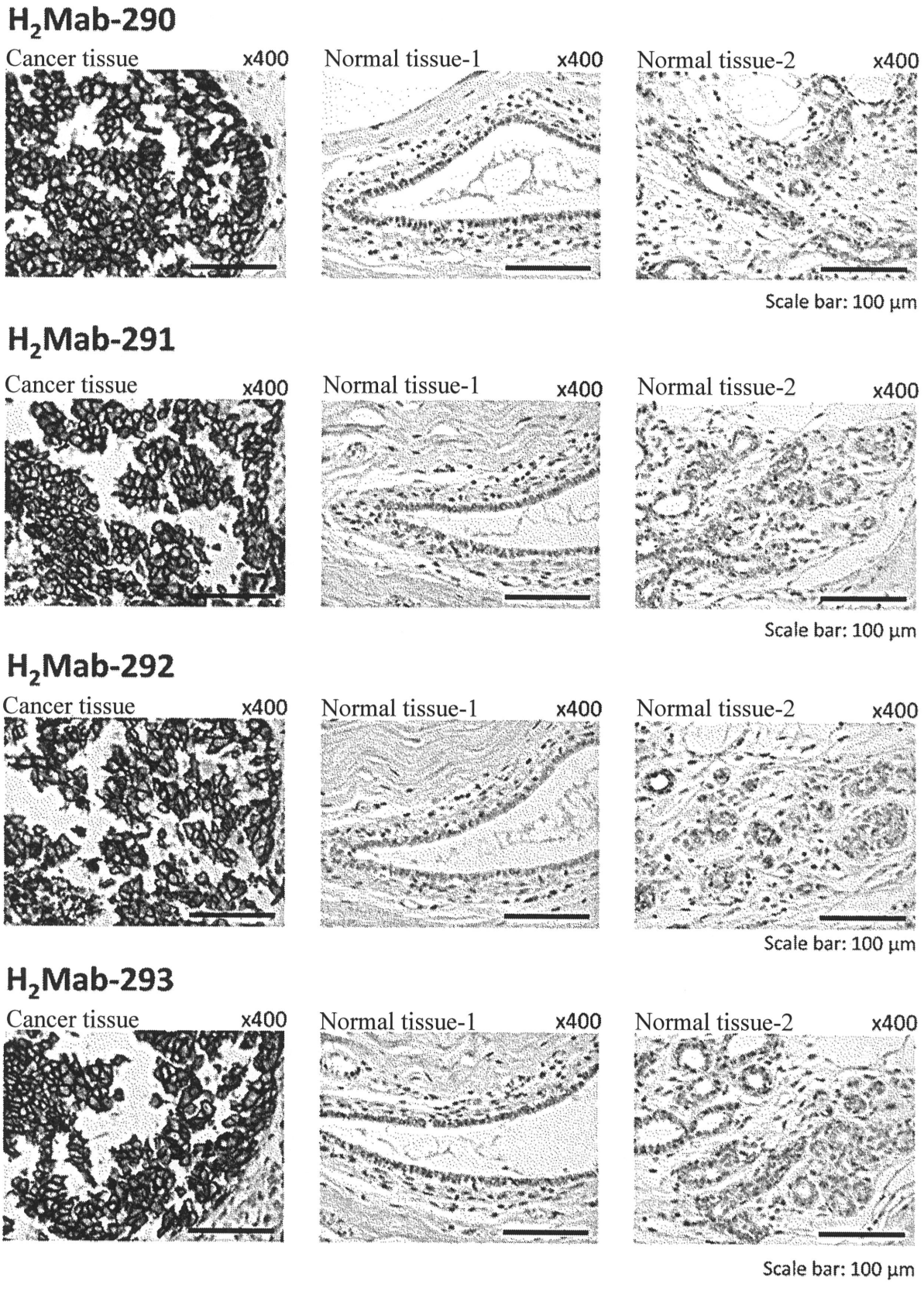
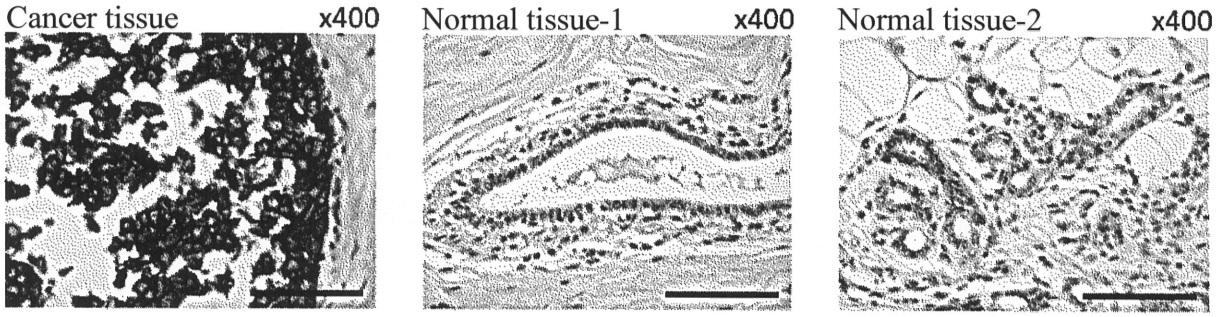
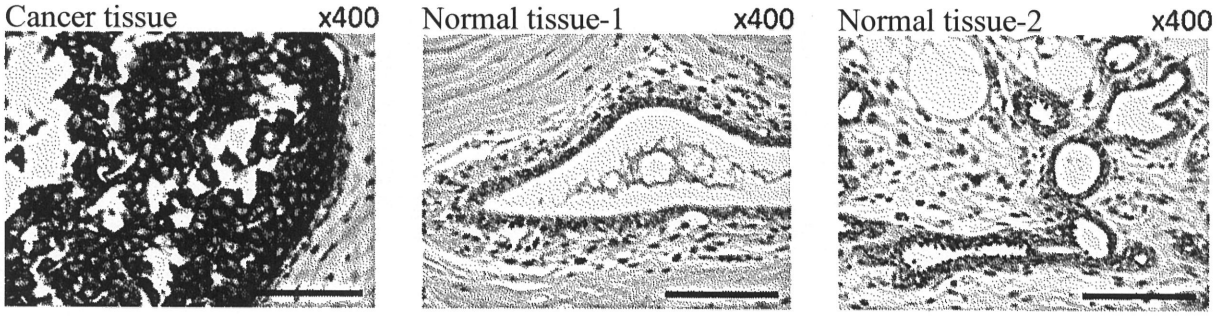

H2Mab-290
Cancer tissue x400
Normal tissue-1 x400
Normal tissue-2 x400
Scale bar: 100 μm
H2Mab-291
Cancer tissue x400
Normal tissue-1 x400
Normal tissue-2 x400
Scale bar: 100 μm
H2Mab-292
Cancer tissue x400
Normal tissue-1 x400
Normal tissue-2 x400
Scale bar: 100 μm
H2Mab-293
Cancer tissue x400
Normal tissue-1 x400
Normal tissue-2 x400
Scale bar: 100 μm

FIG. 8E

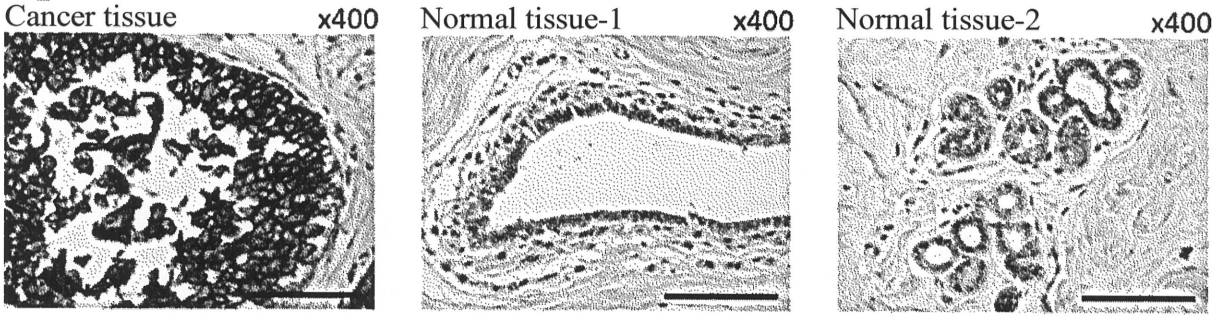
H_2Mab-294



H_2Mab-295



H_2Mab-296



H_2Mab-298

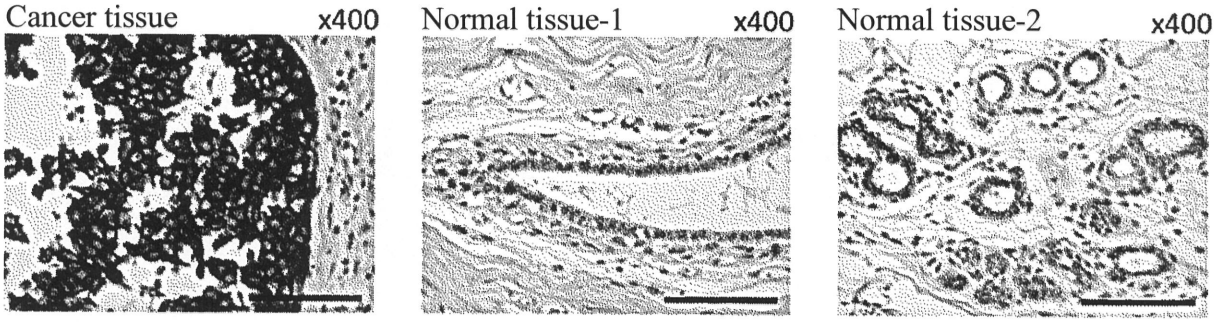
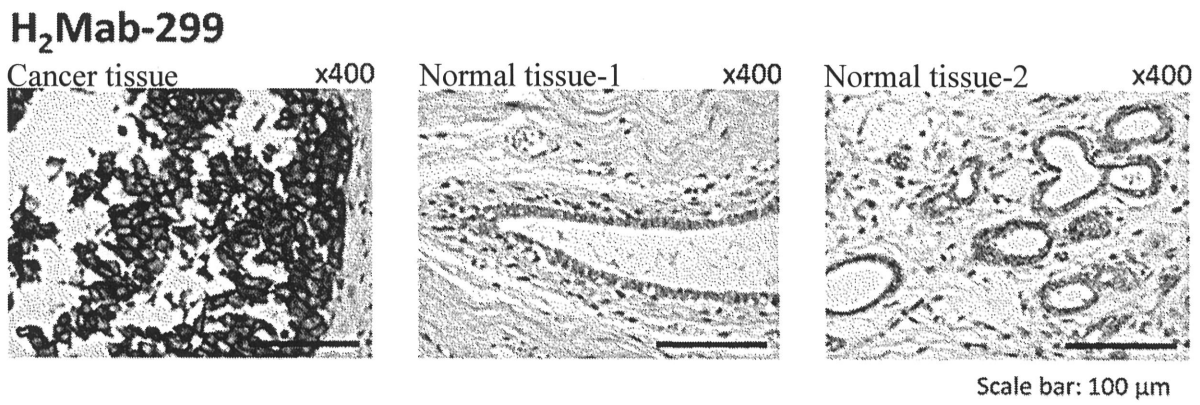


FIG. 8F


H2Mab-299
Cancer tissue
x400
Normal tissue-1
x400
Normal tissue-2
x400
Scale bar: 100 μm