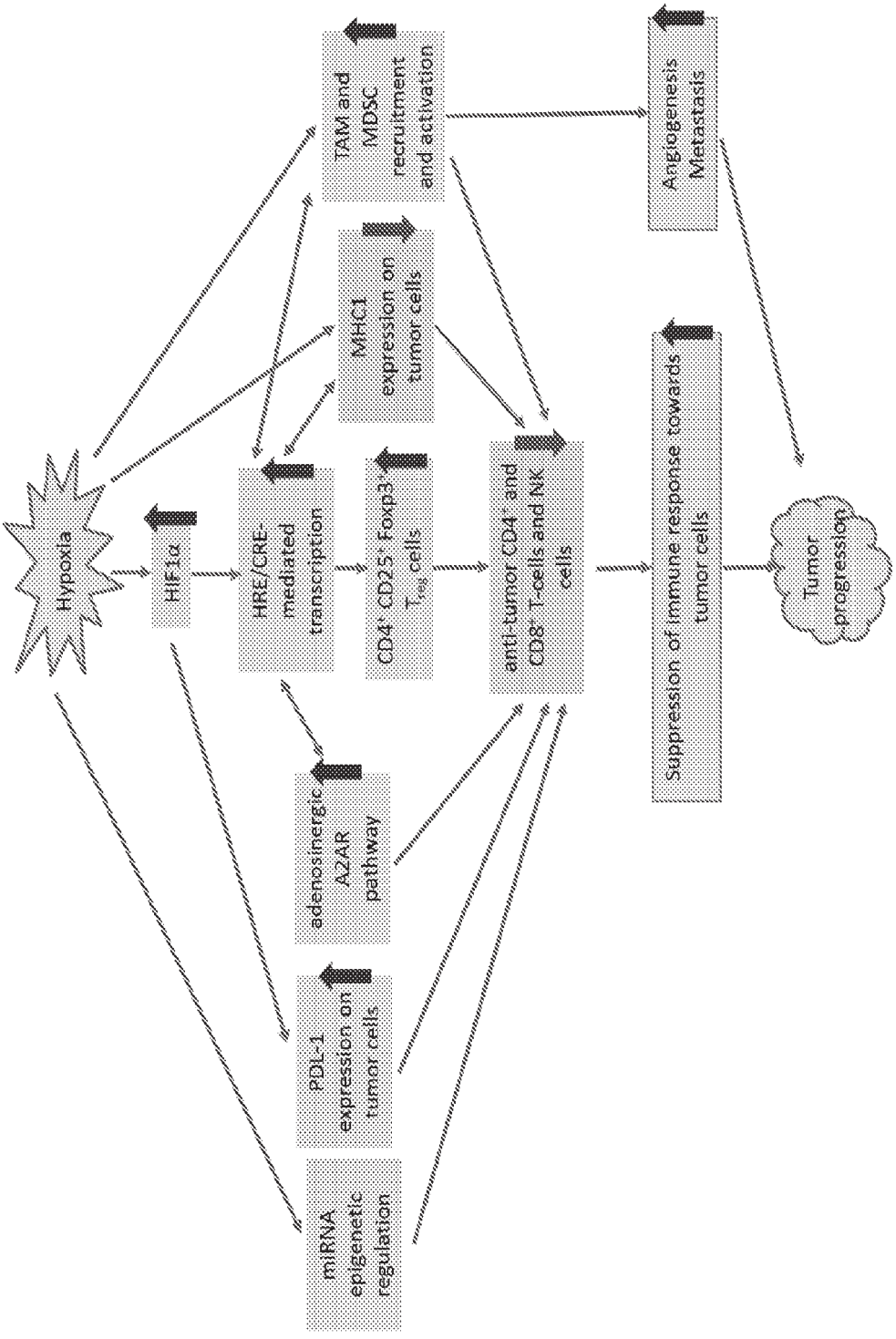

Hypoxia
HIF1α
HRE/CRE-mediated transcription
TAM and MDSC recruitment and activation
MHC1 expression on tumor cells
CD4+ CD25+ Foxp3+ Treg cells
anti-tumor CD4+ and CD8+ T-cells and NK cells
adenosinergic A2AR pathway
PDL-1 expression on tumor cells
miRNA epigenetic regulation
Angiogenesis Metastasis
Suppression of immune response towards tumor cells
Tumor progression

Fig. 1A

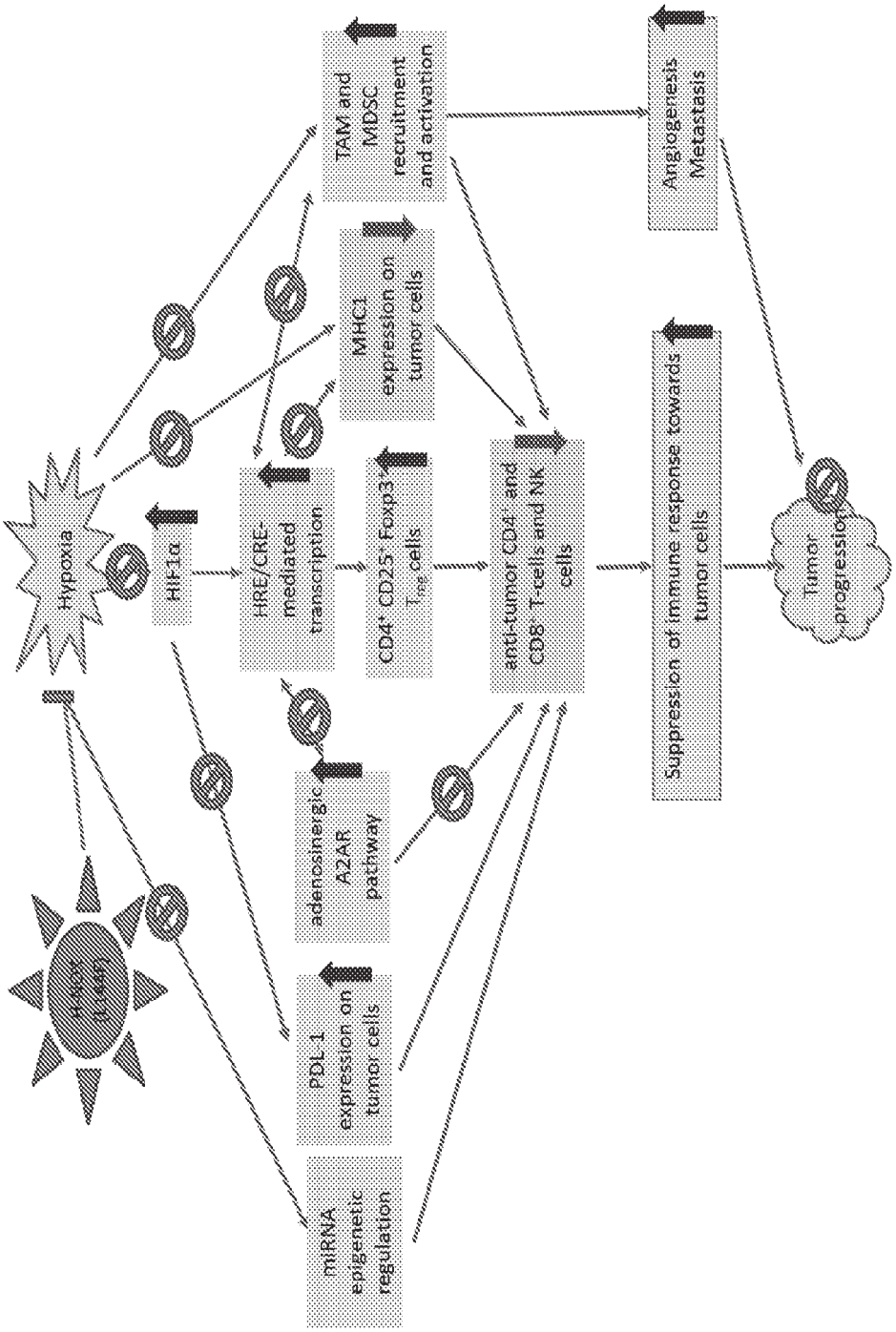

Hypoxia
HIF1α
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Suppression of immune response towards tumor cells
Tumor progression
adenosinergic A2AR pathway
PDL-1 expression on tumor cells
miRNA epigenetic regulation

Fig. 1B

Fig. 2A

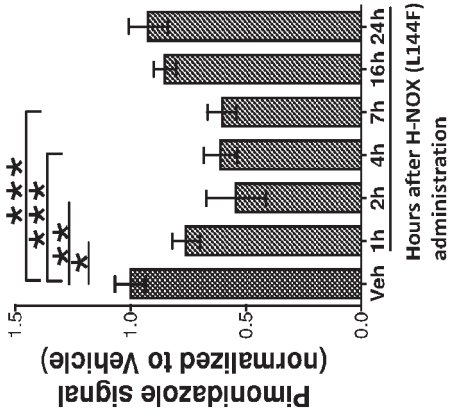


Fig. 2B

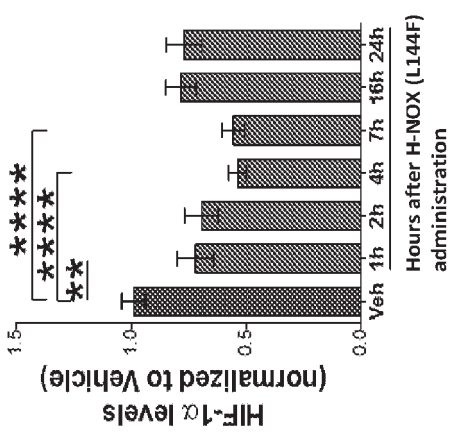


Fig. 2C

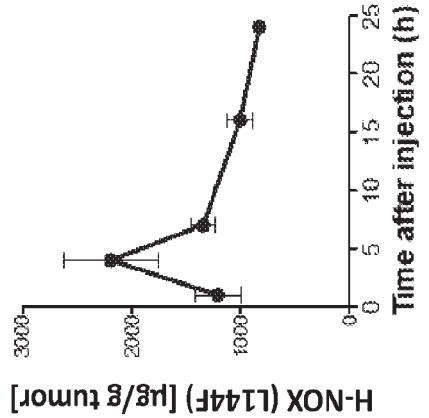


Fig. 3A

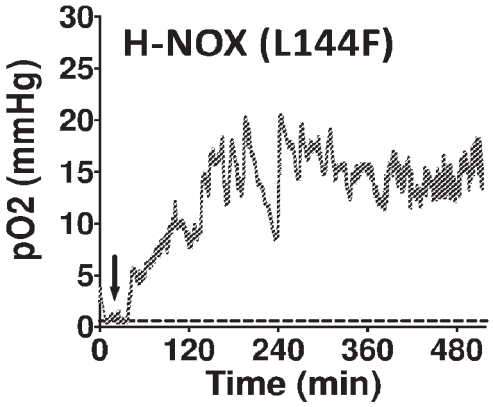


Fig. 3B

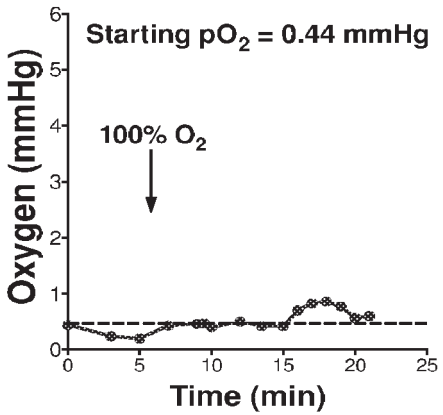


Fig. 3C

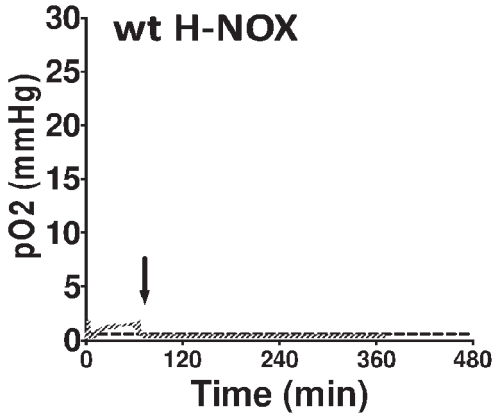


Fig. 3D

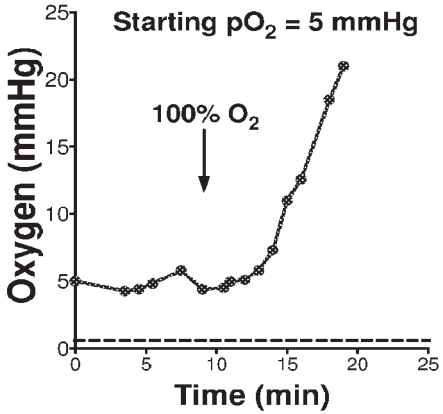


Fig. 4

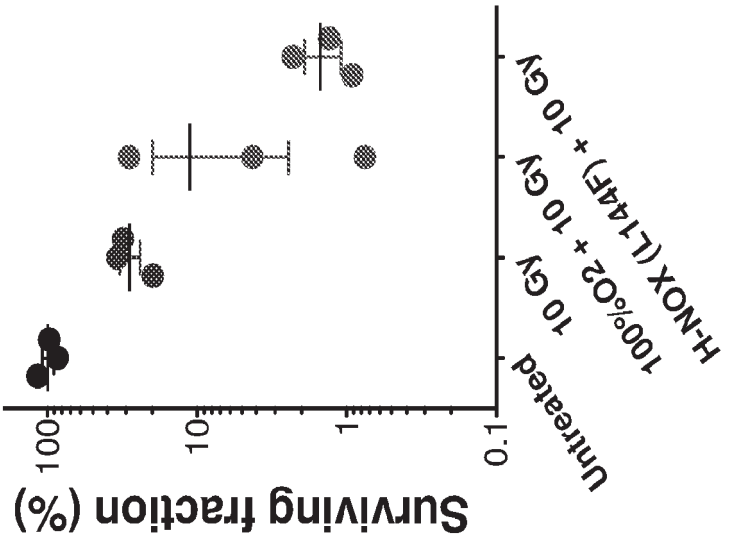

Surviving fraction (%)
100
10
1
0.1
Untreated
10 Gy
100%O2 + 10 Gy
H-NOX (L14AF) + 10 Gy

Fig. 5A

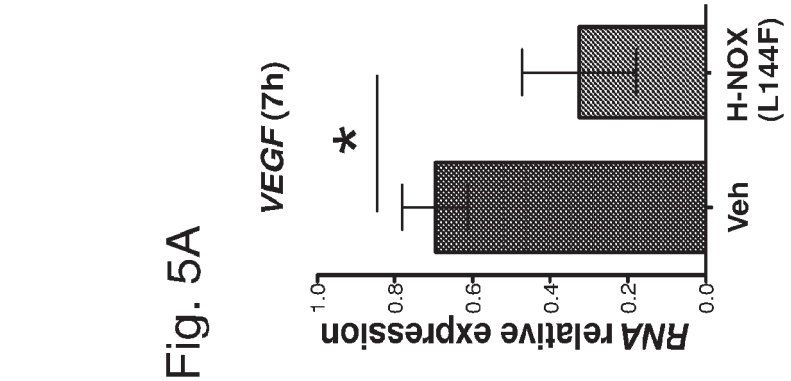


Fig. 5B

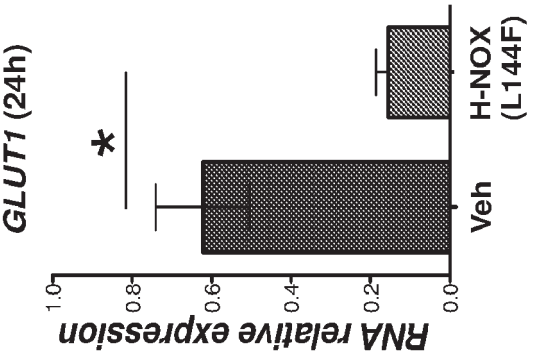


Fig. 5C

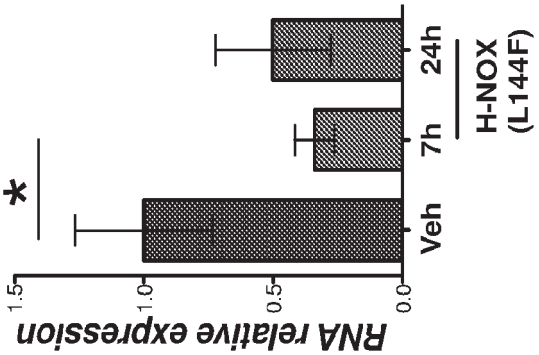


Fig. 6A

pCW-Tt(L144F)+Foldon.gb
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From 2521 to 3210.
Translation 229 a.a. MW=26677.059999999972

```
2521 ATG AAG GCG ACA ATC GTC GCG ACA TGG ATA AAG ACC CTG AGC GAC CTT TAC GGG AAT GAT  2580
   1  M   K   G   T   I   V   G   T   W   I   K   T   L   R   D   L   Y   G   N   D   20

2581 GTG GTT GAT GAA TCT TTA AAA AGT GTG GCT TGG GAA CCA GAT AGG GTA ATT ACA CCT CTG  2640
  21  V   V   D   E   S   L   K   S   V   G   W   E   P   D   R   V   I   T   P   L   40

2641 GAG GAT ATT GAT GAC GAT GAG GTT AGG AGA ATT TTT GCT AAG GTG AGT GAA AAA ACT GGT  2700
  41  E   D   I   D   D   D   E   V   R   R   I   F   A   K   V   S   E   K   T   G   60

2701 AAA AAT GTC AAC GAA ATA TGG AGA GAG GTA GGA AGG CAG AAC ATA AAA ACT TTC AGC GGA  2760
  61  K   N   V   N   E   I   W   R   E   V   G   R   Q   N   I   K   T   F   S   E   80

2761 TGG TTT CCC TCC TAT TTT GCA GGC AGA AGC CTA GTG AAT TTT TTA ATG ATG ATG GAT CAG  2820
  81  W   F   P   S   Y   F   A   G   R   R   L   V   N   F   L   M   M   M   D   E  100

2821 GTA CAC CTA CAG CTT ACC AAG ATG ATA AAA GGA GCC ACT CCT CCA AGG CTT ATT GCA AAG  2880
 101  V   H   L   Q   L   T   K   M   I   K   G   A   T   P   P   R   L   I   A   K  120

2881 CCT GTT GCA AAA GAT GCC ATT GAA ATG GAG TAC GTT TCT AAA AGA AAG ATG TAC GAT TAC  2940
 121  P   V   A   K   D   A   I   E   M   E   Y   V   S   K   R   K   M   Y   D   Y  140

2941 TTT TTA GGG cTT ATA GAG GGT AGT TCT AAA TTT TTC AAG GAA GAA ATT TCA GTG GAA GAG  3000
 141  F   L   G   F   I   E   G   S   S   K   F   F   K   E   E   I   S   V   E   E  160

3001 GTC GAA AGA GGC GAA AAA GAT GGC TTT TCA AGG CTA AAA GTC AGG ATA AAA TTT AAA AAC  3060
 161  V   E   R   G   E   K   D   G   F   S   R   L   K   V   R   I   K   F   K   N  180

3061 CCC GTT TTT GAG TAT AAG AAA AAT CTC GAG ggc agc ggc GGT TAT ATT CCT GAA GCT CCA  3120
 181  P   V   F   E   Y   K   K   N   L   E   G   S   G   G   Y   I   P   E   A   P  200

3121 AGA GAT GGG CAG GCT TAC GTT CGT AAA GAT GGC GAA TGG GTA TTA CTT TCT ACC TTT TTA  3180
 201  R   D   G   Q   A   Y   V   R   K   D   G   E   W   V   L   L   S   T   F   L  220

3181 AGG GGT AGT CAC CAT CAC CAT CAC CAT TGA  3210
 221  R   G   S   H   H   H   H   H   H   *  230
```

Fig. 6B

```
Thu Jan 03, 2013 12:16 PST
pCW-f802.5.gb
/Users/omnioxlab2/DNA/pCW-f802.5.gb
From 2521 to 3183.
Translation 220 a.a. MW=25553.899999999976

   2521 ATG AAG CGC ACA ATC GTC CGC ACA TGG ATA AAC ACC CTG ACG GAC CTT TAC GGG AAT GAT  2580
      1  M   K   G   T   I   V   G   T   W   I   K   T   L   R   D   L   Y   G   N   D   20

   2581 GTC GTT GAT GAA TCT TTA AAA ACT GTC CGT TGG GAA CCA GAT ACG GTA ATT ACA CCT CTG  2640
     21  V   V   D   E   S   L   K   S   V   G   W   E   P   D   T   V   I   T   P   L   40

   2641 GAG GAT ATT GAT GAC GAT GAC CTT ACG ACA ATT TTT GCT AAG GTG AGT GAA AAA ACT CGT  2700
     41  E   D   I   D   D   D   E   V   R   R   I   F   A   K   V   S   E   K   T   G   60

   2701 AAA AAT GTC AAC GAA ATA TGG ACA GAC CTA CGA AGG CAG AAC ATA AAA ACT TTC AGC GAA  2760
     61  K   N   V   N   E   I   W   R   E   V   G   R   Q   N   I   K   T   F   S   E   80

   2761 TGG TTT CCC TCC TAT TTT GCA GGC AGA AGG CTA GTG AAT TTT TTA ATG ATG ATG GAT GAG  2820
     81  W   F   P   S   Y   F   A   G   R   R   L   V   N   F   L   M   M   M   D   E   100

   2821 GTA CAC CTA CAG CTT ACC AAC ATG ATA AAA CGA GCC ACT CCT CCA AGC CTT ATT GCA AAG  2880
    101  V   H   L   Q   L   T   K   M   I   K   G   A   T   P   P   R   L   I   A   K   120

   2881 CCT GTT GCA AAA GAT GCC ATT GAA ATG CAG TAC GTT TCT AAA AGA AAG ATG TAC GAT TAC  2940
    121  P   V   A   K   D   A   I   E   M   E   Y   V   S   K   R   K   M   Y   D   Y   140

   2941 TTT TTA GGG tTT ATA GAG GGT AGT TCT AAA TTT TTC AAG GAA GAA ATT TCA GTG GAA GAG  3000
    141  F   L   G   F   I   E   G   S   S   K   F   F   K   E   E   I   S   V   E   E   160

   3001 GTC GAA AGA GGC GAA AAA GAT GGC TTT TCA AGG CTA AAA GTC AGG ATA AAA TTT AAA AAC  3060
    161  V   E   R   G   E   K   D   G   F   S   R   L   K   V   R   I   K   F   K   N   180

   3061 CCC GTT TTT GAG TAT AAG AAA AAT GTC CAG ggc agc ggc GGT TAT ATT CCT GAA GCT CCA  3120
    181  P   V   F   E   Y   K   K   N   L   E   G   S   G   G   Y   I   P   E   A   P   200

   3121 AGA GAT GGC CAG GCT TAC GTT CGT AAA GAT GGC GAA TGG GTA TTA CTT TCT ACC TTT TTA  3180
    201  R   D   G   Q   A   Y   V   R   K   D   G   E   W   V   L   L   S   T   F   L   220

   3181 tga  3183
    221  *   221
```

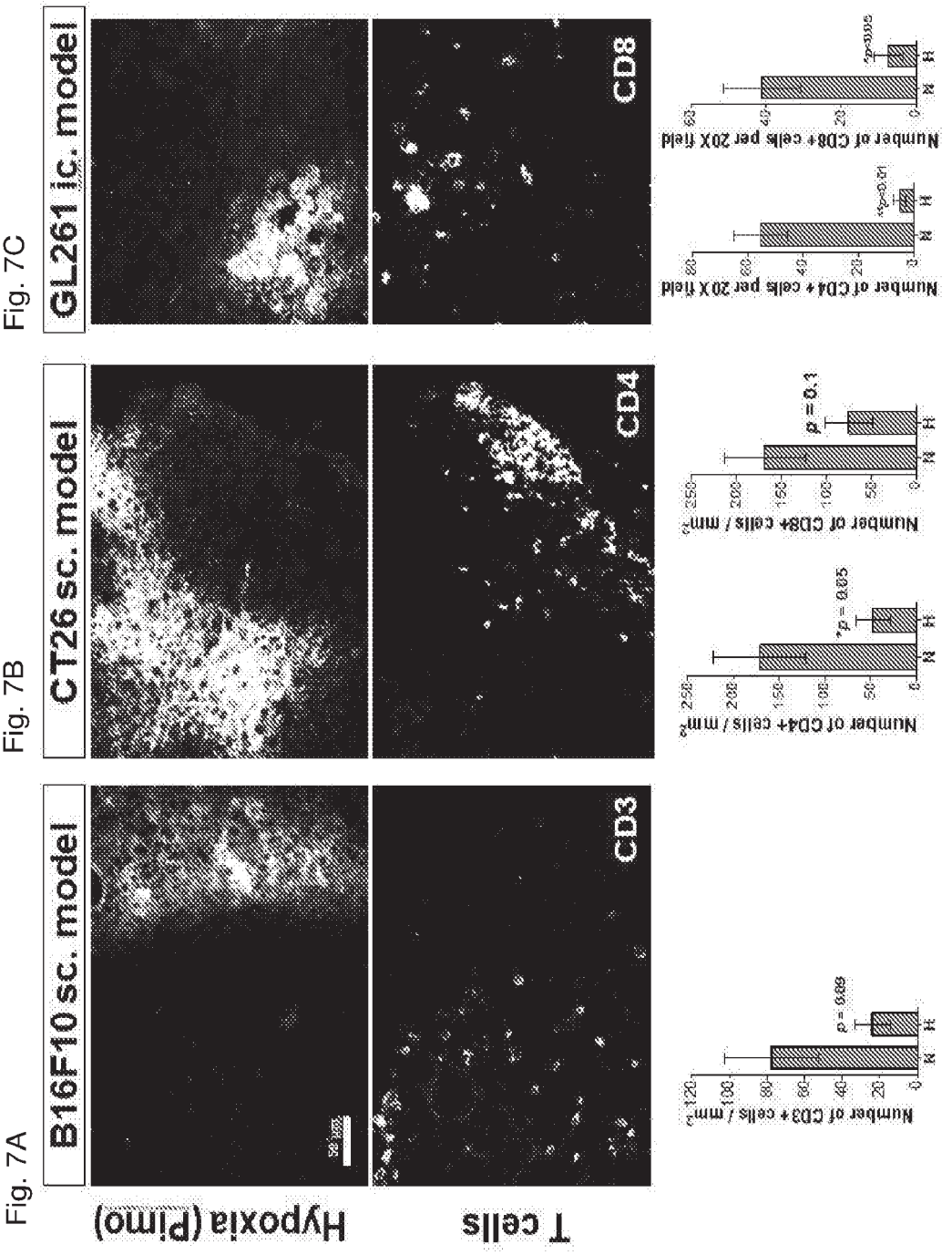


Fig. 7A

Fig. 7B

Fig. 7C

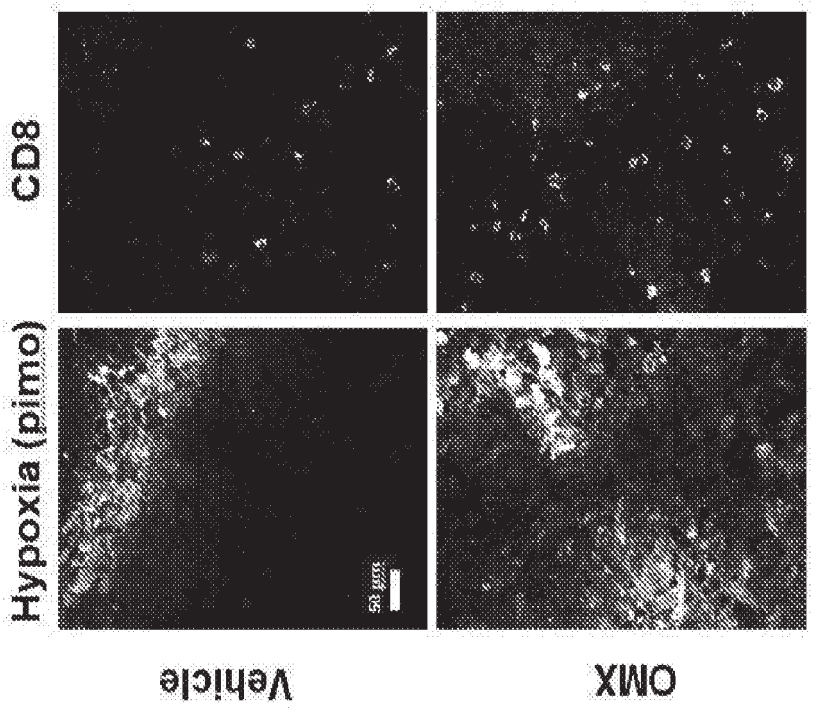


Fig.8

Fig. 9A

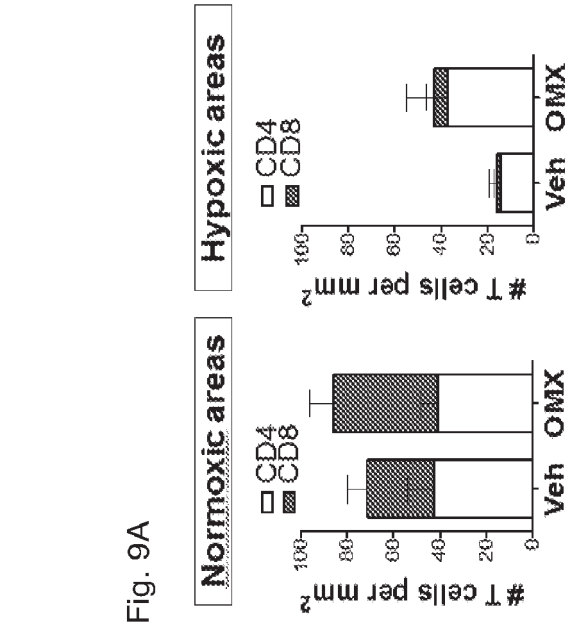

Normoxic areas
Hypoxic areas
CD4
CD8
T cells per mm²
100
80
60
40
20
0
Veh
OMX

Fig. 9B

Vehicle
OMX
CD4
Hypoxia (CAIX)

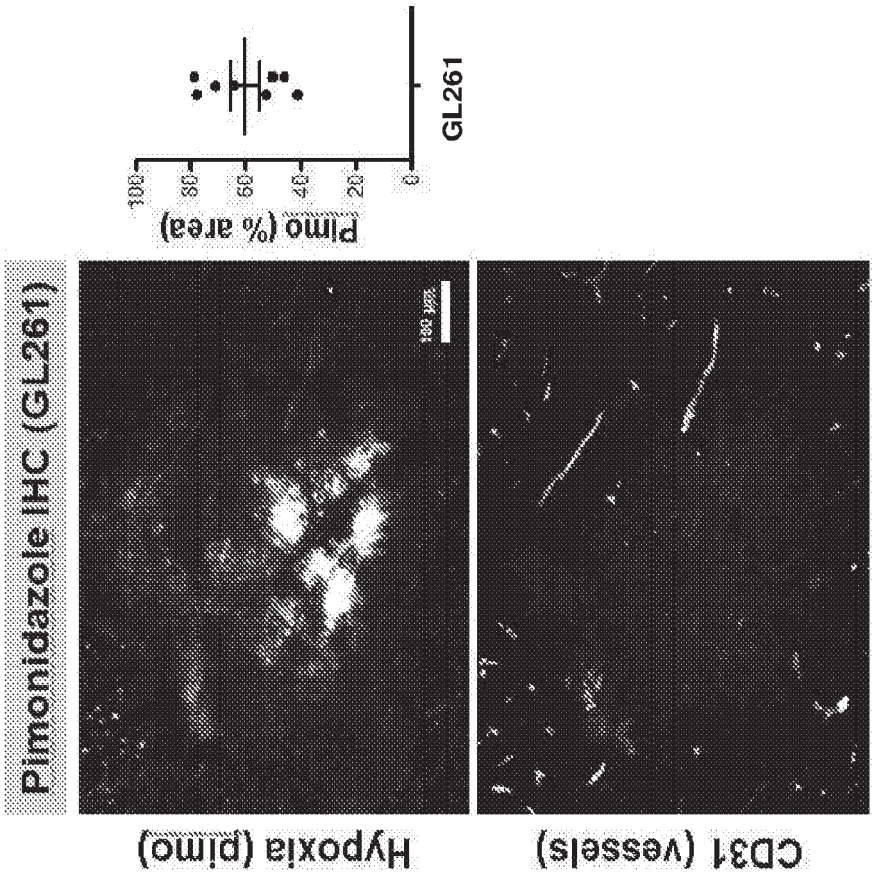

Pimonidazole IHC (GL261)
Hypoxia (pimo)
CD31 (vessels)
Pimo (% area)
100
80
60
40
20
0
GL261

Fig. 10

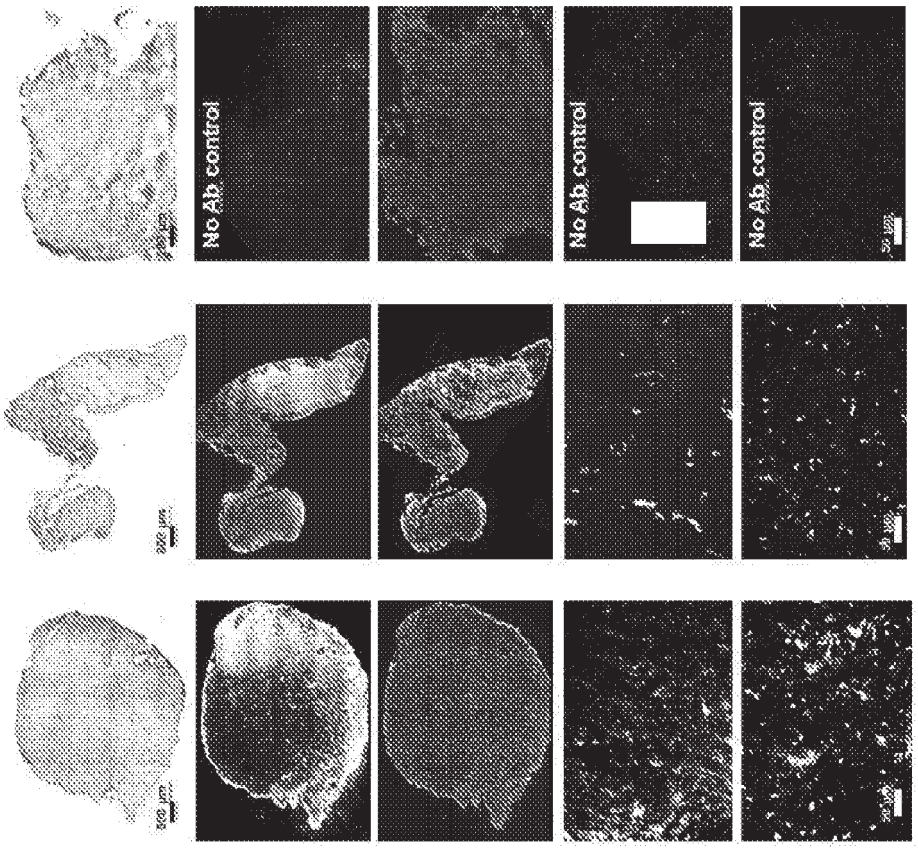


Fig. 11

Fig. 12A

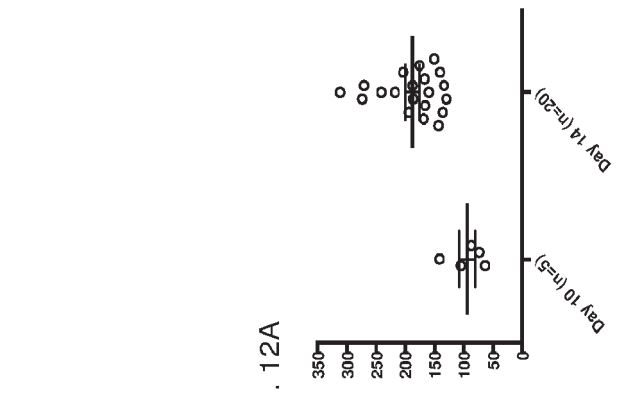


Fig. 12B

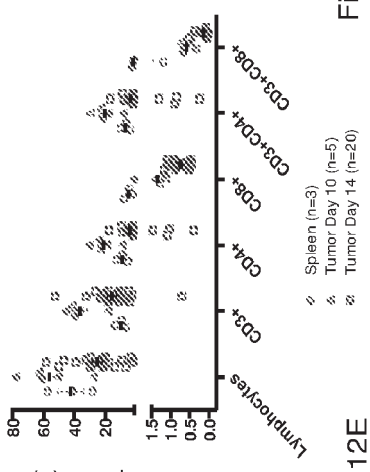


Fig. 12C

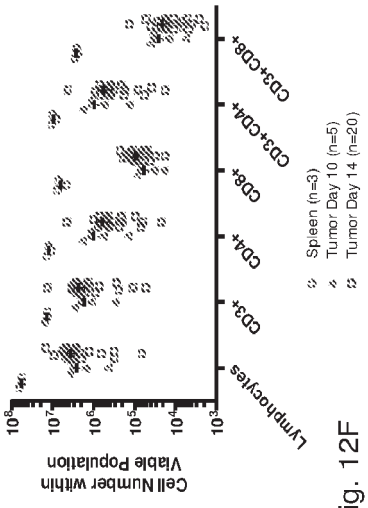
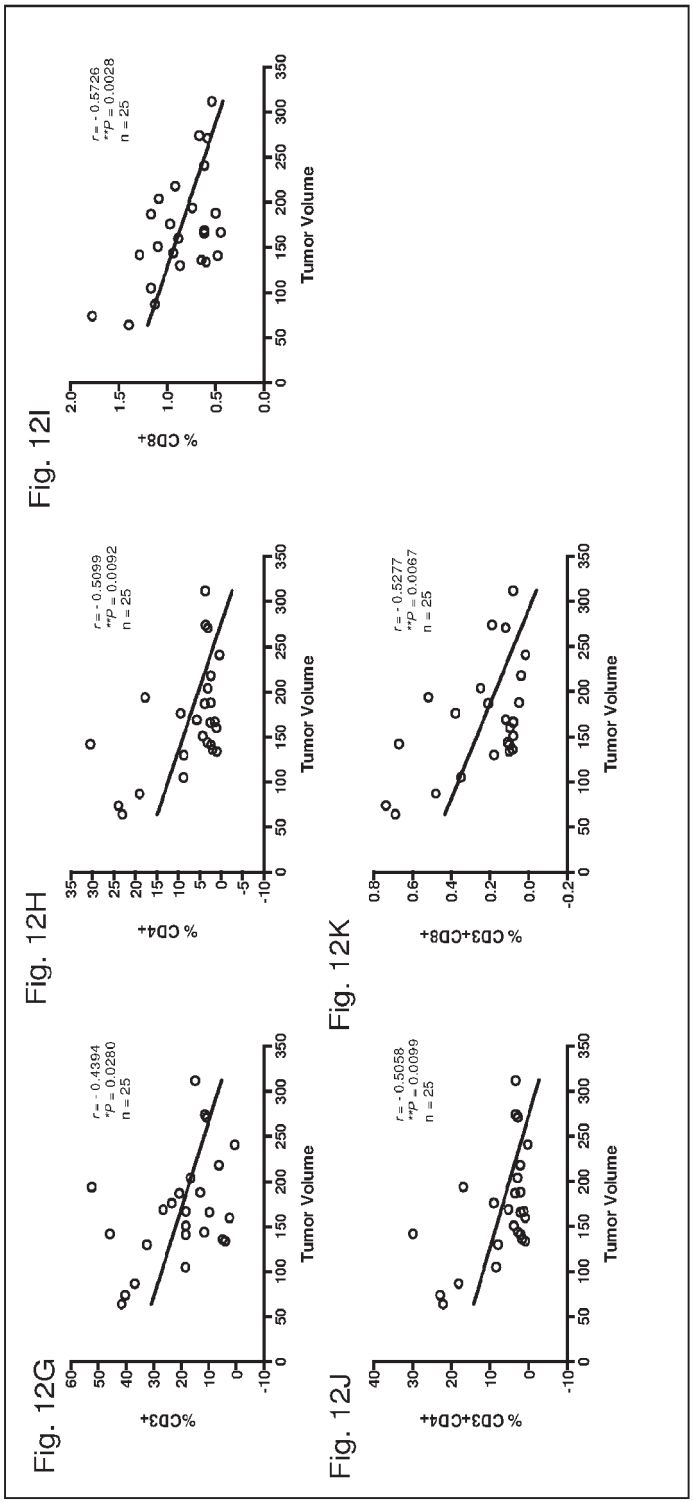
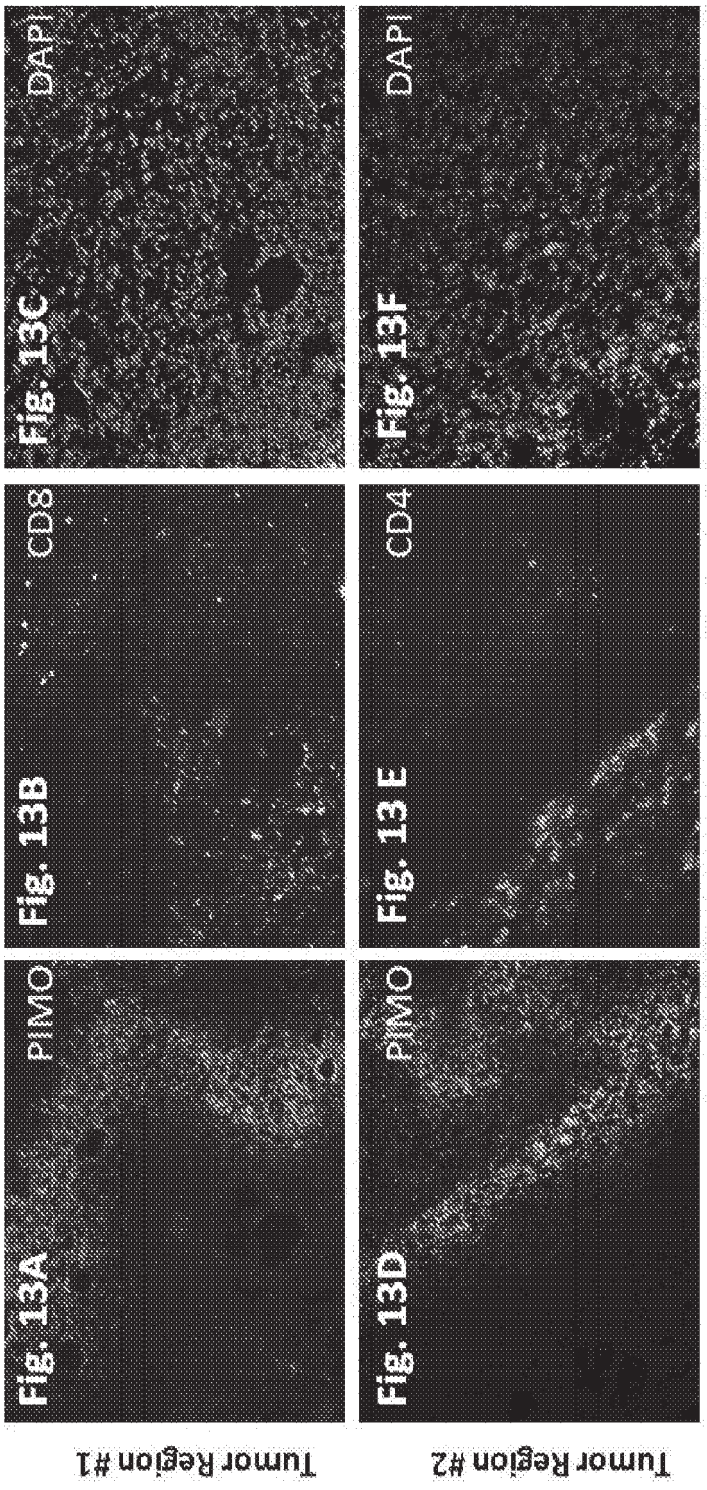


Fig. 12D

Fig. 12E

Fig. 12F


Fig. 12G
%CD3+
r = - 0.4394
**P = 0.0280
n = 25
Tumor Volume
Fig. 12H
% CD4+
r = - 0.5099
**P = 0.0092
n = 25
Tumor Volume
Fig. 12I
% CD8+
r = - 0.5726
**P = 0.0028
n = 25
Tumor Volume
Fig. 12J
% CD3+CD4+
r = - 0.5058
**P = 0.0099
n = 25
Tumor Volume
Fig. 12K
% CD3+CD8+
r = - 0.5277
**P = 0.0067
n = 25
Tumor Volume


Fig. 13A
PIMO
Fig. 13B
CD8
Fig. 13C
DAPI
Fig. 13D
PIMO
Fig. 13 E
CD4
Fig. 13F
DAPI
Tumor Region #1
Tumor Region #2