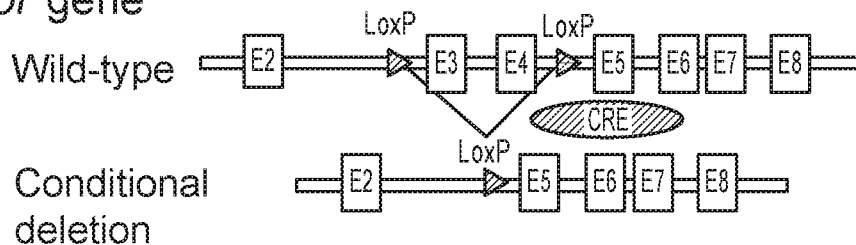
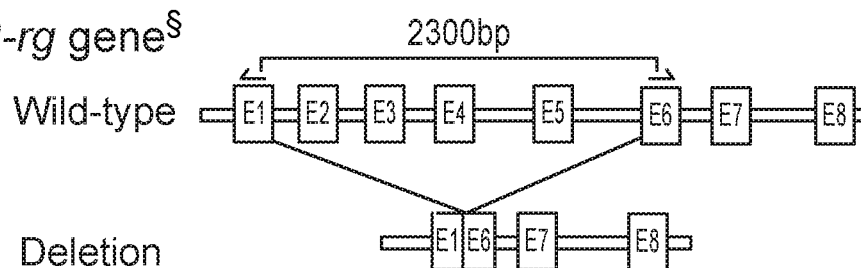
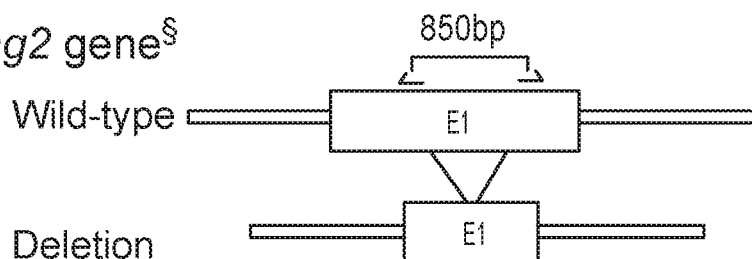
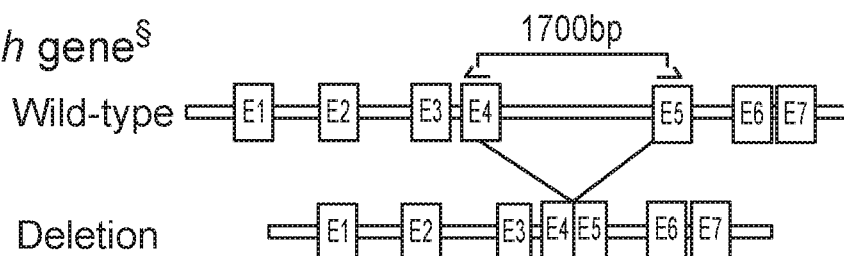


1/31

Figure 1A

PIRF* mouse strain**Por* gene******Ii2-rg* gene[§]*****Rag2* gene[§]*****Fah* gene[§]**

*Embryonic stem cell targeting (See, Figure 4)

§ Zygote injection with Cas9 and gRNA (See, Figure 5)

2/31

Figure 1B

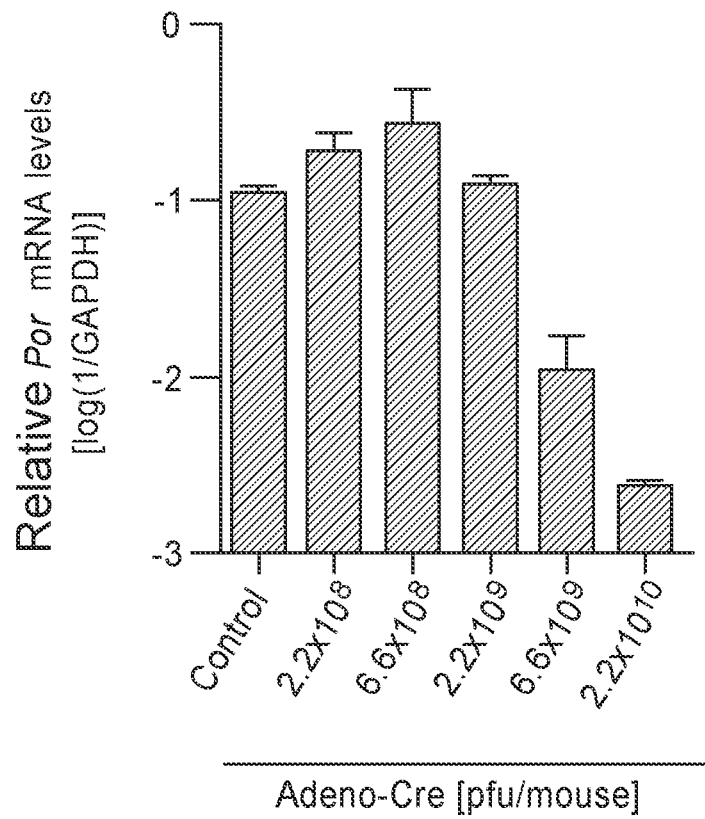
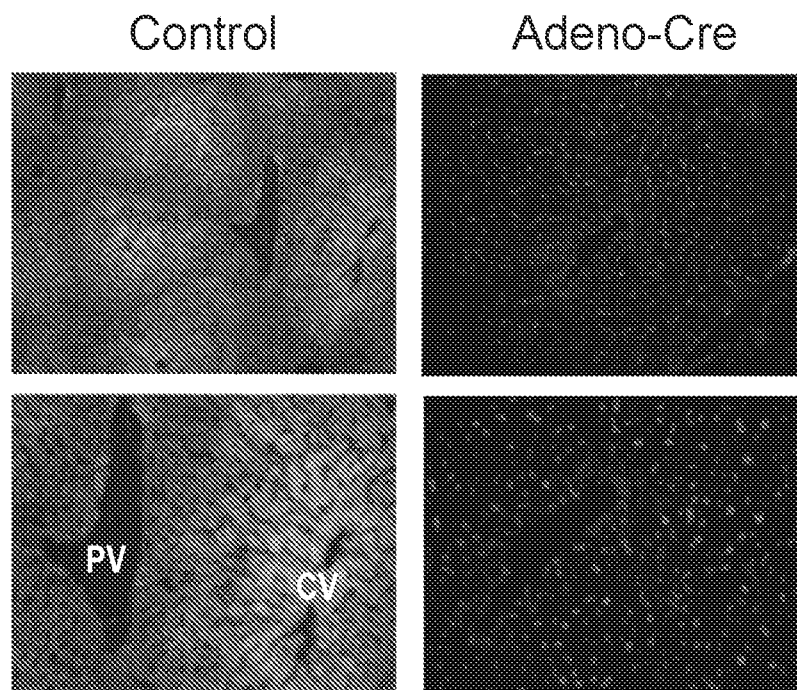
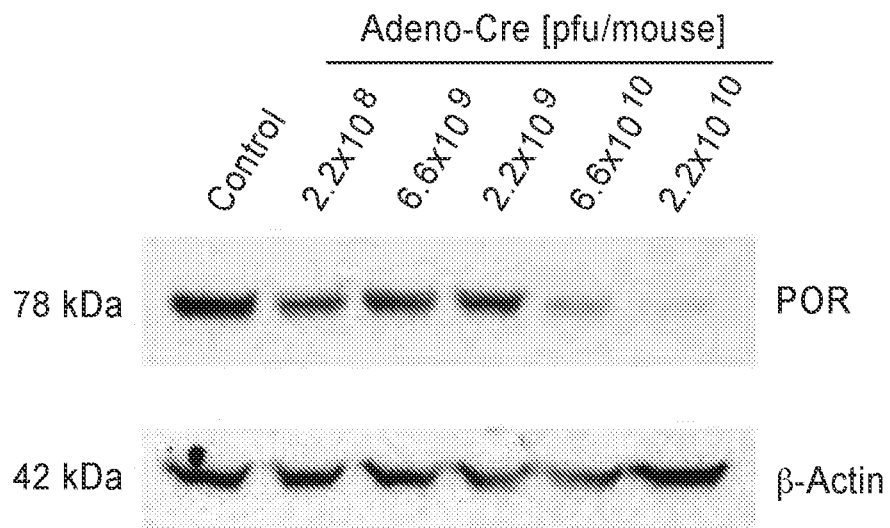


Figure 1C



3/31

Figure 1D



4/31

Figure 2A

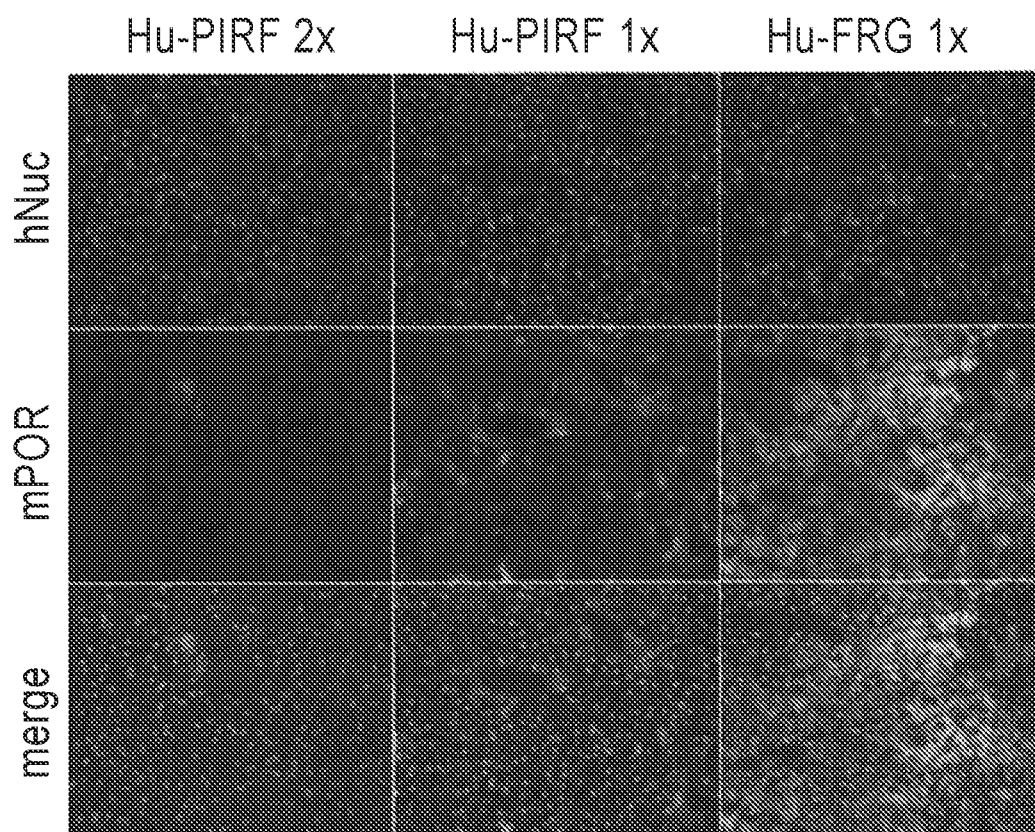
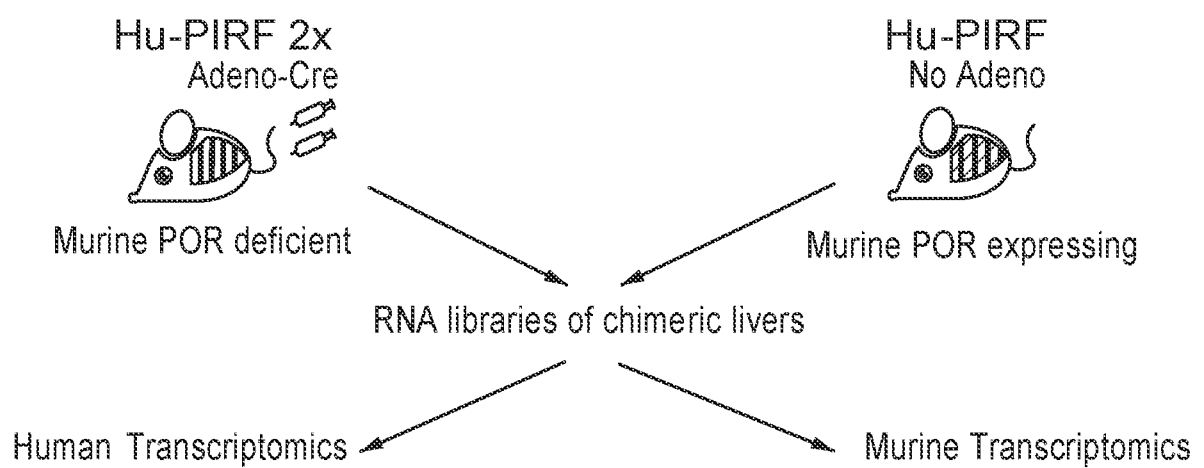
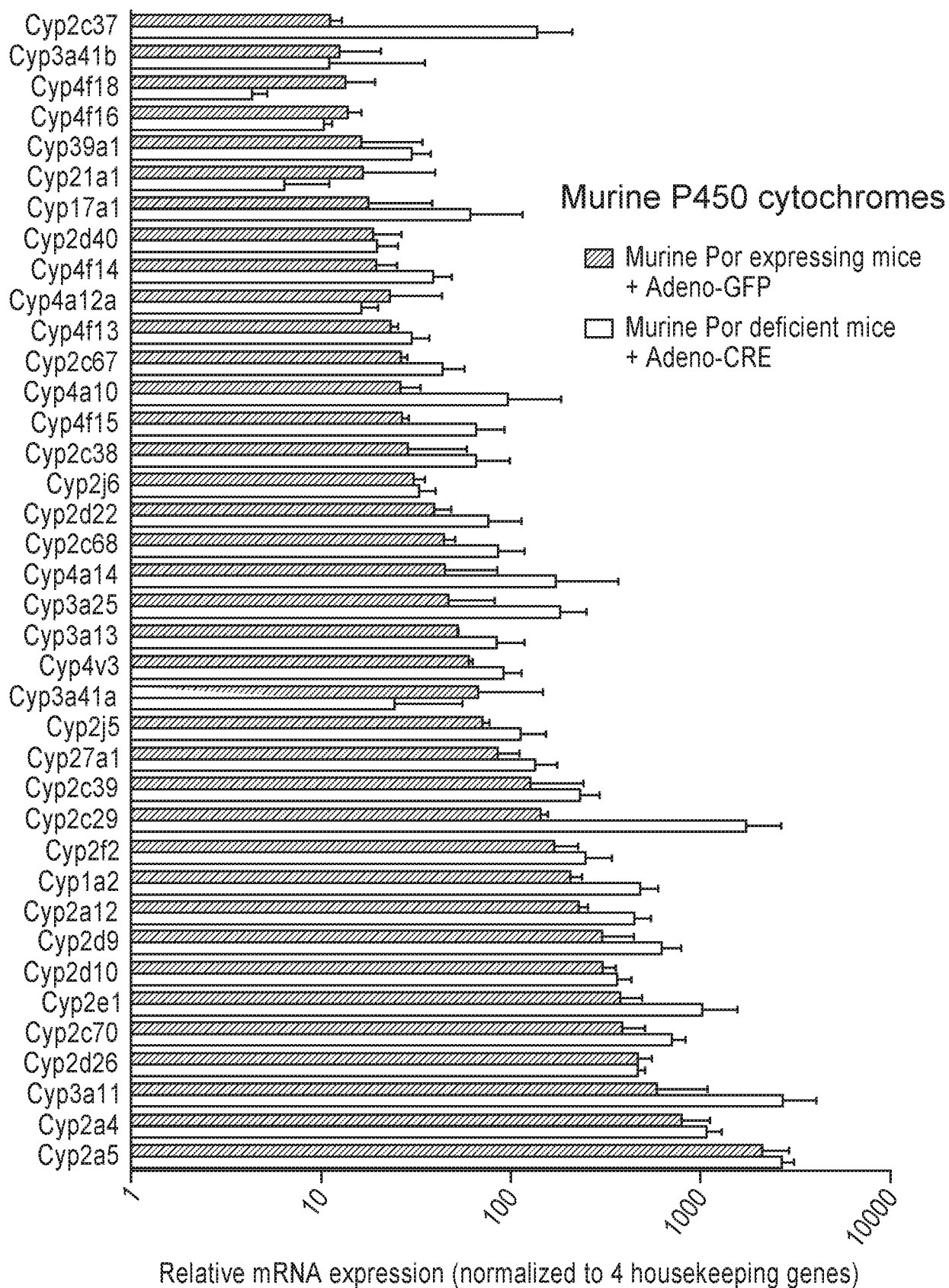


Figure 2B



5/31

Figure 2C



6/31

Figure 2D

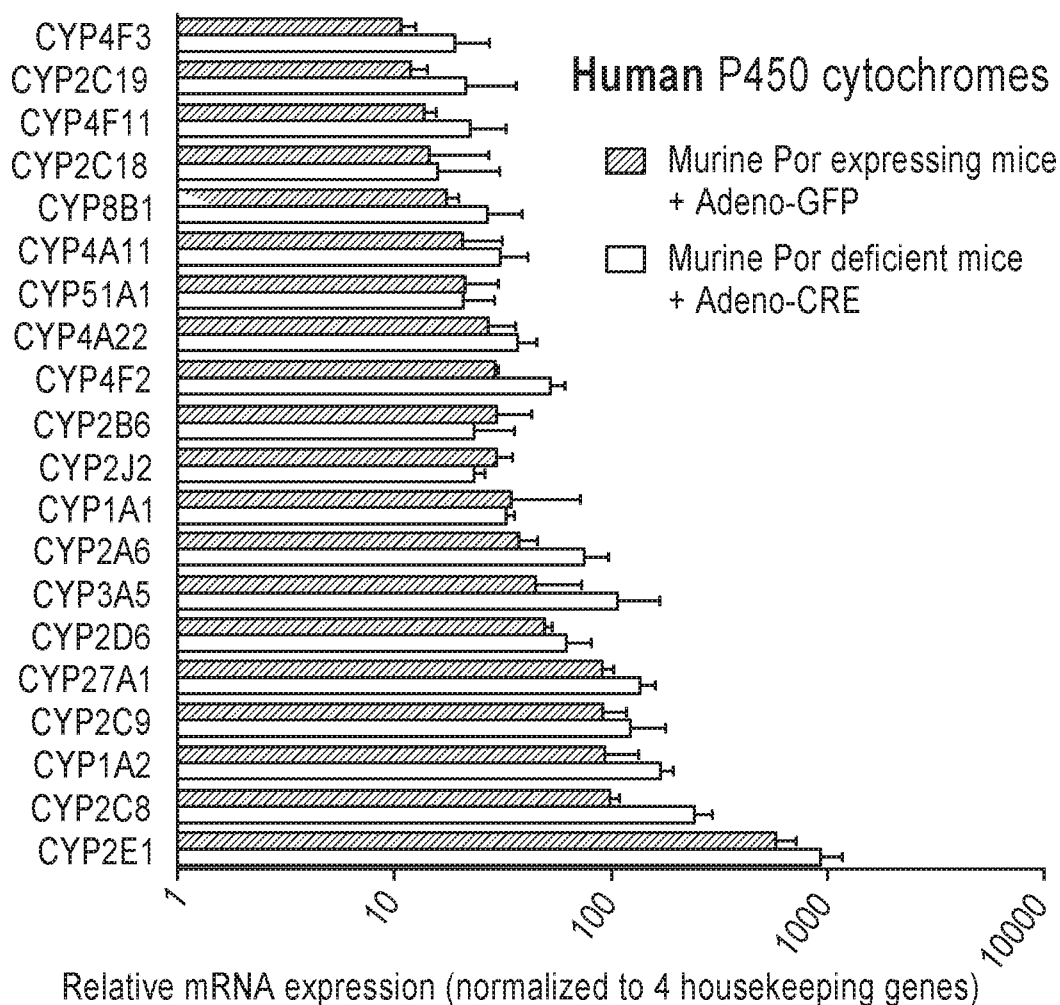
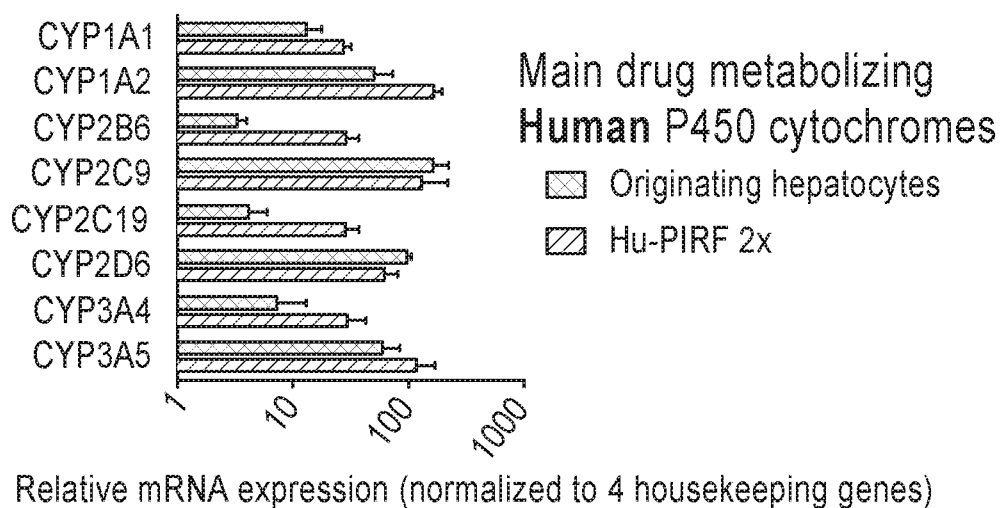


Figure 2E



7/31

Figure 3A

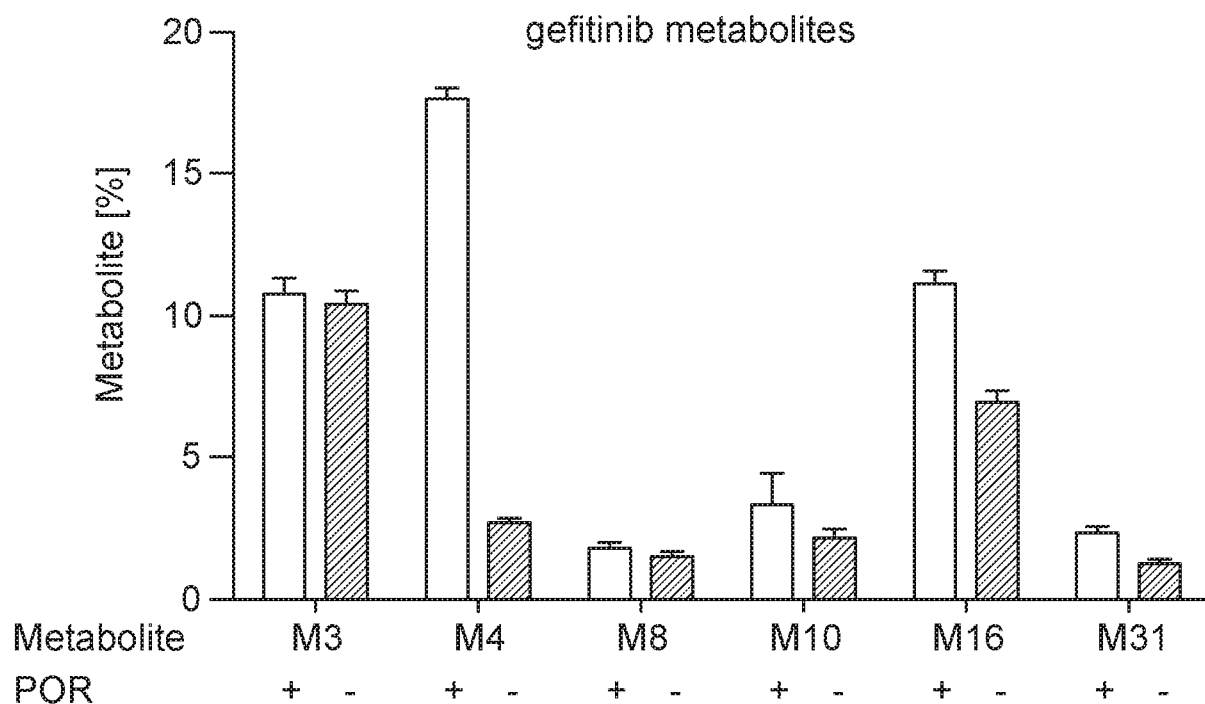
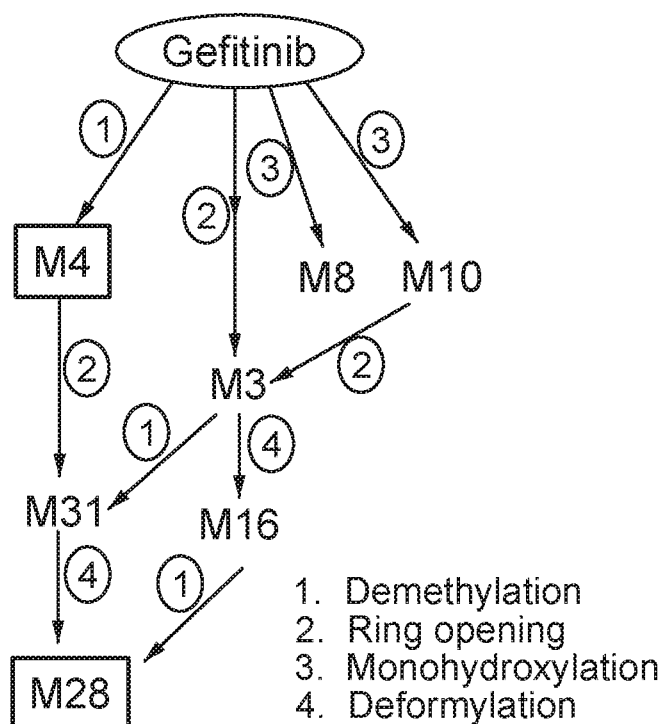


Figure 3B



8/31

Figure 3C

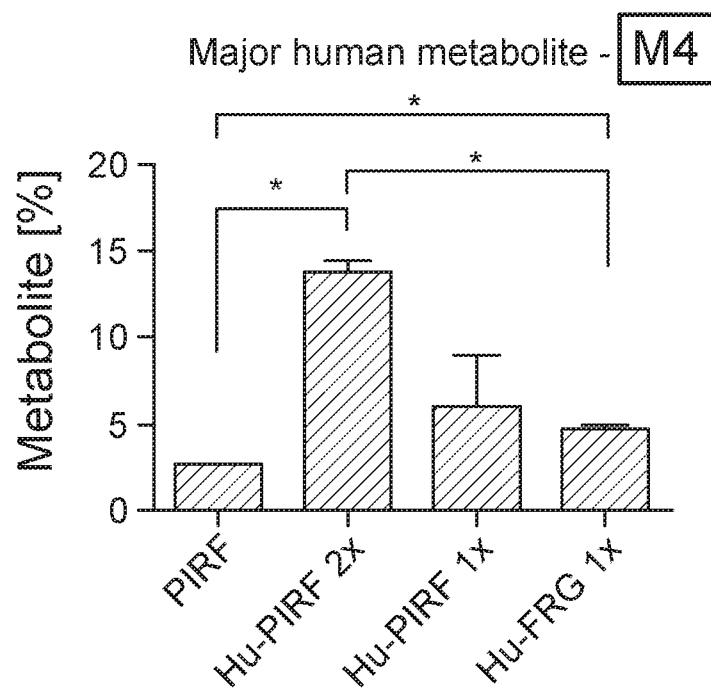
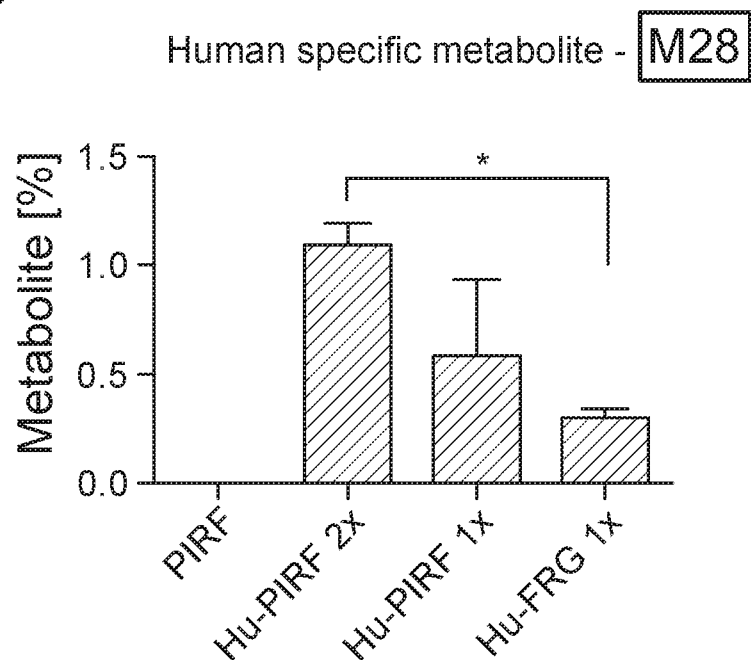


Figure 3D



9/31

Figure 3E

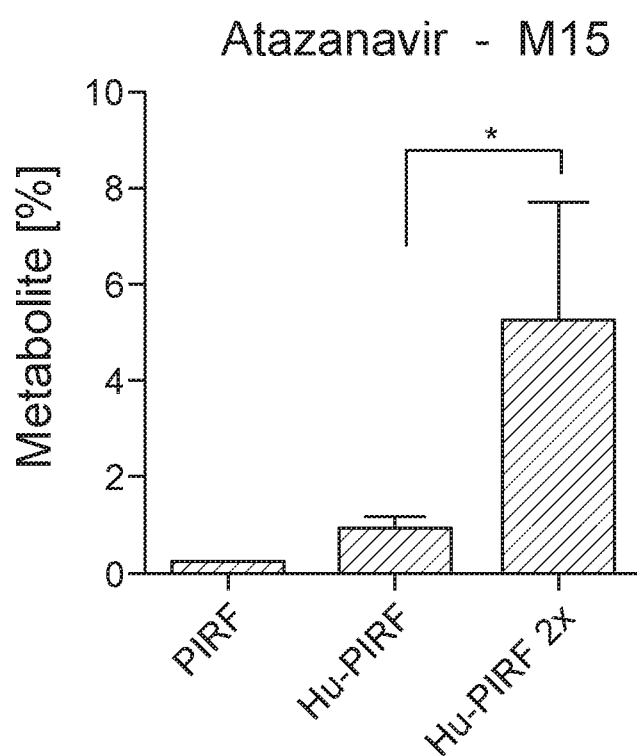
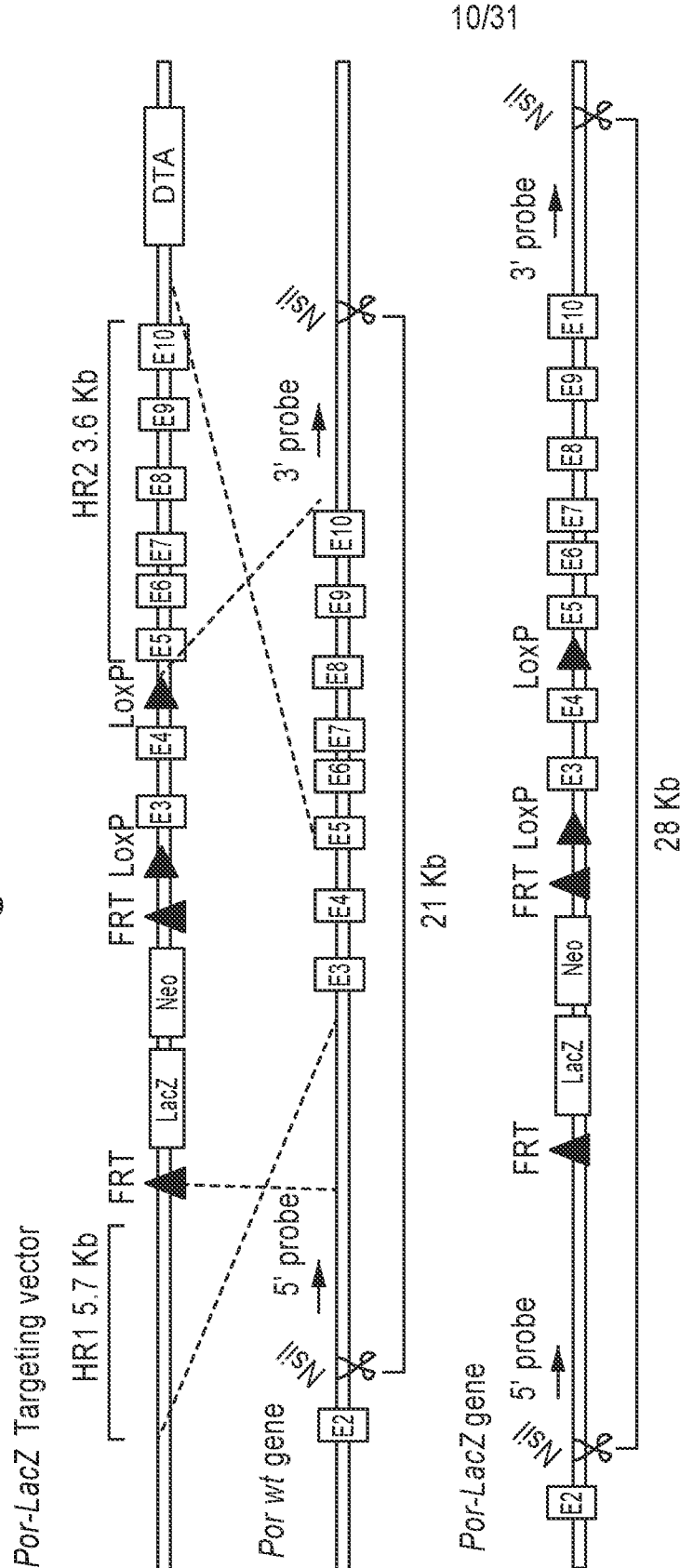


Figure 4A



10/31

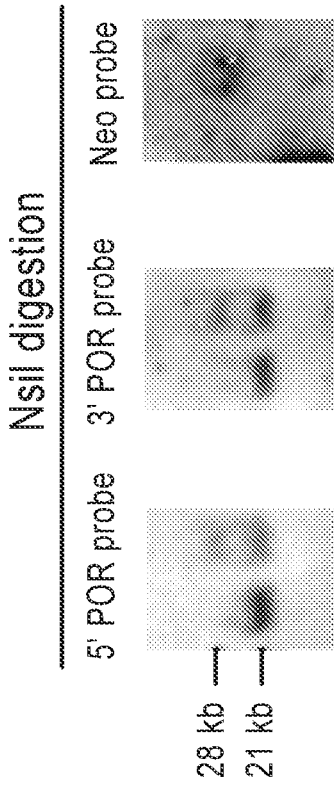
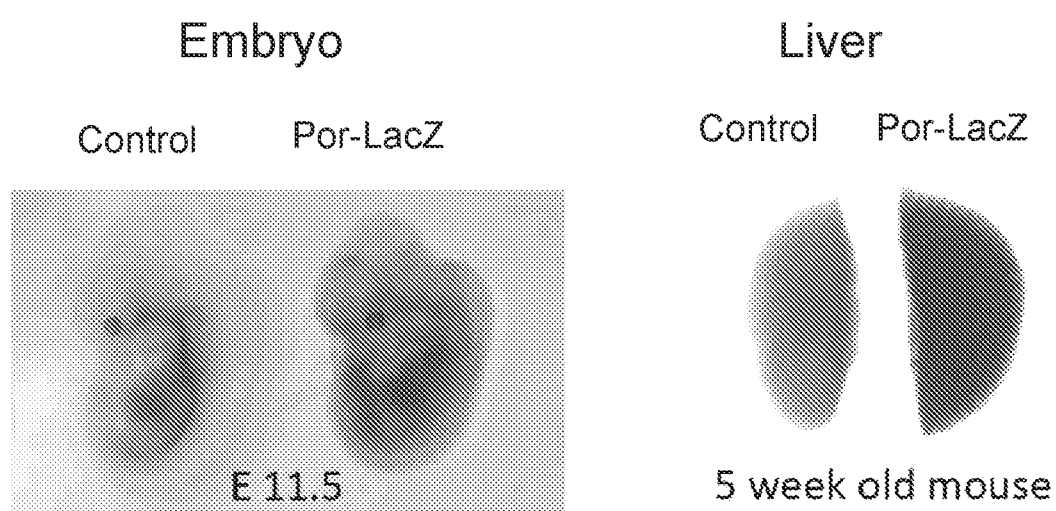


Figure 4B

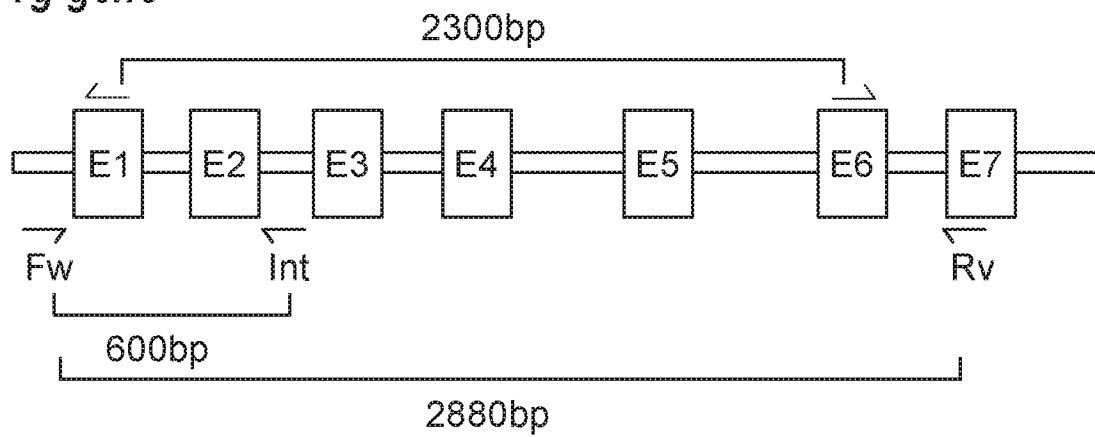
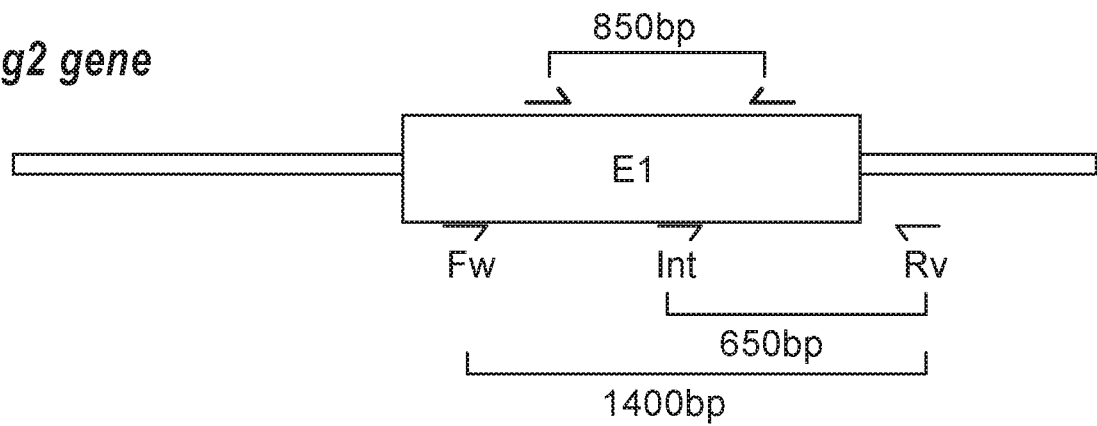
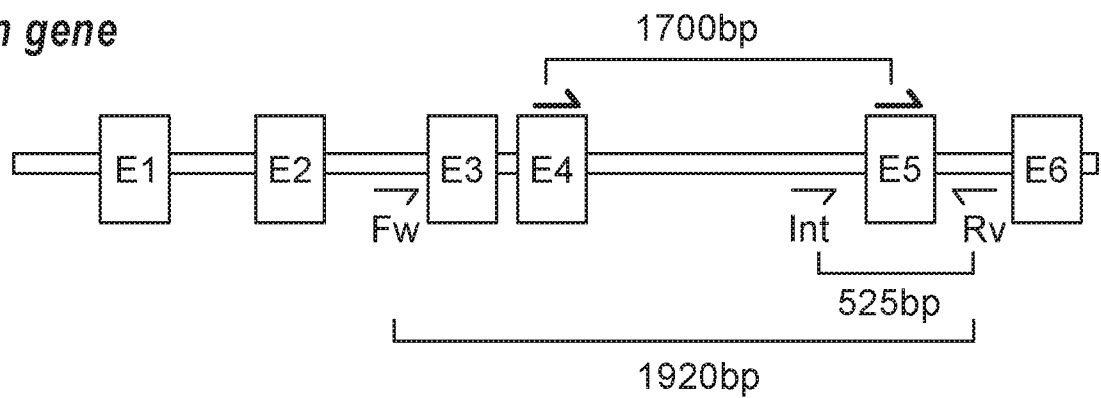
11/31

Figure 5



12/31

Figure 6A

Il2 rg gene*Rag2 gene**Fah gene*

13/31

Figure 6B

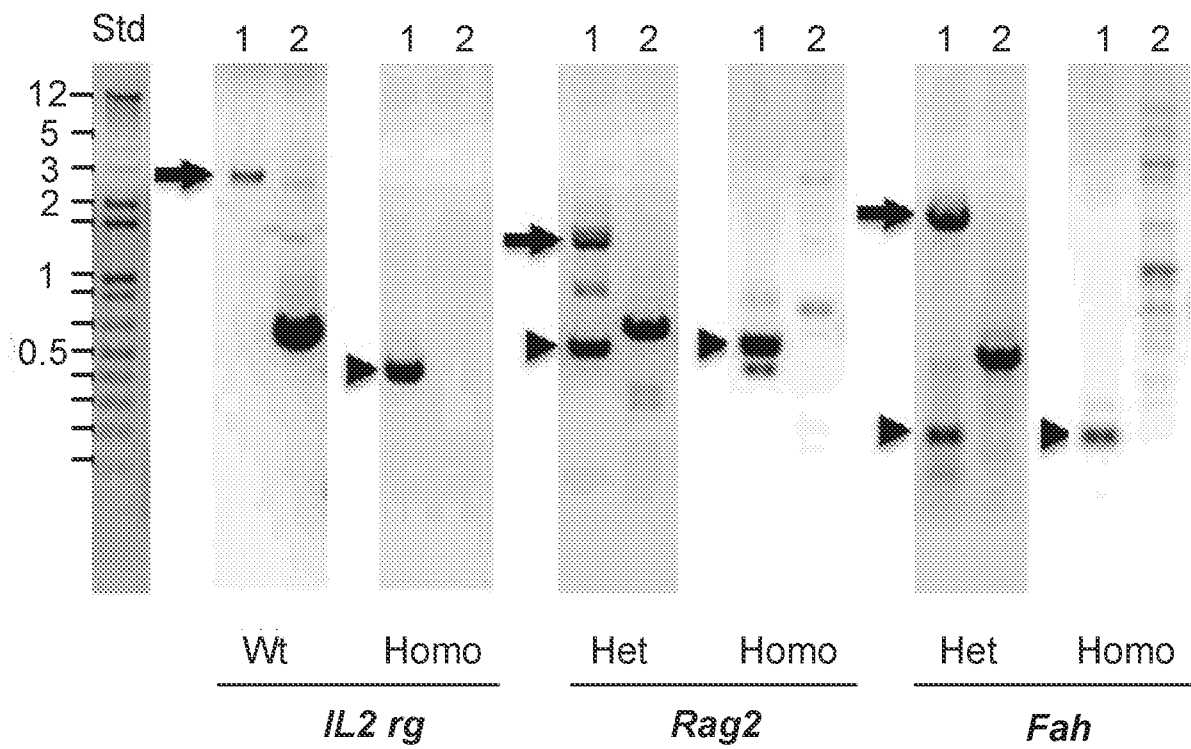
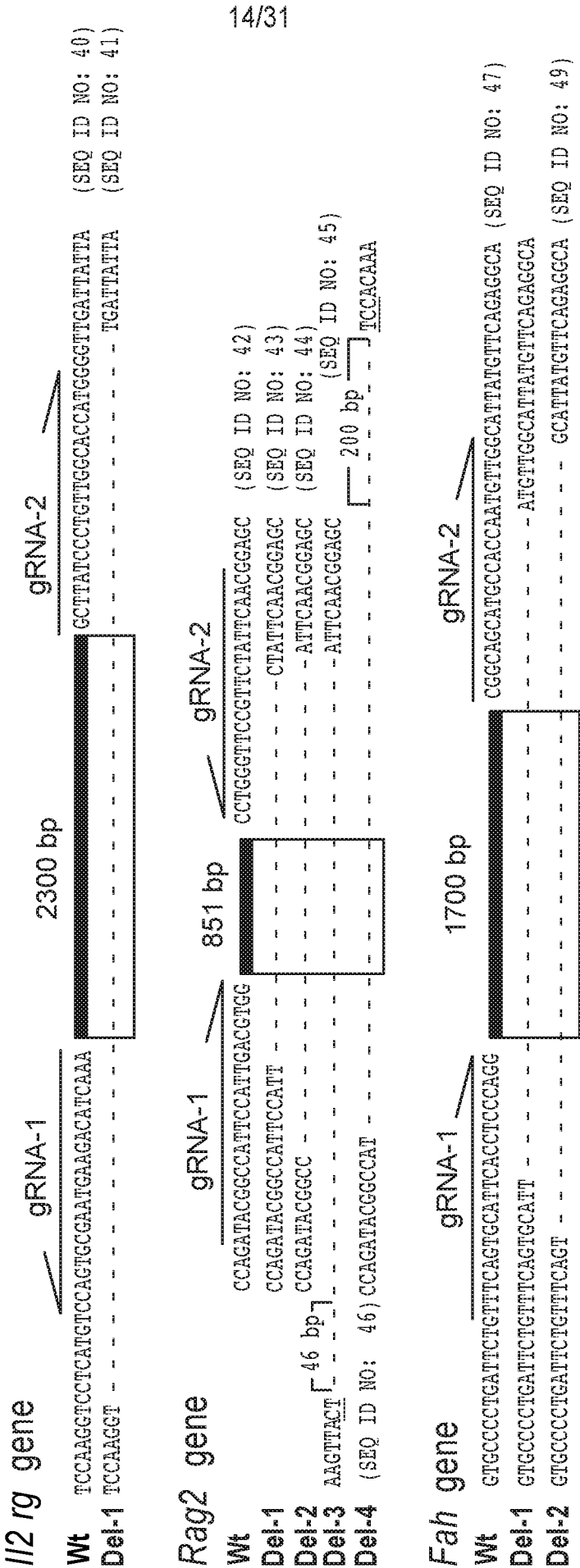


Figure 7A



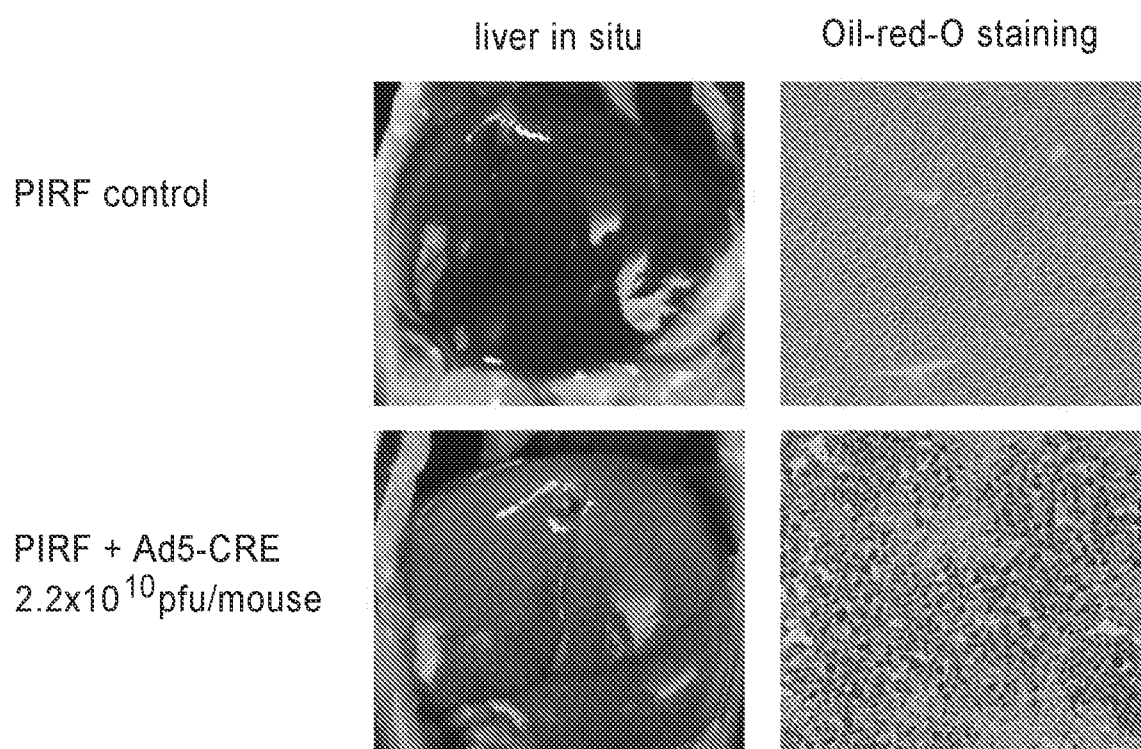
15/31

Figure 7B

Gene KO	Deletion size (bp)	Protein modification
Il2 KO Del-1	2422bp	Frame shift from aminoacid 28: (SEQ ID NO: 50) LCWHYVQRQGECAVAKLAPLTGIPWPSFLHCGIWNPD SKTHGADET+STOP
Rag2 KO Del-1	871bp	Frame shift from aminoacid 143: ILFNGAQ+STOP (SEQ ID NO: 51)
Rag2 KO Del-2	877bp	Frame shift from aminoacid 141: IQRSSINPP+STOP (SEQ ID NO: 52)
Rag2 KO Del-3	936bp	Frame shift from aminoacid 122: IQRSSINPP+STOP (SEQ ID NO: 53)
Rag2 KO Del-4	1088bp	Frame shift from aminoacid 142: TKKALGKS+STOP (SEQ ID NO: 54)
Fah KO Del-1	1717bp	Frame shift from aminoacid 107: (SEQ ID NO: 55) LCWHYVQRQGECAVAKLAPLTGIPWPSFLHCGIWNPD SKTHGADET+STOP
Fah KO Del-2	1720bp	Frame shift from aminoacid 107: (SEQ ID NO: 56) LCSEARRMRCCQIGSTYLWDTMAELPPLWLEPRFEDPWGR+STOP

16/31

Figure 8



17/31

Figure 9

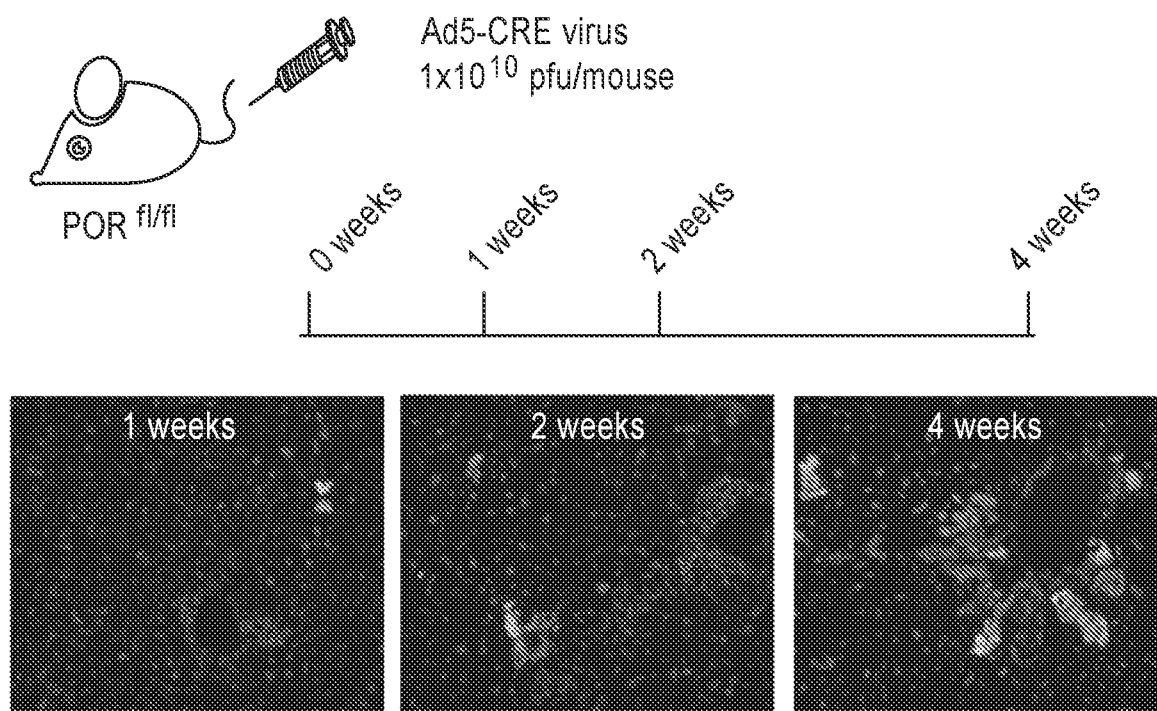
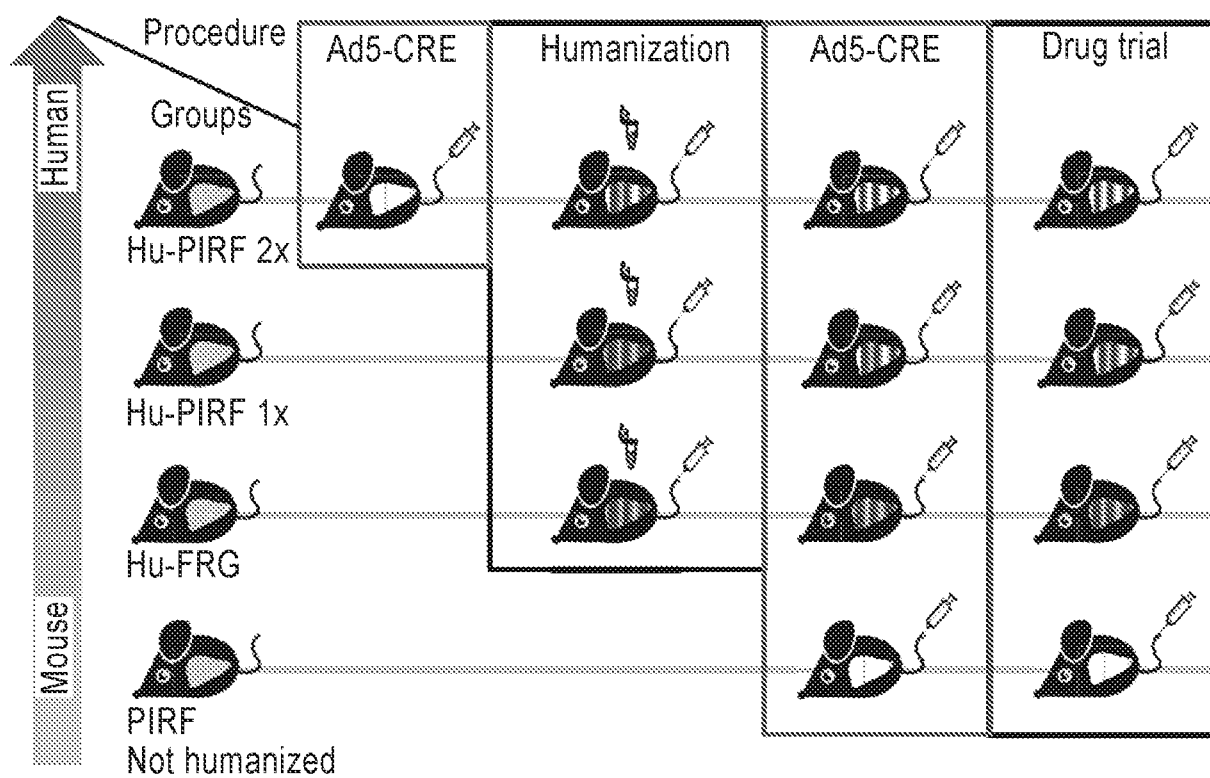


Figure 10



18/31

Figure 11A

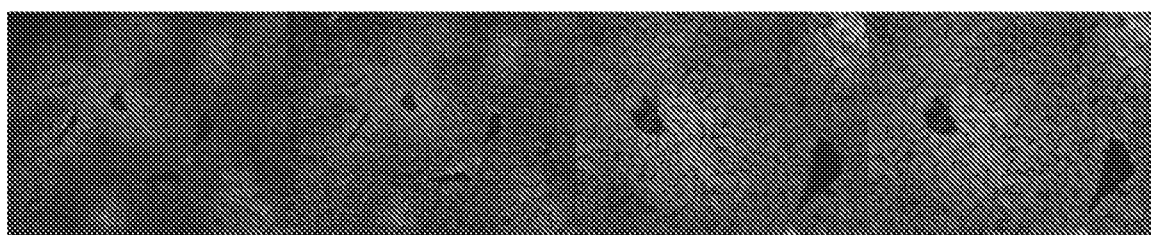
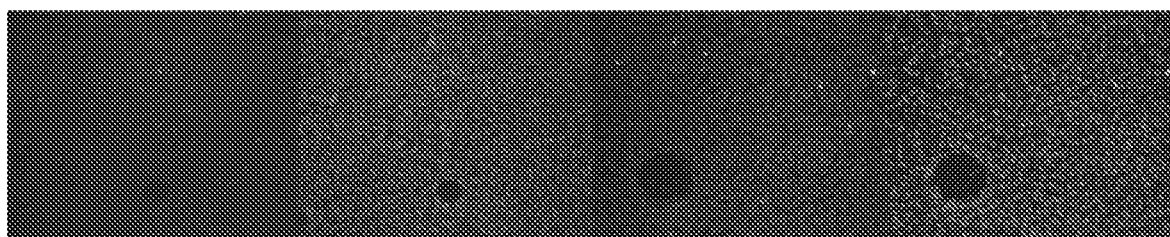
 $Alb-CRE^{+/-}/PQR^{c/+}$ 

Figure 11B

 $Alb-CRE^{+/-}/PQR^{c/c}$ 

19/31

Figure 12A

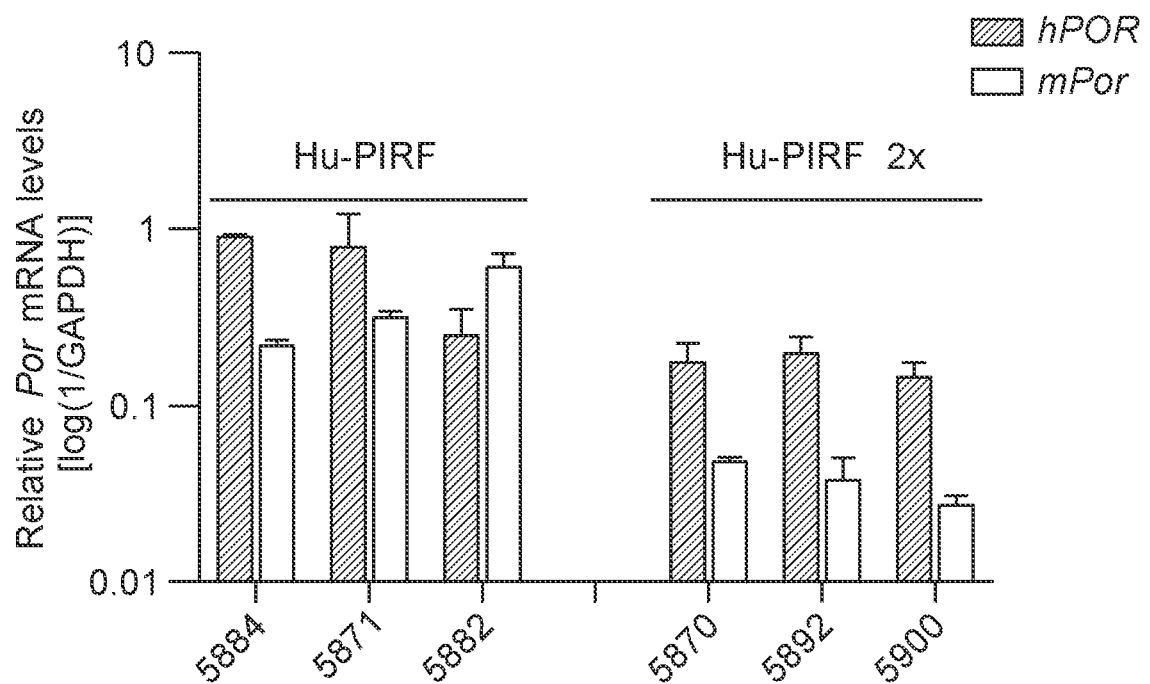
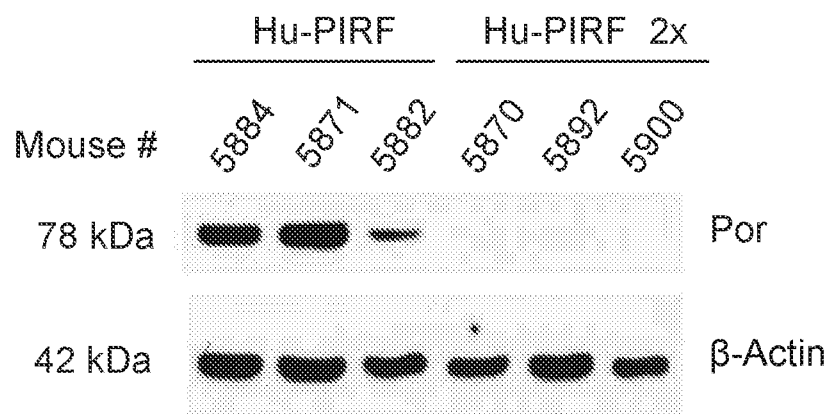


Figure 12B



20/31

Figure 13A

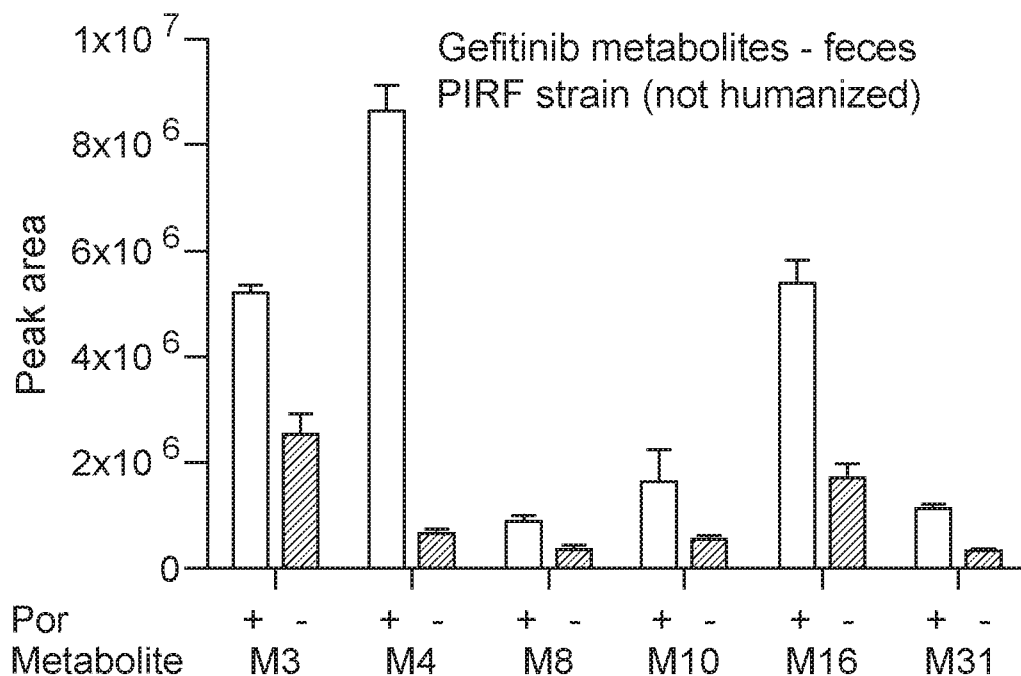
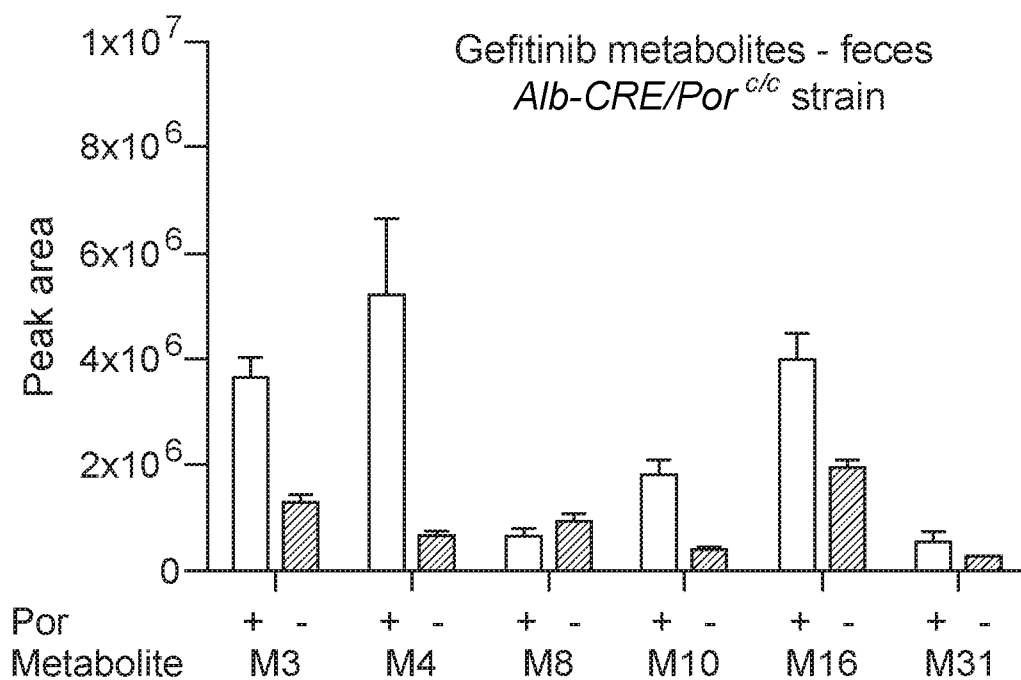


Figure 13B



21/31

Figure 14A

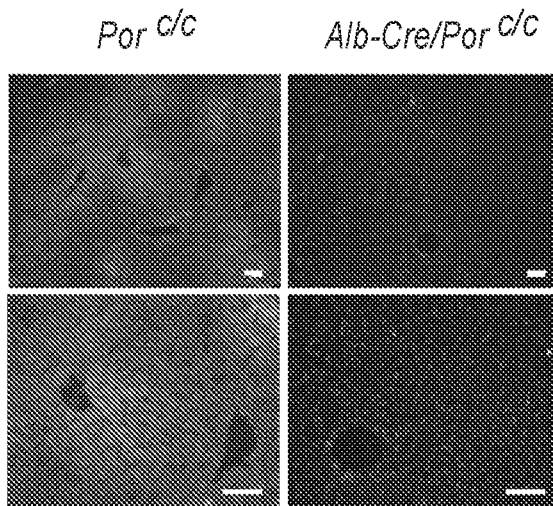


Figure 14B

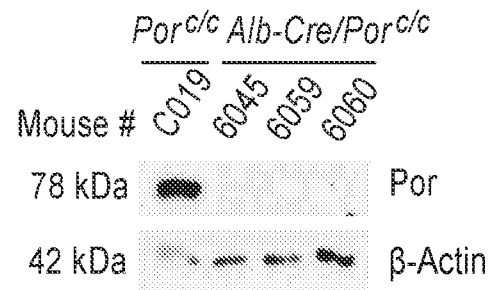
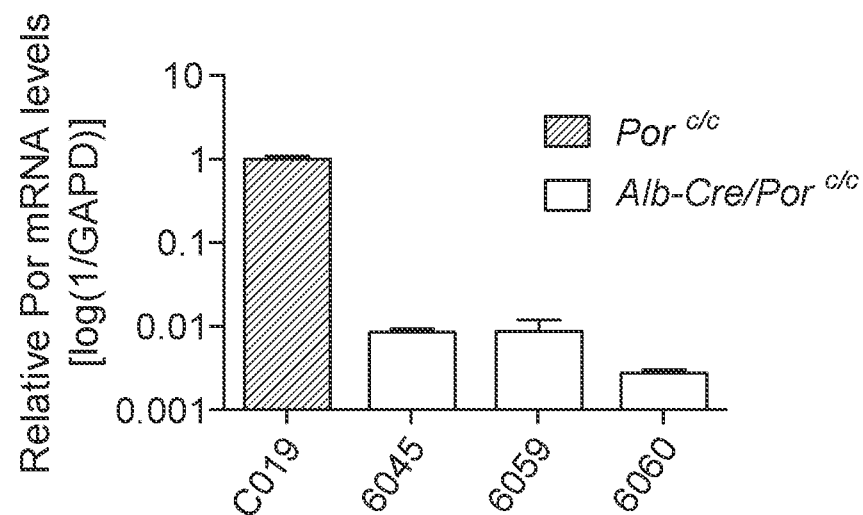
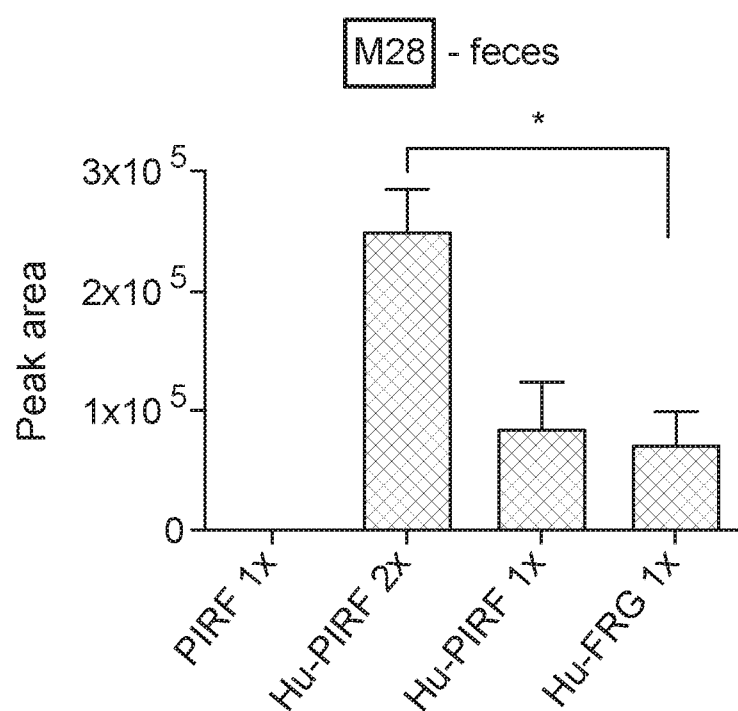


Figure 14C



22/31

Figure 15



23/31

Figure 16A

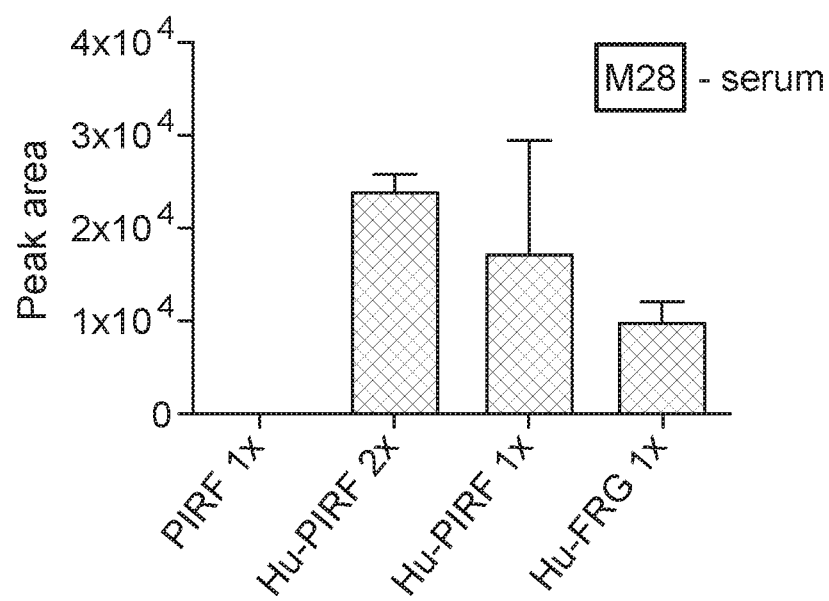
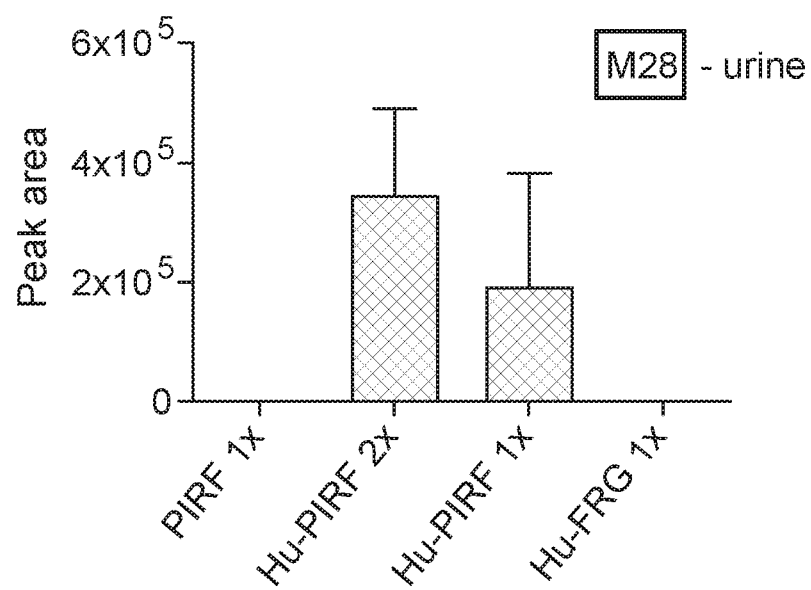
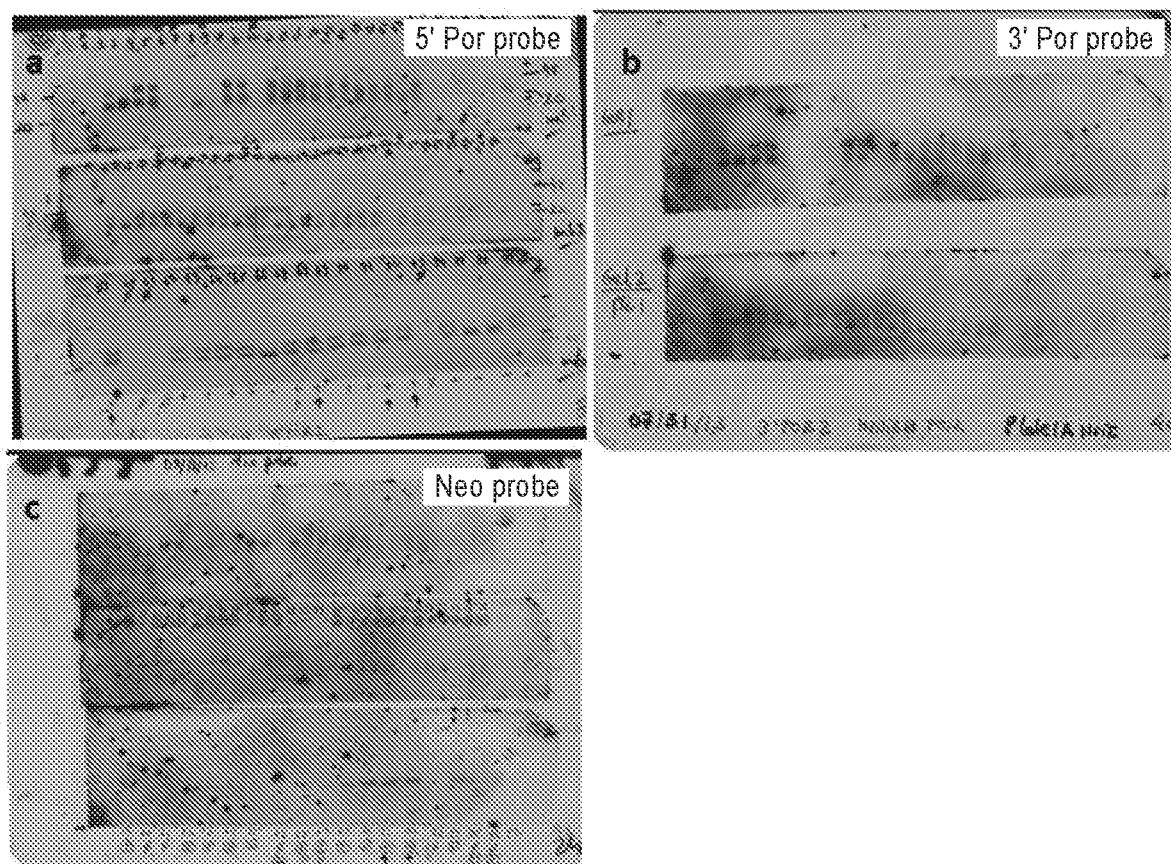


Figure 16B



24/31

Figure 17



25/31

Figure 18

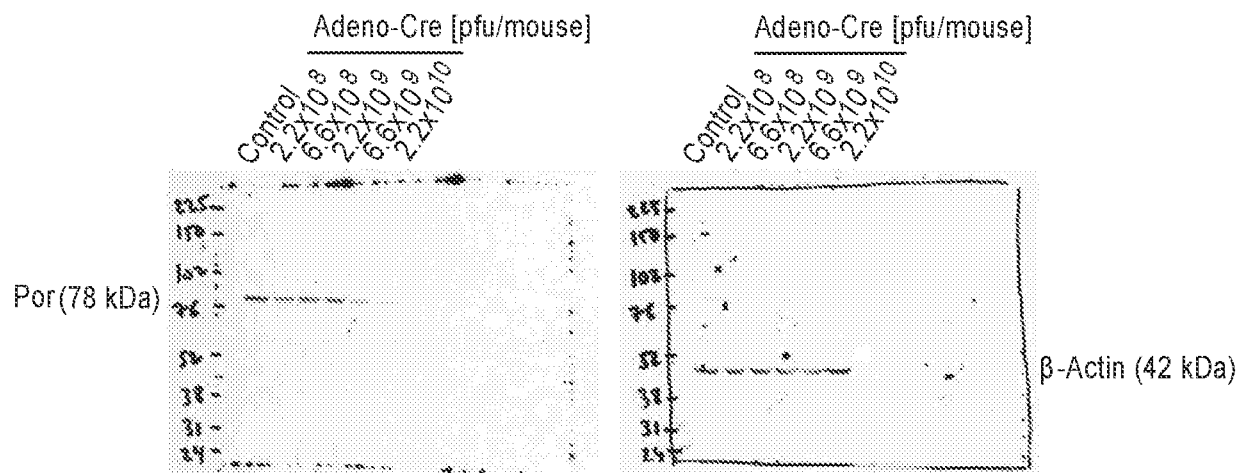


Figure 19A

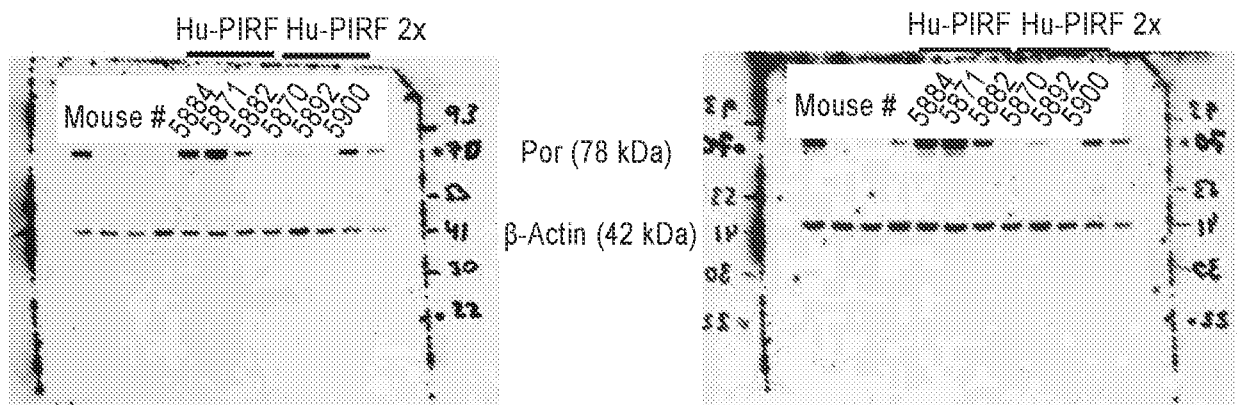
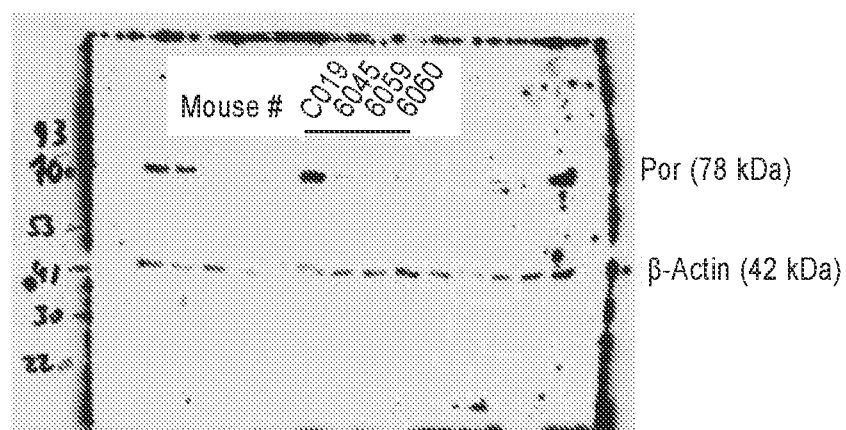
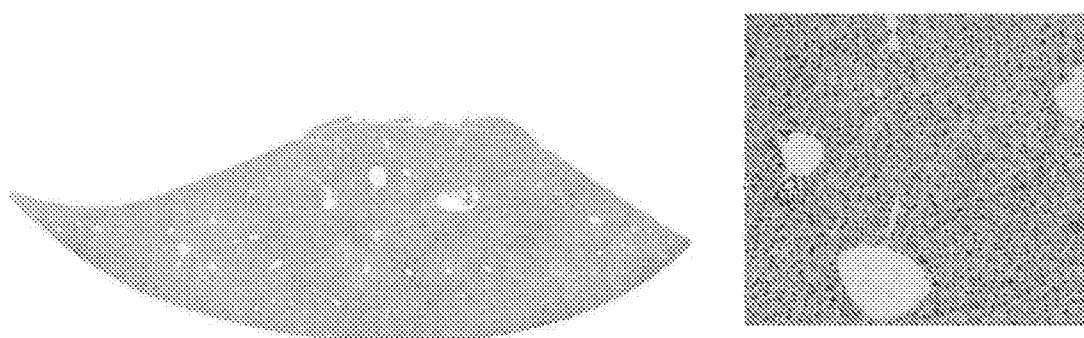


Figure 19B



26/31

Figure 20



27/31

Figure 21A

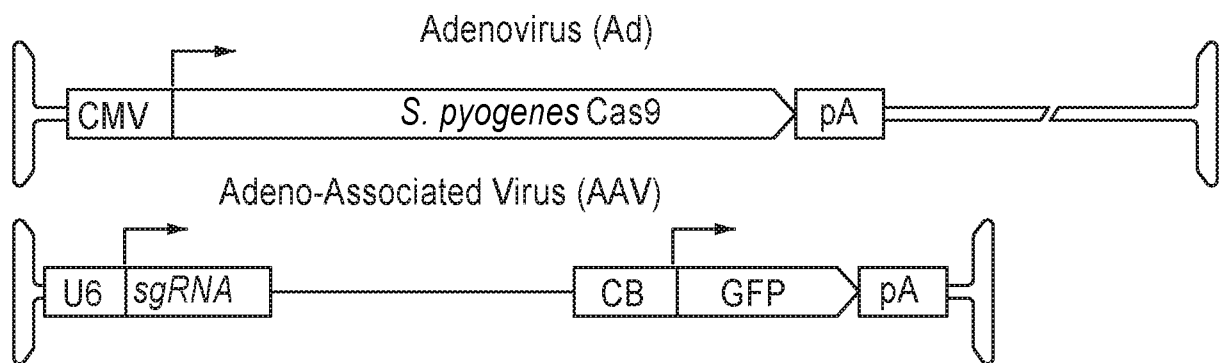


Figure 21B

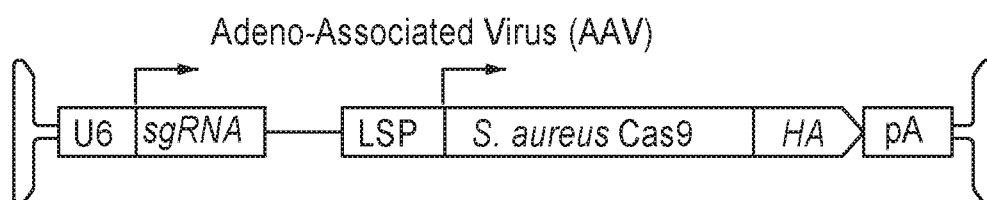


Figure 22

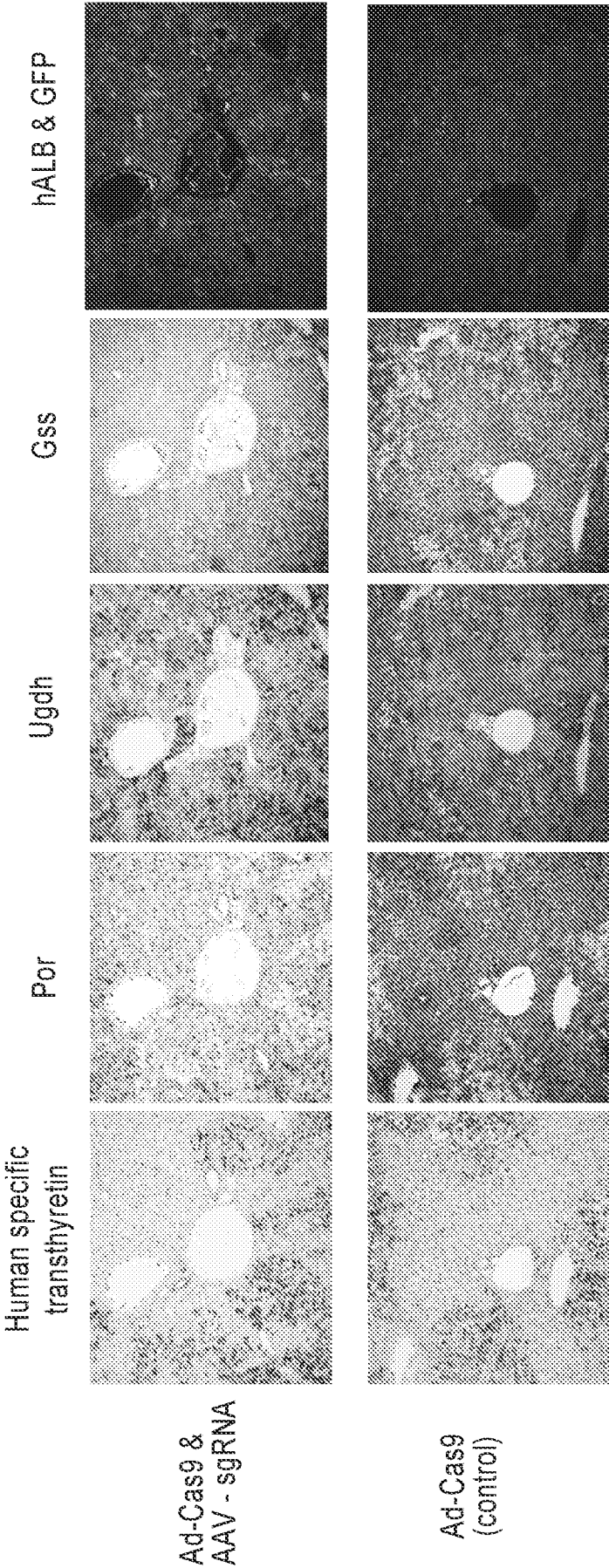
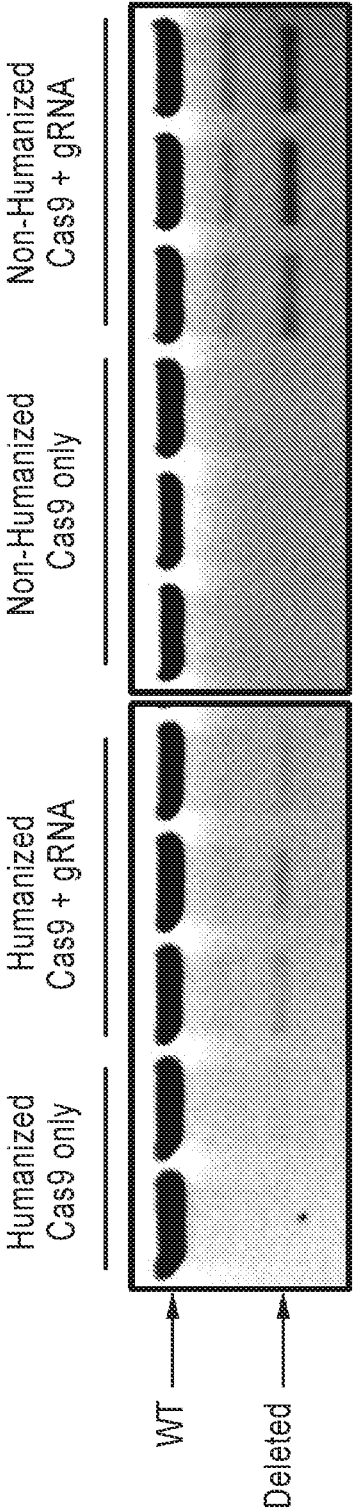
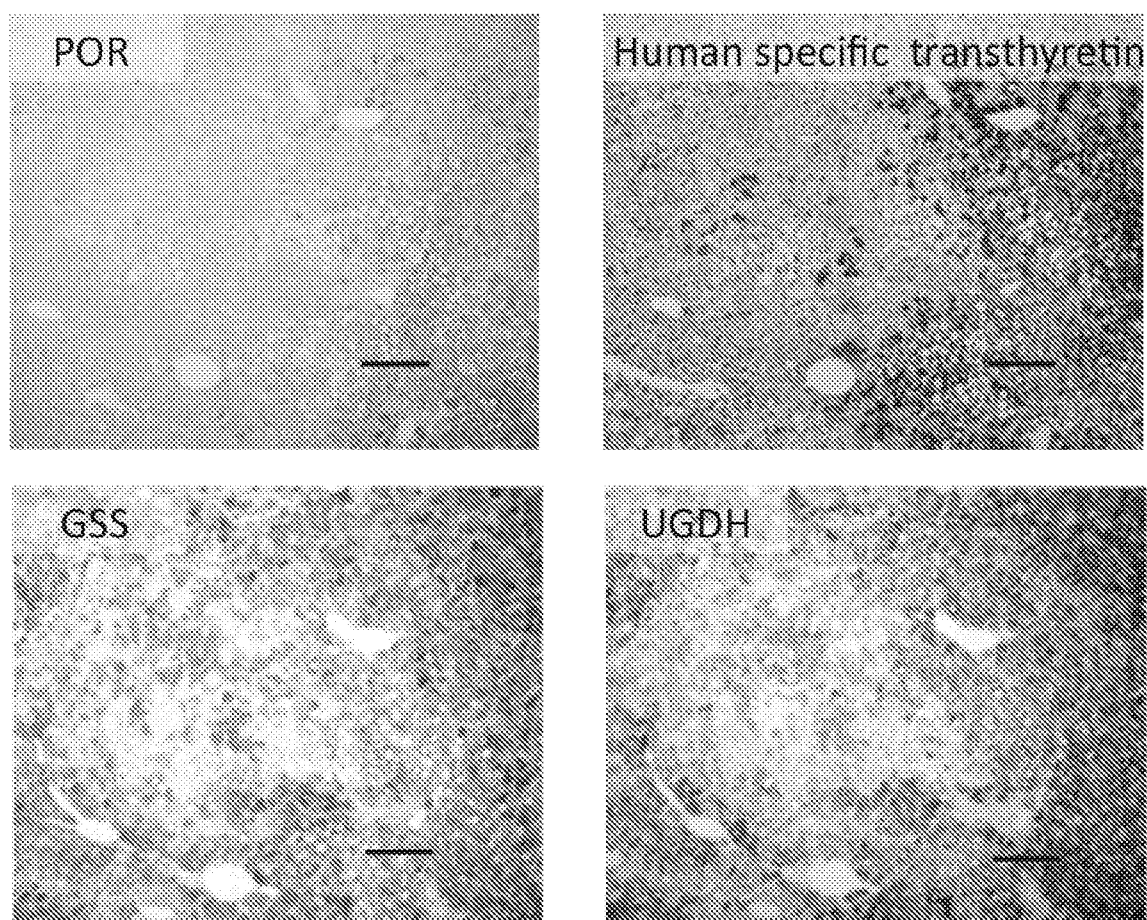


Figure 23



30/31

Figure 24



31/31

Figure 25A

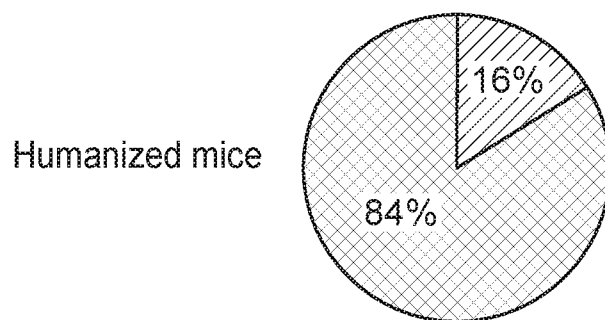


Figure 25B

POR deleted
UGDH deleted

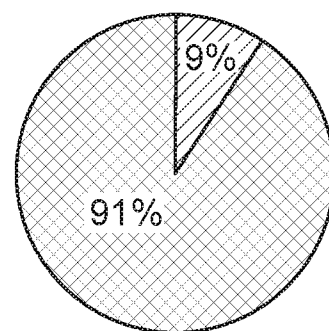


Figure 25C

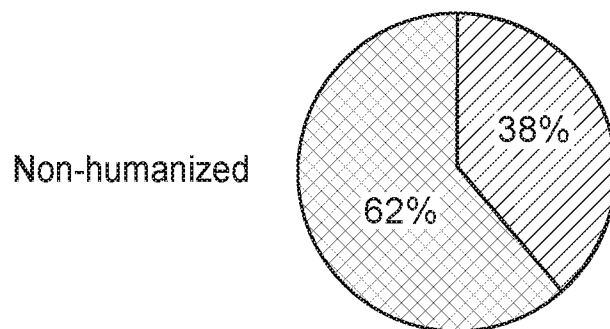


Figure 25D

