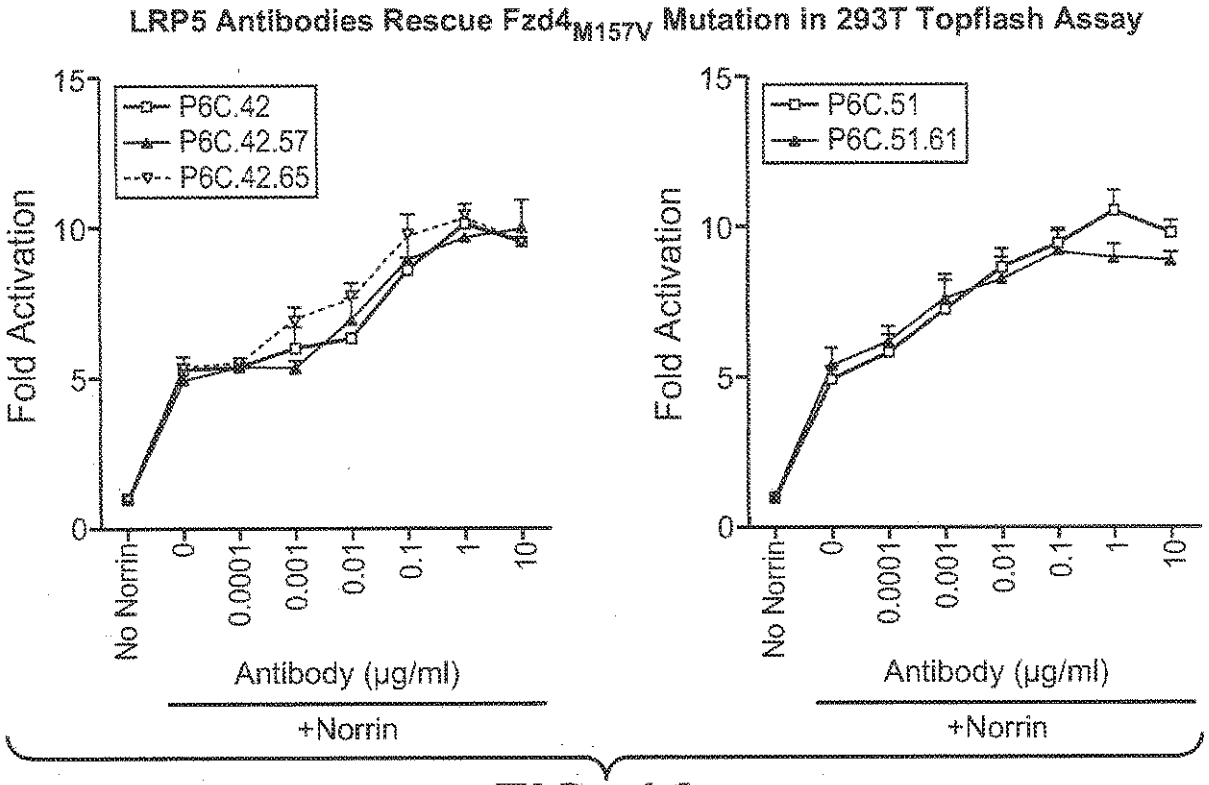

LRP5 Antibodies Rescue Fzd4M157V Mutation in 293T Topflash Assay
P6C.42
P6C.42.57
P6C.42.65
P6C.51
P6C.51.61
Fold Activation
No Norrin
0
0.0001
0.001
0.01
0.1
1
10
Antibody (µg/ml)
+Norrin

FIG. 1A

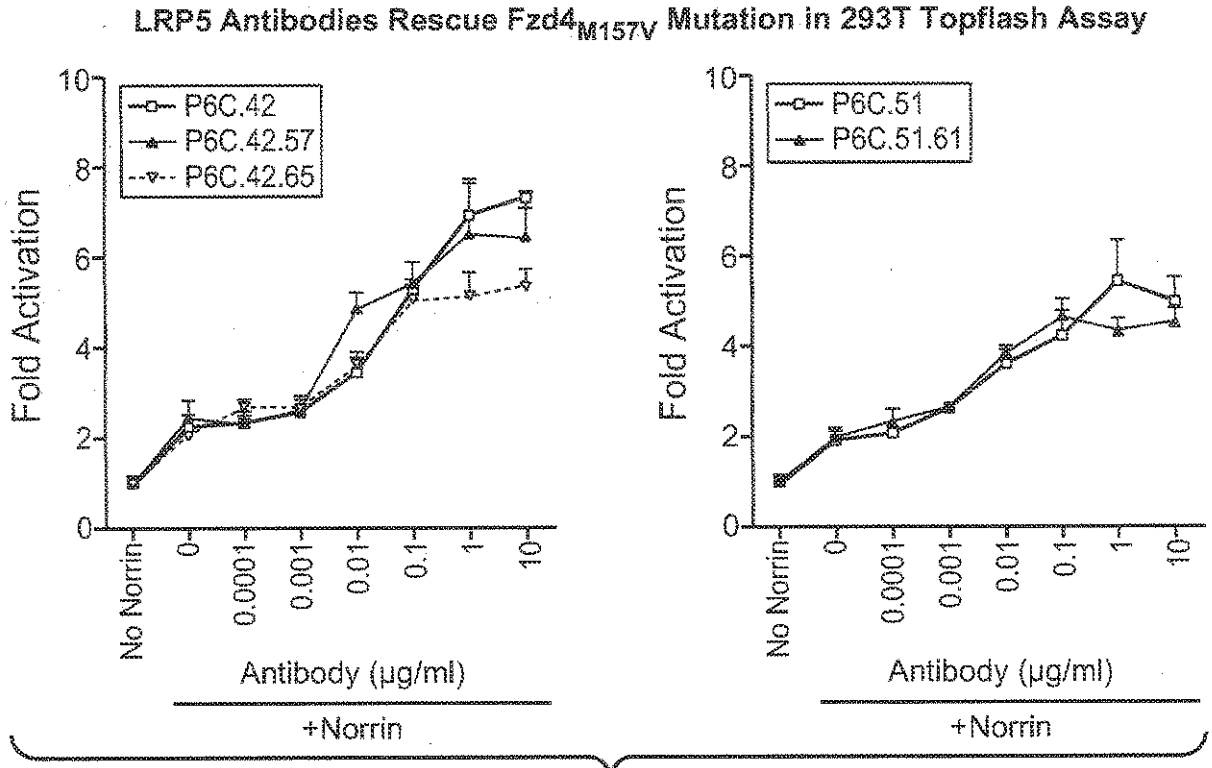

LRP5 Antibodies Rescue Fzd4M157V Mutation in 293T Topflash Assay
P6C.42
P6C.42.57
P6C.42.65
P6C.51
P6C.51.61
Fold Activation
No Norrin
0
0.0001
0.001
0.01
0.1
1
10
Antibody (µg/ml)
+Norrin

FIG. 1B

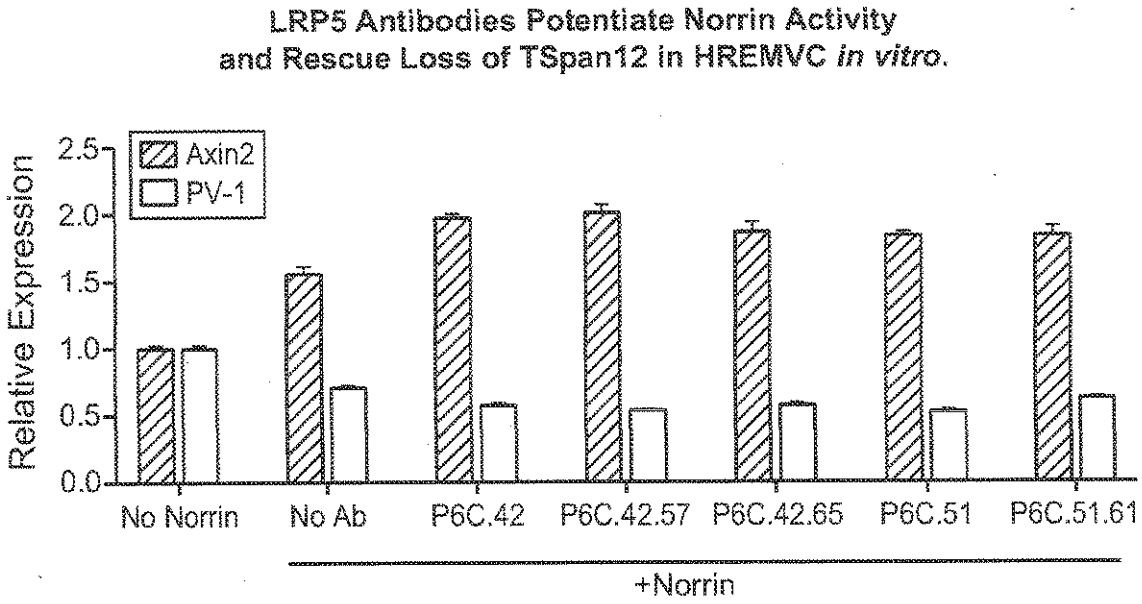

LRP5 Antibodies Potentiate Norrin Activity
and Rescue Loss of TSpan12 in HREMVC *in vitro*.
Relative Expression
2.5
2.0
1.5
1.0
0.5
0.0
Axin2
PV-1
No Norrin
No Ab
P6C.42
P6C.42.57
P6C.42.65
P6C.51
P6C.51.61
+Norrin

FIG. 2A

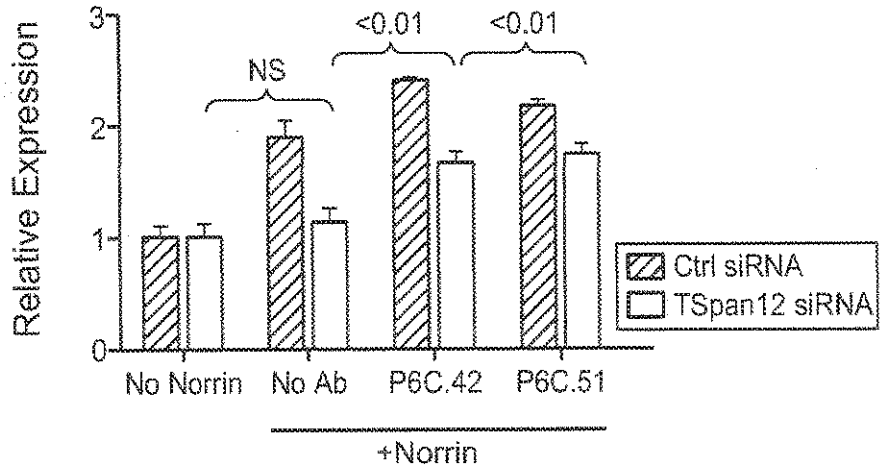

Relative Expression
3
2
1
0
NS
<0.01
<0.01
Ctrl siRNA
TSpan12 siRNA
No Norrin
No Ab
P6C.42
P6C.51
+Norrin

FIG. 2B

LRP5 Antibody, P6C.42, Partially Rescues Vascular Defects in the TSpan12 Knockout Mice *in vivo*.

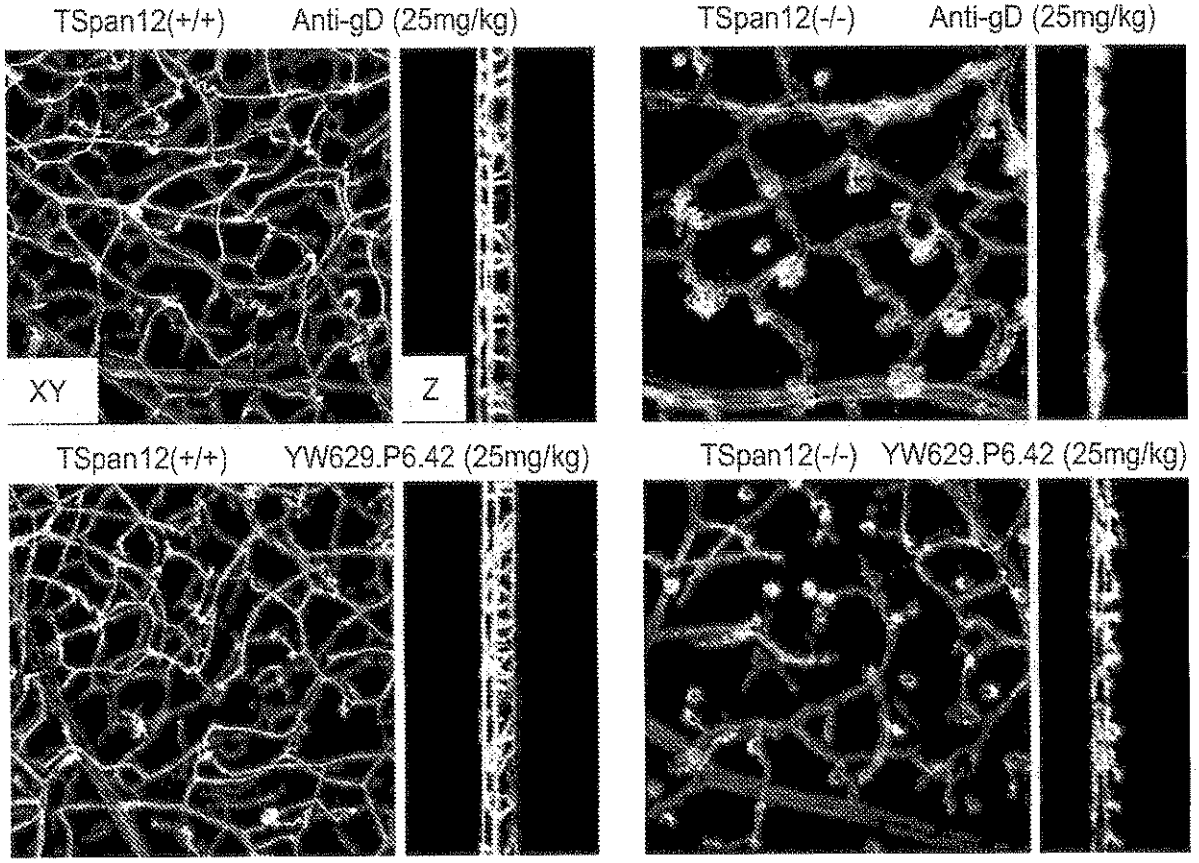


FIG. 3A

LRP5 Antibody, P6C.42, Partially Rescues Vascular Defects in the TSpan12 Knockout Mice *in vivo*.

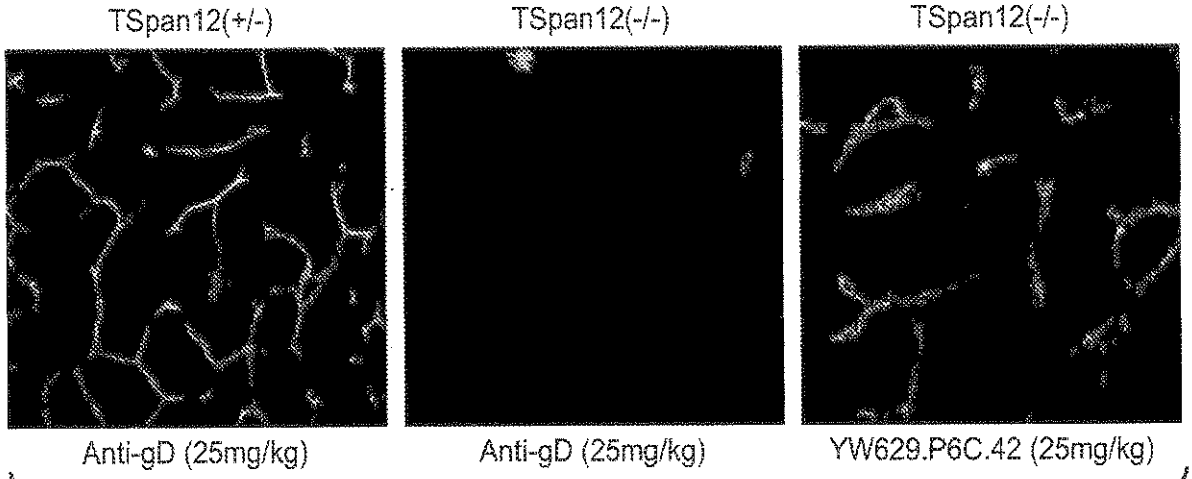


FIG. 3B

FIG. 4

FIG. 4A

FIG. 4B

Kabat#	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
																															Kabat - CDR H1										
																														Chothia - CDR H1				Contact - CDR H1						
YW629.42	E	V	Q	L	V	E	S	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	A	M	S	W	V	R	Q	A
YW629.42.57	E	V	Q	L	V	E	S	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	A	M	S	W	V	R	Q	A
YW629.42.58	E	V	Q	L	V	E	S	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	A	M	S	W	V	R	Q	A
YW629.42.65	E	V	Q	L	V	E	S	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	A	M	S	W	V	R	Q	A
YW629.51	E	V	Q	L	V	E	S	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	A	M	H	W	V	R	Q	A
YW629.51.13	E	V	Q	L	V	E	S	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	A	M	H	W	V	R	Q	A
YW629.51.61	E	V	Q	L	V	E	S	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	A	M	H	W	V	R	Q	A
YW629.51.63	E	V	Q	L	V	E	S	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	A	M	H	W	V	R	Q	A
YW629.51.77	E	V	Q	L	V	E	S	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	A	M	H	W	V	R	Q	A
YW629.51.78	E	V	Q	L	V	E	S	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	A	M	H	W	V	R	Q	A
YW629.51.80	E	V	Q	L	V	E	S	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	T	F	S	S	Y	A	M	H	W	V	R	Q	A

FIG. 4A

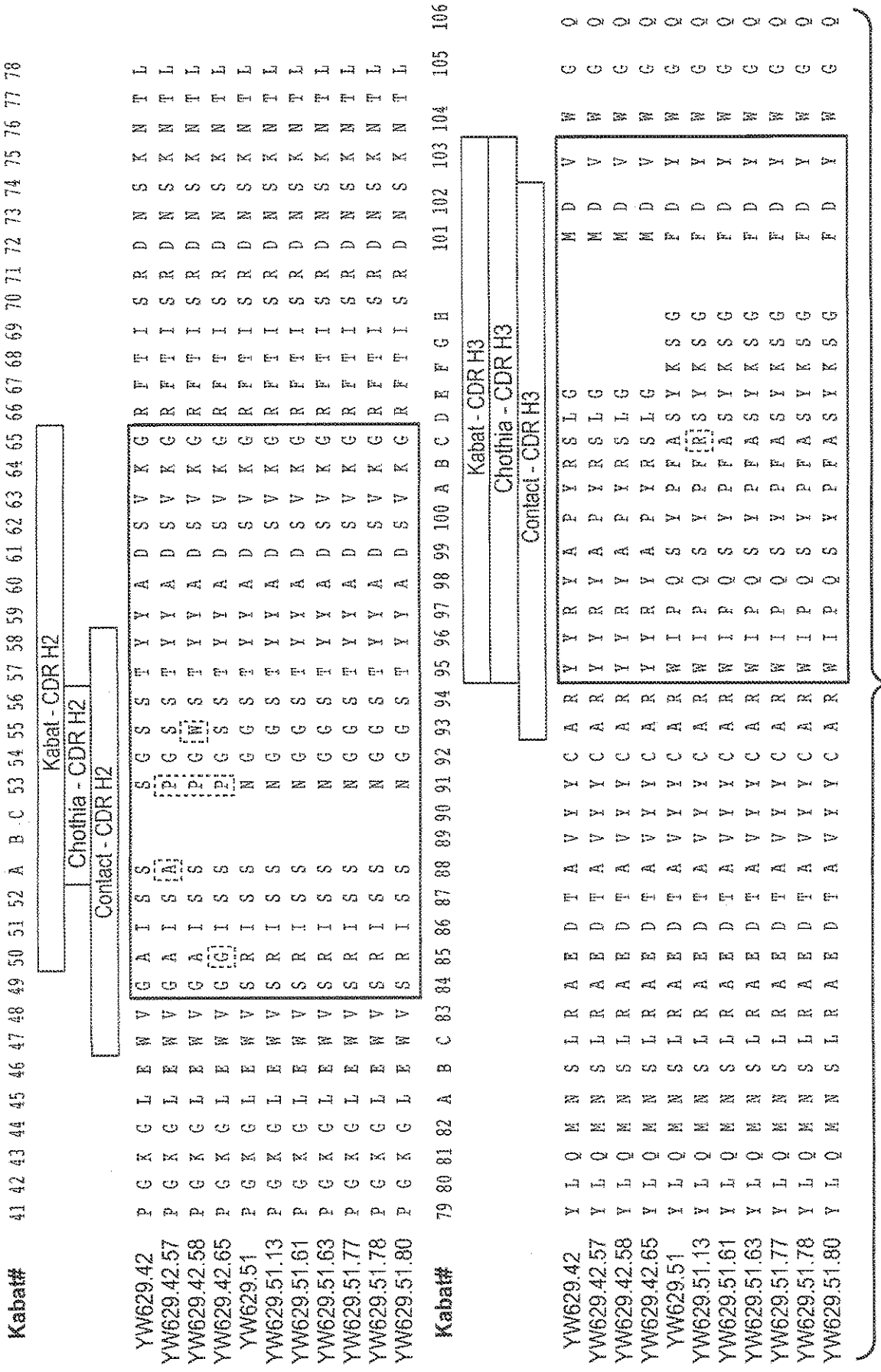

Kabat - CDR H2
Chothia - CDR H2
Contact - CDR H2
Kabat - CDR H3
Chothia - CDR H3
Contact - CDR H3

FIG. 4B

FIG. 5A

FIG. 5B

FIG. 5

Kabat#	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	A	B	C	D	E	F	28	29	30	31	32	33	34	35	36	37
																								Kabat - CDR L1																			
																								Chothia - CDR L1																		
																																				Contact - CDR L1						
YW629.42	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q						G	I	S	S	Y	L	A	W	Y	Q
YW629.42.57	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q						G	I	S	S	Y	L	A	W	Y	Q
YW629.42.58	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q						G	I	S	S	Y	L	A	W	Y	Q
YW629.42.65	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q						G	I	S	S	Y	L	A	W	Y	Q
YW629.51	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q						G	I	S	S	Y	L	A	W	Y	Q
YW629.51.13	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q						G	I	S	S	Y	L	A	W	Y	Q
YW629.51.61	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q						V	M	G	Y	Y	L	A	W	Y	Q
YW629.51.63	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q						S	I	Y	Y	Y	L	A	W	Y	Q
YW629.51.77	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q						V	I	Y	G	Y	L	A	W	Y	Q
YW629.51.78	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q						G	I	F	Y	Y	L	A	W	Y	Q
YW629.51.80	D	I	Q	M	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q						A	I	Y	S	Y	L	A	W	Y	Q

FIG. 5A

Kabat#	38	39	40	41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80
													Kabat - CDR L2																																
													Chothia - CDR L2																																
												Contact - CDR L2																																		
YW629.42	Q	K	P	G	K	A	P	K	L	L	I	Y	A	A	S	S	L	Q	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
YW629.42.57	Q	K	P	G	K	A	P	K	L	L	I	Y	A	A	S	S	L	Q	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
YW629.42.58	Q	K	P	G	K	A	P	K	L	L	I	Y	A	A	S	S	L	Q	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
YW629.42.65	Q	K	P	G	K	A	P	K	L	L	I	Y	A	A	S	S	L	Q	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
YW629.51	Q	K	P	G	K	A	P	K	L	L	I	Y	D	A	S	S	L	E	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
YW629.51.13	Q	K	P	G	K	A	P	K	L	L	I	Y	D	A	S	S	L	E	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
YW629.51.61	Q	K	P	G	K	A	P	K	L	L	I	Y	D	A	S	S	L	E	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
YW629.51.63	Q	K	P	G	K	A	P	K	L	L	I	Y	D	A	S	S	L	E	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
YW629.51.77	Q	K	P	G	K	A	P	K	L	L	I	Y	D	A	S	T	R	E	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
YW629.51.78	Q	K	P	G	K	A	P	K	L	L	I	Y	D	A	S	T	L	E	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
YW629.51.80	Q	K	P	G	K	A	P	K	L	L	I	Y	D	A	S	S	L	E	S	G	V	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P

Kabat#	81	82	83	84	85	86	87	88	89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108
									Kabat - CDR L3																			
									Chothia - CDR L3																			
									Contact - CDR L3																			
YW629.42	E	D	F	A	T	Y	Y	C	Q	Q	Y	Y	S	Y	P	F	T	F	G	Q	G	T	K	V	E	I	K	R
YW629.42.57	E	D	F	A	T	Y	Y	C	Q	Q	Y	Y	S	Y	P	F	T	F	G	Q	G	T	K	V	E	I	K	R
YW629.42.58	E	D	F	A	T	Y	Y	C	Q	Q	Y	Y	S	Y	P	F	T	F	G	Q	G	T	K	V	E	I	K	R
YW629.42.65	E	D	F	A	T	Y	Y	C	Q	Q	Y	Y	L	Y	P	F	T	F	G	Q	G	T	K	V	E	I	K	R
YW629.51	E	D	F	A	T	Y	Y	C	Q	Q	Y	Y	S	Y	P	F	T	F	G	Q	G	T	K	V	E	I	K	R
YW629.51.13	E	D	F	A	T	Y	Y	C	Q	Q	Y	Y	S	Y	P	F	T	F	G	Q	G	T	K	V	E	I	K	R
YW629.51.61	E	D	F	A	T	Y	Y	C	Q	Q	Y	Y	S	Y	P	F	T	F	G	Q	G	T	K	V	E	I	K	R
YW629.51.63	E	D	F	A	T	Y	Y	C	Q	Q	Y	Y	S	Y	P	F	T	F	G	Q	G	T	K	V	E	I	K	R
YW629.51.77	E	D	F	A	T	Y	Y	C	Q	Q	Y	Y	S	Y	P	F	T	F	G	Q	G	T	K	V	E	I	K	R
YW629.51.78	E	D	F	A	T	Y	Y	C	Q	Q	Y	Y	S	Y	P	F	T	F	G	Q	G	T	K	V	E	I	K	R
YW629.51.80	E	D	F	A	T	Y	Y	C	Q	Q	Y	Y	S	Y	P	F	T	F	G	Q	G	T	K	V	E	I	K	R

FIG. 5B

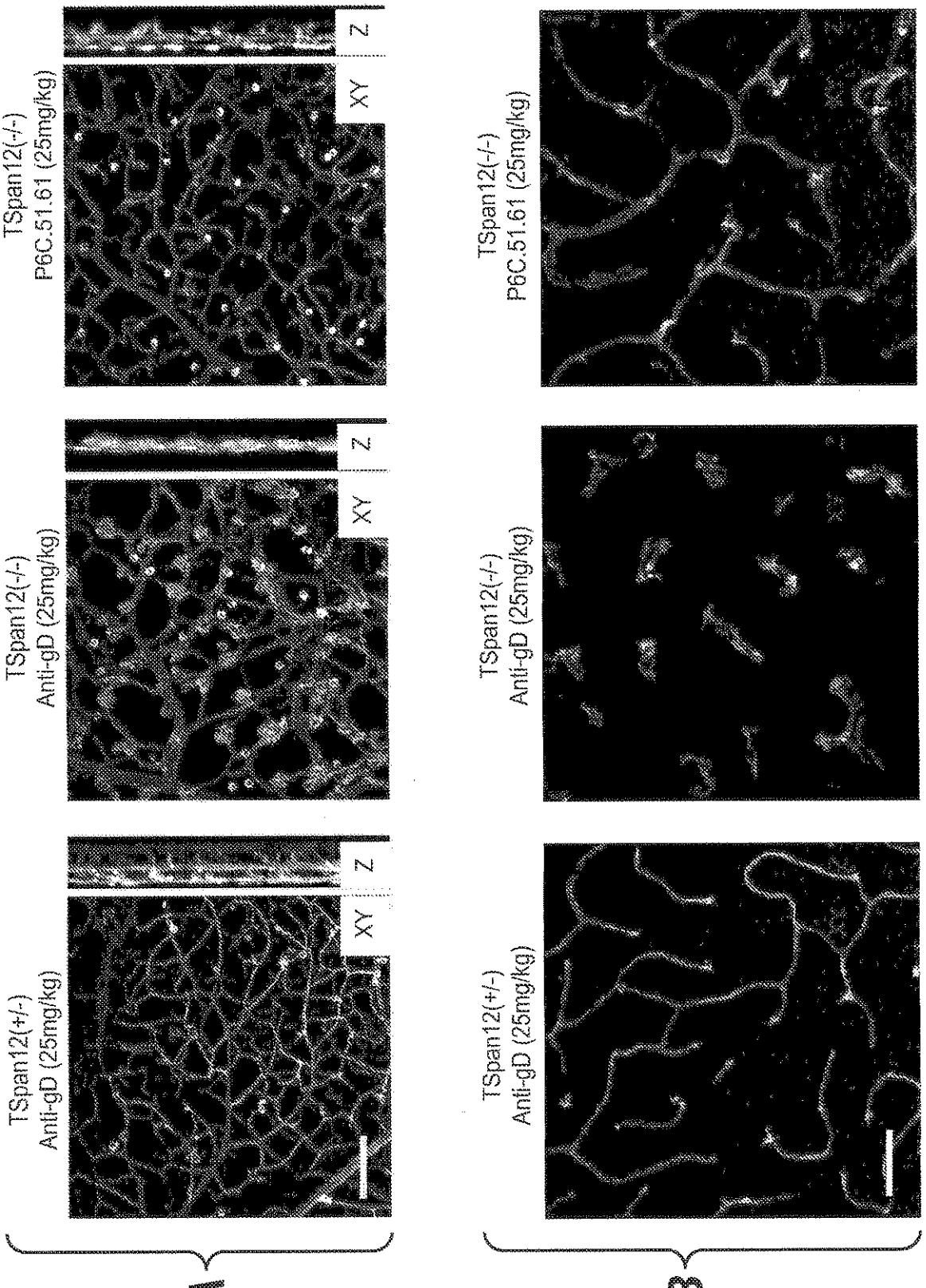

TSpan12(+/-)
Anti-gD (25mg/kg)
XY
Z
TSpan12(-/-)
Anti-gD (25mg/kg)
XY
Z
TSpan12(-/-)
P6C.51.61 (25mg/kg)
XY
Z

FIG. 6A

TSpan12(+/-)
Anti-gD (25mg/kg)
TSpan12(-/-)
Anti-gD (25mg/kg)
TSpan12(-/-)
P6C.51.61 (25mg/kg)

FIG. 6B

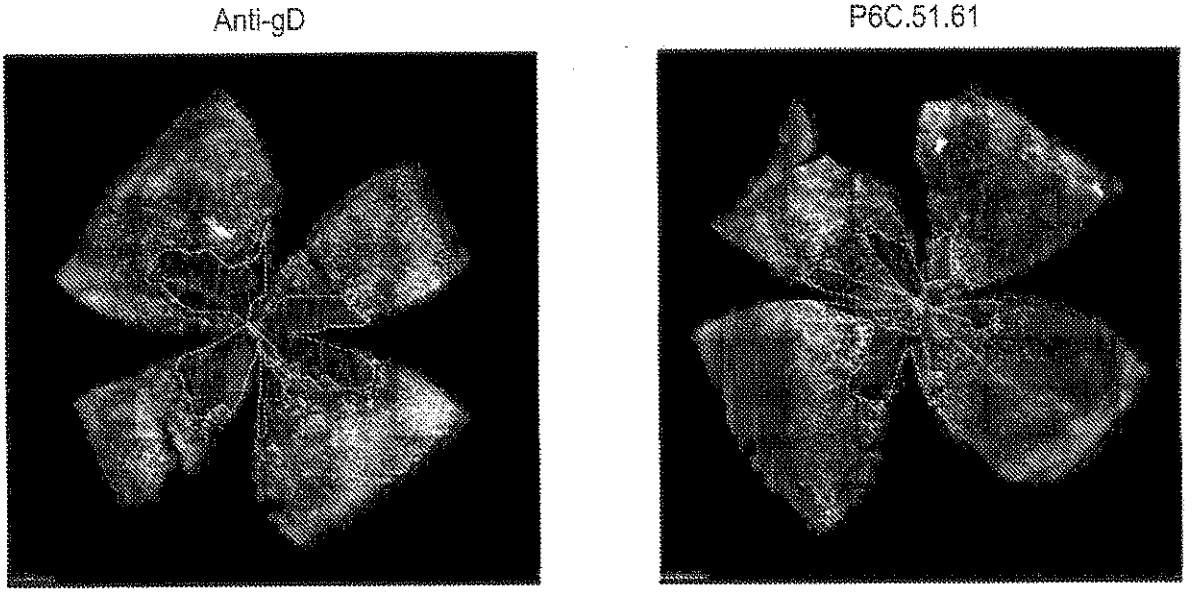


FIG. 7A

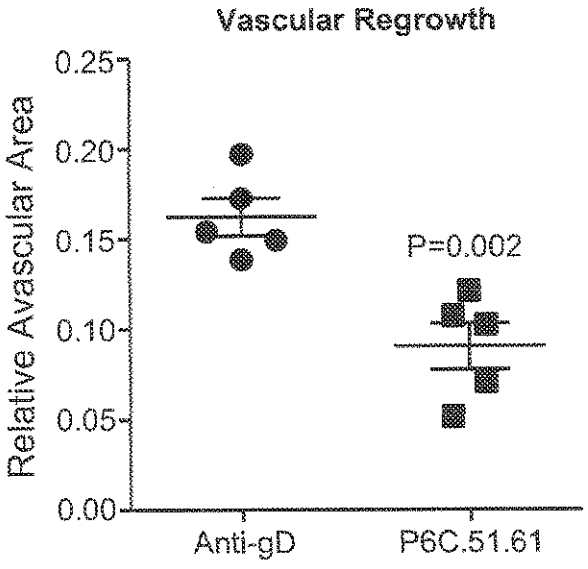


FIG. 7B

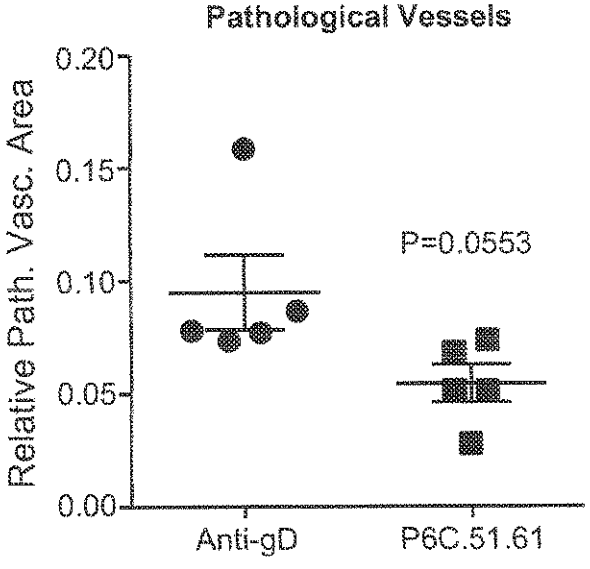


FIG. 7C

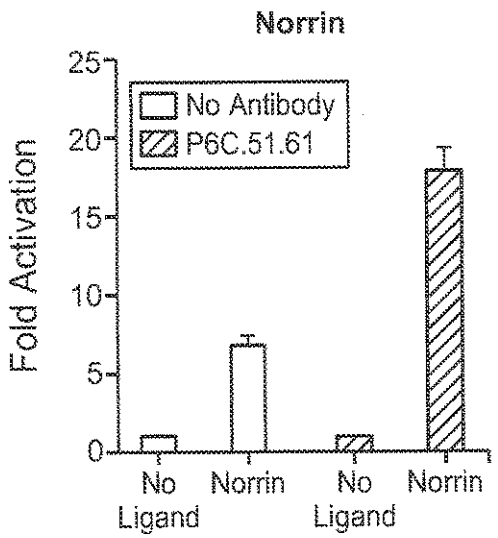


FIG. 8A

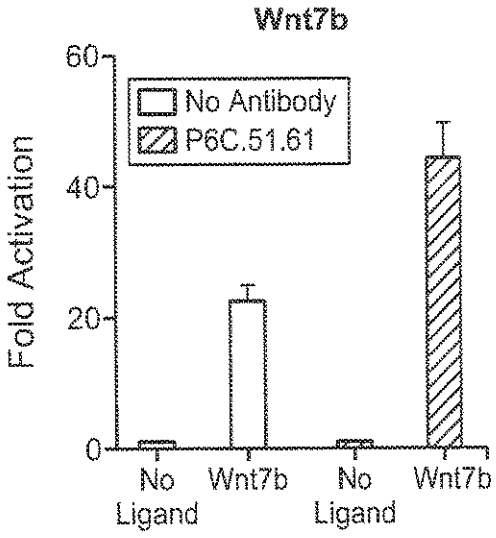


FIG. 8B

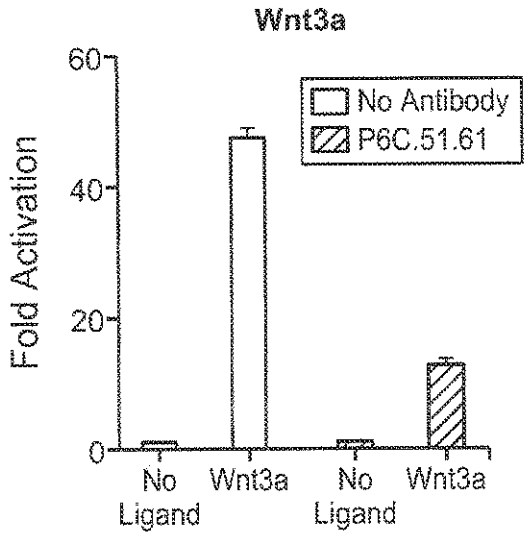


FIG. 8C

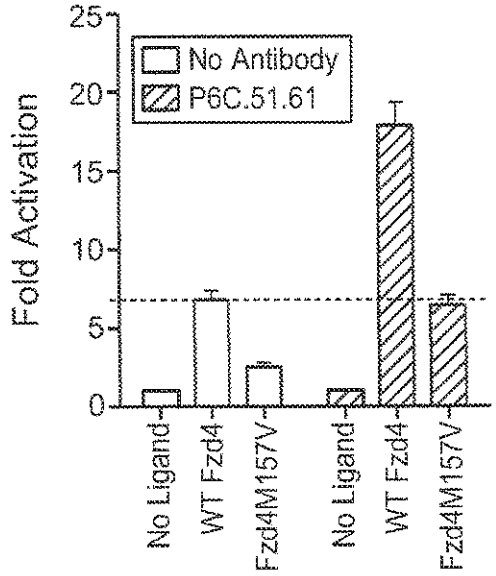


FIG. 9A

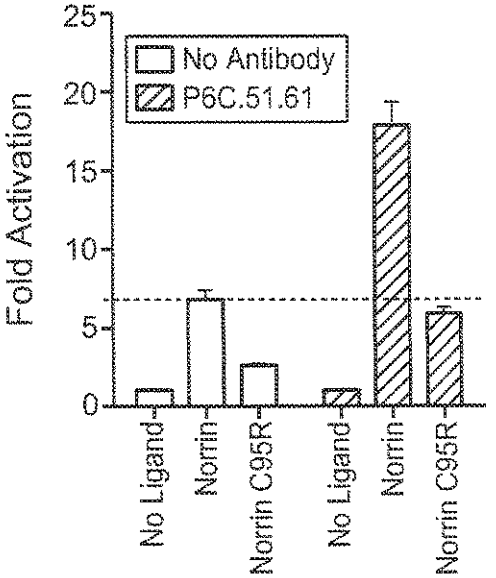


FIG. 9B

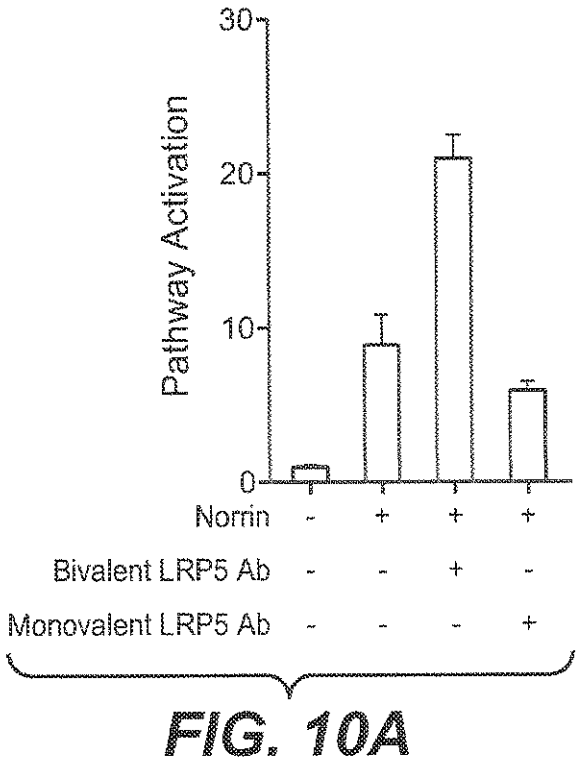


FIG. 10A

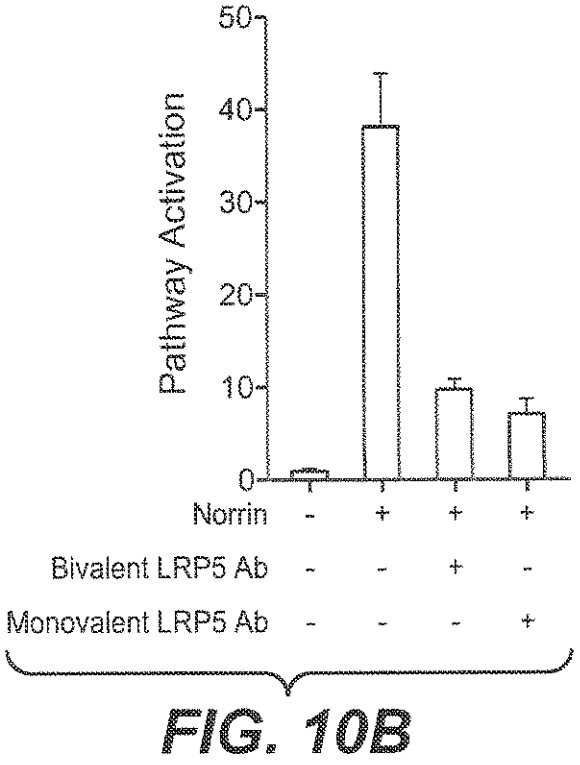


FIG. 10B