

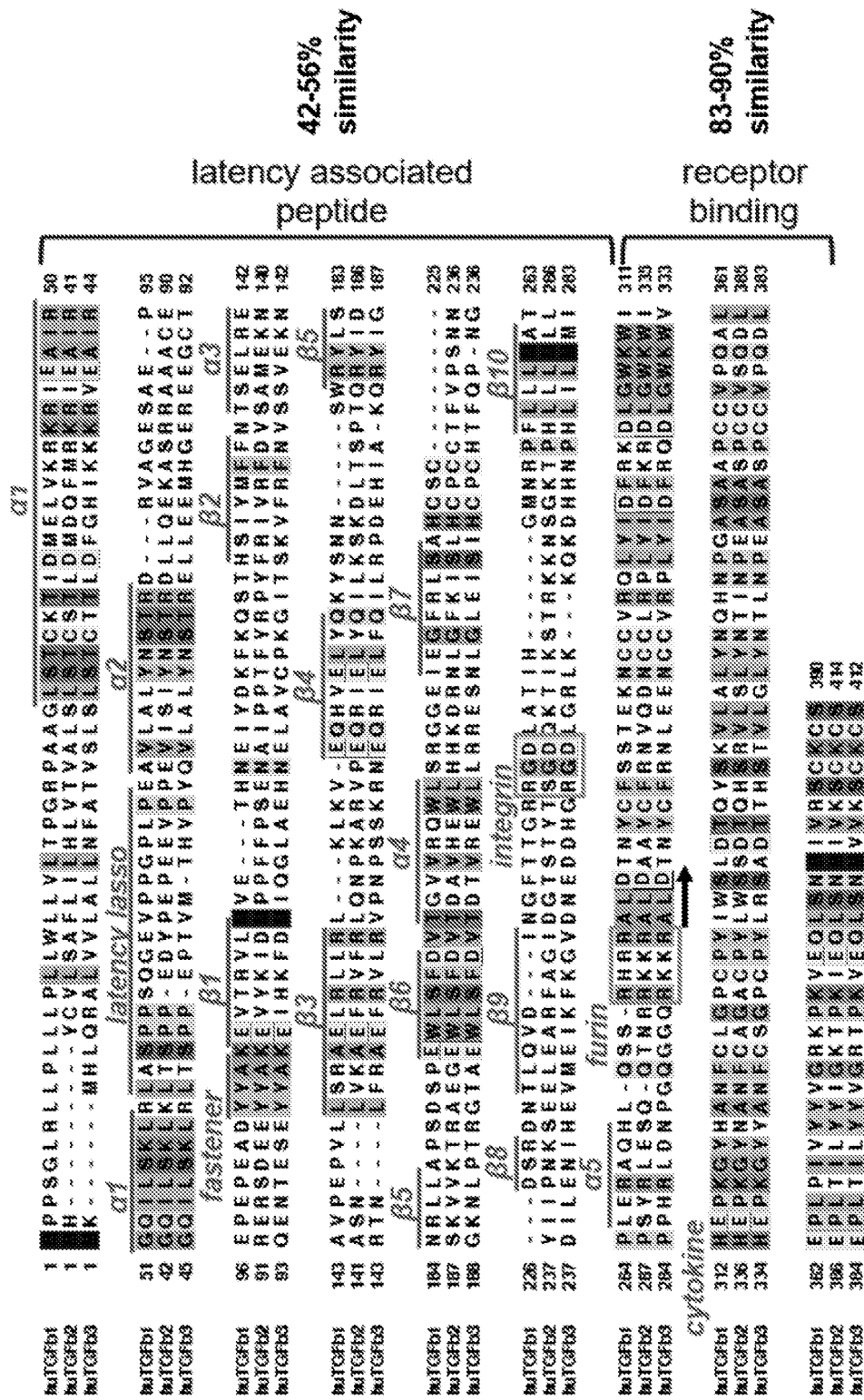


FIG. 1

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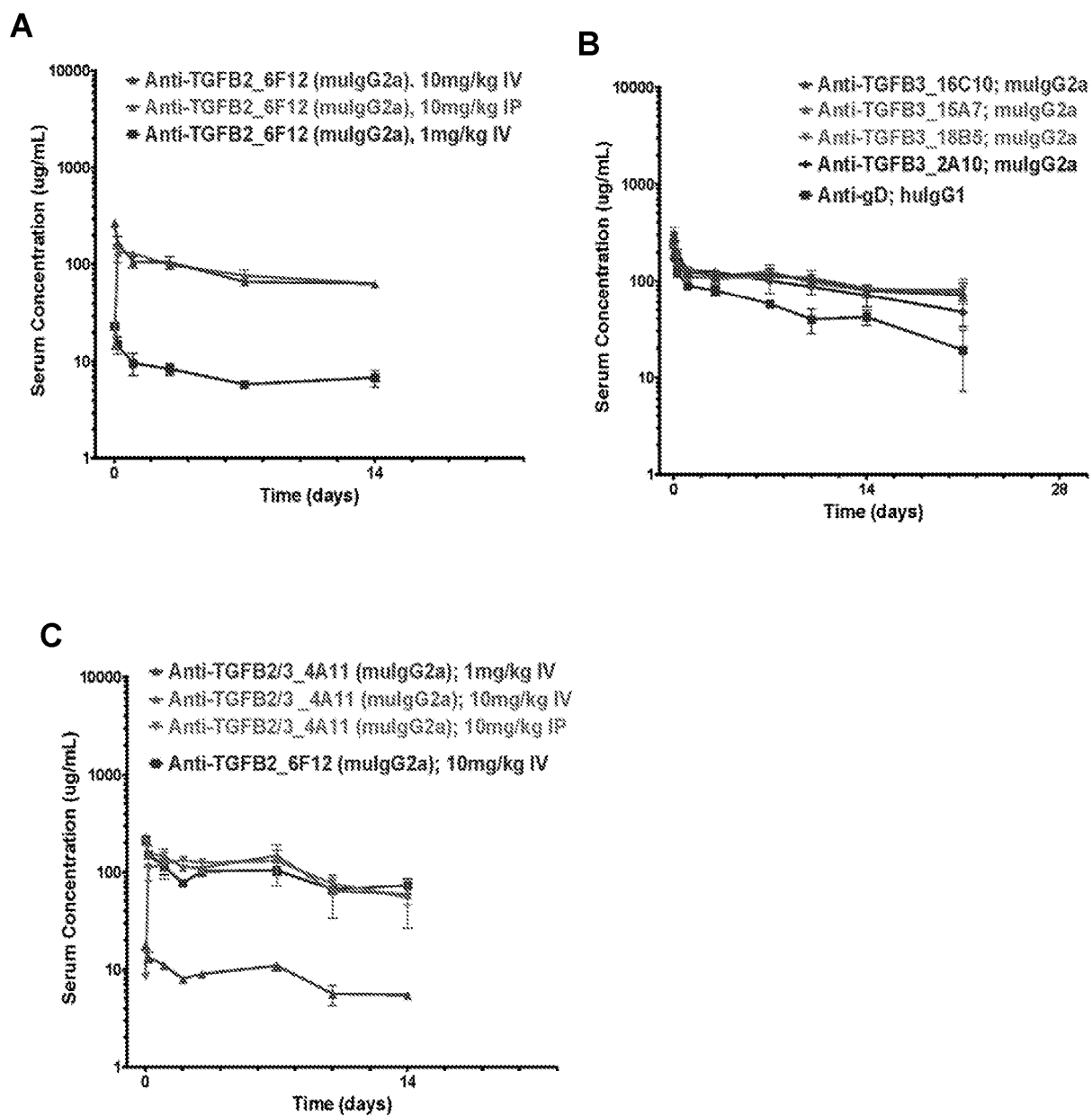


FIG. 2

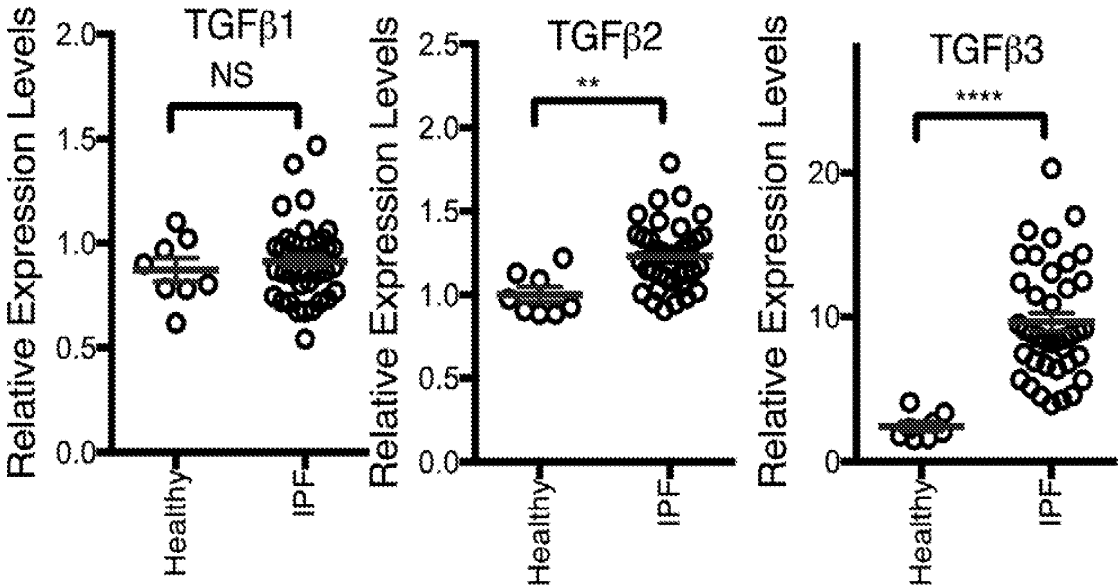


FIG. 3A

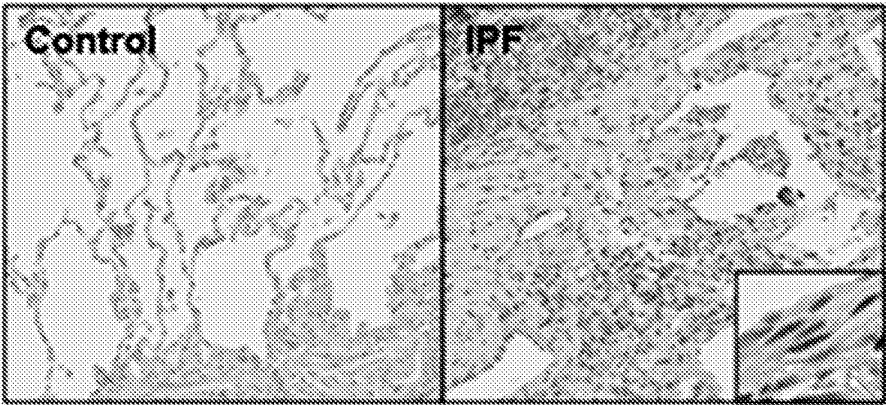
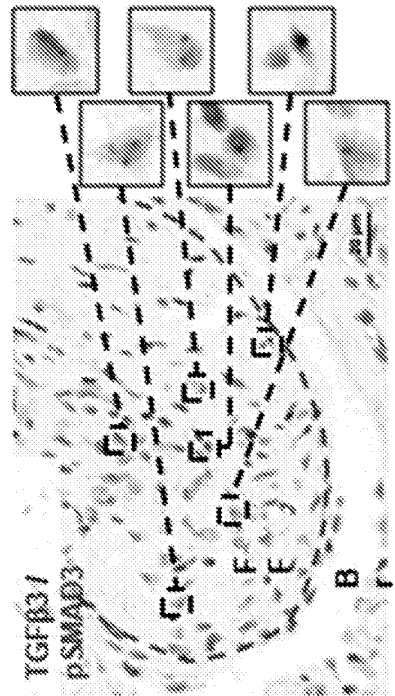


FIG. 3B



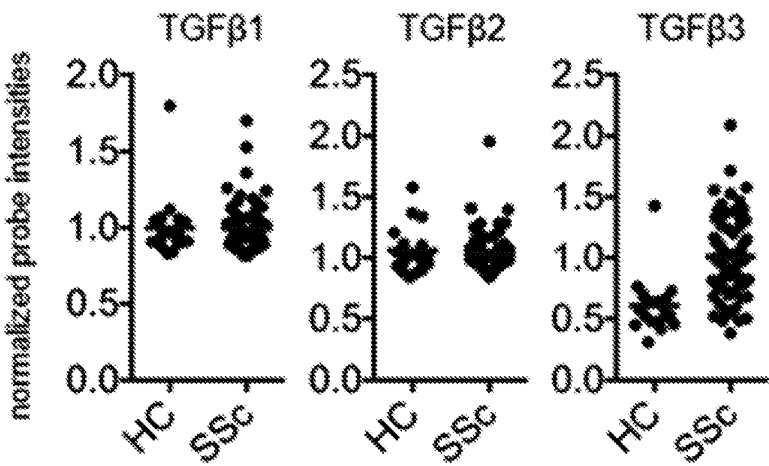


FIG. 5A

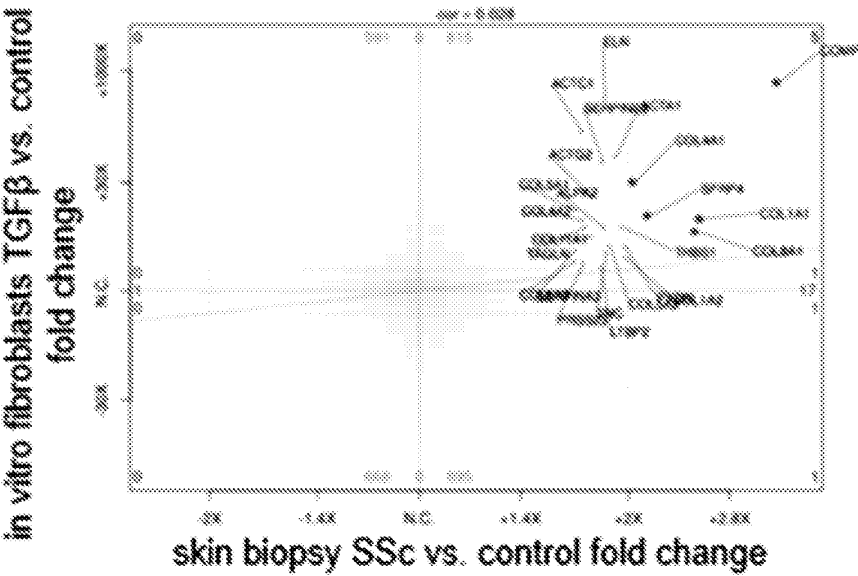


FIG. 5B

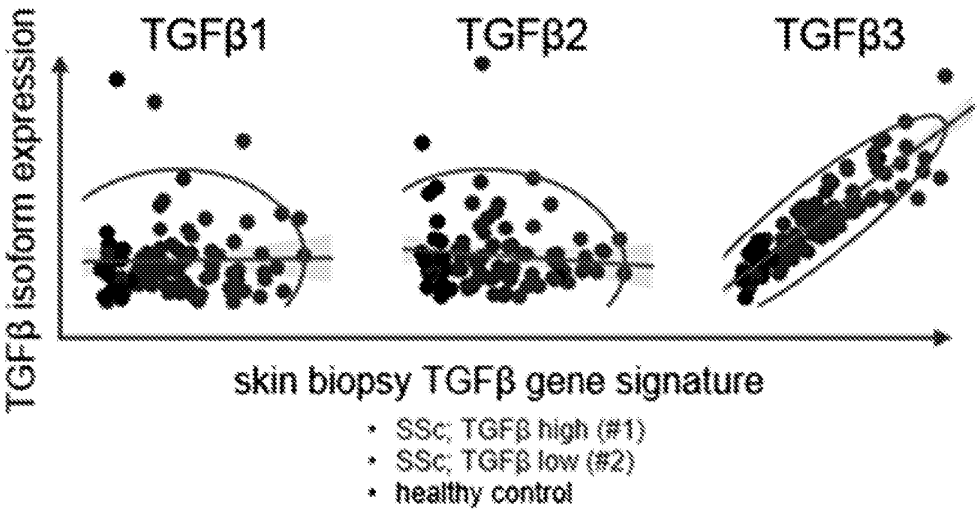


FIG. 6A

intercorrelations with skin TGFβ gene signature

variable	Spearman ρ	p-value
TGFβ1 expression	0.03	0.8
TGFβ2 expression	-0.1	0.4
TGFβ3 expression	0.92	<10⁻⁴
POSTN expression	0.76	<10⁻⁴
COMP expression	0.89	<10⁻⁴
serum periostin	0.55	<10⁻⁴
serum COMP	0.39	0.002

FIG. 6B

intercorrelations with baseline MRSS

serum periostin	0.76	<10⁻⁴
serum COMP	0.70	<10⁻⁴

FIG. 6C

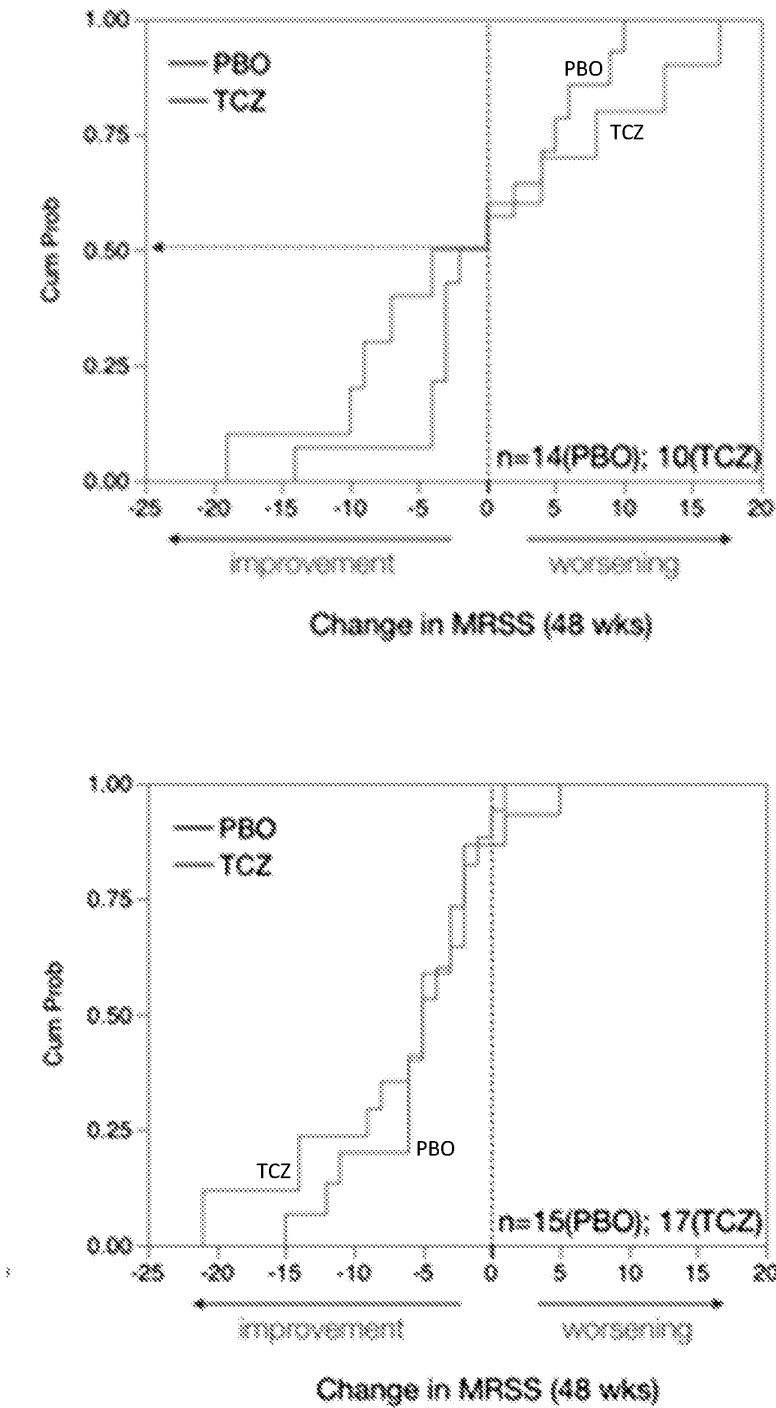


FIG. 7

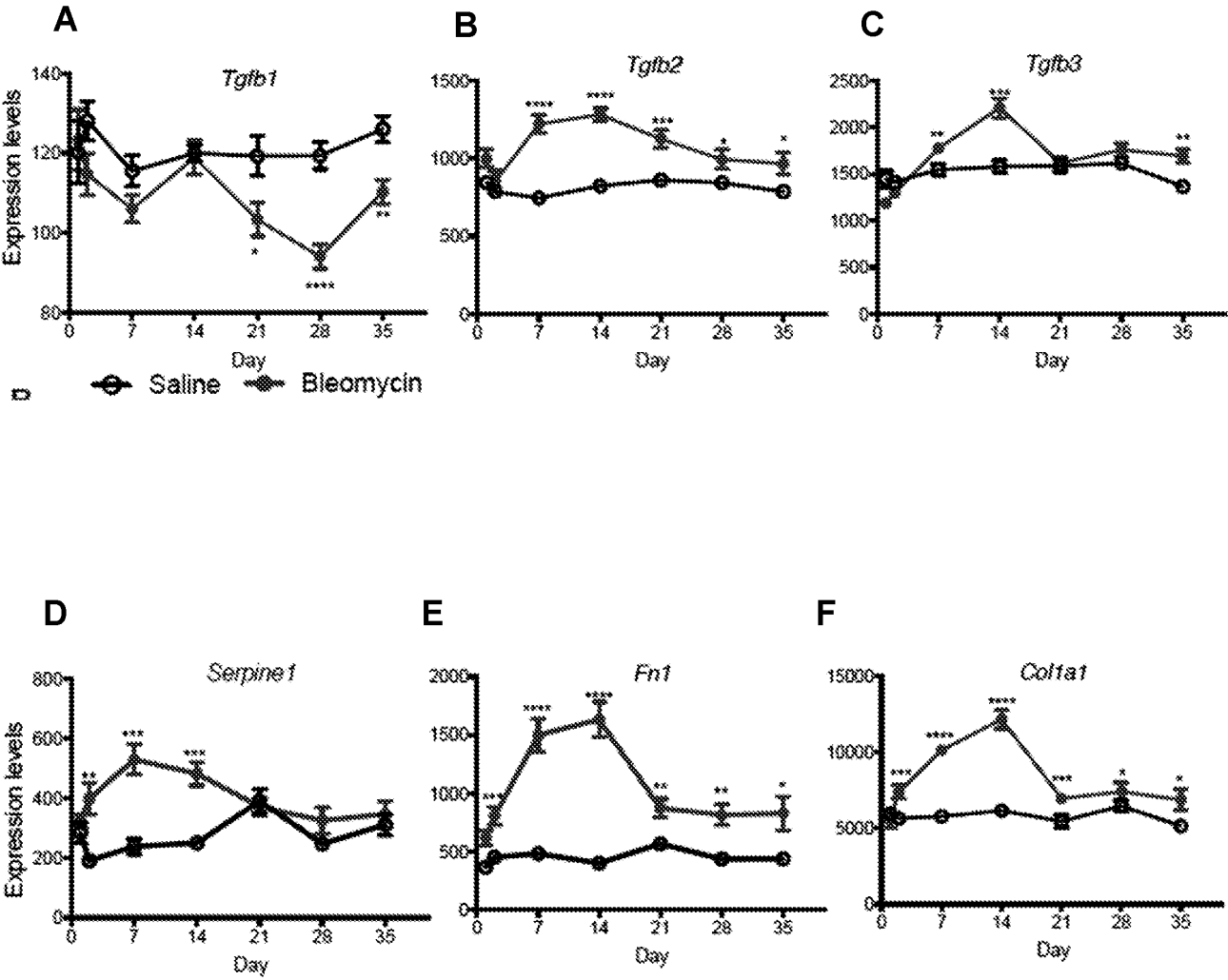


FIG. 8

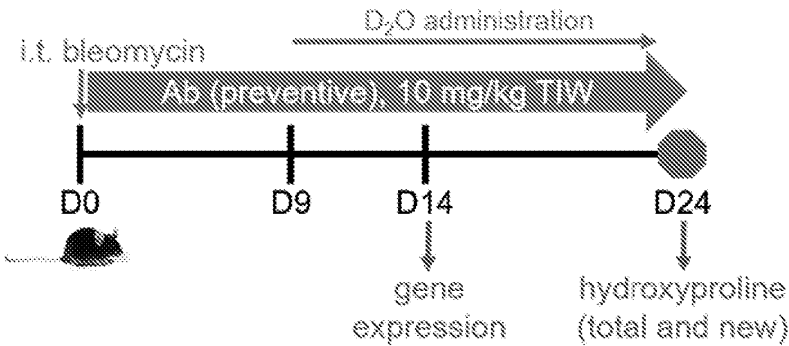


FIG. 9A

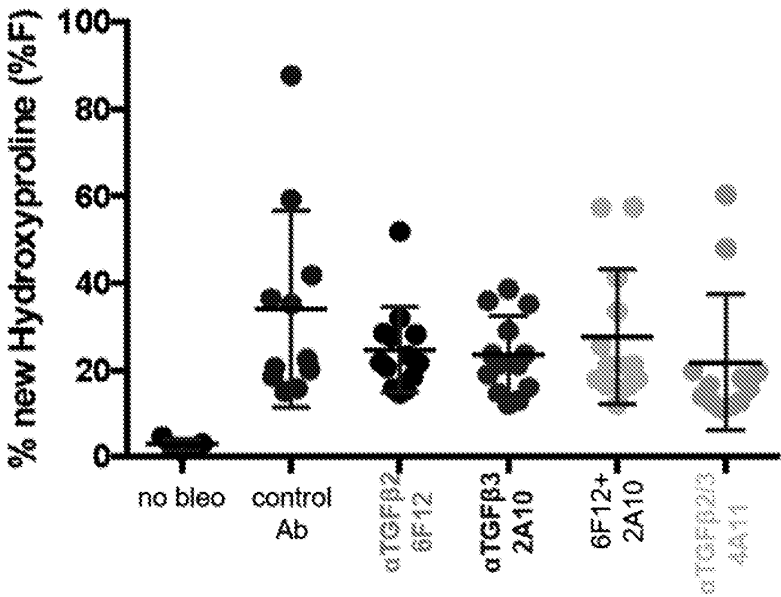


FIG. 9B

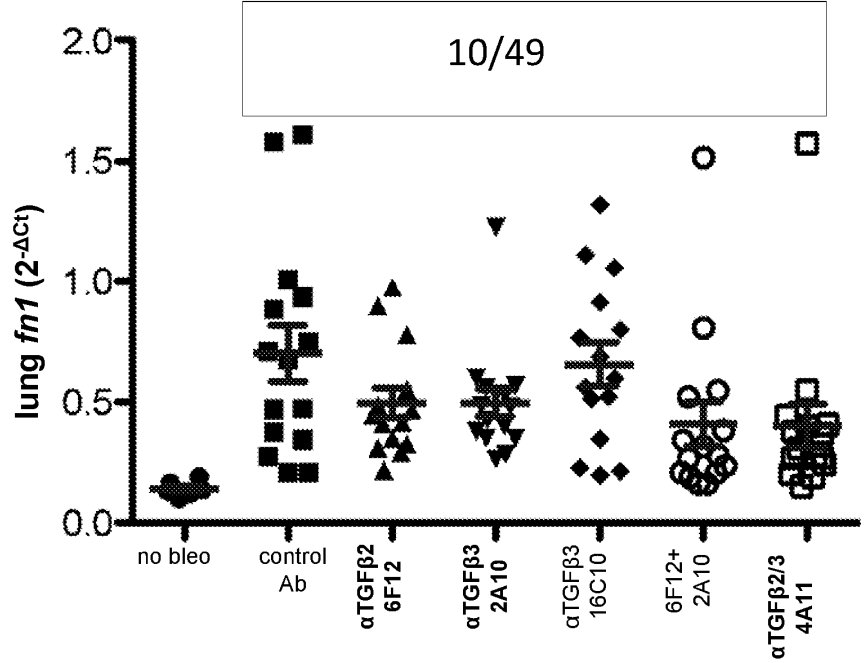


FIG. 9C

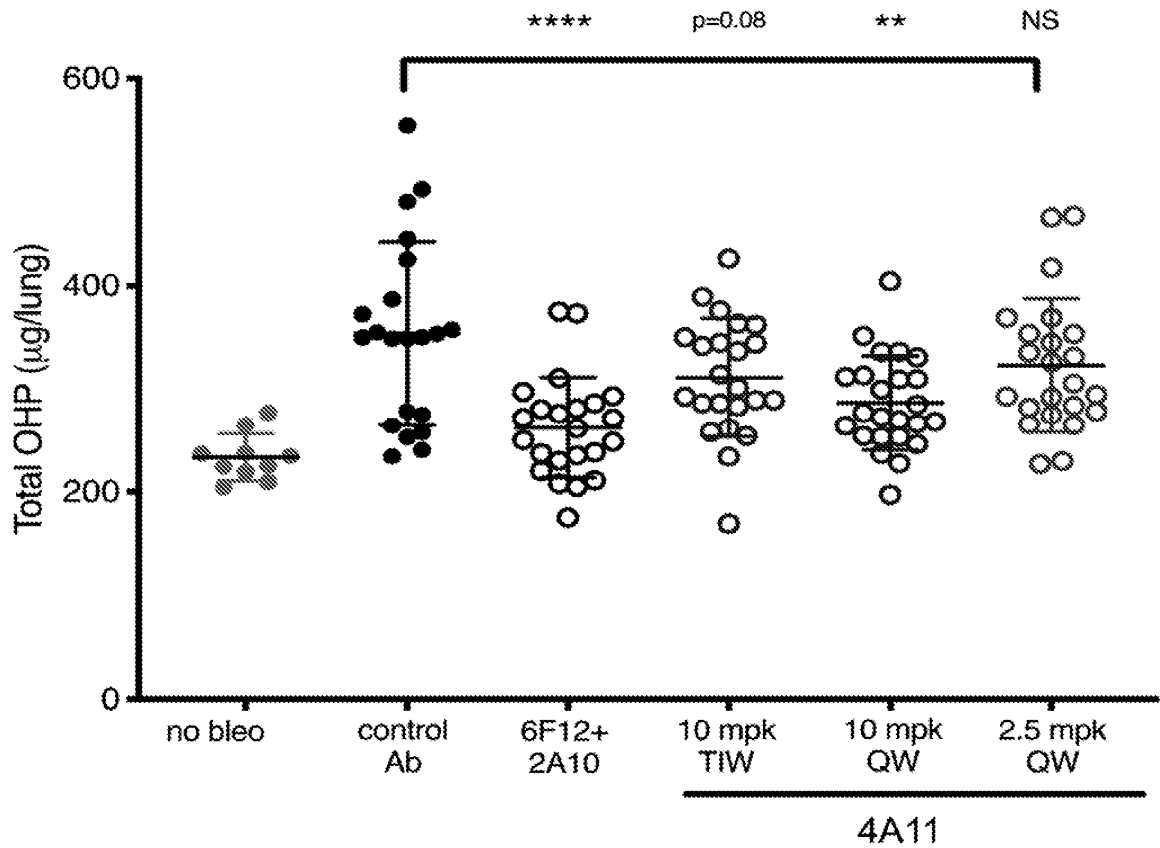


FIG. 9D

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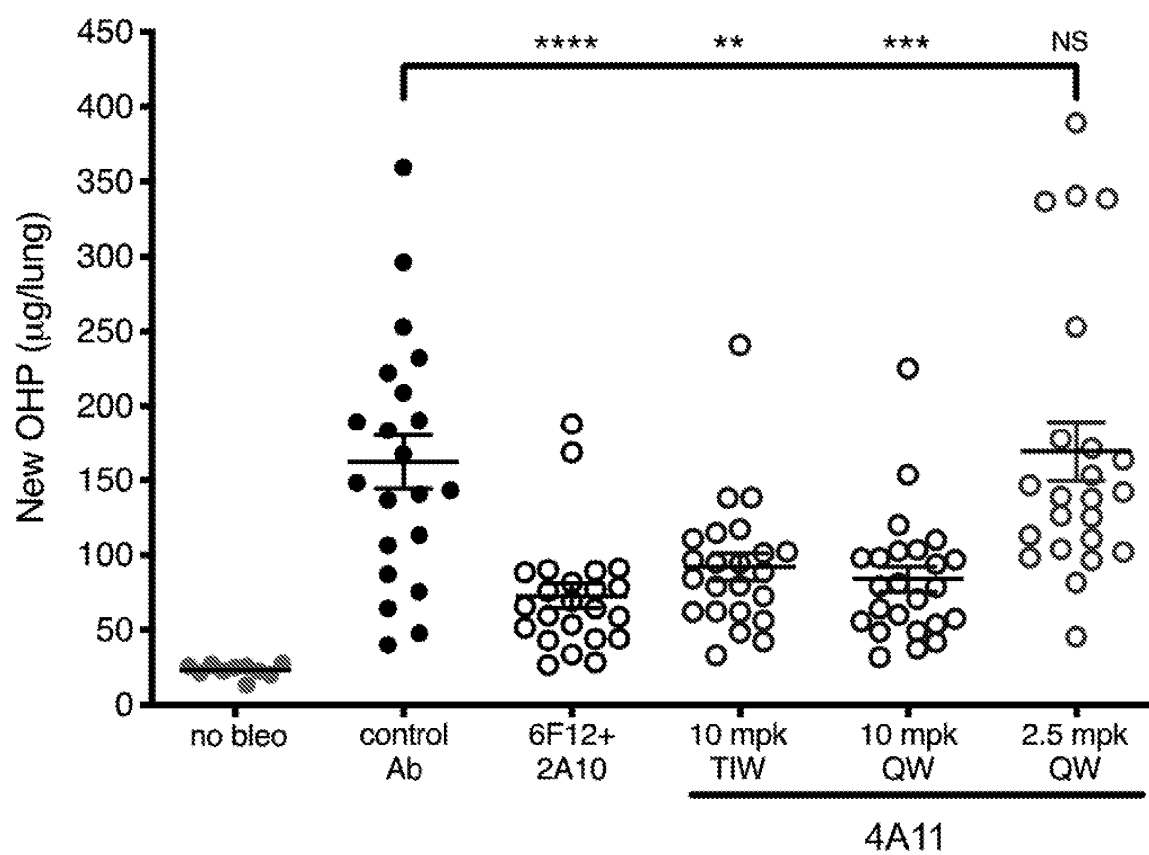


FIG. 9E

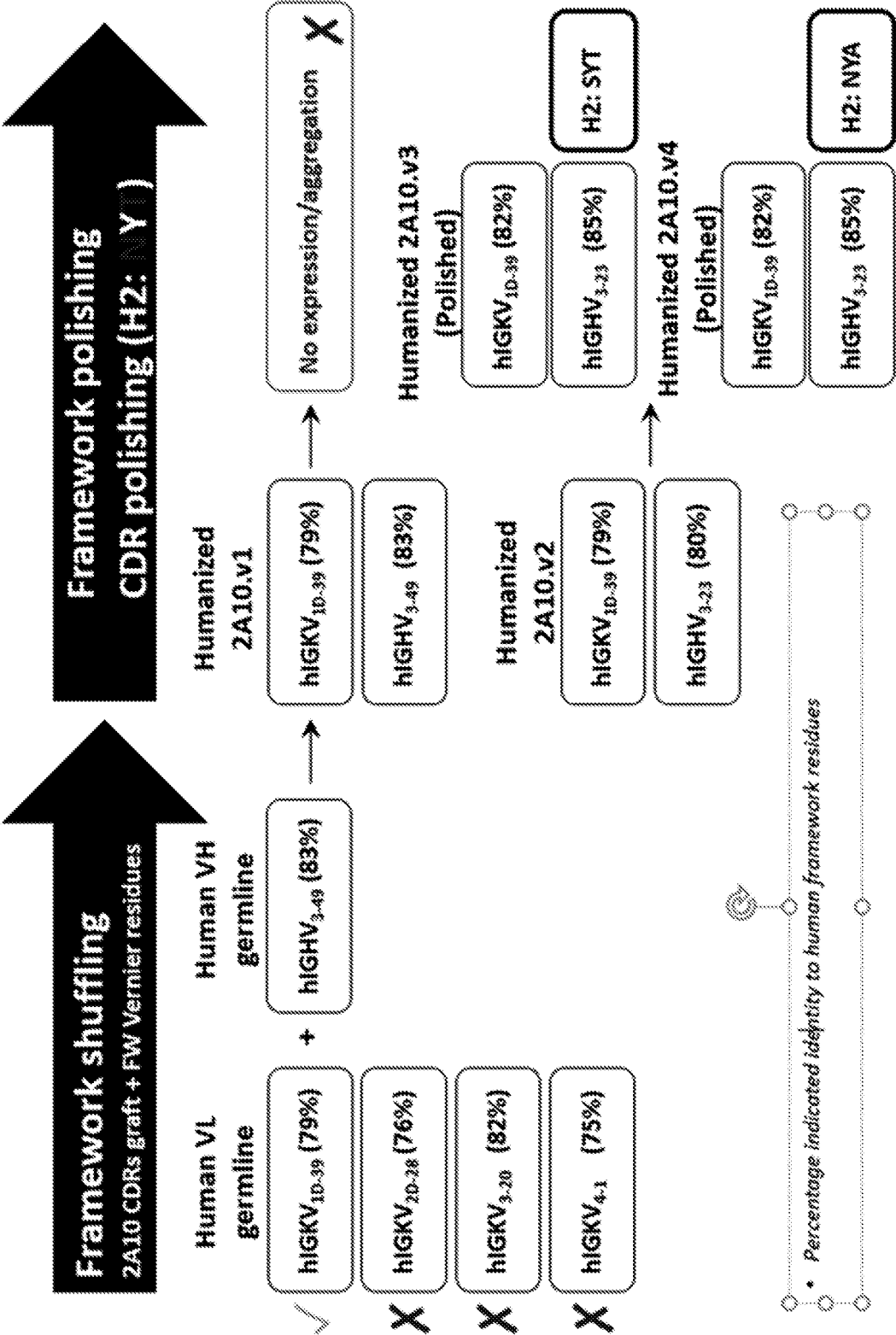


FIG. 10

2A10 variants	Human Framework	Framework mutation	BIAcore (pM)			HERBlue TGFβ blocking IC50 (nM)			SEC Monomer (%)
			TGFβ1	TGFβ2	TGFβ3	TGFβ1	TGFβ2	TGFβ3	
Ref 2A10	-	-	-	62.8	1.2	>200	70	0.01	-
h2A10.v1	K ₁₀₋₃₉ H ₃₋₄₉	-	-	-	4.4	-	-	-	88.97
h2A10.v1.1	K ₁₀₋₃₉ H ₃₋₄₉	LC: L4M	No expression			-	-	-	-
h2A10.v1.2	K ₁₀₋₃₉ H ₃₋₄₉	LC: H38Q	-	-	2.8	-	-	-	97.7
h2A10.v1.3	K ₁₀₋₃₉ H ₃₋₄₉	LC: Q43A	-	-	3.3	-	-	-	92.0
h2A10.v1.4	K ₁₀₋₃₉ H ₃₋₄₉	LC: I58V	-	-	3.0	-	-	-	93.1
h2A10.v1.5	K ₁₀₋₃₉ H ₃₋₄₉	HC: L47W	-	-	493	-	-	-	98.6
h2A10.v1.6	K ₁₀₋₃₉ H ₃₋₄₉	HC: A49G	-	-	5.3	-	-	-	94.0
h2A10.v1.7	K ₁₀₋₃₉ H ₃₋₄₉	HC: V78A	-	-	3.9	-	-	-	96.5
h2A10.v1.N54S	K ₁₀₋₃₉ H ₃₋₄₉	-	No expression			-	-	-	-
h2A10.v1.N54Q	K ₁₀₋₃₉ H ₃₋₄₉	-	No expression			-	-	-	-
h2A10.v1.T56A	K ₁₀₋₃₉ H ₃₋₄₉	-	-	-	2.3	-	-	-	72.3
h2A10.v2	K ₁₀₋₃₉ H ₃₋₂₃	-	-	31.4	1.3	>200	>200	0.01	99.6
h2A10.v2.1	K ₁₀₋₃₉ H ₃₋₂₃	LC: L4M	-	238	3.1	>200	>200	0.01	99.4
h2A10.v2.2	K ₁₀₋₃₉ H ₃₋₂₃	LC: H38Q	-	124	1.2	>200	>200	0.01	99.5
h2A10.v2.3	K ₁₀₋₃₉ H ₃₋₂₃	LC: Q43A	-	242	1.5	>200	>200	0.01	99.5
h2A10.v2.4	K ₁₀₋₃₉ H ₃₋₂₃	LC: I58V	-	190	2.1	>200	>200	0.01	99.5
h2A10.v2.5	K ₁₀₋₃₉ H ₃₋₂₃	HC: L47W	-	2830	500	>200	>200	27.4	99.6
h2A10.v2.6	K ₁₀₋₃₉ H ₃₋₂₃	HC: A49S	-	249	1.5	>200	>200	0.01	99.8
h2A10.v2.7	K ₁₀₋₃₉ H ₃₋₂₃	HC: D73N	-	921	3.2	>200	>200	0.12	99.5
h2A10.v2.8	K ₁₀₋₃₉ H ₃₋₂₃	HC: S76N	-	365	1.2	>200	>200	0.01	99.6
h2A10.v2.9	K ₁₀₋₃₉ H ₃₋₂₃	HC: V78L	-	768	0.7	>200	>200	0.01	99.6
h2A10.v2.N54S	K ₁₀₋₃₉ H ₃₋₂₃	-	-	425	2.4	>200	>200	0.01	99.5
h2A10.v2.N54Q	K ₁₀₋₃₉ H ₃₋₂₃	-	-	378	2.5	>200	>200	0.01	99.6
h2A10.v2.T56A	K ₁₀₋₃₉ H ₃₋₂₃	-	-	247	1.0	>200	>200	0.01	99.6

Detrimental mutation
(>2 fold drop compared to h2A10.v1)

- L47W (HC FW2)

✓ No expression for some variants
✓ Potential aggregation (6-28%)

Detrimental mutation
(>2 fold drop compared to h2A10.v2)

- L4M (LC FW1)
- L47W (HC FW2)
- D73N (HC FW3)

✓ No aggregation observed

Final humanized polished versions based on h2A10.v2

- h2A10.v3: Keep L4, L47, D73 + CDRH2:N54S (NYT -> SYT)
- h2A10.v4: Keep L4, L47, D73 + CDRH2:T56A (NYT -> NYA)

FIG. 11

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* Vernier zone

Light chain variable region

Light chain variable region

		CDRL1-Contact																						
		CDRL1-Contact																						
		CDRL1-Kabat																						
Kabat number		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	
Rat 2A10		D	I	V	L	T	Q	S	P	A	L	A	V	S	L	G	Q	R	A	T	I	S	C	R
h2A10.v1		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C
h2A10.v2		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C
h2A10.v3		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C
h2A10.v4		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C
		*		*																				
			</																					

Heavy chain variable region

		CDRH1-Contact																					
		CDRH1-Kabat																					
Kabat number		67	68	69	70	71	72	73	74	75	76	77	78	79	80	81	82	83	84	85	86	87	88
Rat 2A10		E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	K	G	S	L	K	L	S	C
h2A10.v1		E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	P	S	L	R	L	S	C
h2A10.v2		E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C
h2A10.v3		E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C
h2A10.v4		E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C
		*		*		*		*		*		*		*		*		*		*		*	

		CDRH2-Contact																					
		CDRH2-Kabat																					
Kabat number		89	90	91	92	93	94	95	96	97	98	99	100	101	102	103	104	105	106	107	108	109	110
Rat 2A10		K	G	L	D	L	V	A	D	I	V	S	K	T	Y	N	T	T	Y	S	D	S	V
h2A10.v1		K	G	L	E	L	V	A	D	I	V	S	K	T	Y	N	T	T	Y	S	D	S	V
h2A10.v2		K	G	L	E	L	V	A	D	I	V	S	K	T	Y	N	T	T	Y	S	D	S	V
h2A10.v3		K	G	L	E	L	V	S	D	I	V	S	K	T	Y	S	Y	T	T	Y	S	D	S
h2A10.v4		K	G	L	E	L	V	S	D	I	V	S	K	T	Y	N	Y	A	T	Y	S	D	S
		*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*	*

		CDRH3-Contact																					
		CDRH3-Kabat																					
Kabat number		111	112	113	114	115	116	117	118	119	120	121	122	123	124	125	126	127	128	129	130	131	132
Rat 2A10		M	D	N	L	K	T	E	D	T	A	L	Y	Y	C	T	V	A	P	G	G	S	F
h2A10.v1		M	N	S	L	K	T	E	D	T	A	V	Y	Y	C	T	V	A	P	G	G	S	F
h2A10.v2		M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	T	V	A	P	G	G	S	F
h2A10.v3		M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	T	V	A	P	G	G	S	F
h2A10.v4		M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	T	V	A	P	G	G	S	F
		*		*		*		*		*		*		*		*		*		*		*	

FIG. 12

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* Vernier zone

Light chain variable region

																						CDR11 - Contact																					
																						CDR11 - Kabat																					
Kabat number		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										
Rat 2A10		D	I	V	L	T	Q	S	P	A	.	L	A	V	S	L	G	Q	R	A	T	I	S	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H
h2A10.v2		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H
h2A10.v2.1		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	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H
h2A10.v2.2		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H
h2A10.v2.3		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H
h2A10.v2.4		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H
h2A10.v2.5		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H
h2A10.v2.6		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H
h2A10.v2.7		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H
h2A10.v2.8		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H
h2A10.v2.9		D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H
		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	
																						CDR12 - Contact																					
																						CDR12 - Kabat																					
Kabat number		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										
Rat 2A10		K	P	G	Q	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	A	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	N	P	V	Q	A	
h2A10.v2		K	P	G	K	Q	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
h2A10.v2.1		K	P	G	K	Q	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
h2A10.v2.2		K	P	G	K	Q	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
h2A10.v2.3		K	P	G	K	A	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
h2A10.v2.4		K	P	G	K	Q	P	K	L	L	I	Y	R	A	S	N	L	A	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
h2A10.v2.5		K	P	G	K	Q	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
h2A10.v2.6		K	P	G	K	Q	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
h2A10.v2.7		K	P	G	K	Q	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
h2A10.v2.8		K	P	G	K	Q	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
h2A10.v2.9		K	P	G	K	Q	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P
		.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.	.		
																						CDR13 - Contact																					
																						CDR13 - Kabat																					
Kabat number		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										
Rat 2A10		D	D	L	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	L	E	I	K															
h2A10.v2		E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K															
h2A10.v2.1		E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K															
h2A10.v2.2		E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K															
h2A10.v2.3		E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K															
h2A10.v2.4		E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K															
h2A10.v2.5		E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K															
h2A10.v2.6		E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K															
h2A10.v2.7		E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K															
h2A10.v2.8		E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K															
h2A10.v2.9		E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K															

FIG. 13

FIG. 14

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* Vernier zone

Light chain variable region

Light chain variable region

	CDRL1 - Contact																																														
	CDRL1 - Kabat																																														
Kabat number	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	27a	27b	27c	27d	28	29	30	31	32	33	34	35	36	37	38					
Rat 2A10	D	I	V	L	T	Q	S	P	A	.	L	A	V	S	L	G	R	A	T	I	S	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H						
h2A10.v2	D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H					
h2A10.v2.N54S	D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H					
h2A10.v2.N54Q	D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H					
h2A10.v2.T56A	D	I	Q	L	T	Q	S	P	S	S	L	S	A	S	V	G	D	R	V	T	I	T	C	R	A	S	Q	S	V	S	I	S	R	F	N	L	M	H	W	Y	Q	H					
	*		*																																					*	*	*					
	CDRL2 - Contact																				CDRL2 - Kabat																										
Kabat number	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					
Rat 2A10	K	P	G	Q	K	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	A	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	N	P	V	Q	A	.	.	.	.	
h2A10.v2	K	P	G	K	Q	K	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P	.	.	.	.
h2A10.v2.N54S	K	P	G	K	Q	K	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P	.	.	.	.
h2A10.v2.N54Q	K	P	G	K	Q	K	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P	.	.	.	.
h2A10.v2.T56A	K	P	G	K	Q	K	P	K	L	L	I	Y	R	A	S	N	L	A	S	G	I	P	S	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	S	L	Q	P	.	.	.	.
			*	*		*	*	*	*	*									*						*	*	*	*	*	*	*																
	CDRL3 - Contact																				CDRL3 - Kabat																										
Kabat number	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																				
Rat 2A10	D	D	L	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	L	E	I	K																				
h2A10.v2	E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K																				
h2A10.v2.N54S	E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K																				
h2A10.v2.N54Q	E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K																				
h2A10.v2.T56A	E	D	F	A	T	Y	Y	C	Q	H	S	R	E	S	P	W	T	F	G	G	G	T	K	V	E	I	K																				

Heavy chain variable region

heavy chain variable region

CDRH1 - Contact

CDRH1 - Kabat

Kabat number	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	41	42
Rat 2A10	E	V	Q	L	V	E	S	G	G	G	L	V	Q	P	K	G	S	L	K	L	S	C	A	A	S	G	F	D	F	N	S	Y	G	M	S	W	V	R	Q	A	P	G
h2A10.v2	E	V	Q	L	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	D	F	N	S	Y	G	M	S	W	V	R	Q	A	P	G	
h2A10.v2.N54S	E	V	Q	L	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	D	F	N	S	Y	G	M	S	W	V	R	Q	A	P	G	
h2A10.v2.N54Q	E	V	Q	L	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	D	F	N	S	Y	G	M	S	W	V	R	Q	A	P	G	
h2A10.v2.T56A	E	V	Q	L	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	A	S	G	F	D	F	N	S	Y	G	M	S	W	V	R	Q	A	P	G	

CDRH2 - Contact

CDRH2 - Kabat

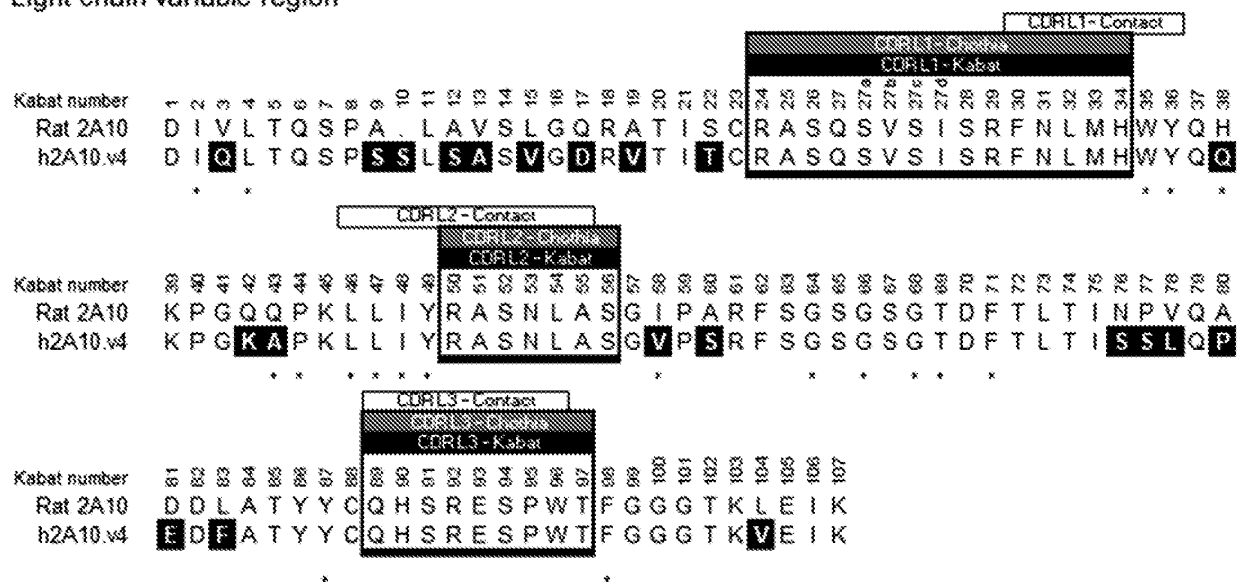
Kabat number	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60	61	62	63	64	65	66	67	68	69	70	71	72	73	74	75	76	77	78	79	80	81		
Rat 2A10	K	G	L	D	L	V	A	D	I	V	S	K	T	Y	N	Y	T	T	Y	S	D	S	V	K	D	R	F	T	I	S	R	D	D	S	Q	S	M	V	Y	L	Q
h2A10.v2	K	G	L	E	L	V	A	D	I	V	S	K	T	Y	N	Y	T	T	Y	S	D	S	V	K	D	R	F	T	I	S	R	D	D	S	K	S	T	V	Y	L	Q
h2A10.v2.N54S	K	G	L	E	L	V	A	D	I	V	S	K	T	Y	S	Y	T	T	Y	S	D	S	V	K	D	R	F	T	I	S	R	D	D	S	K	S	T	V	Y	L	Q
h2A10.v2.N54Q	K	G	L	E	L	V	A	D	I	V	S	K	T	Y	Q	Y	T	T	Y	S	D	S	V	K	D	R	F	T	I	S	R	D	D	S	K	S	T	V	Y	L	Q
h2A10.v2.T56A	K	G	L	E	L	V	A	D	I	V	S	K	T	Y	N	A	T	Y	Y	S	D	S	V	K	D	R	F	T	I	S	R	D	D	S	K	S	T	V	Y	L	Q

CDRH3 - Contact

CDRH3 - Kabat

Kabat number	82	82a	82b	82c	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	109	110	111	112	113
Rat 2A10	M	D	N	L	K	T	E	D	T	A	L	Y	Y	C	T	V	A	P	G	G	S	F	D	Y	W	G	Q	G	V	M	V	T	V	S	S
h2A10.v2	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	T	V	A	P	G	G	S	F	D	Y	W	G	Q	G	T	L	V	T	V	S	S
h2A10.v2.N54S	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	T	V	A	P	G	G	S	F	D	Y	W	G	Q	G	T	L	V	T	V	S	S
h2A10.v2.N54Q	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	T	V	A	P	G	G	S	F	D	Y	W	G	Q	G	T	L	V	T	V	S	S
h2A10.v2.T56A	M	N	S	L	R	A	E	D	T	A	V	Y	Y	C	T	V	A	P	G	G	S	F	D	Y	W	G	Q	G	T	L	V	T	V	S	S

Light chain variable region



Heavy chain variable region

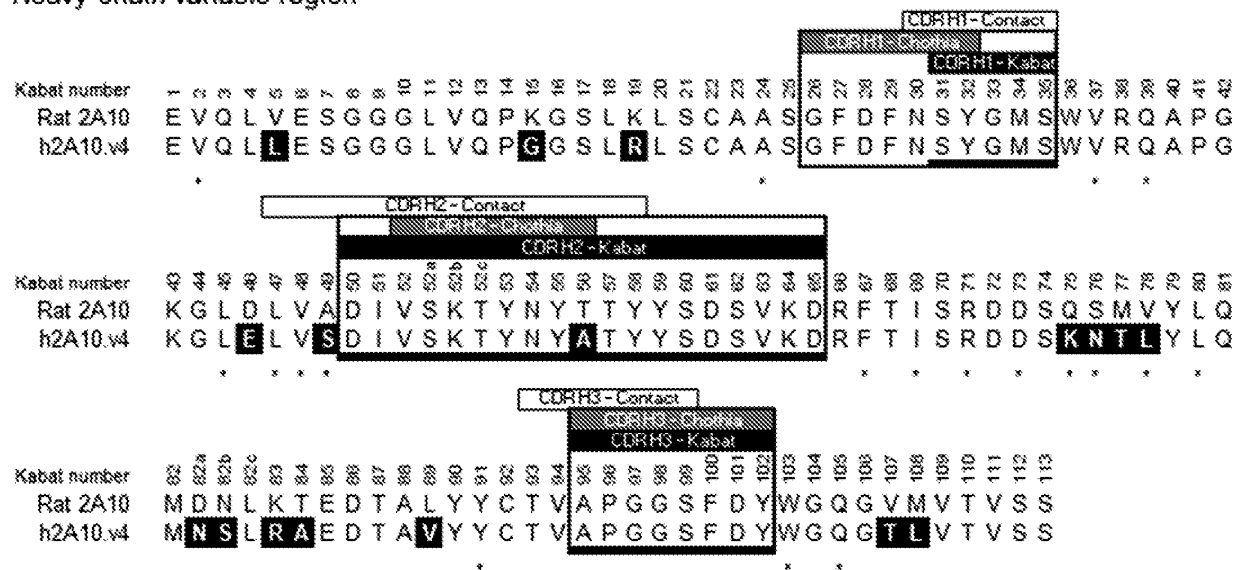


FIG. 16

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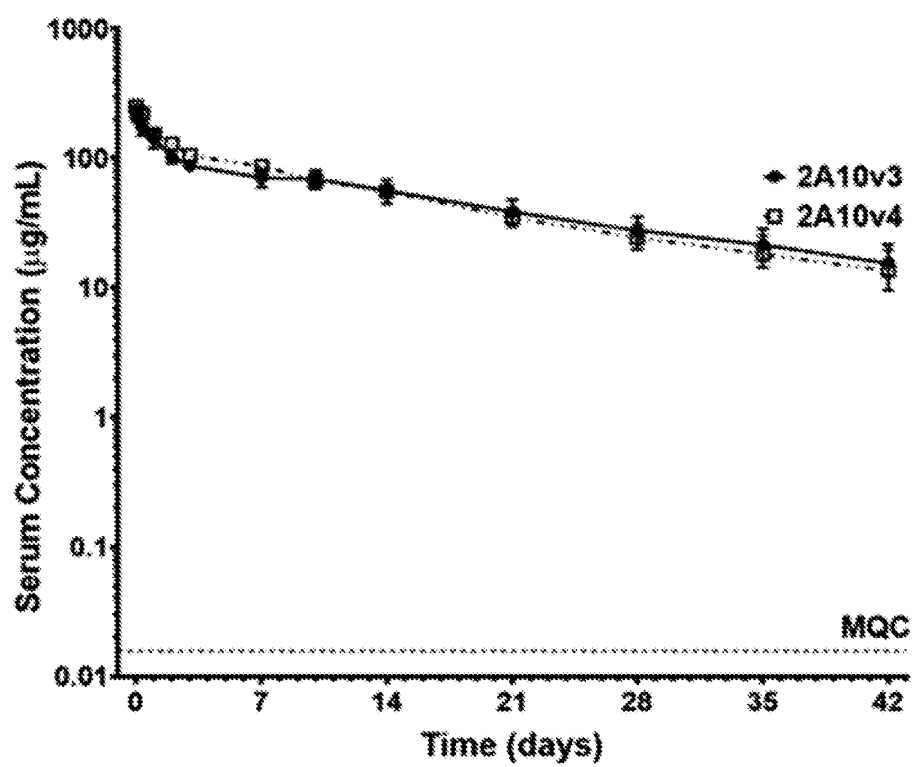


FIG. 17

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Light chain variable region

		CDR11-Context		CDR11-Kabat	
Kabat number	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 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 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100				
Rbr 4A11	A A V L T Q T P S P V S A A V G G T V S I S C Q S S Q S V Y N N N Y L S W F Q Q K P				
h4A11.v1	D A V L T Q S P D S L A V S L G E R A T I N C Q S S Q S V Y N N N Y L S W F Q Q K P				
h4A11.v2	D A Q L T Q S P S S L S A S V G D R V I T I C Q S S Q S V Y N N N Y L S W F Q Q K P				
h4A11.v3	D A V L T Q S P D S L A V S L G E R A T I N C Q S S Q S V Y N N N Y L S W F Q Q K P				
h4A11.v4	D A Q L T Q S P S S L S A S V G D R V I T I C Q S S Q S V Y N N N Y L S W F Q Q K P				
h4A11.v5	E A V L T Q S P G T L S L S P G E R A T L S C Q S S Q S V Y N N N Y L S W F Q Q K P				
h4A11.v6	D A V L T Q T P L S S P V T L G Q P A S I S C Q S S Q S V Y N N N Y L S W F Q Q R P				
h4A11.v7	E A V L T Q S P G T L S L S P G E R A T L S C Q S S Q S V Y N N N Y L S W F Q Q K P				
h4A11.v8	D A V L T Q T P L S S P V T L G Q P A S I S C Q S S Q S V Y N N N Y L S W F Q Q R P				
		CDR12-Context		CDR12-Kabat	
Kabat number	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 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 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100				
Rbr 4A11	G Q P P K L L I Y G A S T L T S G V P S R F K G S G S G T Q F T L T I S D V Q C D D				
h4A11.v1	G Q P P K L L I Y G A S T L T S G V P D R F S G S G S G T D F T L T I S S L Q A E D				
h4A11.v2	G K P P K L L I Y G A S T L T 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 E D				
h4A11.v3	G Q P P K L L I Y G A S T L T S G V P D R F S G S G S G T D F T L T I S S L Q A E D				
h4A11.v4	G K P P K L L I Y G A S T L T 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 E D				
h4A11.v5	G Q P P R L L I Y G A S T L T S G V P D R F S G S G S G T D F T L T I S R L E P E D				
h4A11.v6	G Q P P R L L I Y G A S T L T S G V P D R F S G S G A G T D F T L K I S R V E A E D				
h4A11.v7	G Q P P R L L I Y G A S T L T S G V P D R F S G S G S G T D F T L T I S R L E P E D				
h4A11.v8	G Q P P R L L I Y G A S T L T S G V P D R F S G S G A G T D F T L K I S R V E A E D				
		CDR13-Context		CDR13-Kabat	
Kabat number	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 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 81 82 83 84 85 86 87 88 89 90 91 92 93 94 95 96 97 98 99 100				
Rbr 4A11	A A T Y Y C A G G Y S G S S D K Y A F G G G T E V V V K				
h4A11.v1	V A V Y Y C A G G Y S G S S D K Y A F G G G T K V E I K				
h4A11.v2	F A T Y Y C A G G Y S G S S D K Y A F G G G T K V E I K				
h4A11.v3	V A V Y Y C A G G Y S G S S D K Y A F G G G T K V E I K				
h4A11.v4	F A T Y Y C A G G Y S G S S D K Y A F G G G T K V E I K				
h4A11.v5	F A V Y Y C A G G Y S G S S D K Y A F G G G T K V E I K				
h4A11.v6	V G V Y Y C A G G Y S G S S D K Y A F G G G T K V E I K				
h4A11.v7	F A V Y Y C A G G Y S G S S D K Y A F G G G T K V E I K				
h4A11.v8	V G V Y Y C A G G Y S G S S D K Y A F G G G T K V E I K				

FIG. 18

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Heavy chain variable region

Heavy chain variable region

		CDR H1 - Context																											CDR H1 - Kabat														
Kabat number		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				
Rb1 4A11		Q	S	L	E	S	G	G	R	L	V	T	P	G	T	P	L	T	L	T	C	T	V	S	G	F	S	L	S	S	Y	T	V	N	W	V	R	Q	A	P	G		
h4A11.v1		E	Q	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	V	S	G	F	S	L	S	S	Y	T	V	N	W	V	R	Q	A	P	G
h4A11.v2		E	Q	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	V	S	G	F	S	L	S	S	Y	T	V	N	W	V	R	Q	A	P	G
h4A11.v3		E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L	T	C	T	V	T	G	F	S	L	S	S	Y	T	V	N	W	V	R	Q	A	P	G
h4A11.v4		E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L	T	C	T	V	T	G	F	S	L	S	S	Y	T	V	N	W	V	R	Q	A	P	G
h4A11.v5		E	Q	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	V	S	G	F	S	L	S	S	Y	T	V	N	W	V	R	Q	A	P	G
h4A11.v6		E	Q	Q	L	V	E	S	G	G	G	L	V	Q	P	G	G	S	L	R	L	S	C	A	V	S	G	F	S	L	S	S	Y	T	V	N	W	V	R	Q	A	P	G
h4A11.v7		E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L	T	C	T	V	T	G	F	S	L	S	S	Y	T	V	N	W	V	R	Q	A	P	G
h4A11.v8		E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L	T	C	T	V	T	G	F	S	L	S	S	Y	T	V	N	W	V	R	Q	A	P	G

		CDR H2 - Context																											CDR H2 - Kabat														
Kabat number		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				
Rb1 4A11		K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	Y	A	S	W	A	N	G	R	F	T	I	S	K	T	S	A	T	V	D	L	K	I	T	S		
h4A11.v1		K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	Y	A	S	W	A	N	G	R	F	T	I	S	K	D	S	A	K	N	S	V	Y	L	Q	M	N	S
h4A11.v2		K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	Y	A	S	W	A	N	G	R	F	T	I	S	K	D	S	A	K	N	S	V	Y	L	Q	M	N	S
h4A11.v3		K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	Y	A	S	W	A	N	G	R	F	T	I	S	K	D	S	S	K	N	Q	V	S	L	K	L	S	S
h4A11.v4		K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	Y	A	S	W	A	N	G	R	F	T	I	S	K	D	S	S	K	N	Q	V	S	L	K	L	S	S
h4A11.v5		K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	Y	A	S	W	A	N	G	R	F	T	I	S	K	D	S	A	K	N	S	V	Y	L	Q	M	N	S
h4A11.v6		K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	Y	A	S	W	A	N	G	R	F	T	I	S	K	D	S	A	K	N	S	V	Y	L	Q	M	N	S
h4A11.v7		K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	Y	A	S	W	A	N	G	R	F	T	I	S	K	D	S	S	K	N	Q	V	S	L	K	L	S	S
h4A11.v8		K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	Y	A	S	W	A	N	G	R	F	T	I	S	K	D	S	S	K	N	Q	V	S	L	K	L	S	S

		CDR H3 - Context																												CDR H3 - Kabat												
Kabat number		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			
Rb1 4A11		P	T	I	E	D	T	A	T	Y	F	C	A	R	H	M	Q	V	G	G	A	P	T	G	S	M	A	A	F	D	P	W	G	P	G	T	L	V	T	V	S	S
h4A11.v1		L	R	A	E	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A	P	T	G	S	M	A	A	F	D	P	W	G	P	G	T	L	V	T	V	S	S
h4A11.v2		L	R	A	E	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A	P	T	G	S	M	A	A	F	D	P	W	G	P	G	T	L	V	T	V	S	S
h4A11.v3		V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A	P	T	G	S	M	A	A	F	D	P	W	G	P	G	T	L	V	T	V	S	S
h4A11.v4		V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A	P	T	G	S	M	A	A	F	D	P	W	G	P	G	T	L	V	T	V	S	S
h4A11.v5		L	R	A	E	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A	P	T	G	S	M	A	A	F	D	P	W	G	P	G	T	L	V	T	V	S	S
h4A11.v6		L	R	A	E	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A	P	T	G	S	M	A	A	F	D	P	W	G	P	G	T	L	V	T	V	S	S
h4A11.v7		V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A	P	T	G	S	M	A	A	F	D	P	W	G	P	G	T	L	V	T	V	S	S
h4A11.v8		V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A	P	T	G	S	M	A	A	F	D	P	W	G	P	G	T	L	V	T	V	S	S

FIG. 19

22/49

Light chain variable region

Light Chain variable region																										CDRL1 - Constant																
Kabat number	CDRL1 - 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												
h4A11.v7	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.1	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.2	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.3	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.4	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.5	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.6	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.7	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.8	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.9	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.10	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.11	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.12	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.13	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.14	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.15	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.16	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.17	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.18	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P
h4A11.v7.19	E	A	V	L	T	Q	S	P	G	T	L	S	L	S	P	G	E	R	A	T	L	S	C	Q	S	S	Q	S	V	Y	N	N	N	Y	L	S	W	F	Q	Q	K	P

Kabat number	CDH12 - Contract																																										
	as CDH12 - Contract																																										
	CDH12 - T359																																										
h4A11.v7	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.1	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.2	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.3	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.4	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.5	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.6	G	Q	P	A	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D
h4A11.v7.7	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	I	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.8	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.9	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.10	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.11	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.12	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.13	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.14	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.15	G	Q	P	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	V	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.16	G	Q	P	A	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	I	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D
h4A11.v7.17	G	Q	A	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	I	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.18	G	Q	A	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	I	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	
h4A11.v7.19	G	Q	A	P	R	L	L	I	Y	G	A	S	T	L	T	S	G	I	P	D	R	F	S	G	S	G	S	G	T	D	F	T	L	T	I	S	R	L	E	P	E	D	

Kabat number																													
	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
h4A11.v7	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.1	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.2	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.3	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.4	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.5	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.6	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.7	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.8	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.9	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.10	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.11	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.12	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.13	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.14	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.15	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.16	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.17	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.18	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	
h4A11.v7.19	F	A	V	Y	Y	C	A	G	G	Y	S	G	S	S	D	K	Y	A	F	G	G	G	T	K	V	E	I	K	

FIG. 20

Heavy chain variable region

Heavy chain variable region

		CDRH1 - Contact																			
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20
Kabat number	h4A11.v7	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.1	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.2	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.3	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.4	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.5	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.6	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.7	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.8	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.9	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.10	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.11	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.12	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.13	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.14	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.15	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.16	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.17	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.18	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L
	h4A11.v7.19	E	Q	Q	L	Q	E	S	G	P	G	L	V	K	P	S	E	T	L	S	L

		CDRH2 - Contact																			
		21	22	23	24	25	26	27	28	29	30	31	32	33	34	35	36	37	38	39	40
Kabat number	h4A11.v7	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.1	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.2	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.3	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.4	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.5	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.6	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.7	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.8	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.9	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.10	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.11	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.12	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.13	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.14	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.15	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.16	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.17	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.18	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A
	h4A11.v7.19	K	G	L	E	W	I	G	Y	I	S	Y	G	G	S	A	Y	A	S	W	A

		CDRH3 - Contact																			
		41	42	43	44	45	46	47	48	49	50	51	52	53	54	55	56	57	58	59	60
Kabat number	h4A11.v7	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.1	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.2	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.3	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.4	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.5	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.6	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.7	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.8	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.9	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.10	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.11	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.12	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.13	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.14	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.15	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.16	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.17	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.18	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A
	h4A11.v7.19	V	T	A	A	D	T	A	V	Y	F	C	A	R	H	M	Q	V	G	G	A

FIG. 21

Heavy chain variable region

FIG. 22

FIG. 24

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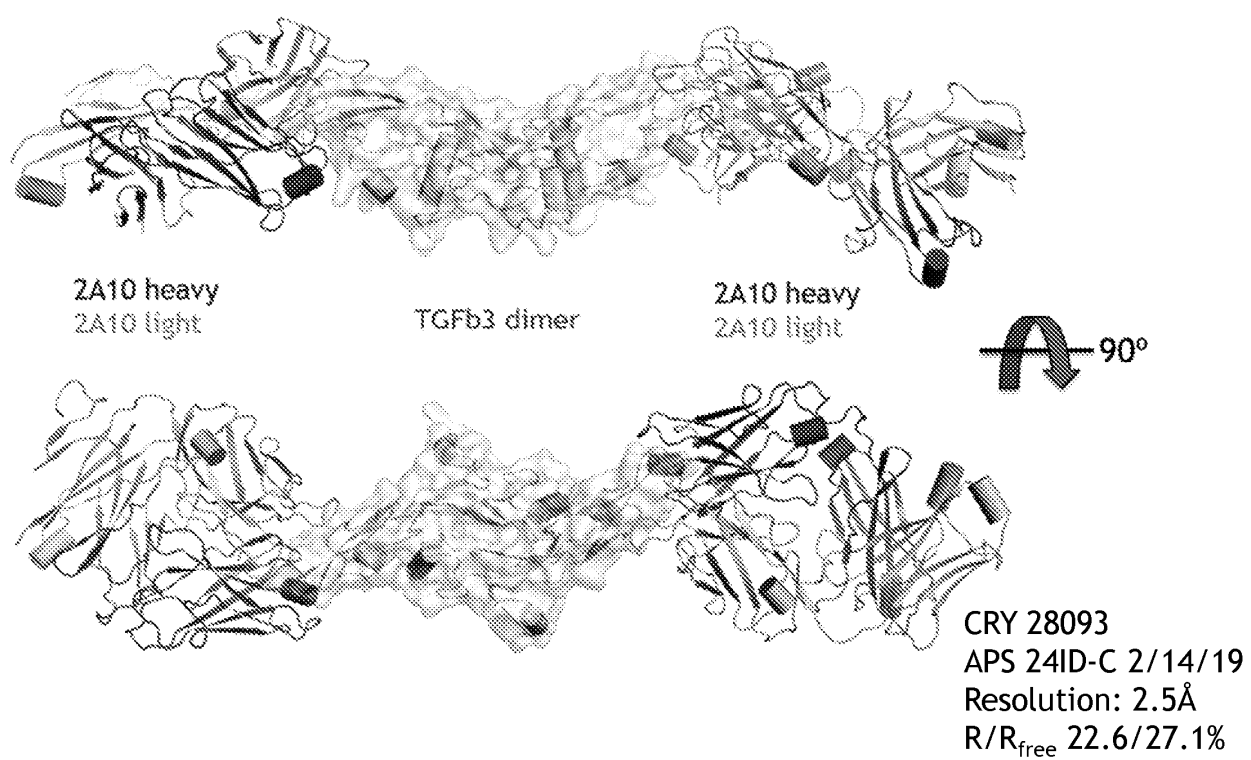


FIG. 25

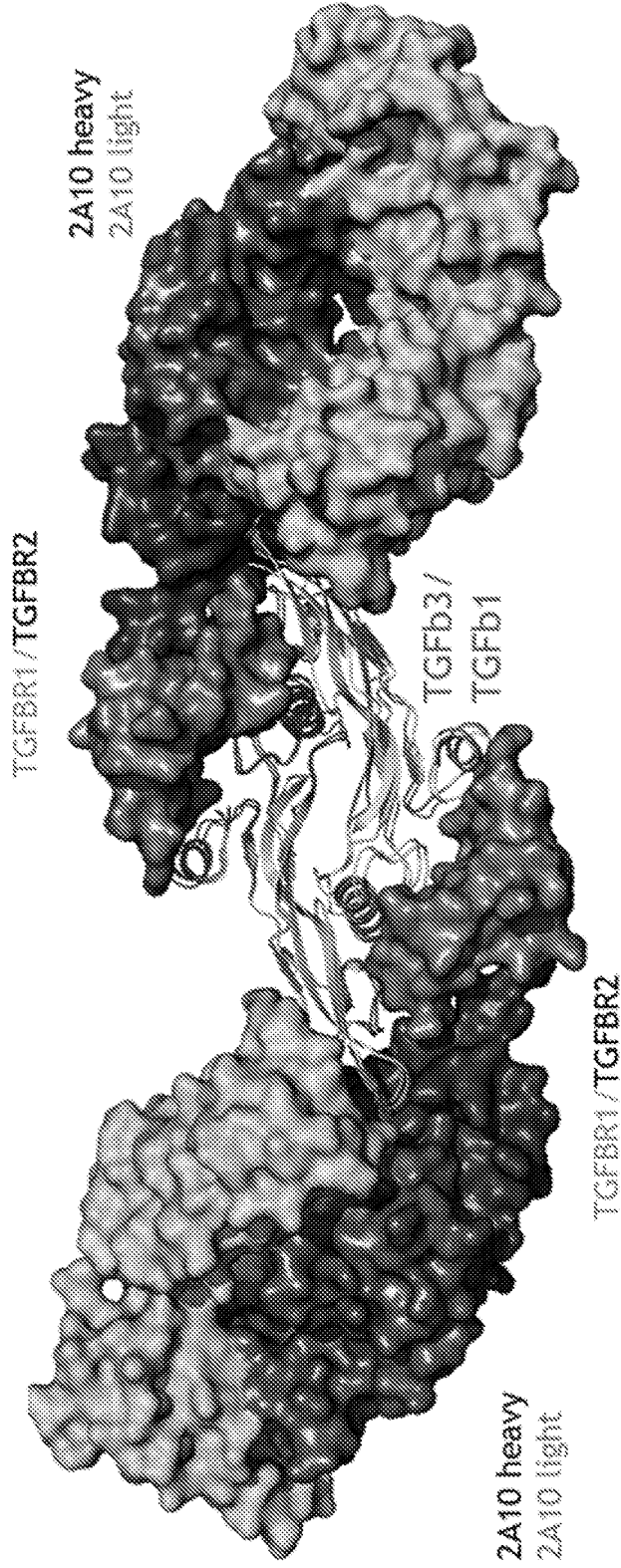


FIG. 26

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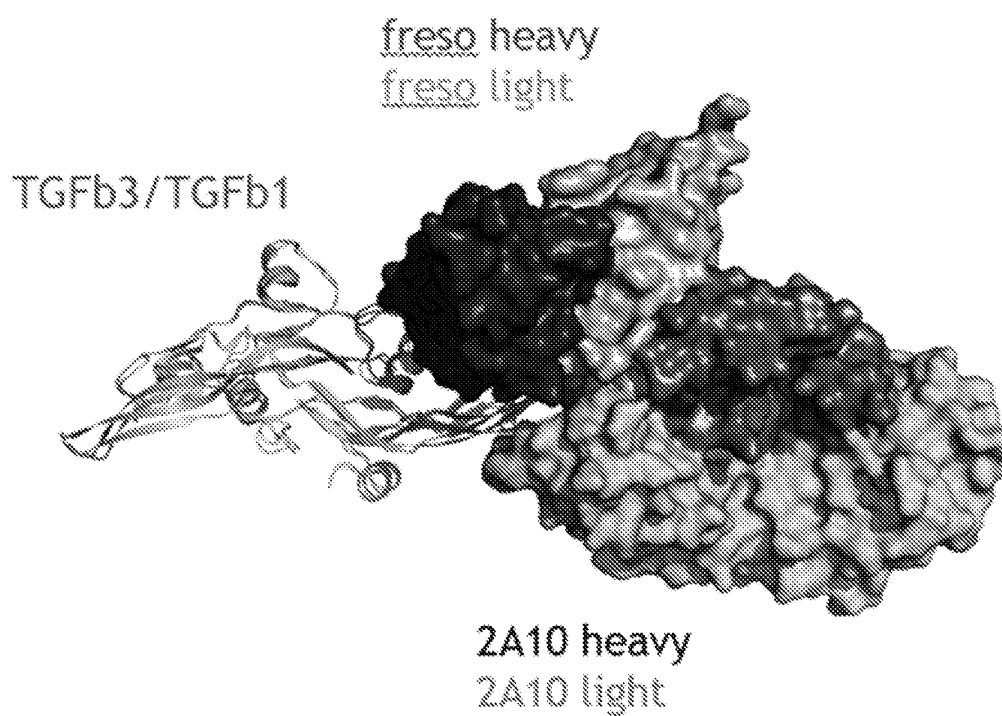
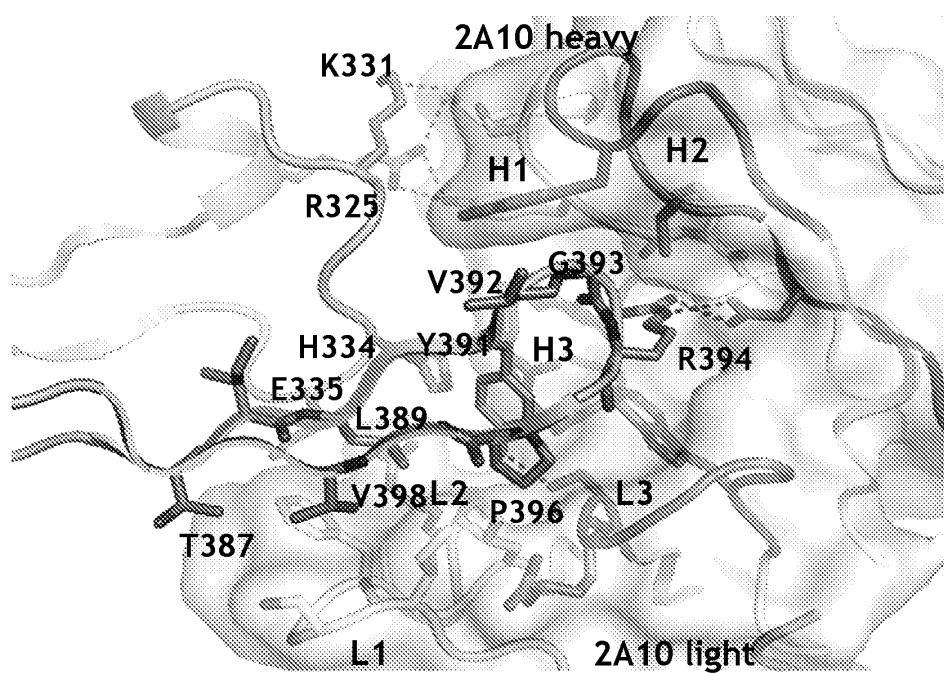
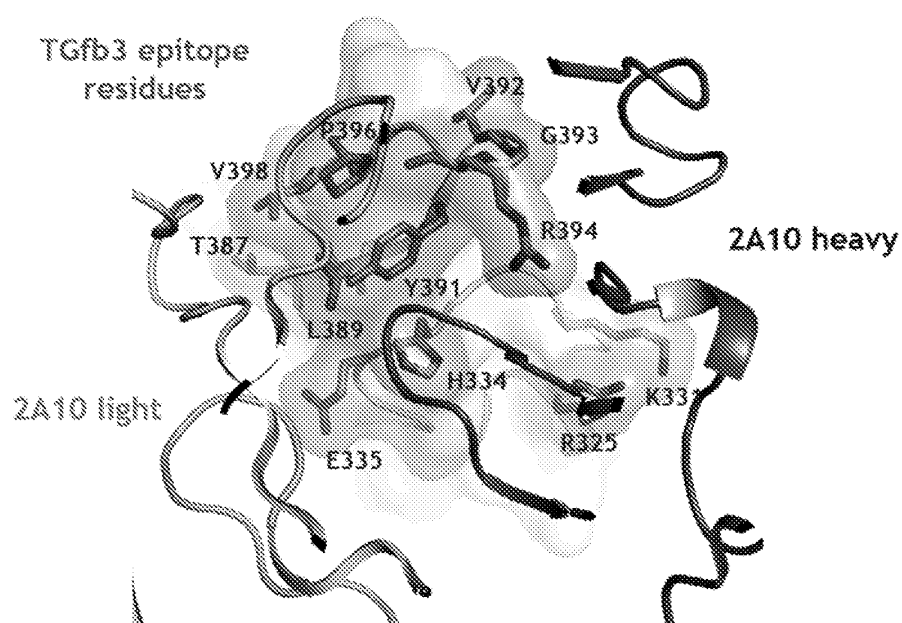


FIG. 27

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**FIG. 28****FIG. 29**

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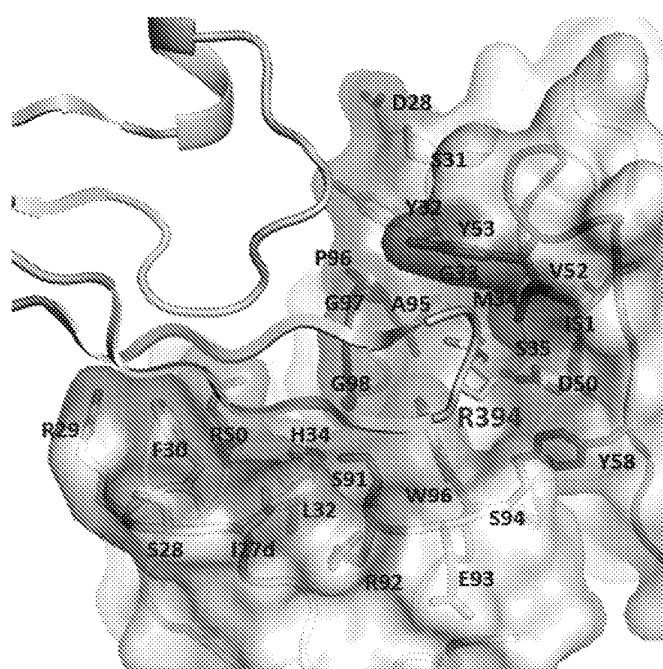


FIG. 30

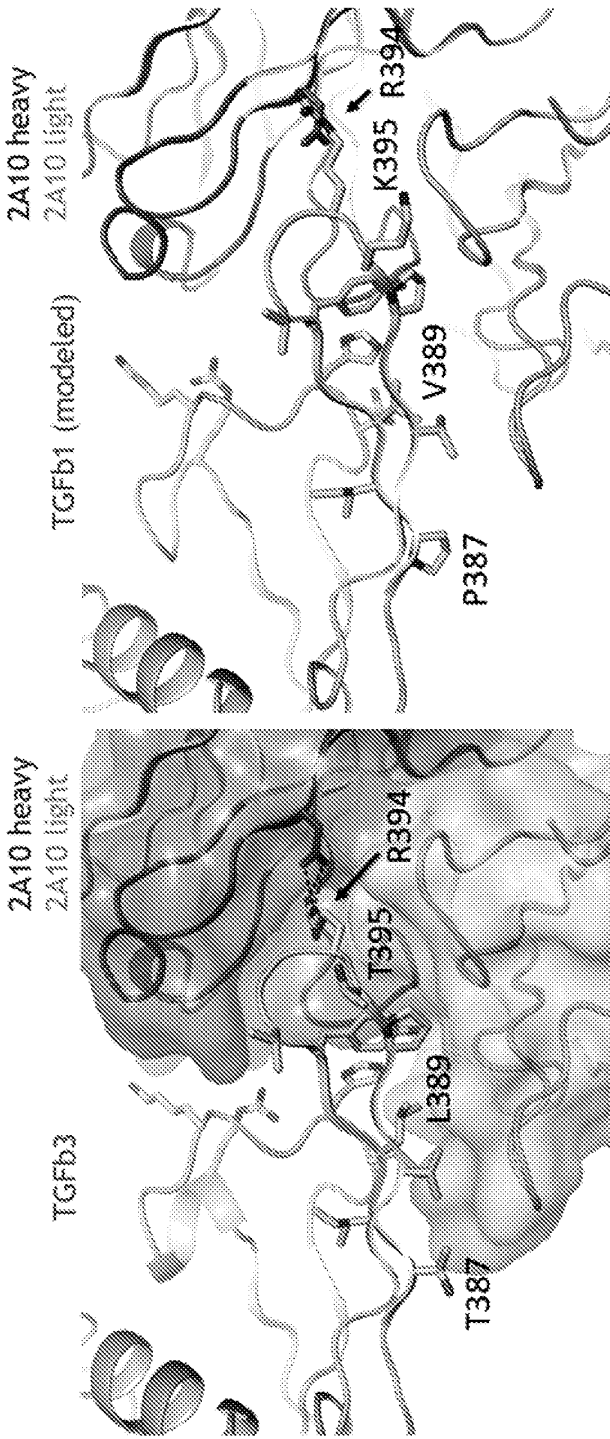


FIG. 31

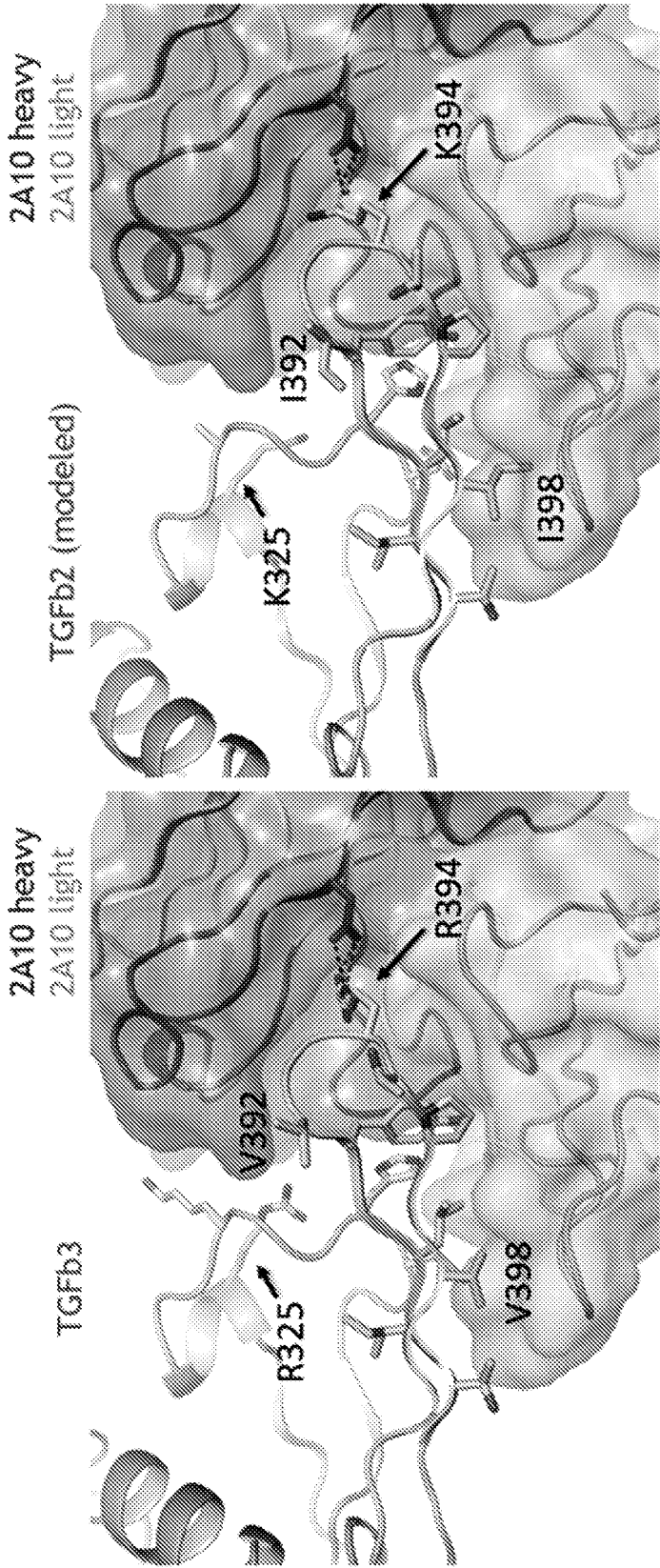


FIG. 32

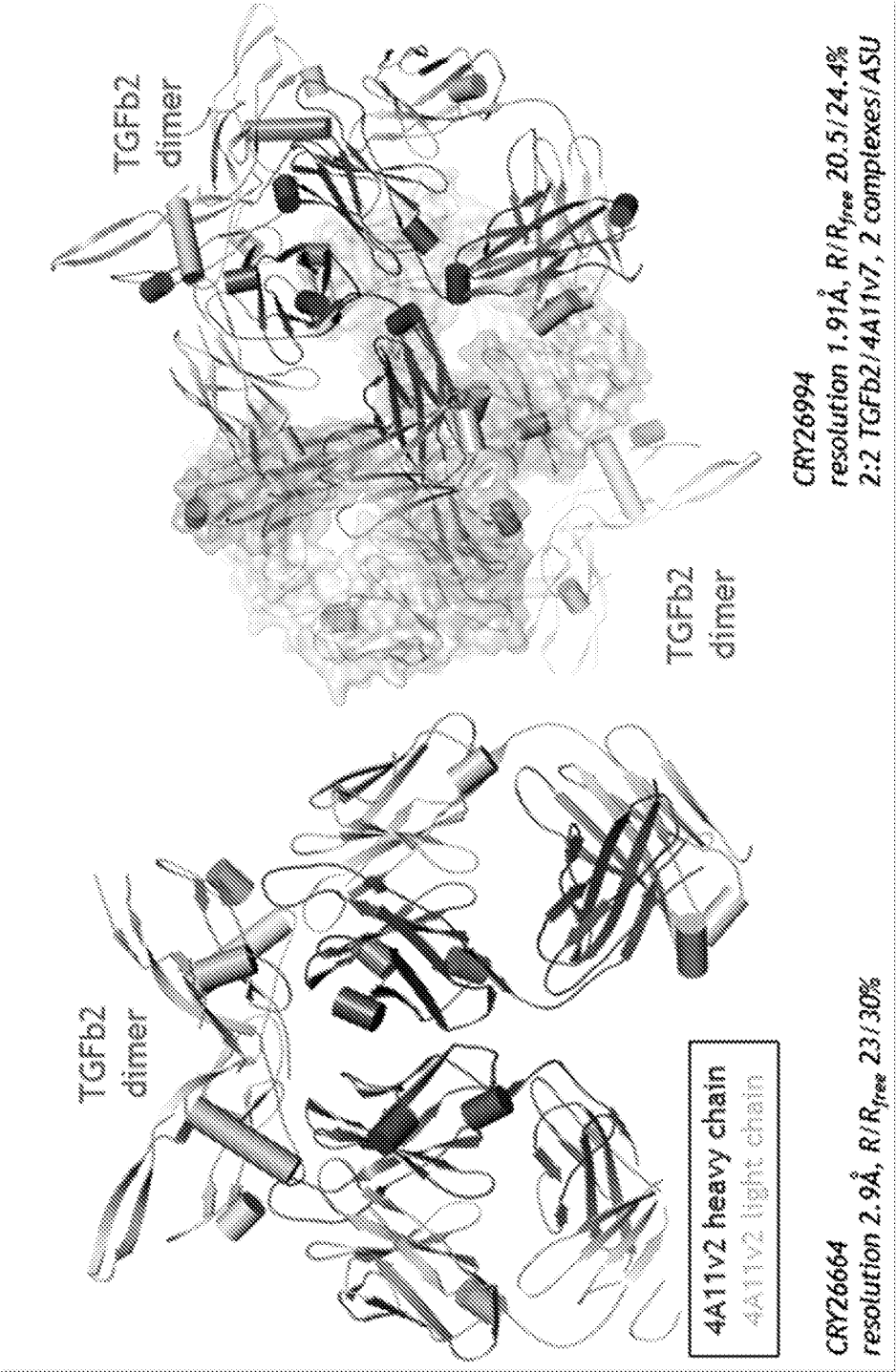


FIG. 33

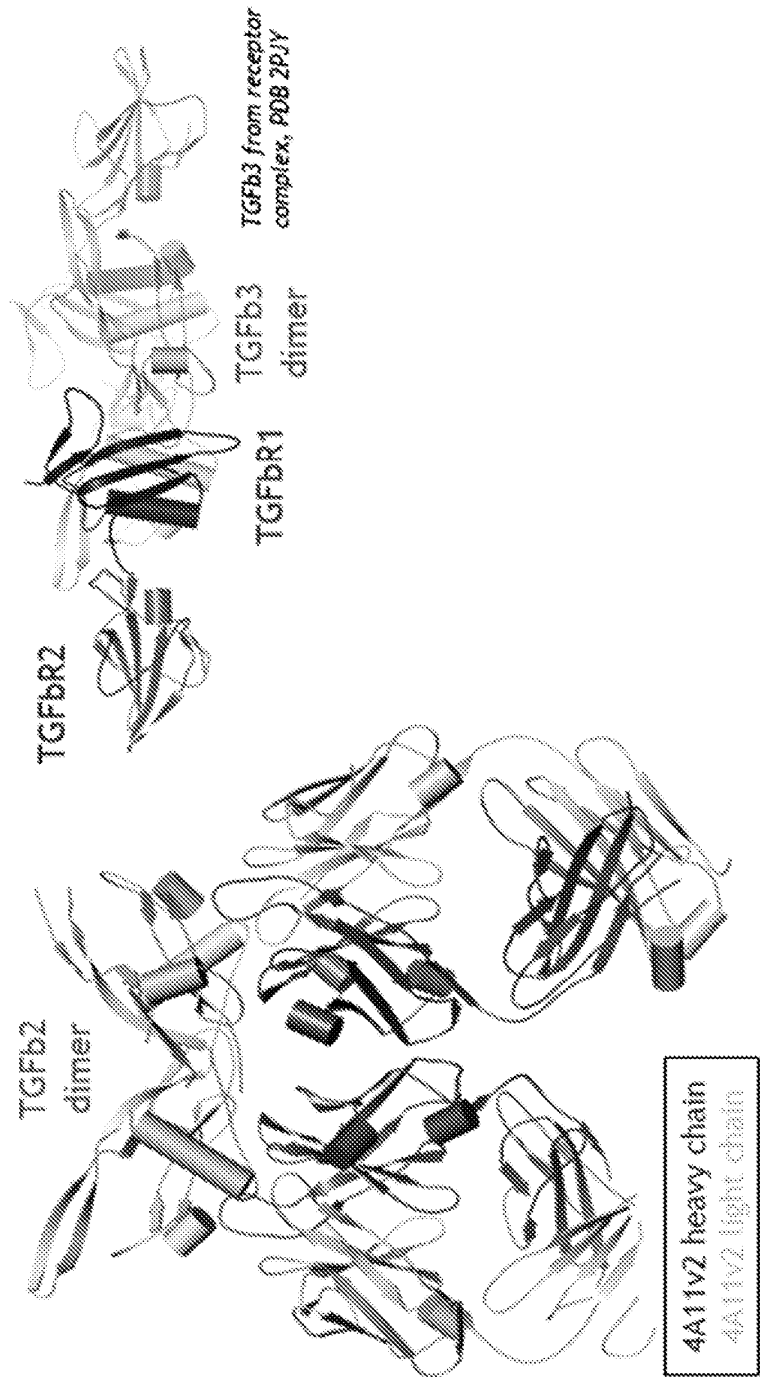
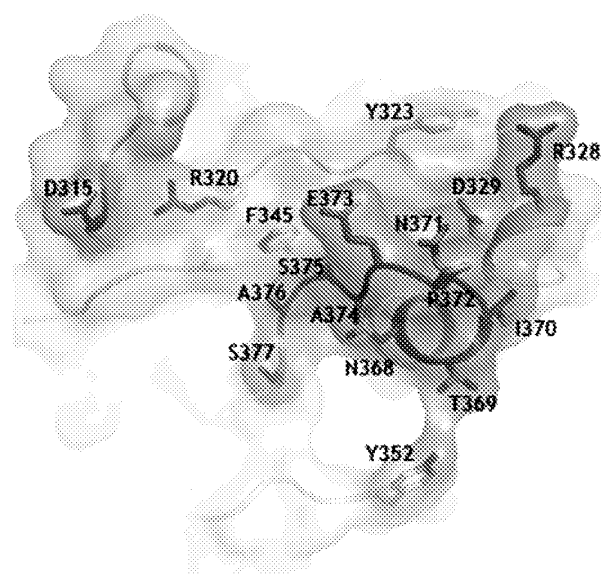
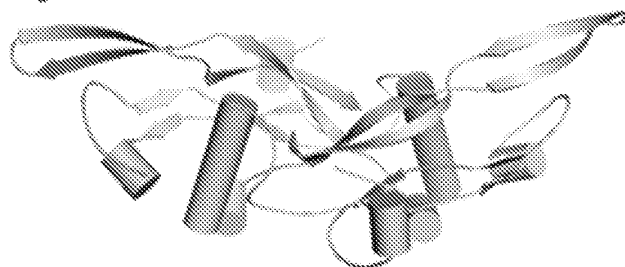


FIG. 34

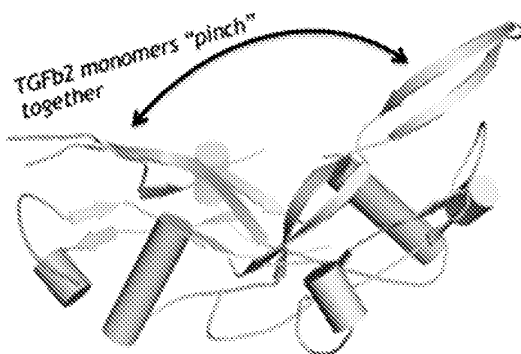
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**FIG. 35**

*TGFβ2 molecules aligned
on green monomer*



TGFβ2 from fresco complex, PDB 4KXZ



TGFβ2 from 4A11v2 complex

FIG. 36

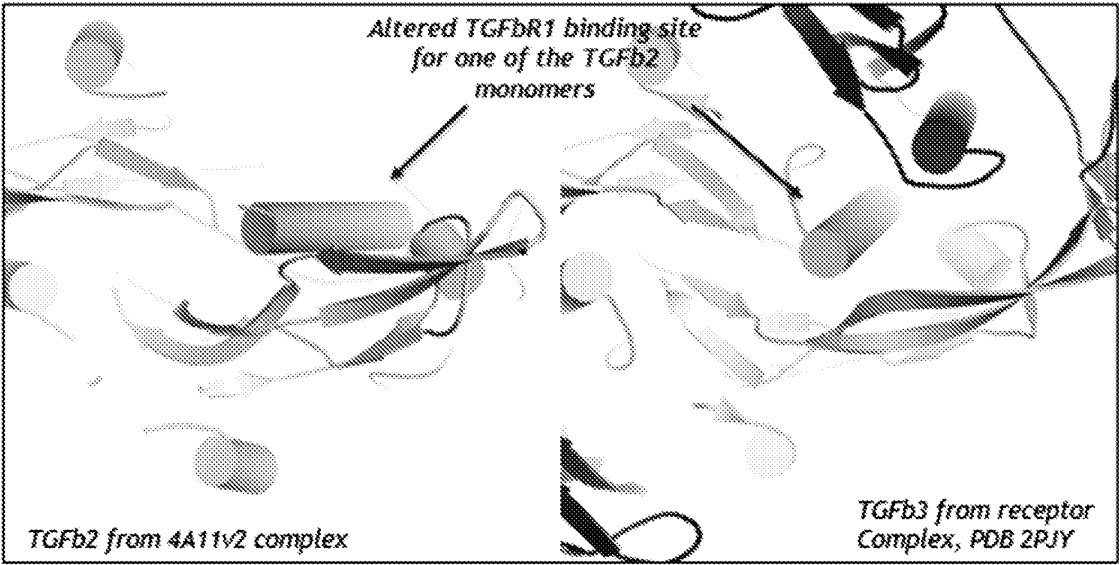


FIG. 37

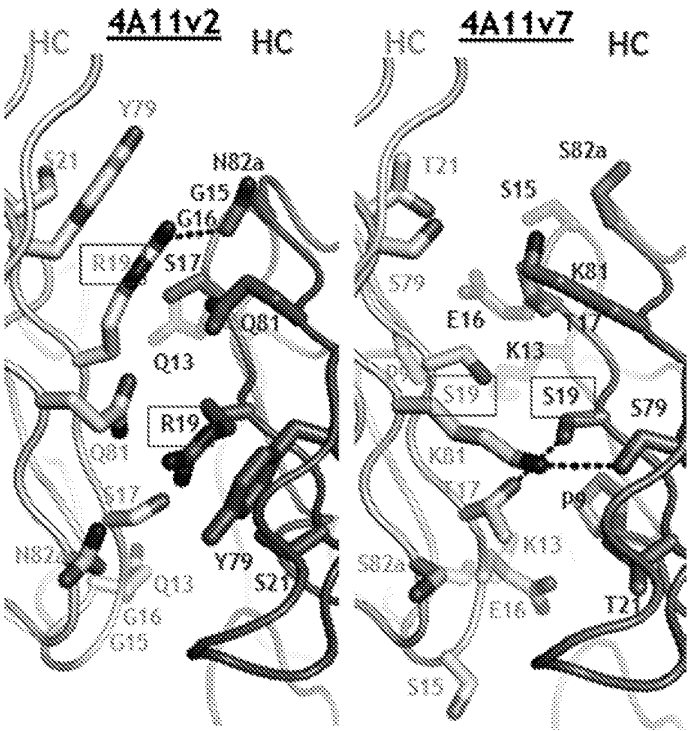


FIG. 38

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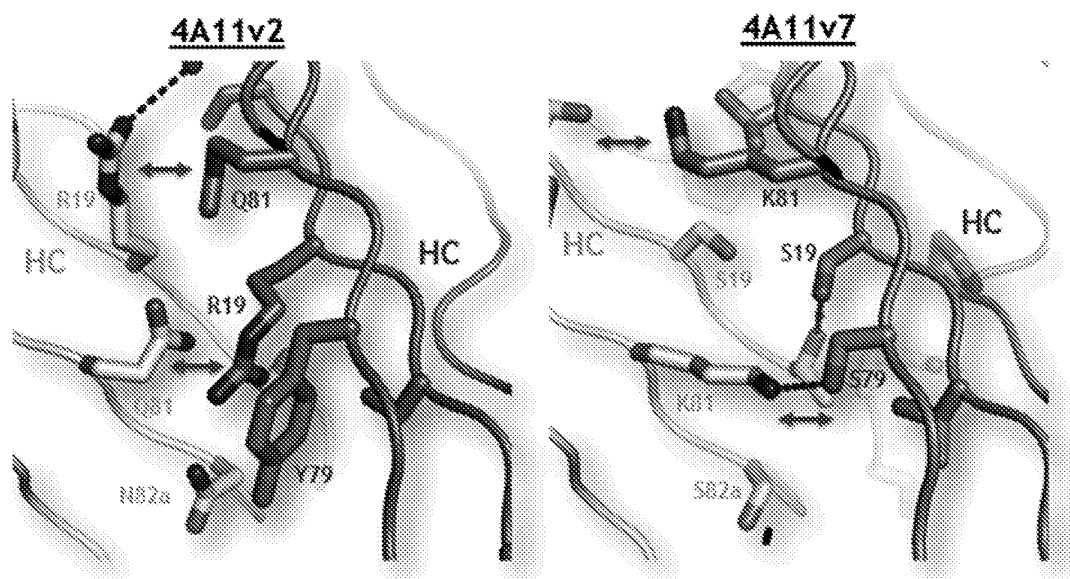


FIG. 39

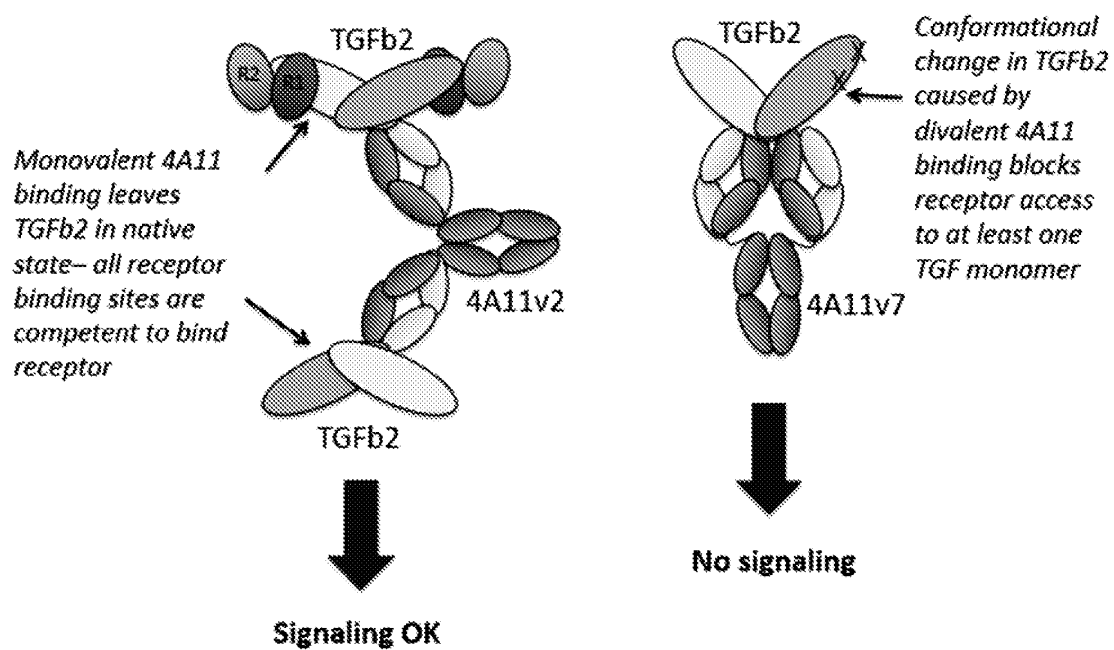


FIG. 40

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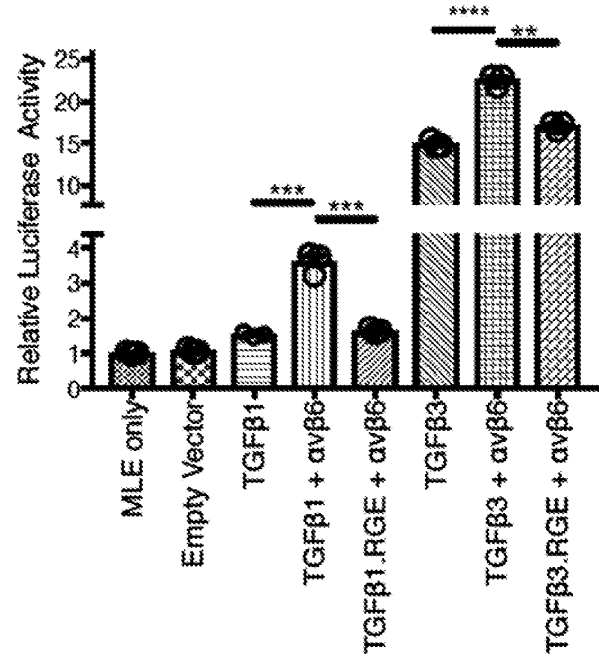


FIG. 41

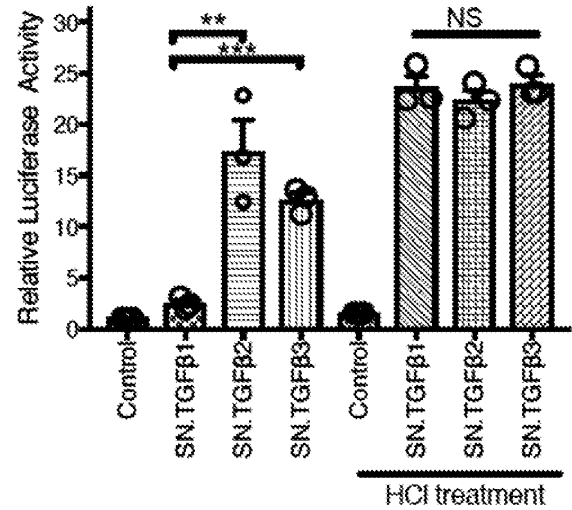


FIG. 42

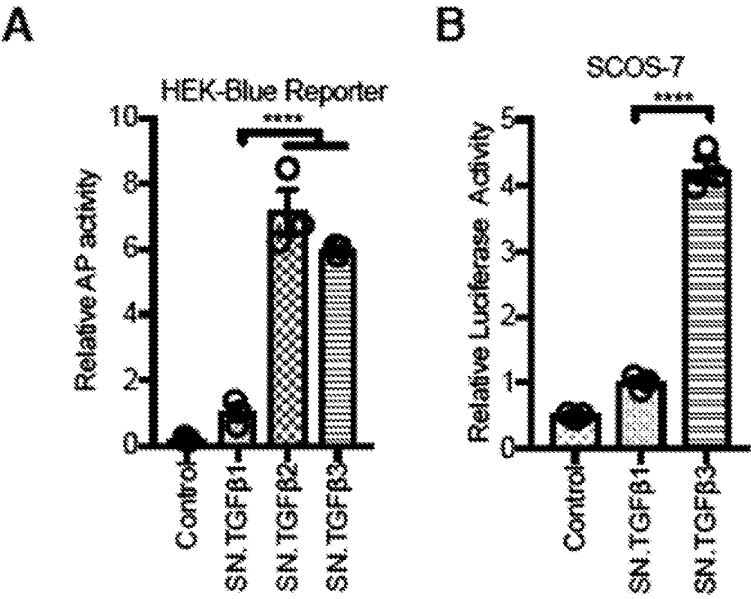


FIG. 43

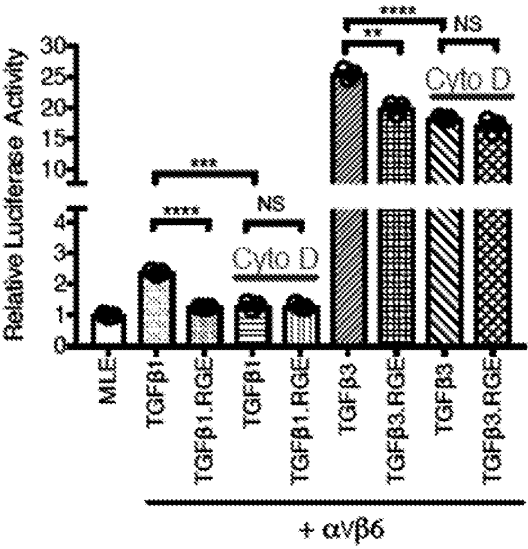


FIG. 44

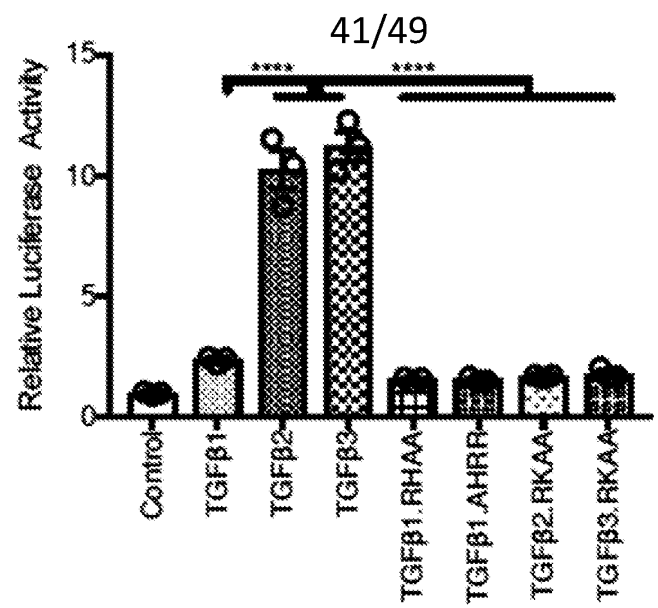


FIG. 45

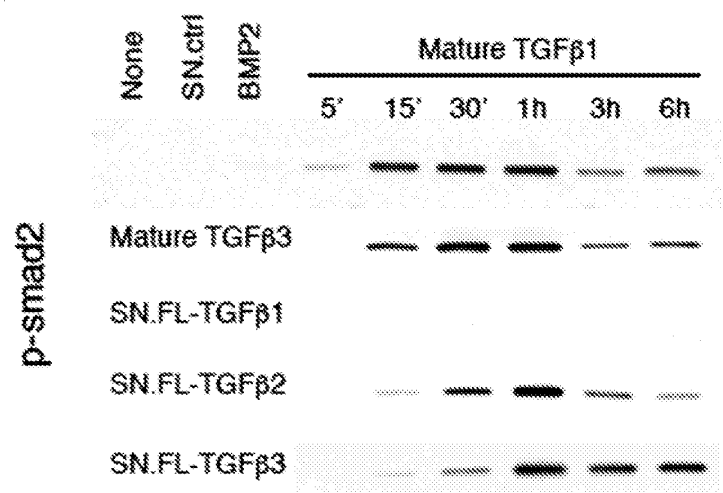


FIG. 46

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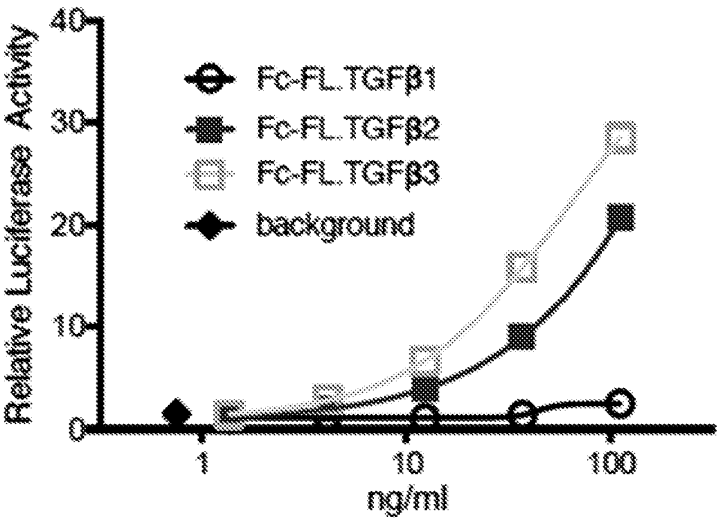


FIG. 47

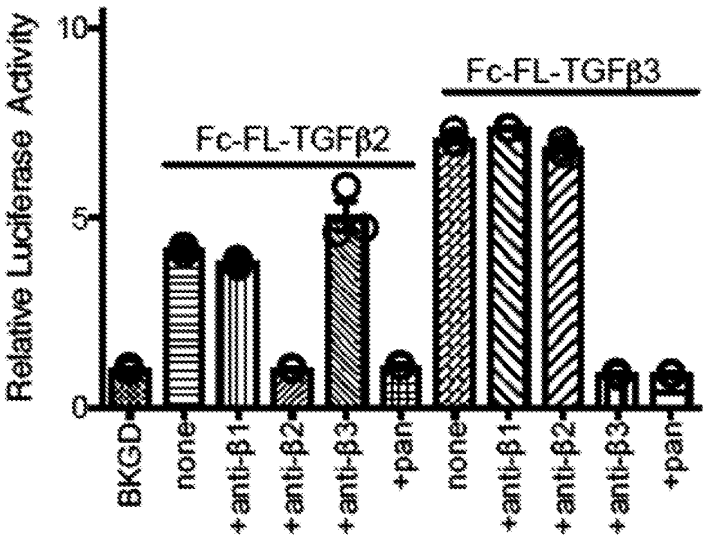


FIG. 48

%	LAP1	LAP2	LAP3
LAP1	—	42	45
LAP2		—	56
LAP3			—

%	mature β1	mature β2	mature β3
mature β1	—	85	83
mature β2		—	90
mature β3			—

FIG. 49

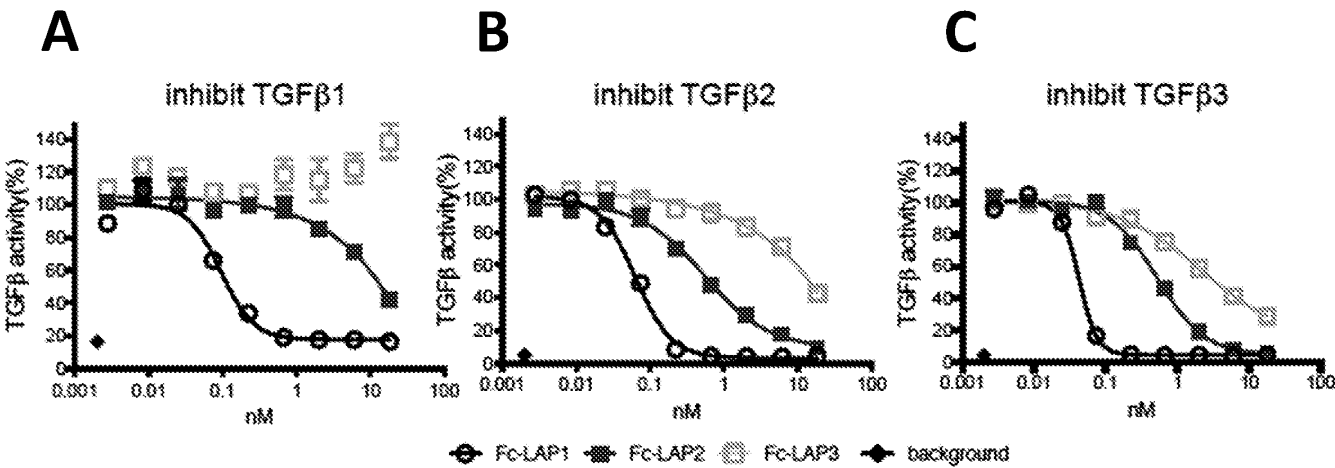


FIG. 50

IC ₅₀ (nM)	TGFβ1	TGFβ2	TGFβ3
Fc-LAP1	96	64	43
Fc-LAP2	10,143	548	525
Fc-LAP3	no inhibition	12,446	2,924

FIG. 51

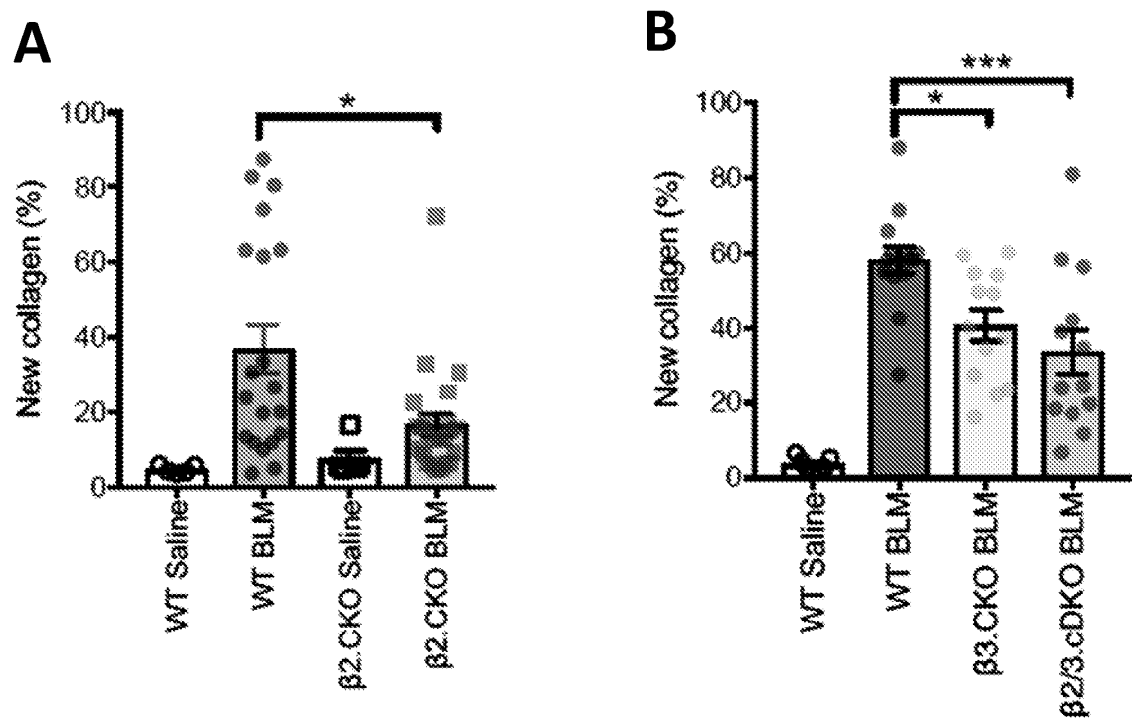


FIG. 52

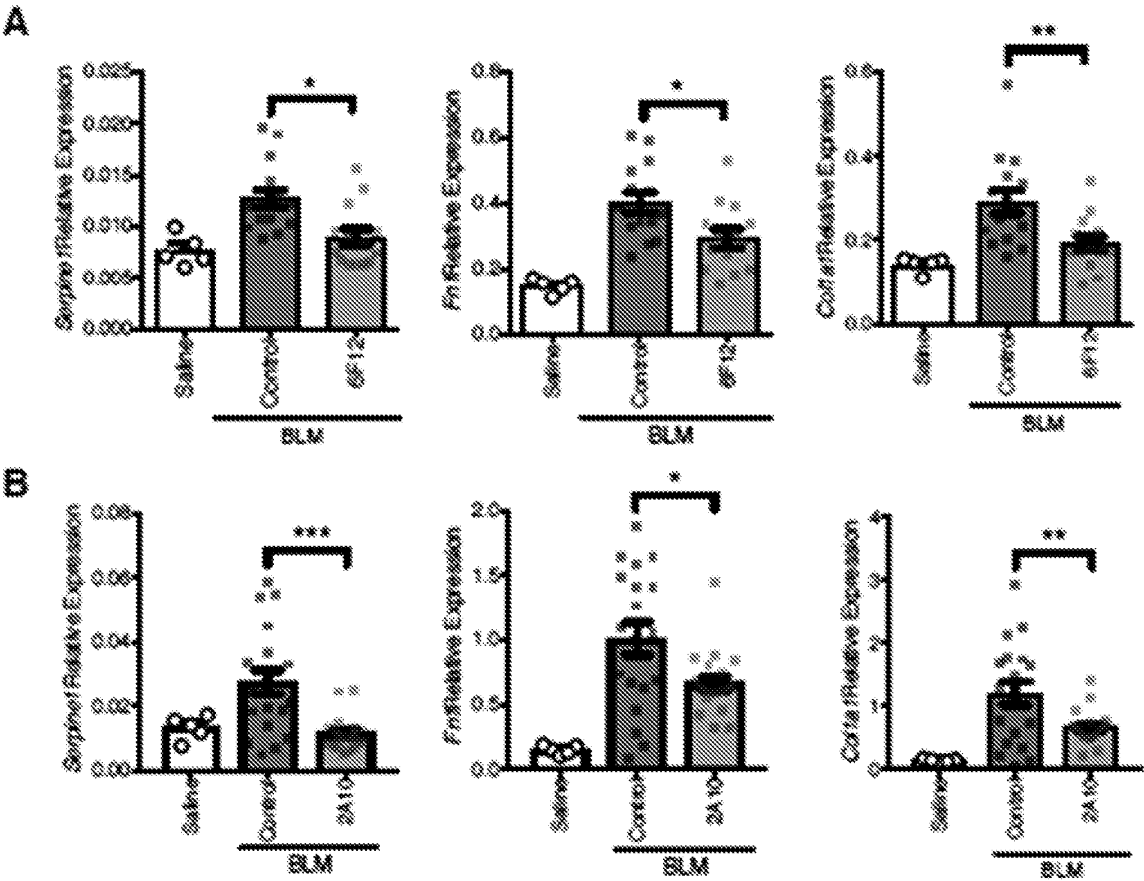


FIG. 53

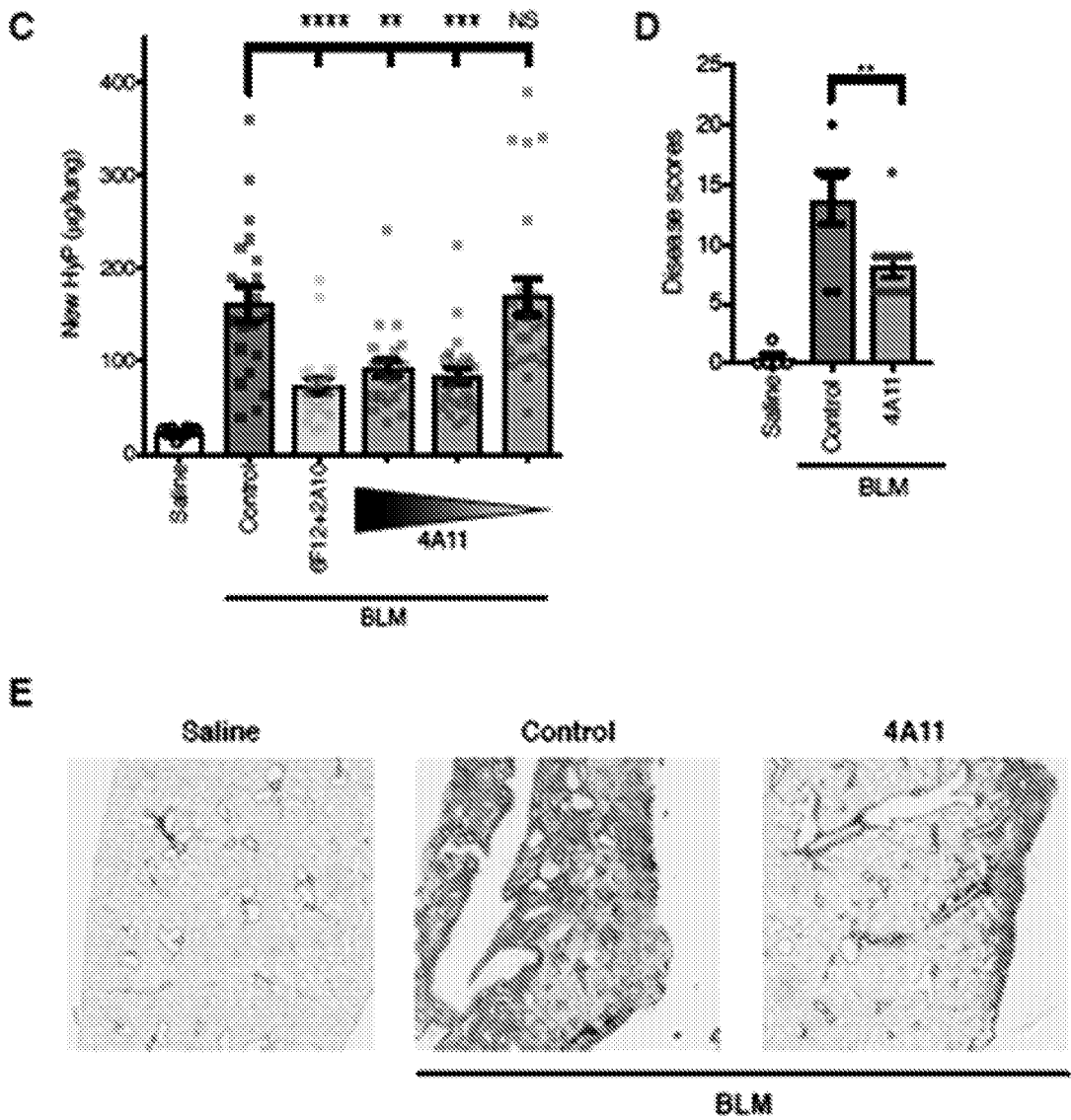


FIG. 53 (cont.)

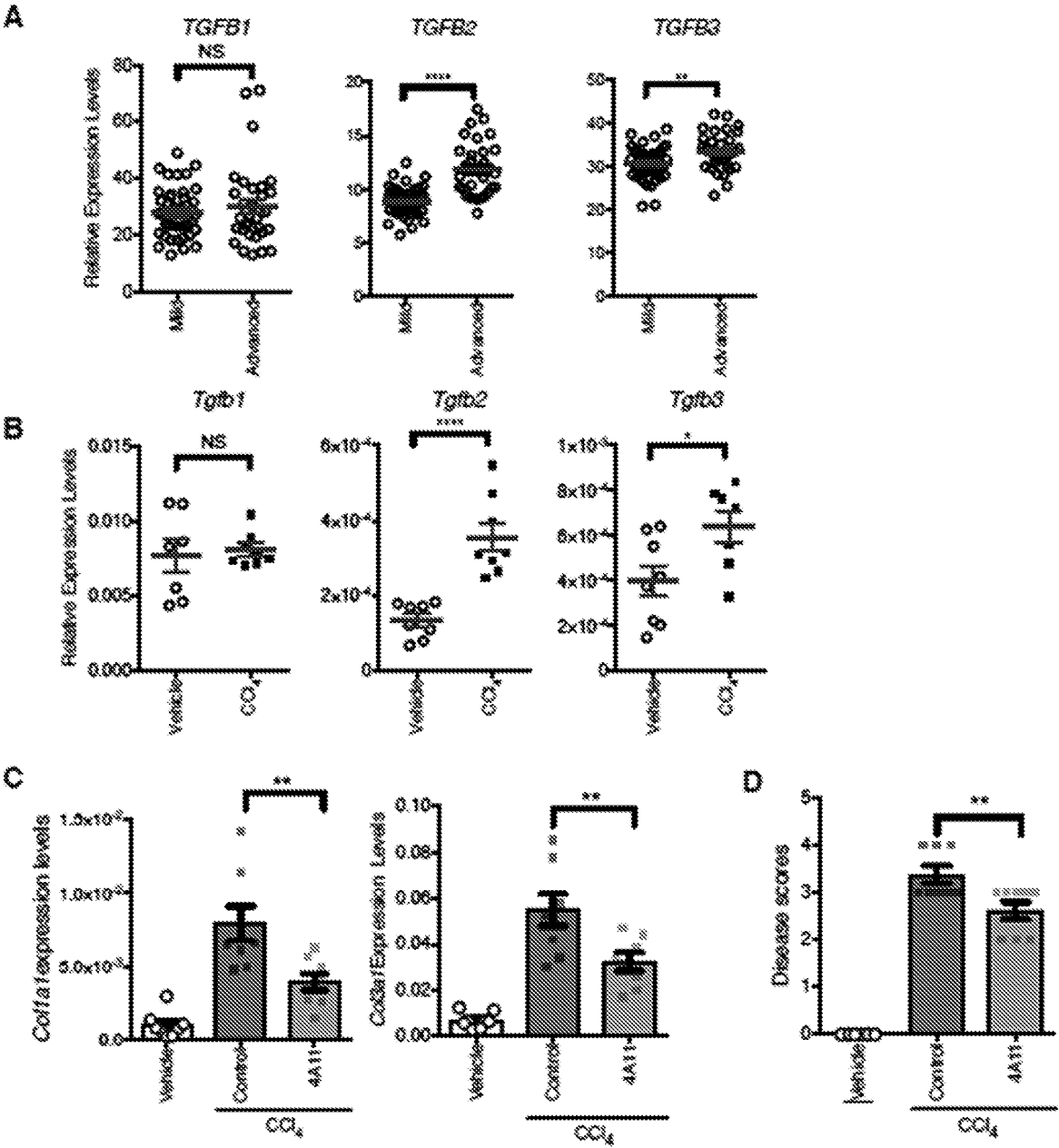


FIG. 54

A

K_D (nM)	Human $\beta 2$	mouse $\beta 2$
6F12	<0.001	<0.001
4A11	0.008	<0.002

B

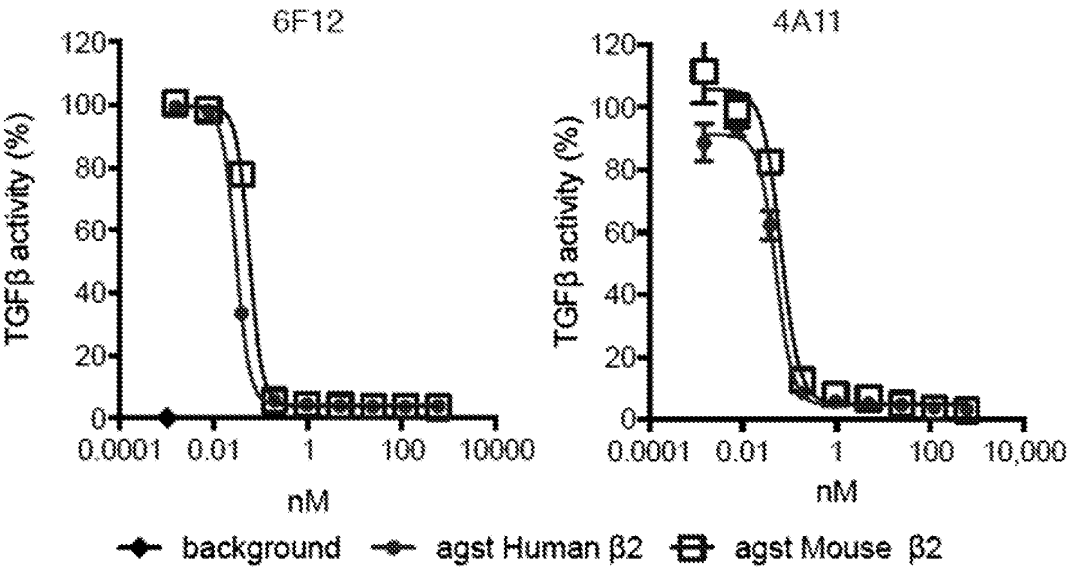


FIG. 55

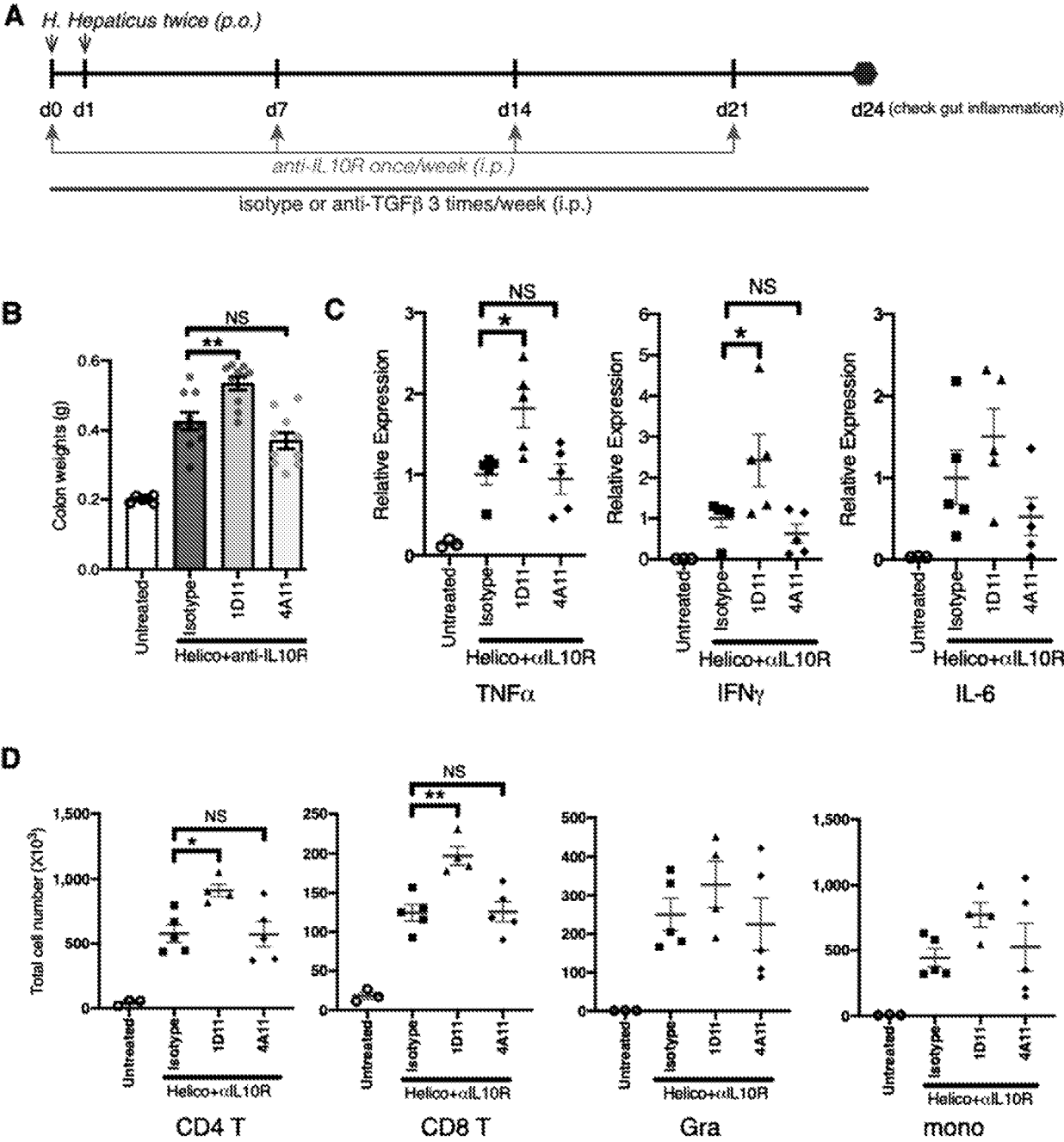


FIG. 56