



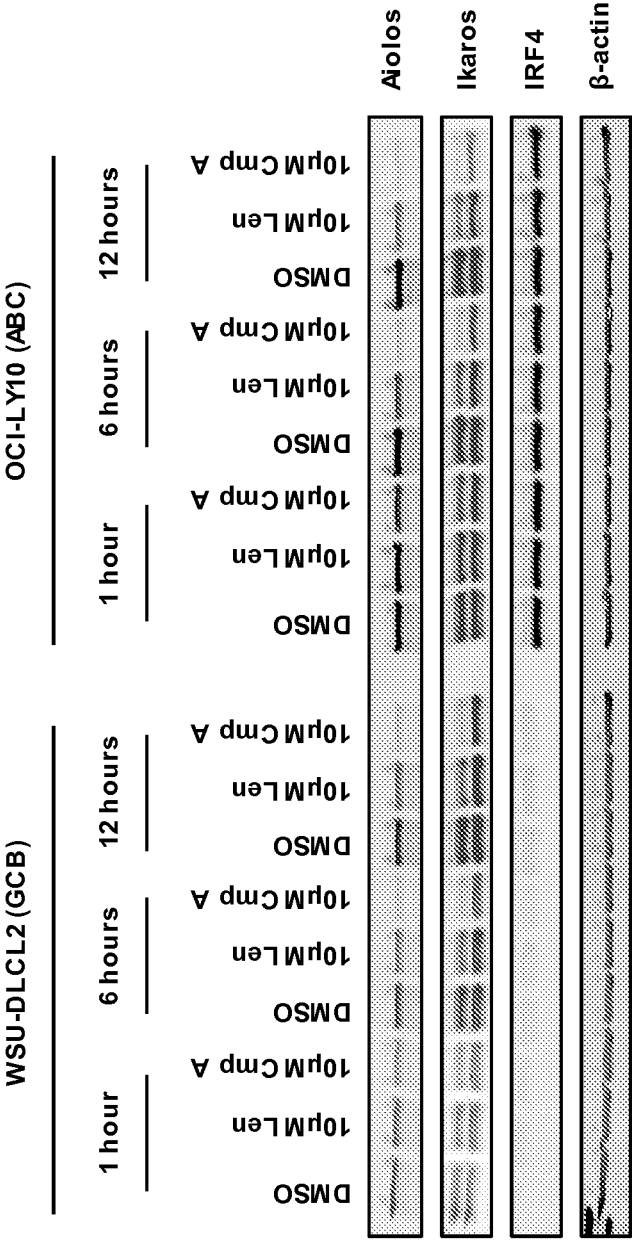


Figure 1B

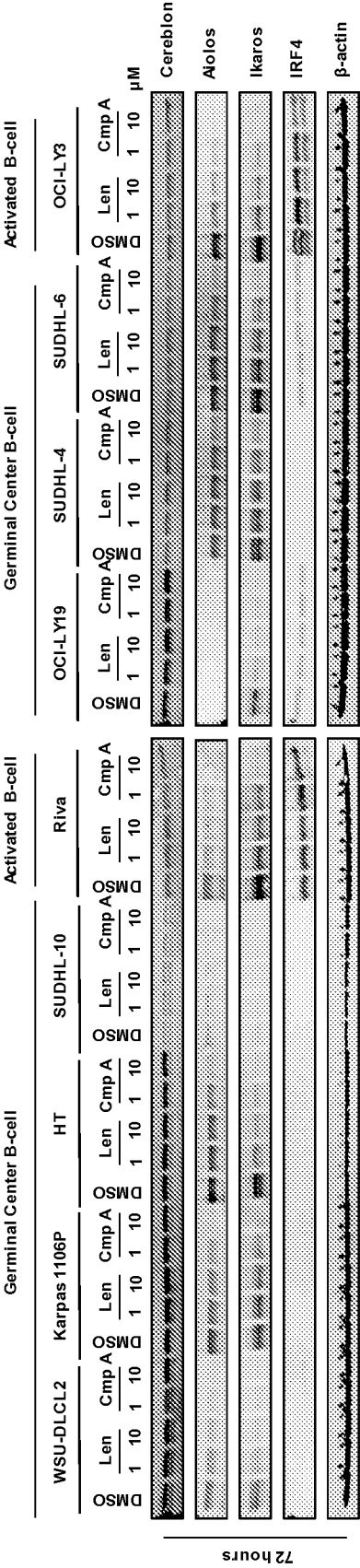


Figure 1C

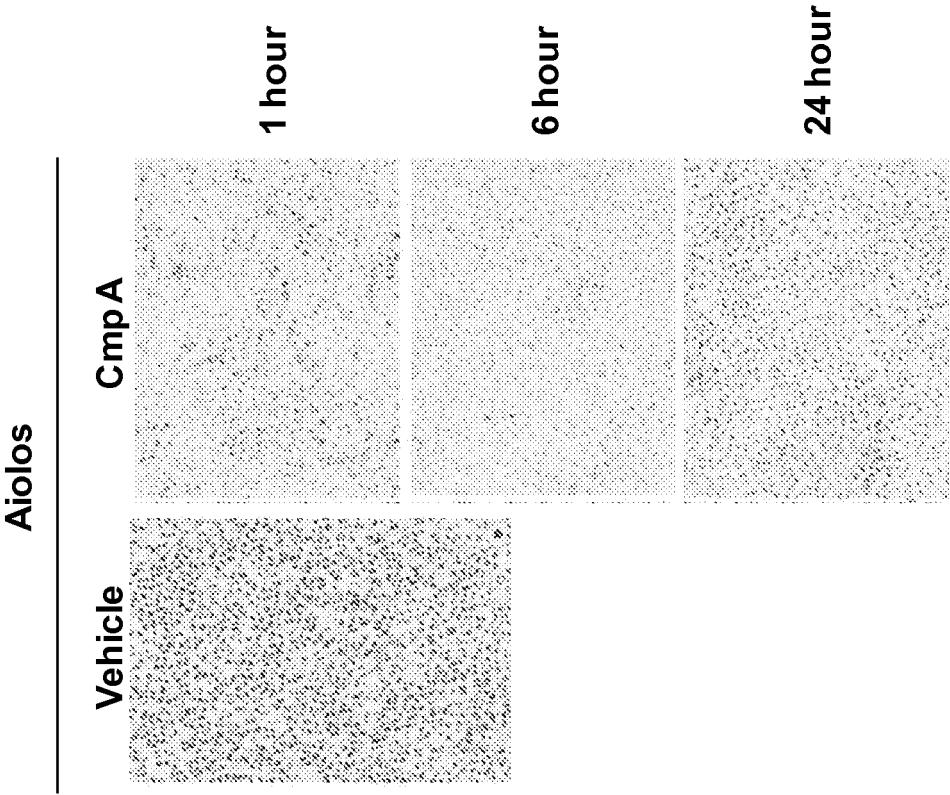


Figure 2A

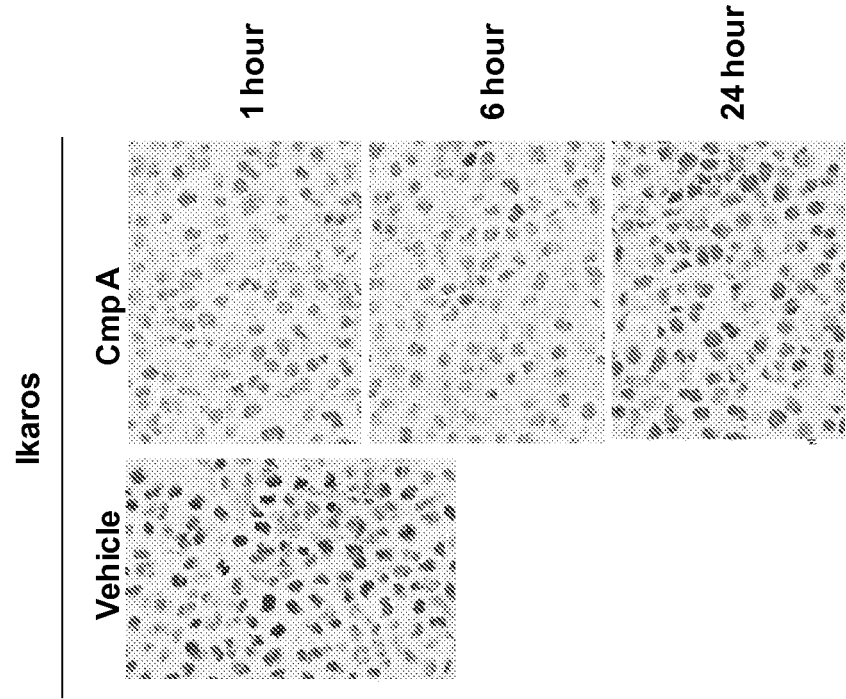


Figure 2B

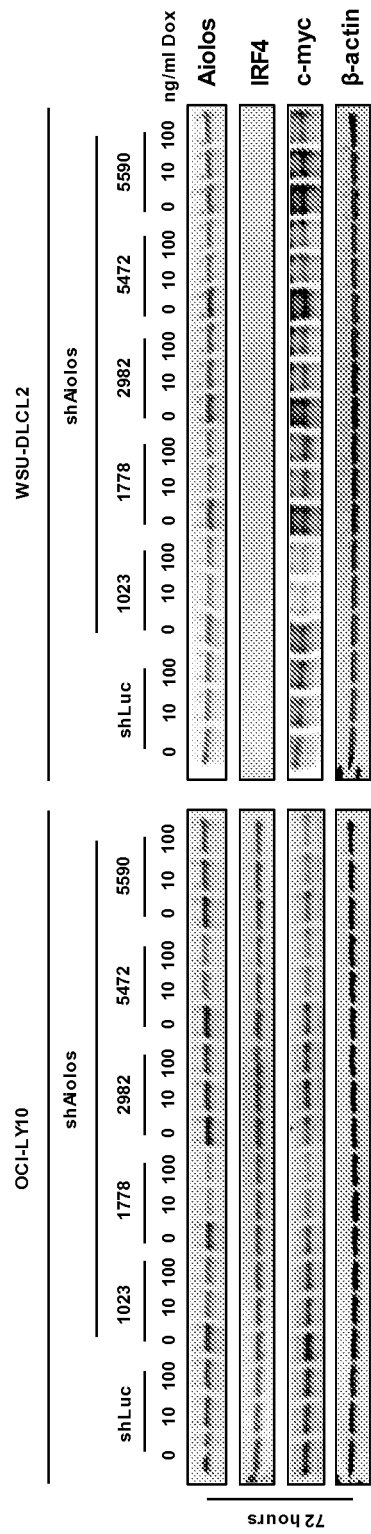


Figure 3A

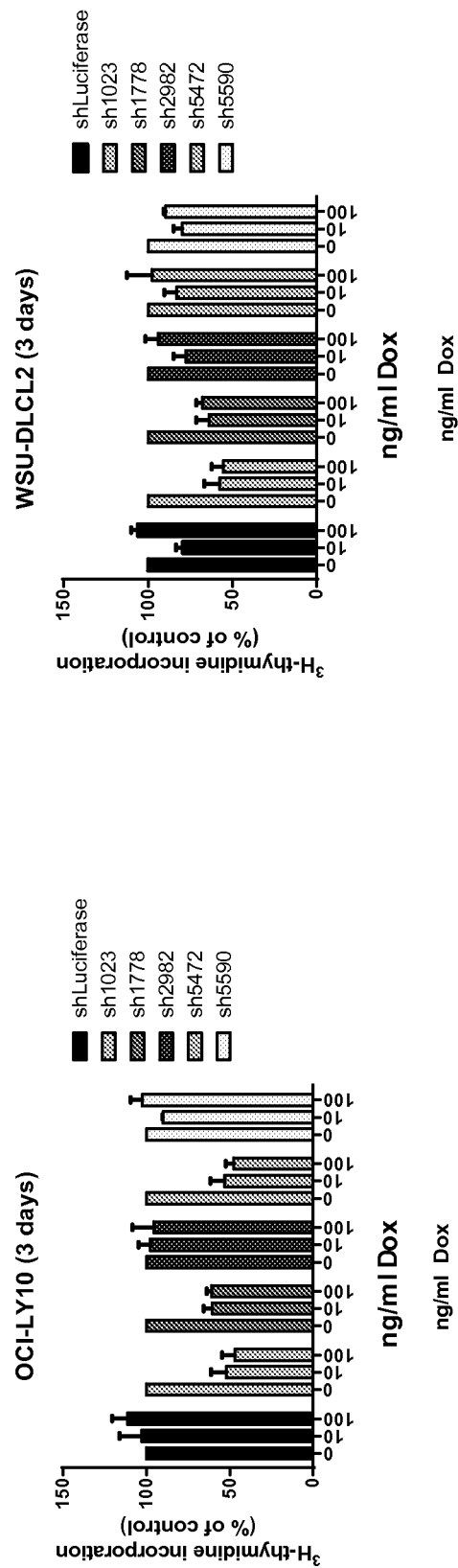


Figure 3B

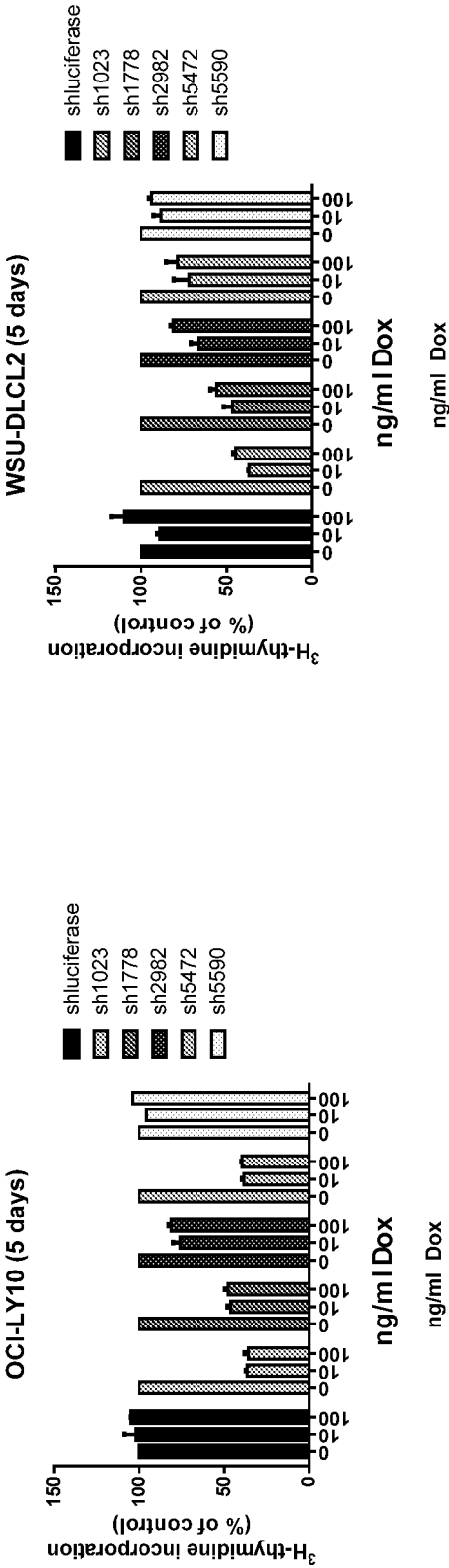


Figure 3C

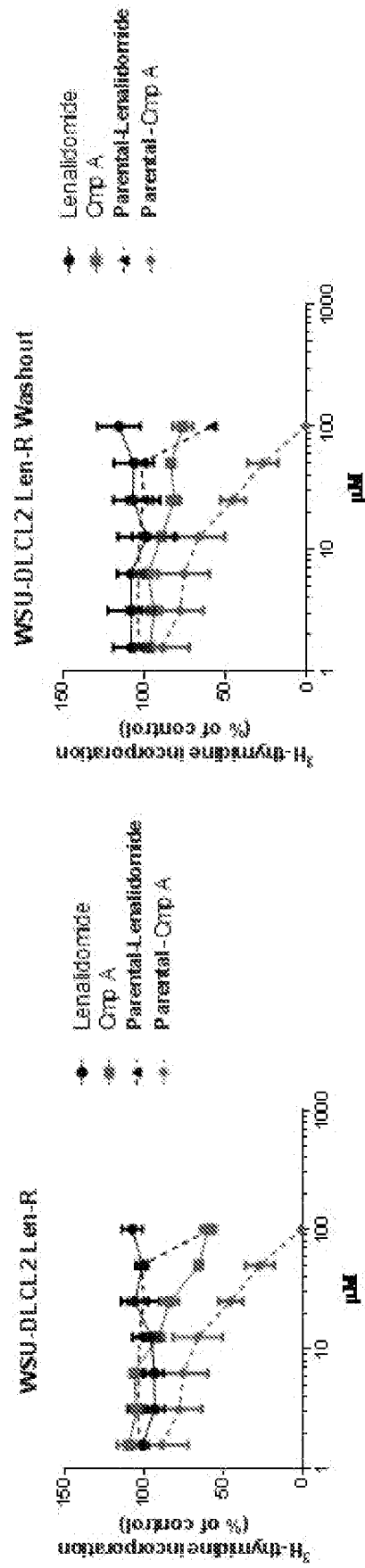


Figure 4A

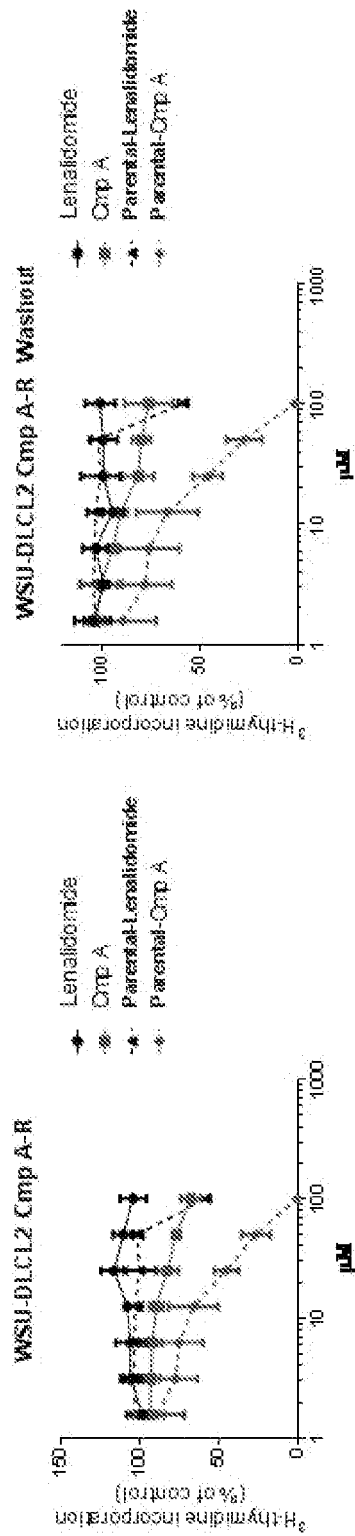


Figure 4B

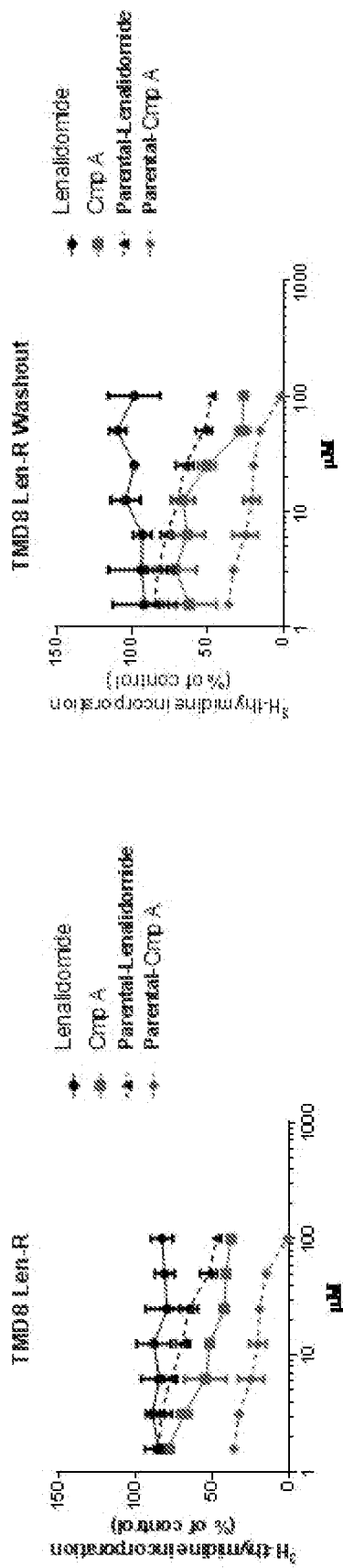


Figure 4C

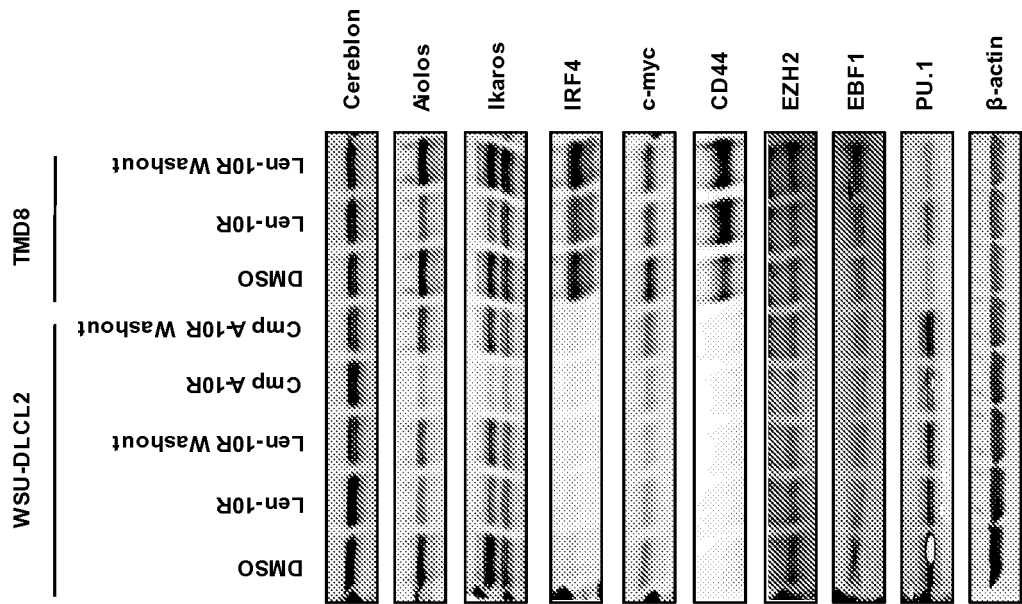


Figure 5A

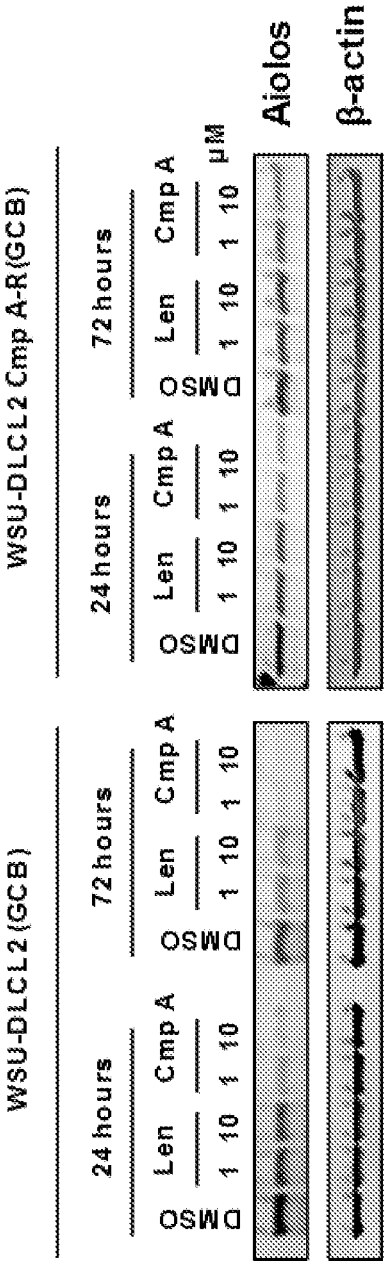


Figure 5B

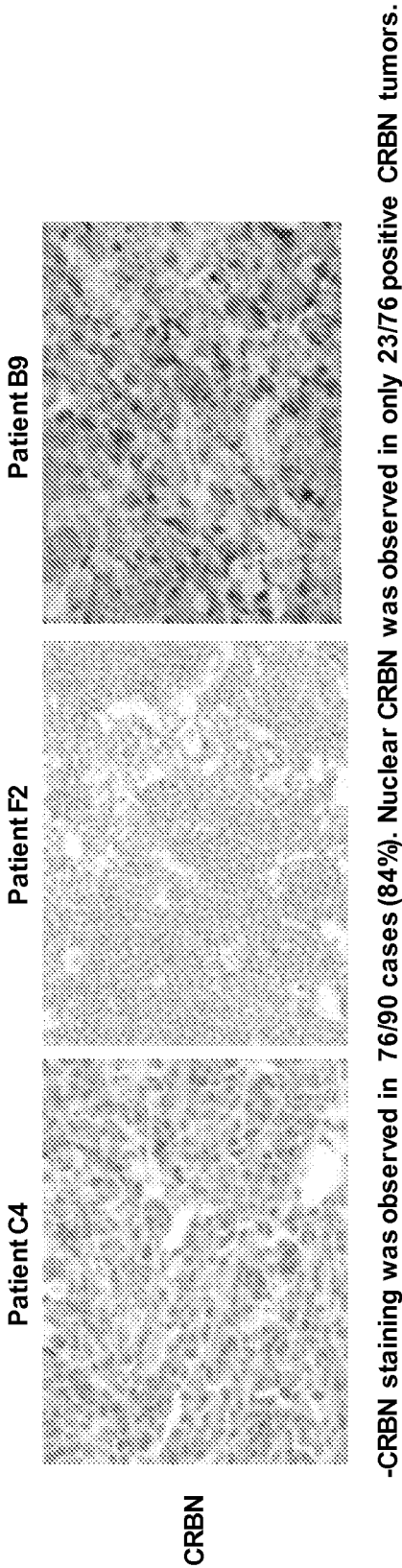


Figure 6A

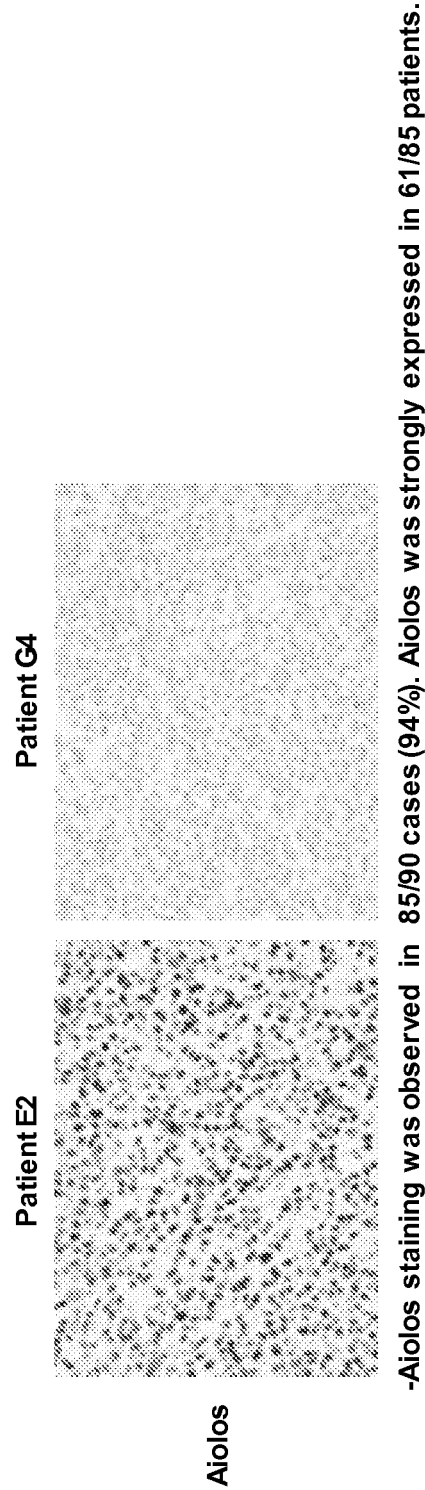


Figure 6B

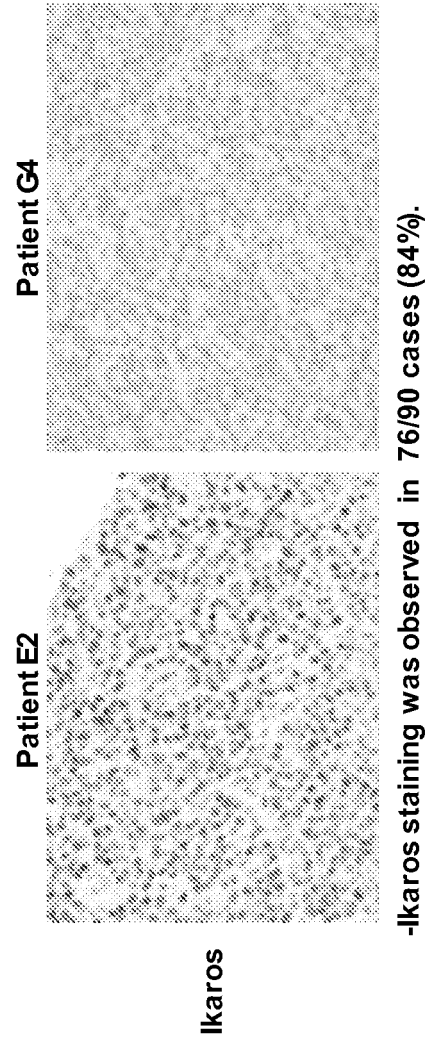


Figure 6C

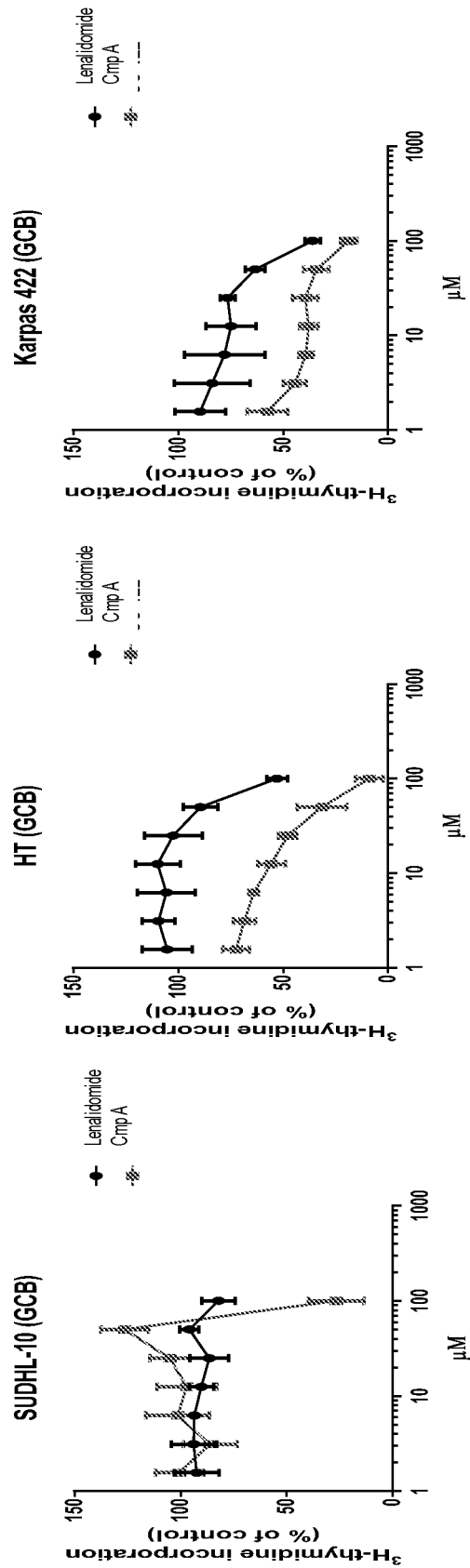


Figure 7A

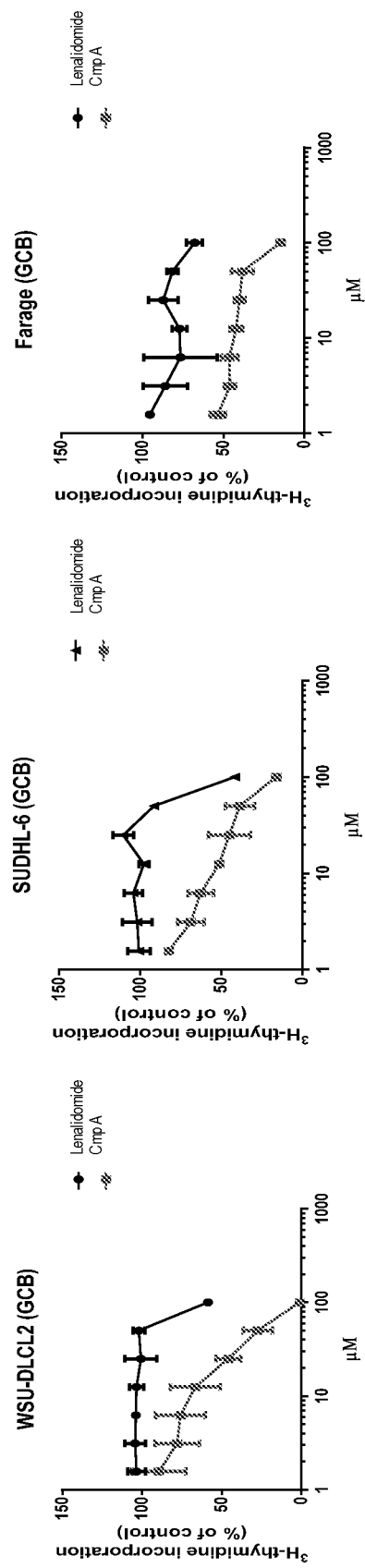


Figure 7B

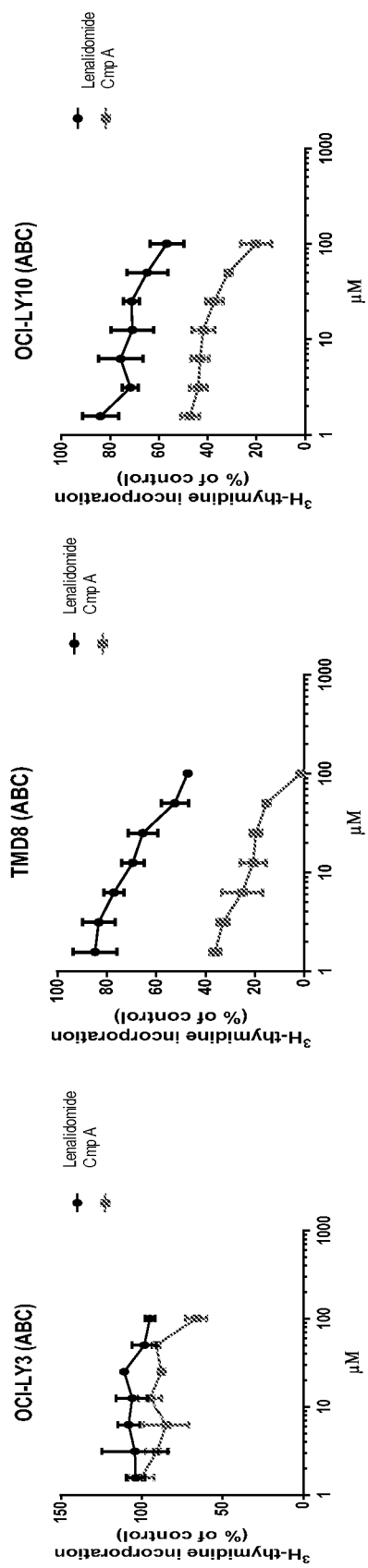


Figure 7C

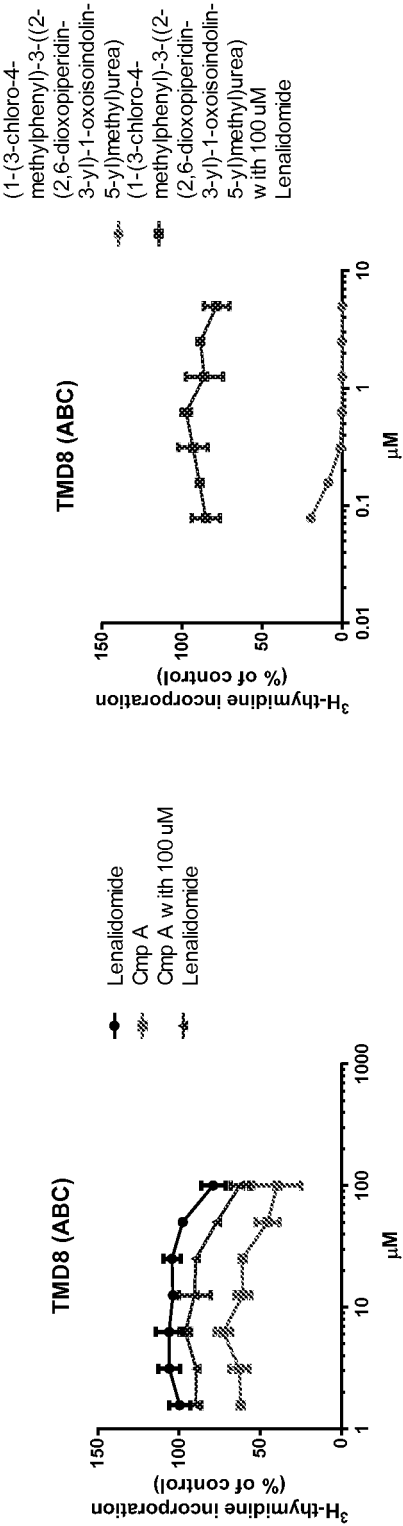


Figure 8A

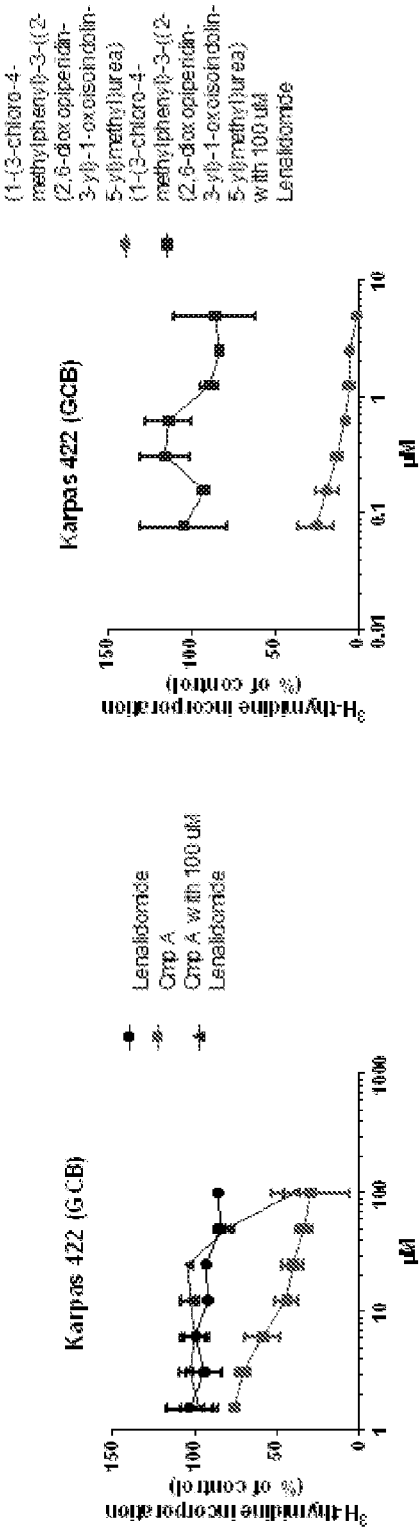


Figure 8B

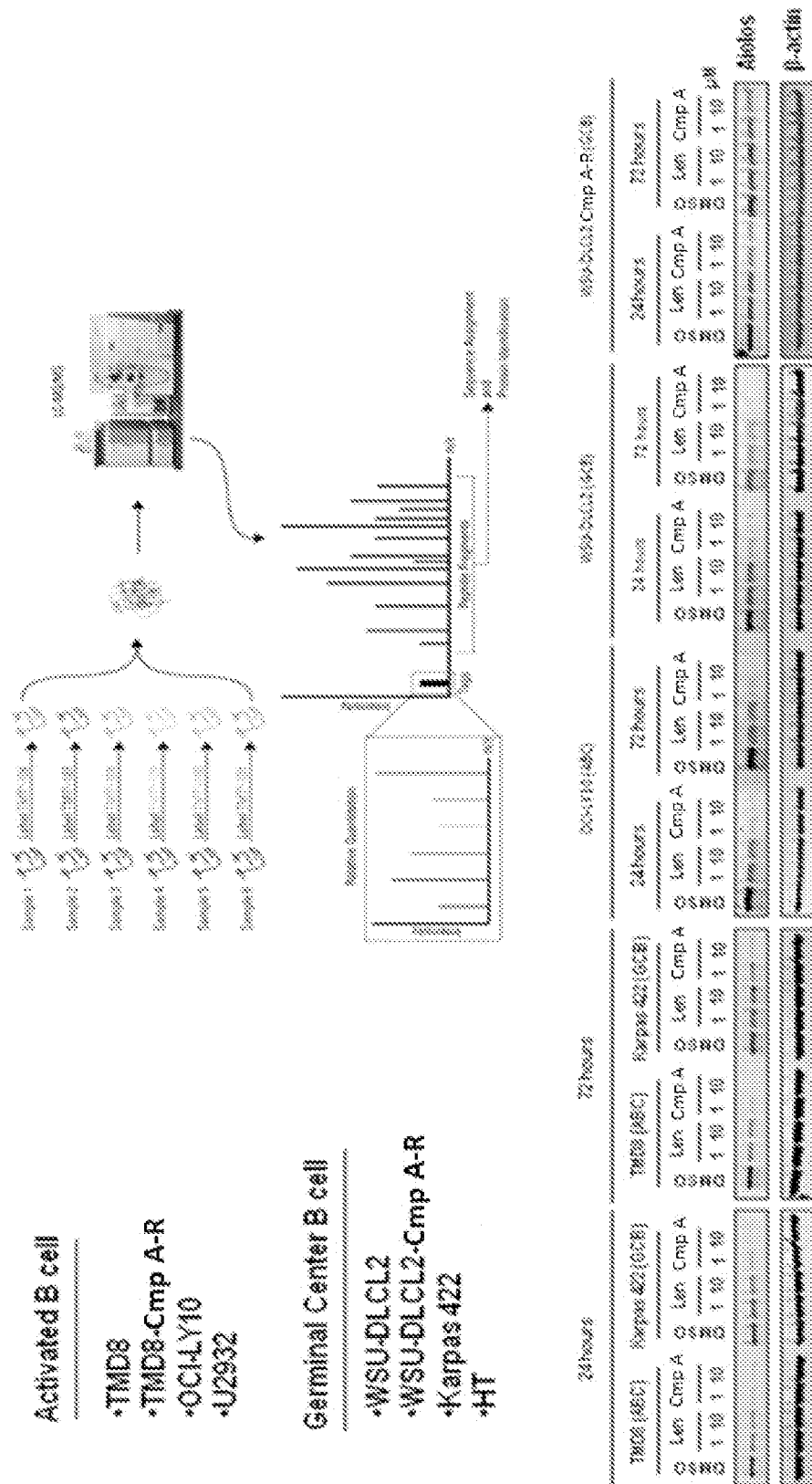


Figure 9

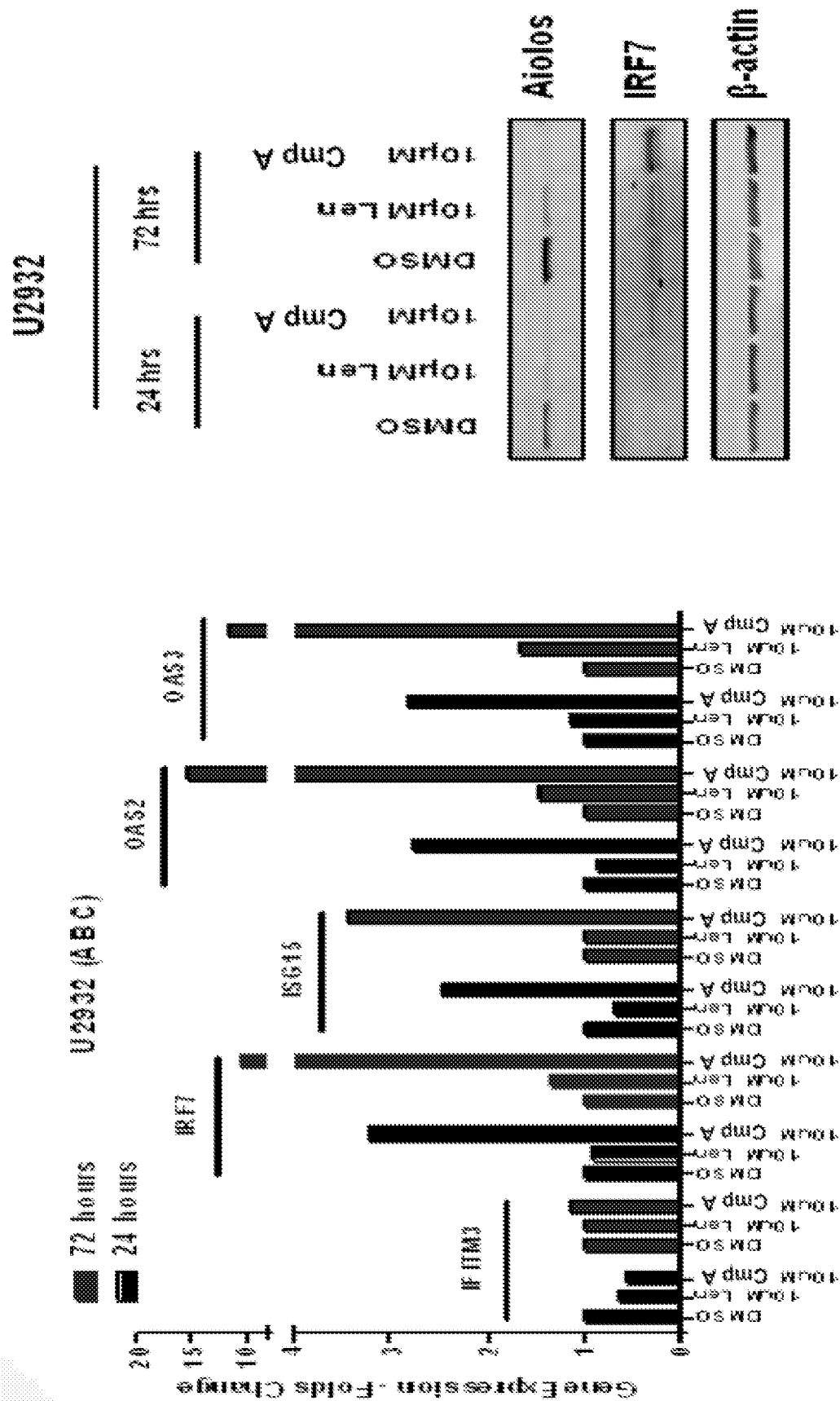


Figure 10A

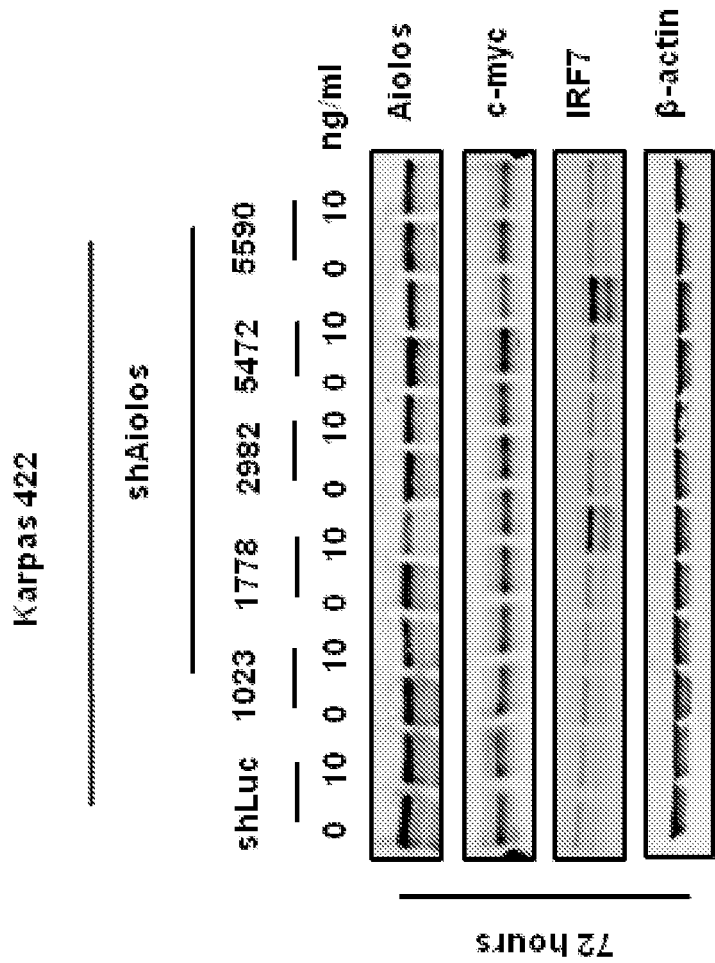


Figure 10B

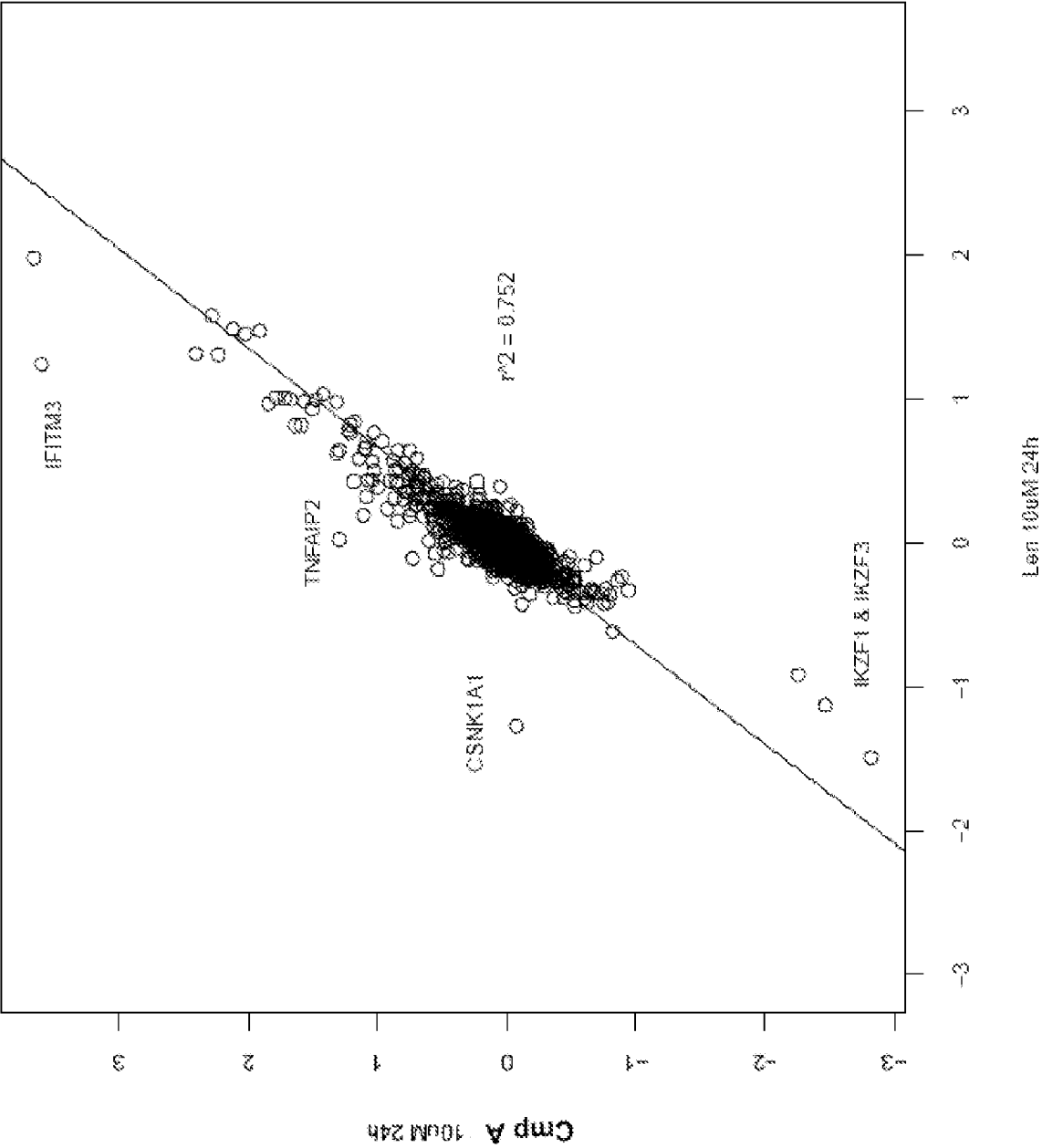


Figure 11

Gene Name	Full Name
IFIT3	interferon-induced protein with tetratricopeptide repeats 3 [Source:HGNC Symbol;Acc:5411]
IFIT1	interferon-induced protein with tetratricopeptide repeats 1 [Source:HGNC Symbol;Acc:5407]
IFI27	interferon, alpha-inducible protein 27 [Source:HGNC Symbol;Acc:5397]
IFIT5	interferon-induced protein with tetratricopeptide repeats 5 [Source:HGNC Symbol;Acc:13328]
IFIT1	interferon-induced protein with tetratricopeptide repeats 1 [Source:HGNC Symbol;Acc:5407]
IFIT2	interferon-induced protein with tetratricopeptide repeats 2 [Source:HGNC Symbol;Acc:5409]
IFIT3	interferon-induced protein with tetratricopeptide repeats 3 [Source:HGNC Symbol;Acc:5411]
DDX58	DEAD (Asp-Glu-Ala-Asp) box polypeptide 58 [Source:HGNC Symbol;Acc:19102]
IFIT3	interferon-induced protein with tetratricopeptide repeats 3 [Source:HGNC Symbol;Acc:5411]
TLR3	toll-like receptor 3 [Source:HGNC Symbol;Acc:11849]
OAS1	2'-5'-oligoadenylate synthetase 1, 40/46kDa [Source:HGNC Symbol;Acc:8086]
ISG15	ISG15 ubiquitin-like modifier [Source:HGNC Symbol;Acc:4053]
MX1	myxovirus (influenza virus) resistance 1, interferon-inducible protein p78 (mouse) [Source:HGNC Symbol;Acc:7532]
IFI44L	interferon-induced protein 44-like [Source:HGNC Symbol;Acc:17817]
IFI44	interferon-induced protein 44 [Source:HGNC Symbol;Acc:16938]
OAS3	2'-5'-oligoadenylate synthetase 3, 100kDa [Source:HGNC Symbol;Acc:8088]
OAS2	2'-5'-oligoadenylate synthetase 2, 69/71kDa [Source:HGNC Symbol;Acc:8087]
MX2	myxovirus (influenza virus) resistance 2 (mouse) [Source:HGNC Symbol;Acc:7533]
ISG20	interferon stimulated exonuclease gene 20kDa [Source:HGNC Symbol;Acc:6130]
GBP1	guanylate binding protein 1, interferon-inducible [Source:HGNC Symbol;Acc:4182]
IFI6	interferon, alpha-inducible protein 6 [Source:HGNC Symbol;Acc:4054]
IFIT5	interferon-induced protein with tetratricopeptide repeats 5 [Source:HGNC Symbol;Acc:13328]
DDX60	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60 [Source:HGNC Symbol;Acc:25942]
DDX60L	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60-like [Source:HGNC Symbol;Acc:26429]
IFIH1	interferon induced with helicase C domain 1 [Source:HGNC Symbol;Acc:18873]
IFI35	interferon-induced protein 35 [Source:HGNC Symbol;Acc:5399]
IFI16	interferon, gamma-inducible protein 16 [Source:HGNC Symbol;Acc:5395]
IFI27	interferon, alpha-inducible protein 27 [Source:HGNC Symbol;Acc:5397]
IFI6	interferon, alpha-inducible protein 6 [Source:HGNC Symbol;Acc:4054]

Figure 12

Gene Name	Full Name
IFI27	interferon, alpha-inducible protein 27 [Source:HGNC Symbol;Acc:5397]
IFI6	interferon, alpha-inducible protein 6 [Source:HGNC Symbol;Acc:4054]
OASL	2'-5'-oligoadenylate synthetase-like [Source:HGNC Symbol;Acc:8090]
DDX60	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60 [Source:HGNC Symbol;Acc:25942]
OAS1	2'-5'-oligoadenylate synthetase 1, 40/46kDa [Source:HGNC Symbol;Acc:8086]
OAS3	2'-5'-oligoadenylate synthetase 3, 100kDa [Source:HGNC Symbol;Acc:8088]
IFI44	interferon-induced protein 44 [Source:HGNC Symbol;Acc:16938]
IFI44	interferon-induced protein 44 [Source:HGNC Symbol;Acc:16938]
DDX60L	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60-like [Source:HGNC Symbol;Acc:26429]
IFIT1	interferon-induced protein with tetratricopeptide repeats 1 [Source:HGNC Symbol;Acc:5407]
TLR1	toll-like receptor 1 [Source:HGNC Symbol;Acc:11847]
TLR4	toll-like receptor 4 [Source:HGNC Symbol;Acc:11850]
IFIH1	interferon induced with helicase C domain 1 [Source:HGNC Symbol;Acc:18873]
TLR7	toll-like receptor 8 [Source:HGNC Symbol;Acc:15632]
TLR8	toll-like receptor 8 [Source:HGNC Symbol;Acc:15632]
OASL	2'-5'-oligoadenylate synthetase-like [Source:HGNC Symbol;Acc:8090]
OAS2	2'-5'-oligoadenylate synthetase 2, 69/71kDa [Source:HGNC Symbol;Acc:8087]
TLR3	toll-like receptor 3 [Source:HGNC Symbol;Acc:11849]
IFIT5	interferon-induced protein with tetratricopeptide repeats 5 [Source:HGNC Symbol;Acc:13328]
IRF8	interferon regulatory factor 8 [Source:HGNC Symbol;Acc:5358]
DDX60	DEAD (Asp-Glu-Ala-Asp) box polypeptide 60 [Source:HGNC Symbol;Acc:25942]
IRF8	interferon regulatory factor 8 [Source:HGNC Symbol;Acc:5358]
MX2	myxovirus (influenza virus) resistance 2 (mouse) [Source:HGNC Symbol;Acc:7533]
ISG20	interferon stimulated exonuclease gene 20kDa [Source:HGNC Symbol;Acc:6130]
IFIT2	interferon-induced protein with tetratricopeptide repeats 2 [Source:HGNC Symbol;Acc:5409]
IFI27	interferon, alpha-inducible protein 27 [Source:HGNC Symbol;Acc:5397]
IRF7	interferon regulatory factor 7 [Source:HGNC Symbol;Acc:6122]
DDX58	DEAD (Asp-Glu-Ala-Asp) box polypeptide 58 [Source:HGNC Symbol;Acc:19102]

Figure 12 (Cont'd)

Gene Name	Full Name
ISG15	ISG15 ubiquitin-like modifier [Source:HGNC Symbol;Acc:4053]
IFITM2	interferon induced transmembrane protein 2 [Source:HGNC Symbol;Acc:5413]
MX2	myxovirus (influenza virus) resistance 2 (mouse) [Source:HGNC Symbol;Acc:7533]
TLR8	toll-like receptor 8 [Source:HGNC Symbol;Acc:15632]
IRF2	interferon regulatory factor 2 [Source:HGNC Symbol;Acc:6117]
IRF1	interferon regulatory factor 1 [Source:HGNC Symbol;Acc:6116]
IRF8	interferon regulatory factor 8 [Source:HGNC Symbol;Acc:5358]
GBP1	guanylate binding protein 1, interferon-inducible [Source:HGNC Symbol;Acc:4182]
IRF1	interferon regulatory factor 1 [Source:HGNC Symbol;Acc:6116]
OAS3	2'-5'-oligoadenylate synthetase 3, 100kDa [Source:HGNC Symbol;Acc:8088]
IFI44L	interferon-induced protein 44-like [Source:HGNC Symbol;Acc:17817]
IFNA16	interferon, alpha 16 [Source:HGNC Symbol;Acc:5421]
TLR4	toll-like receptor 4 [Source:HGNC Symbol;Acc:11850]
IFITM2	interferon induced transmembrane protein 2 [Source:HGNC Symbol;Acc:5413]
IFNA5	interferon, alpha 5 [Source:HGNC Symbol;Acc:5426]
IFI35	interferon-induced protein 35 [Source:HGNC Symbol;Acc:5399]
IFNG	interferon, gamma [Source:HGNC Symbol;Acc:5438]
IFI16	interferon, gamma-inducible protein 16 [Source:HGNC Symbol;Acc:5395]
IFNGR1	interferon gamma receptor 1 [Source:HGNC Symbol;Acc:5439]
TLR3	toll-like receptor 3 [Source:HGNC Symbol;Acc:11849]
IFI27L2	interferon, alpha-inducible protein 27-like 2 [Source:HGNC Symbol;Acc:19753]
IFIT3	interferon-induced protein with tetratricopeptide repeats 3 [Source:HGNC Symbol;Acc:5411]
IRF4	interferon regulatory factor 4 [Source:HGNC Symbol;Acc:6119]

Figure 12 (Cont'd)

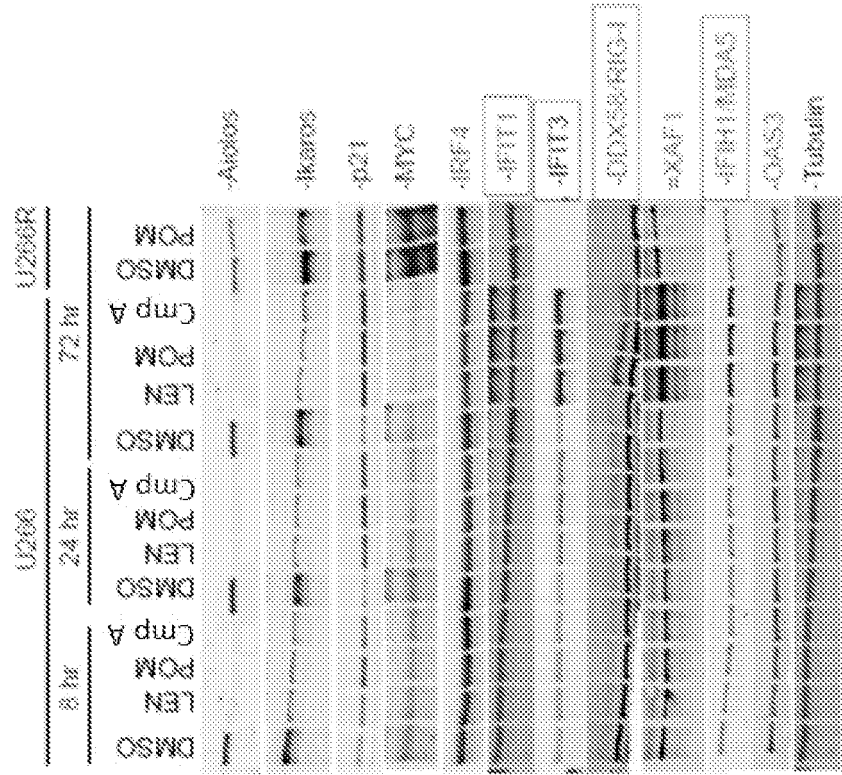


Figure 13A

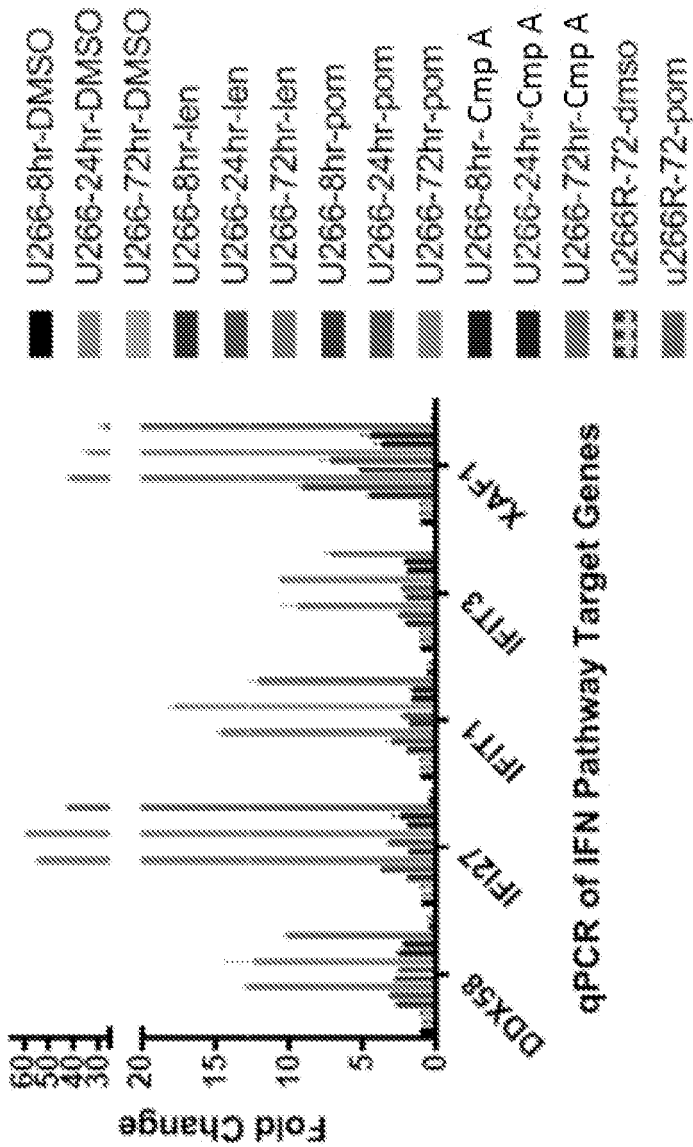


Figure 13B

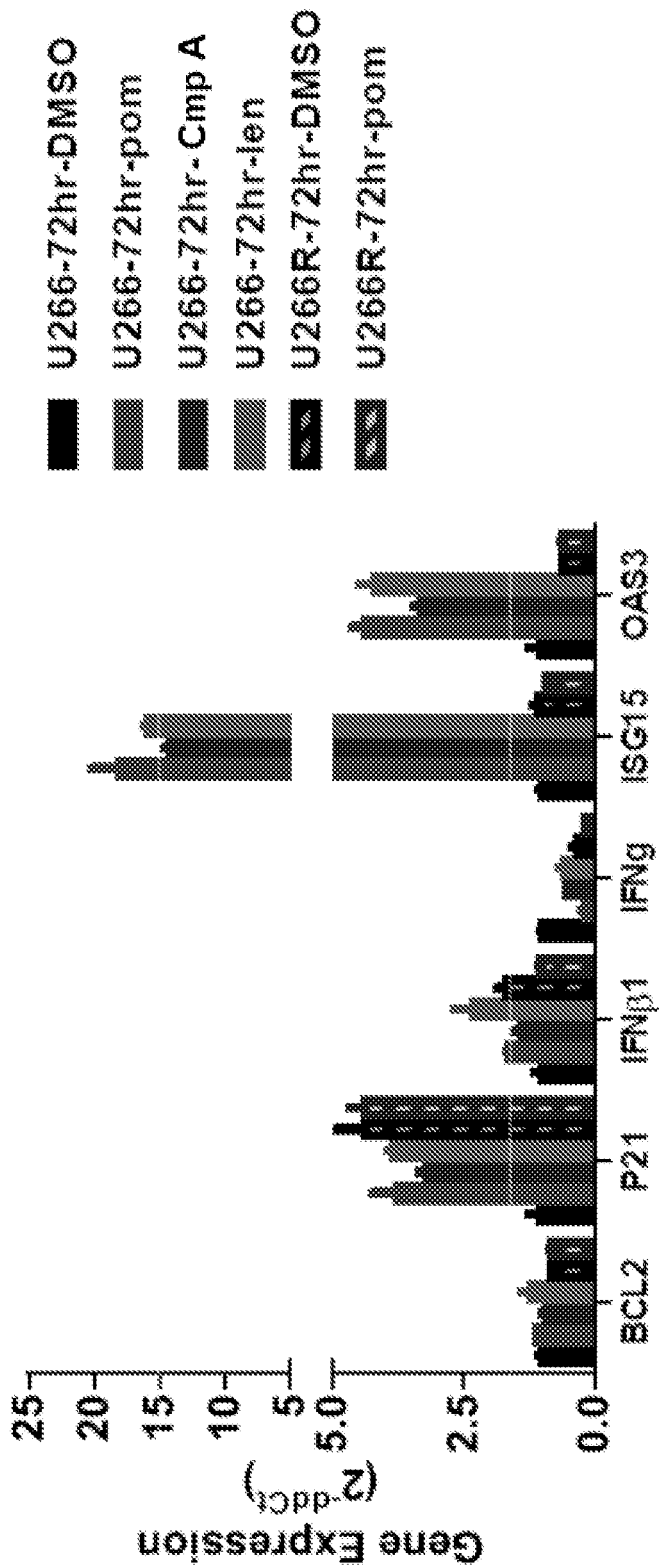


Figure 13C

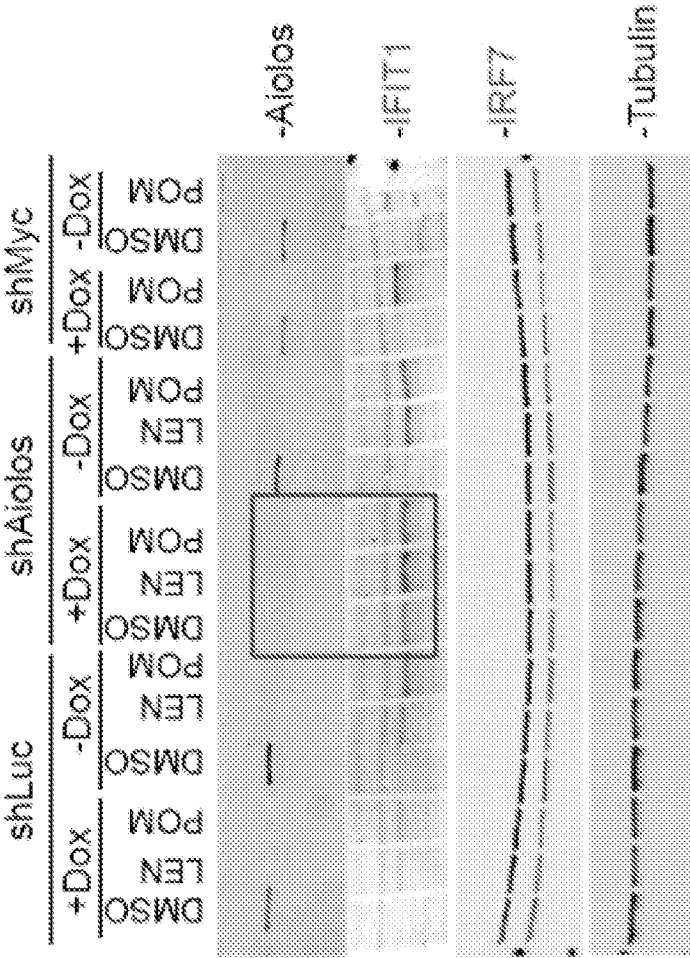


Figure 13D

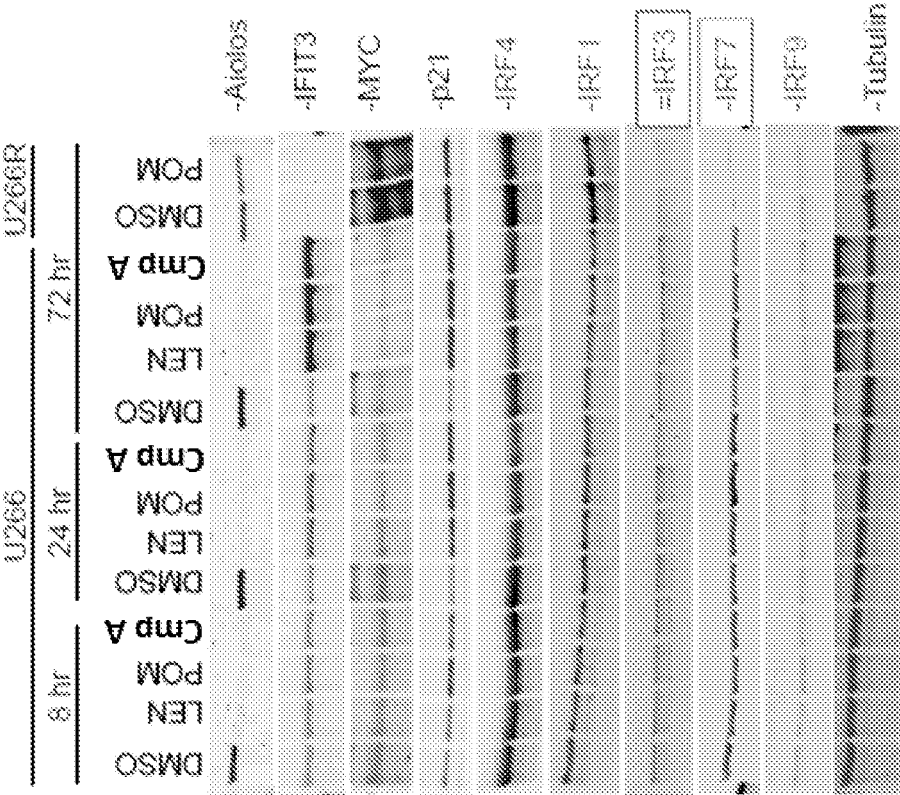


Figure 13E

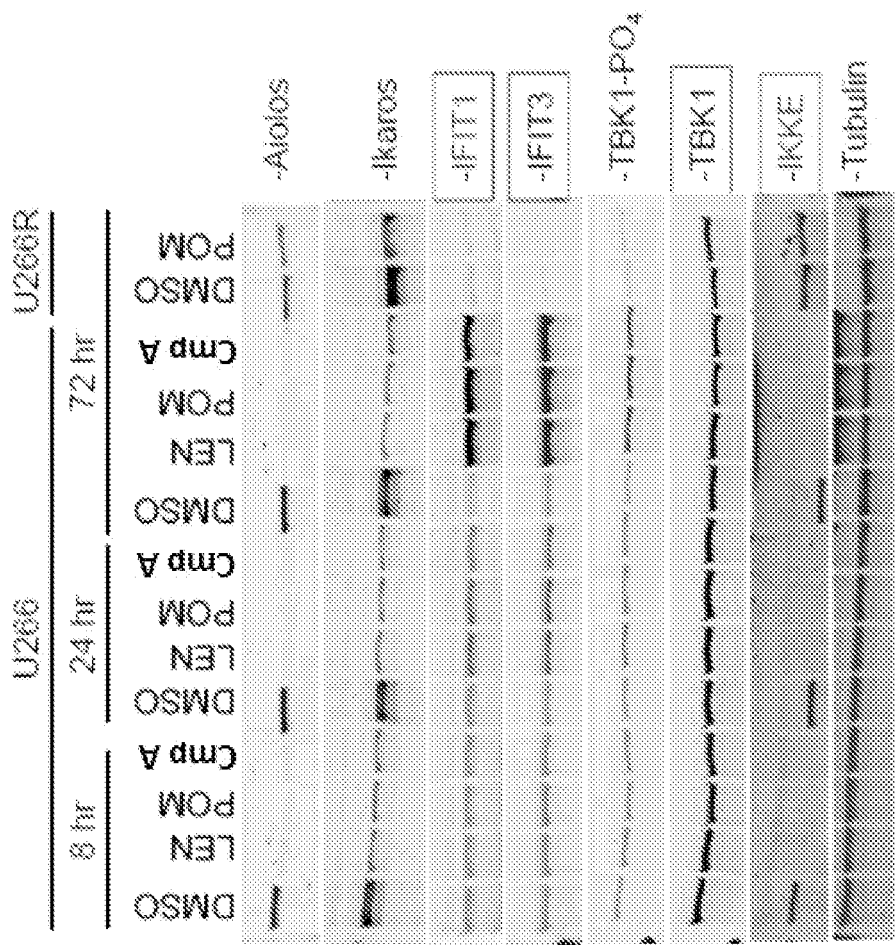


Figure 13F

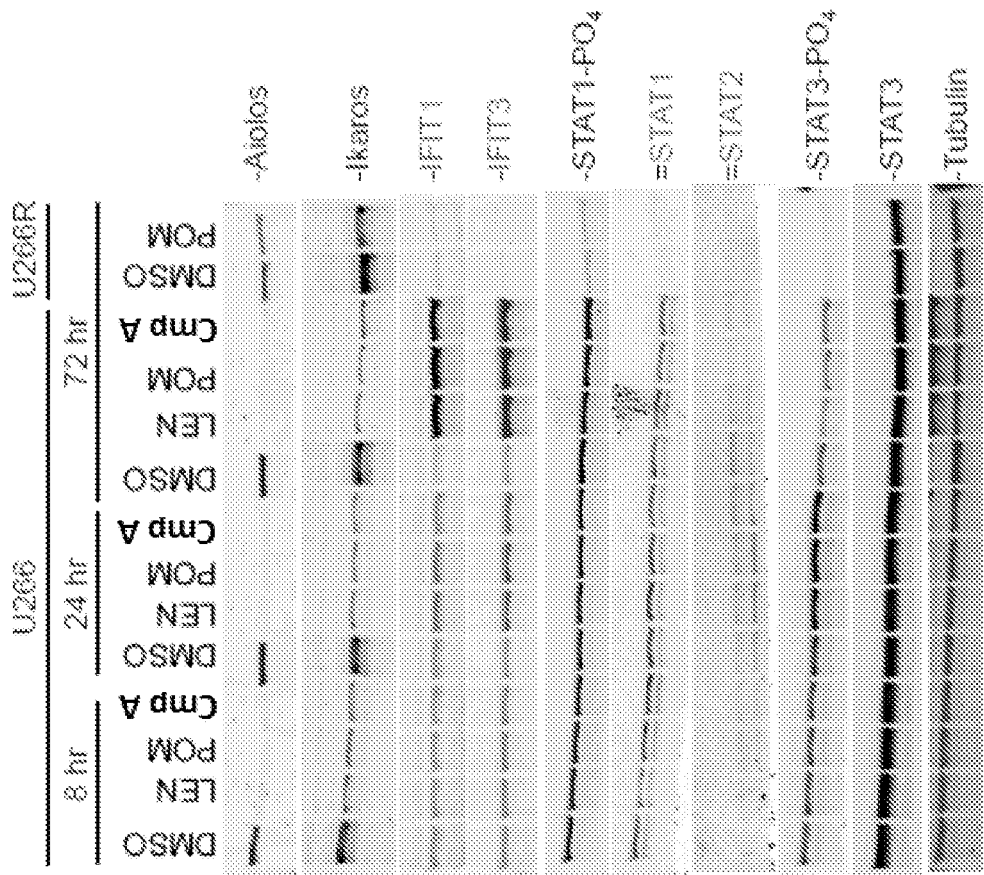


Figure 13G

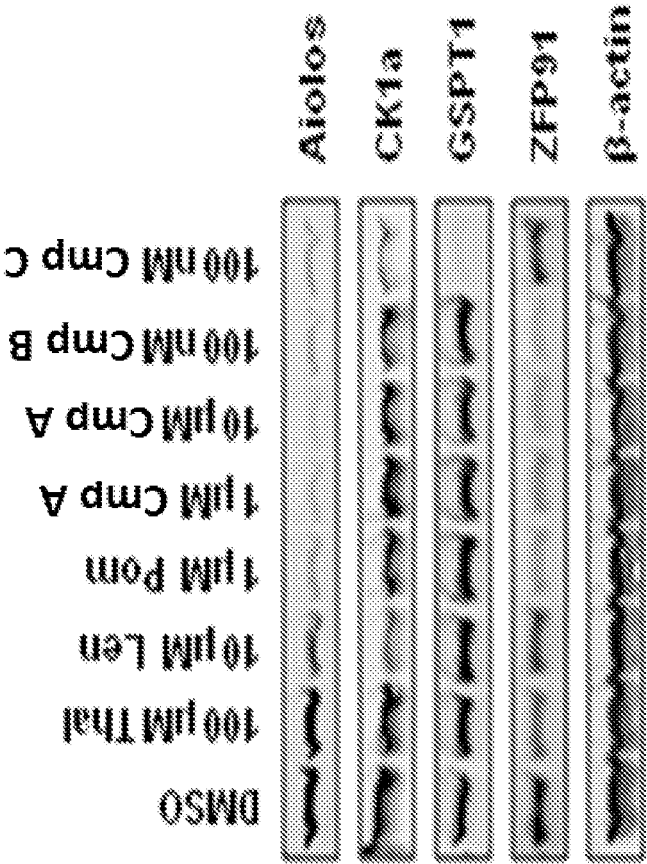


Figure 14A

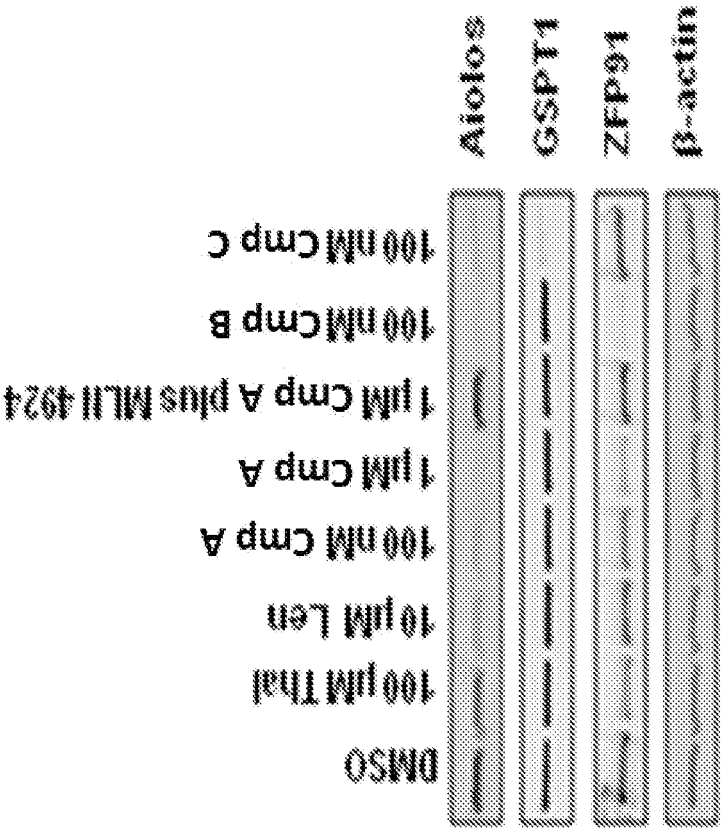


Figure 14B

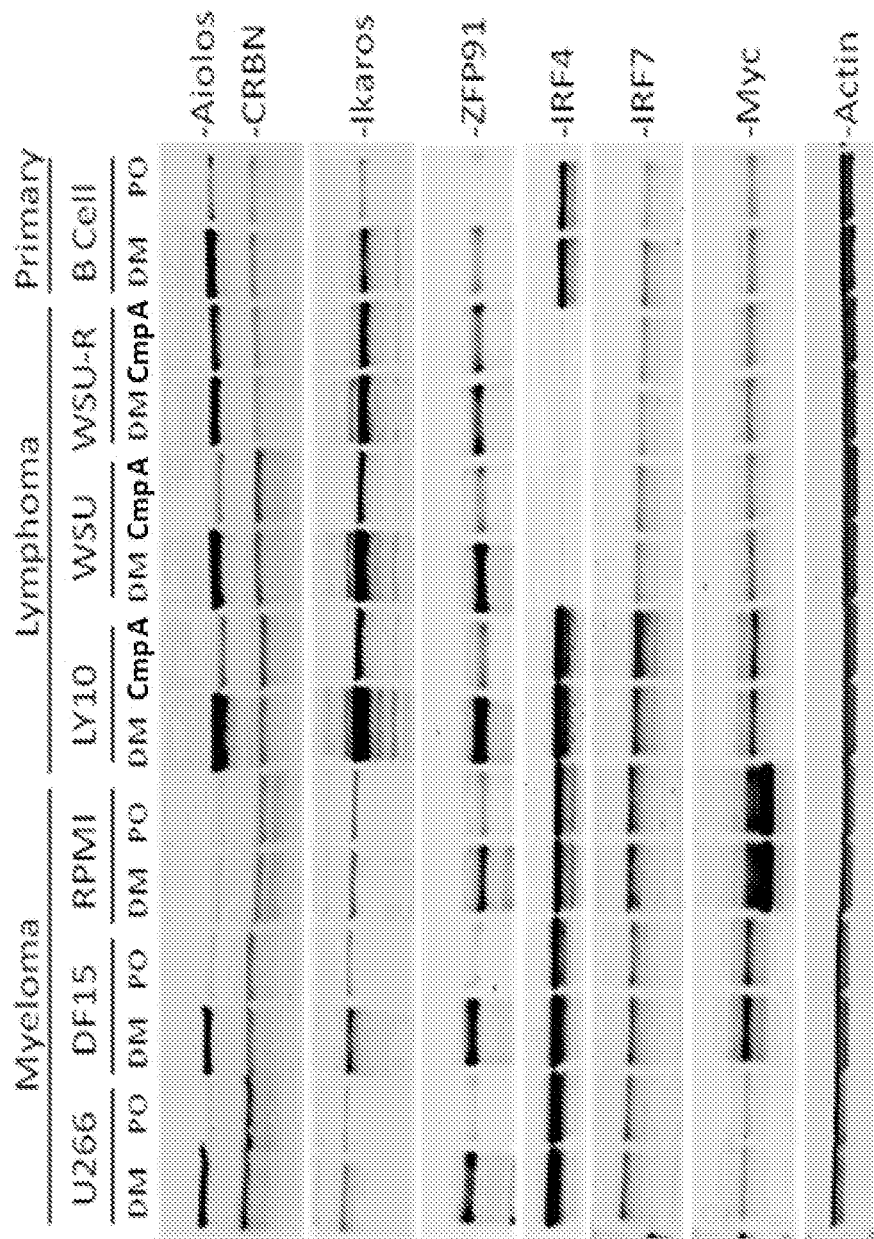


Figure 15

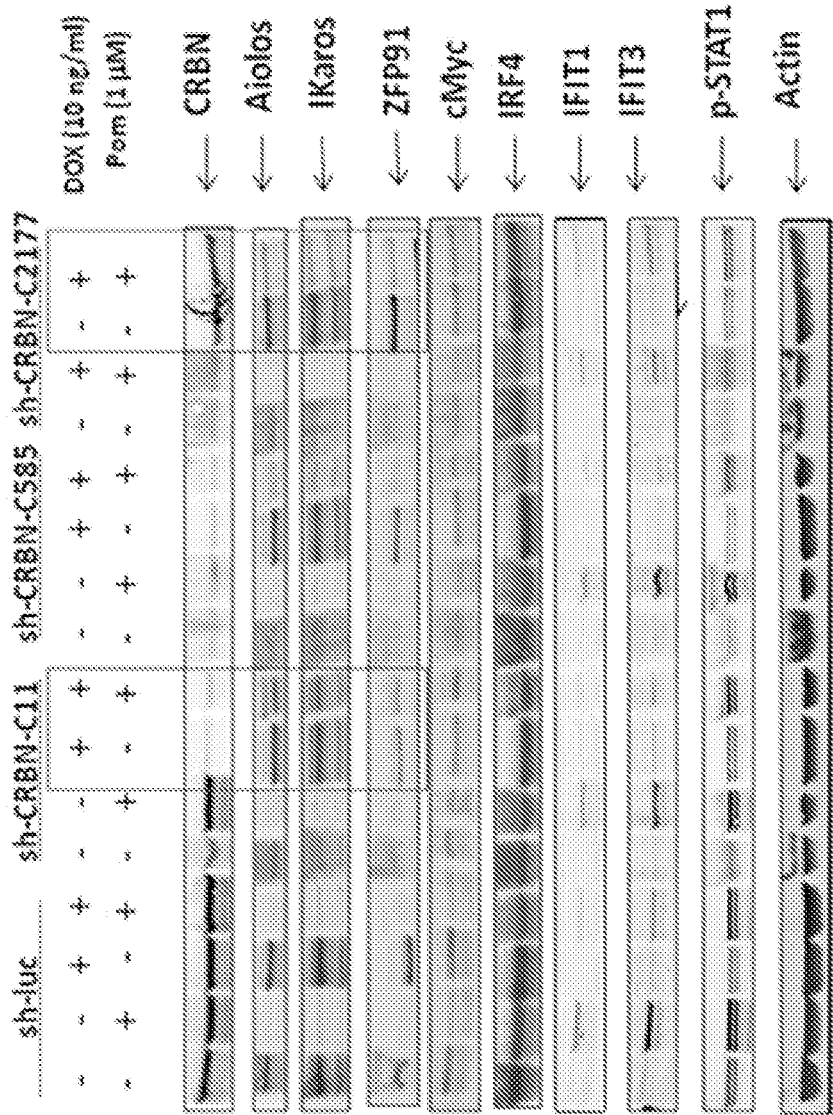


Figure 16A

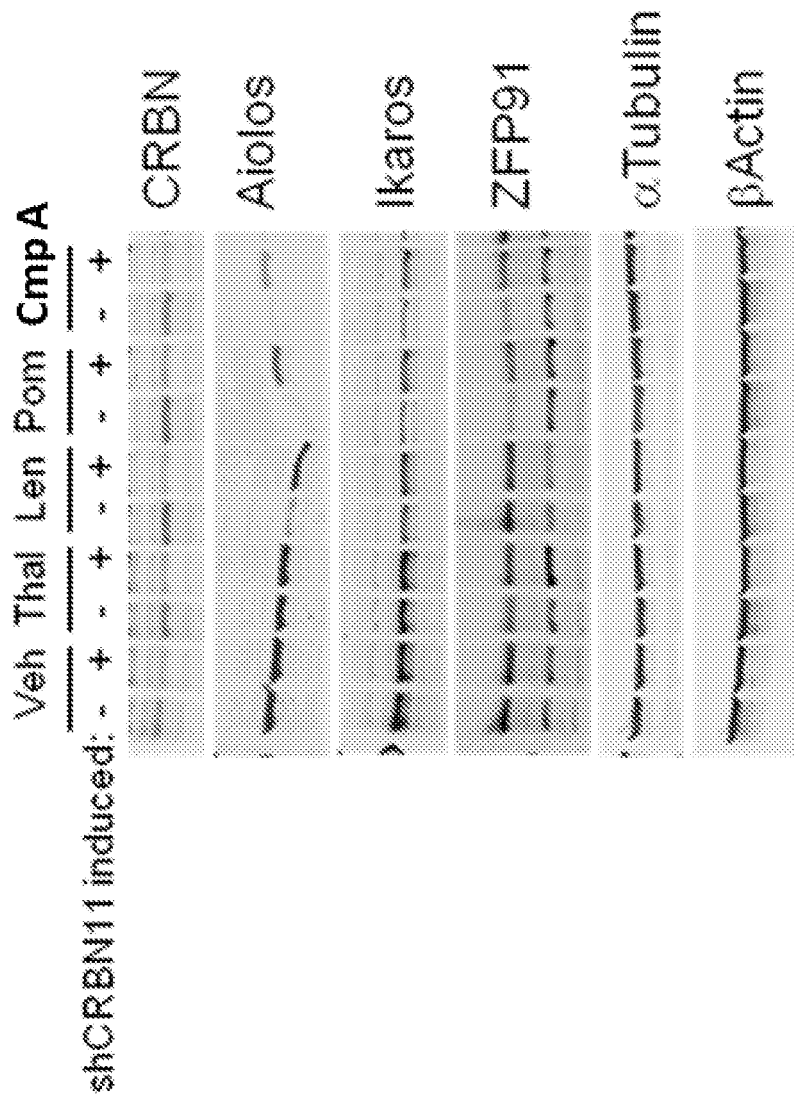


Figure 16B

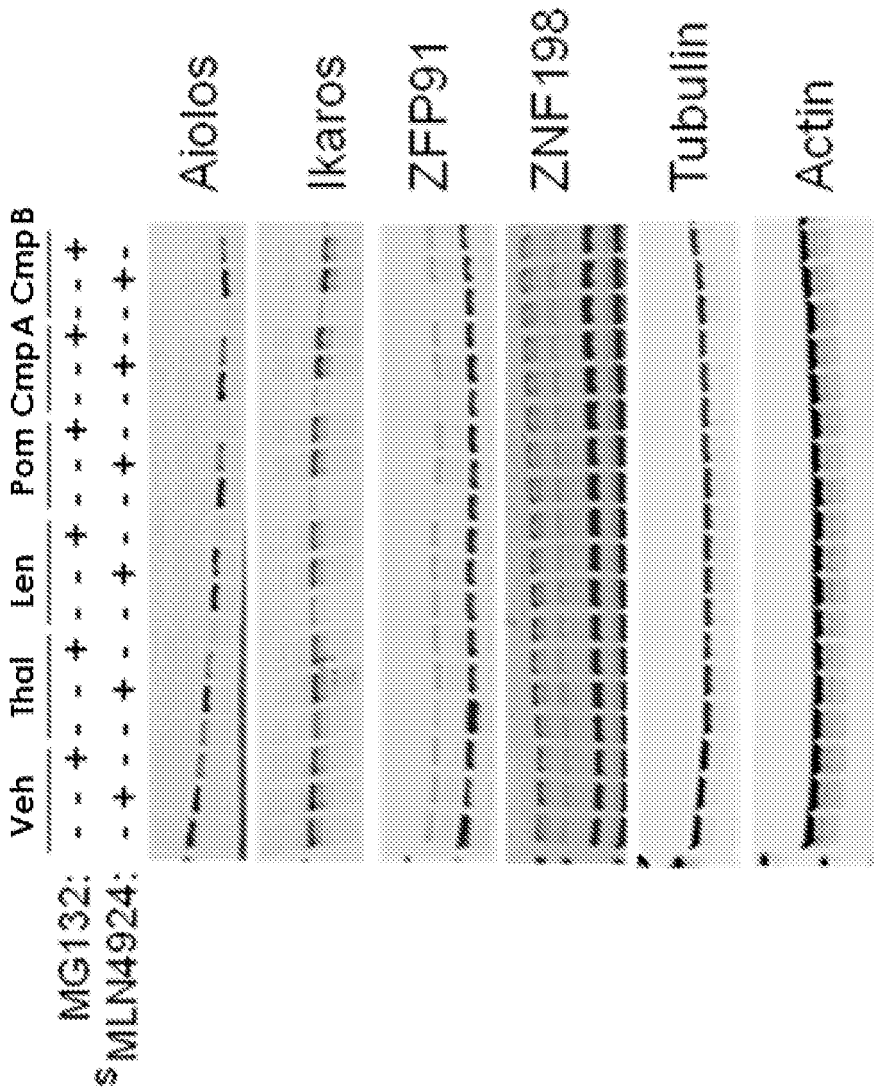


Figure 16C

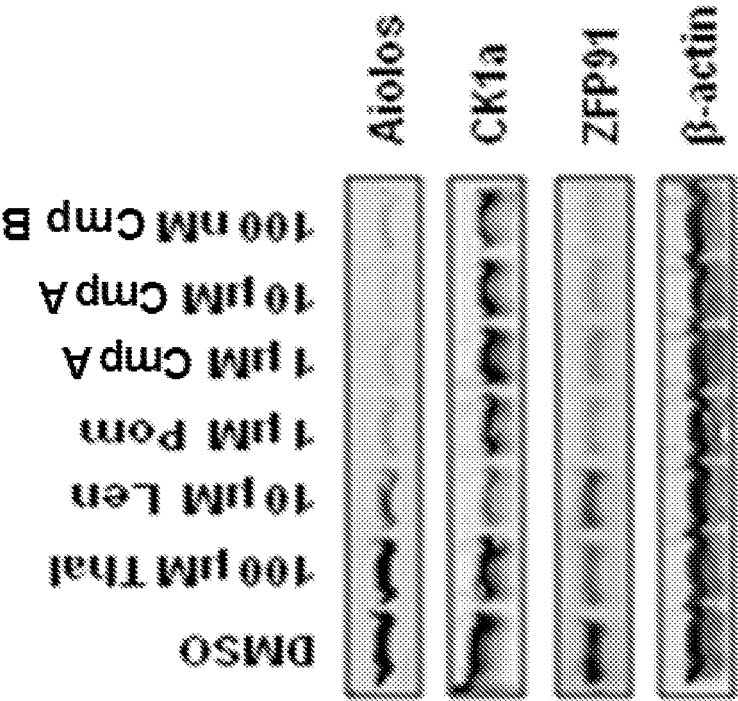


Figure 17A

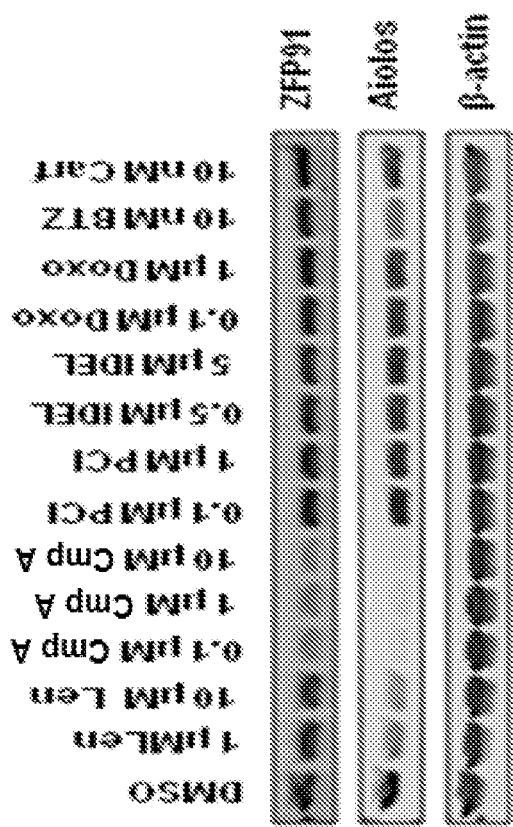


Figure 17B

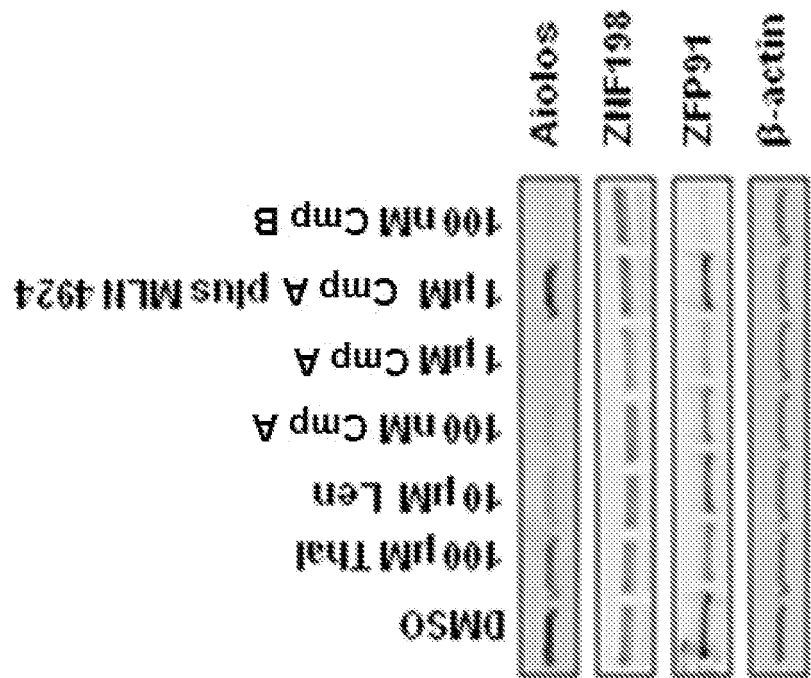


Figure 17C

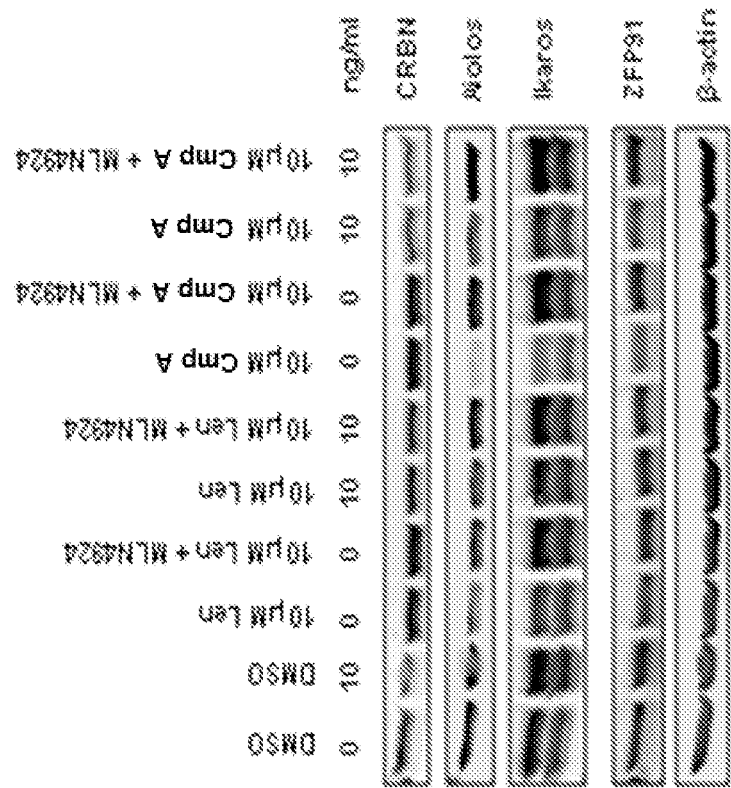


Figure 17D

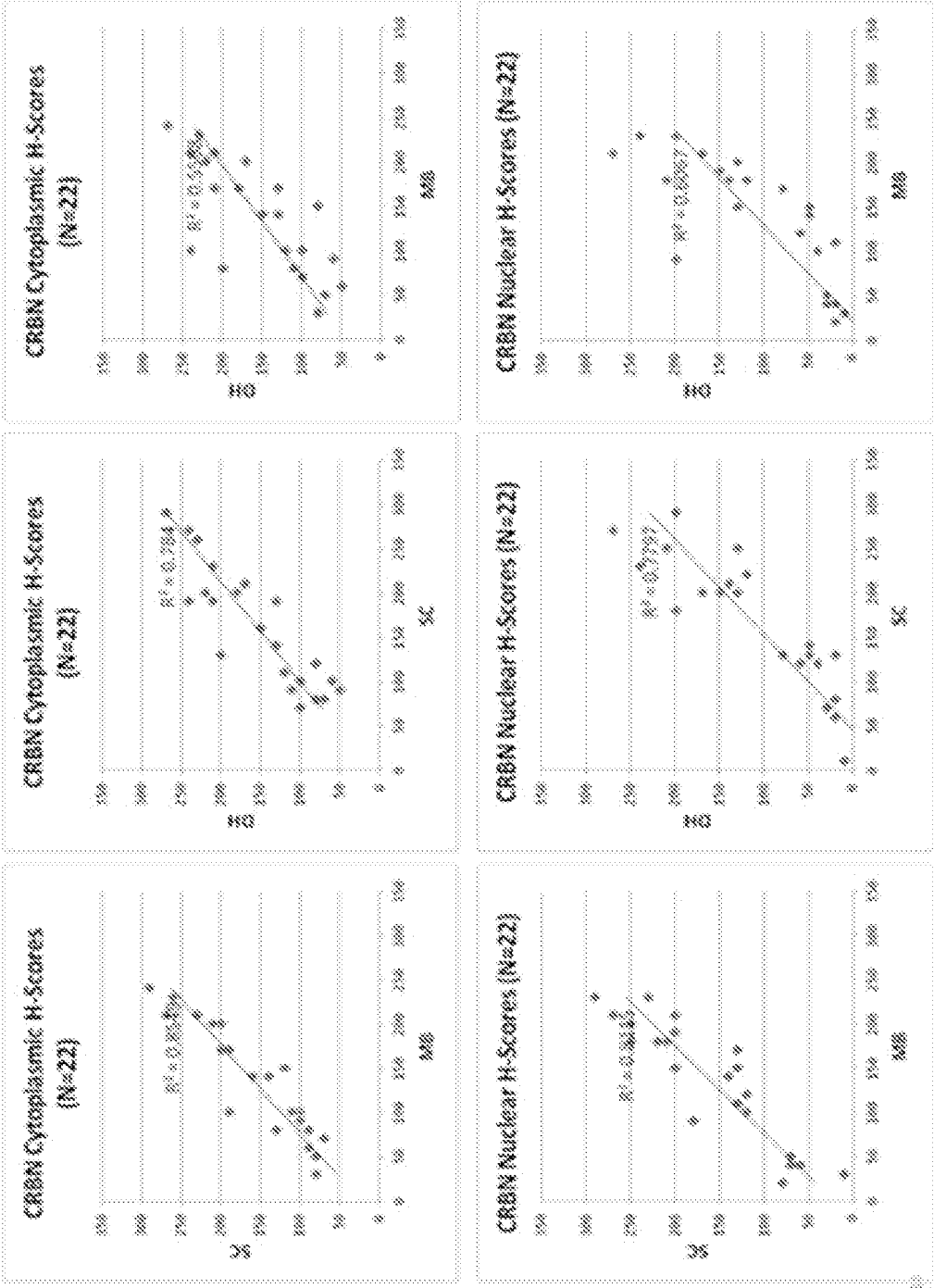
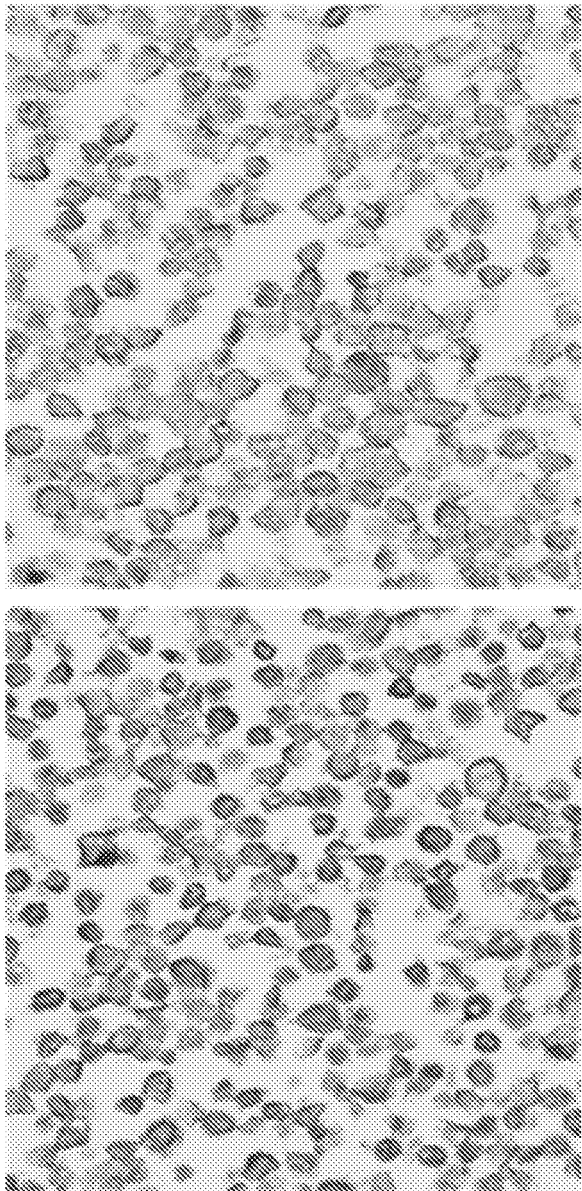


Figure 18



CD138 1/1200; CR8N 1/2000

40X

Figure 19A

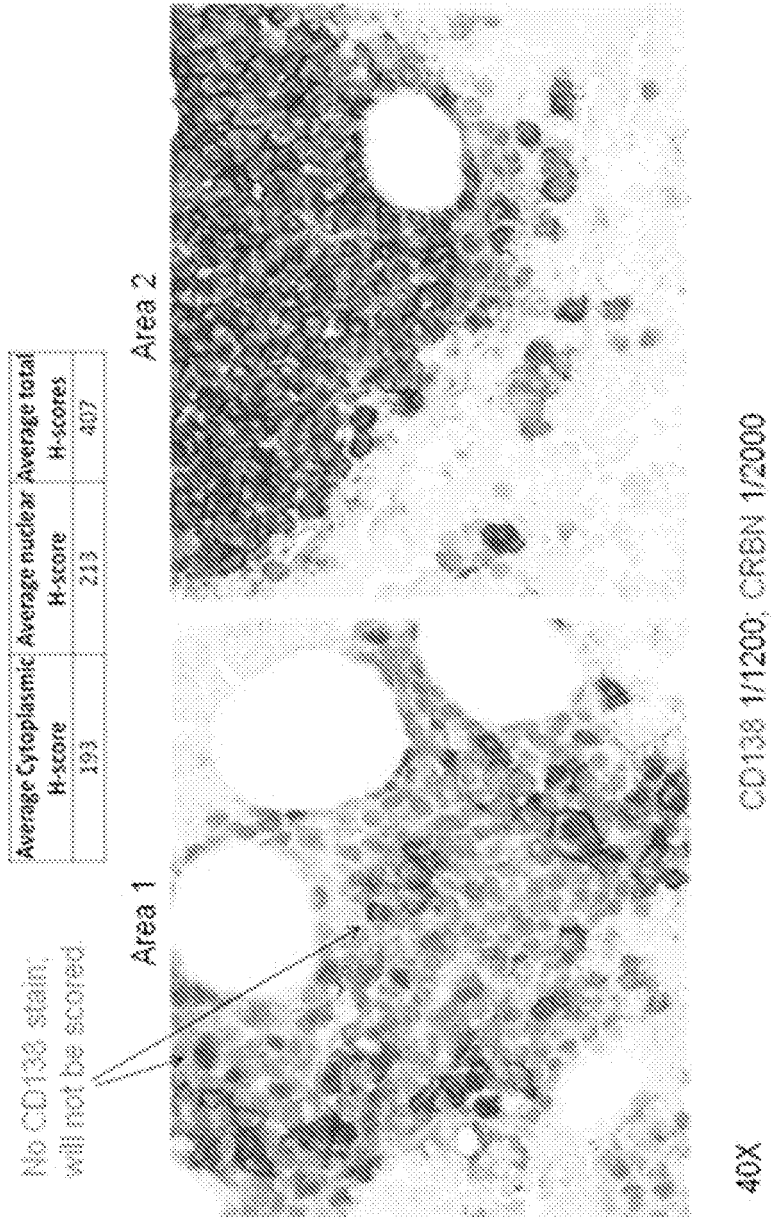


Figure 19B

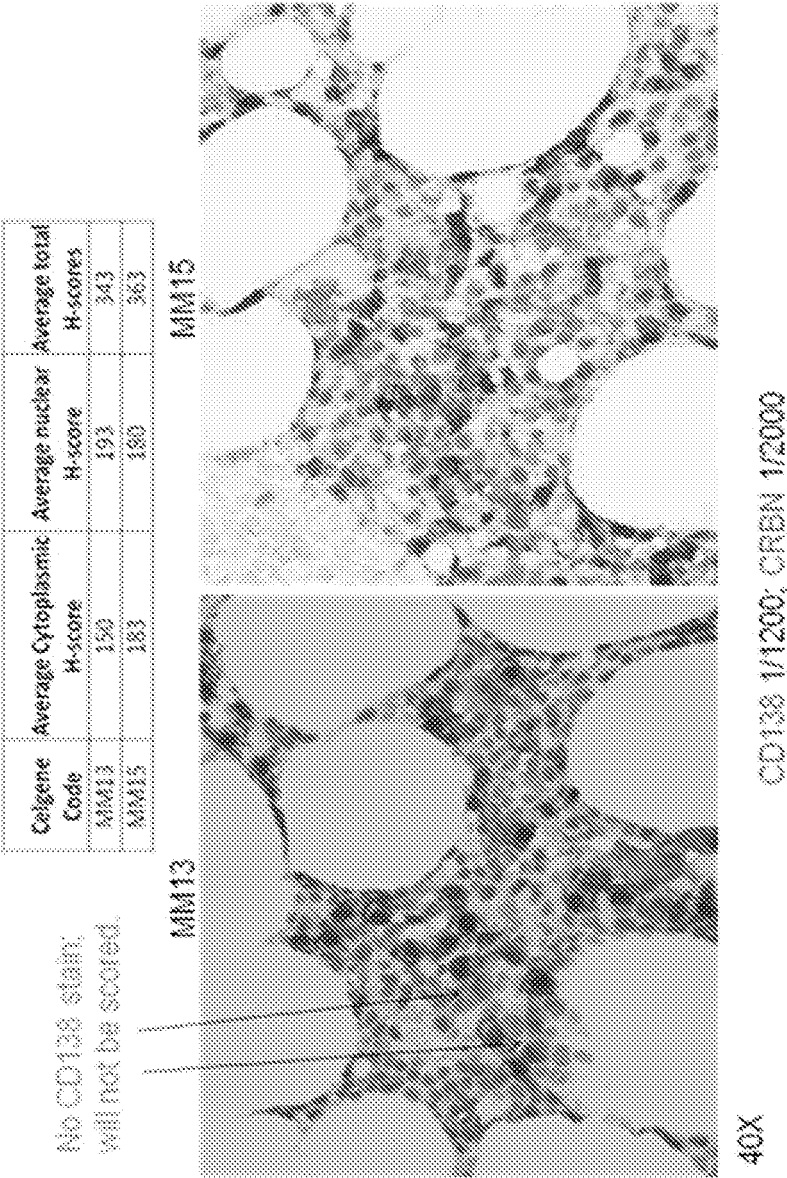


Figure 19C

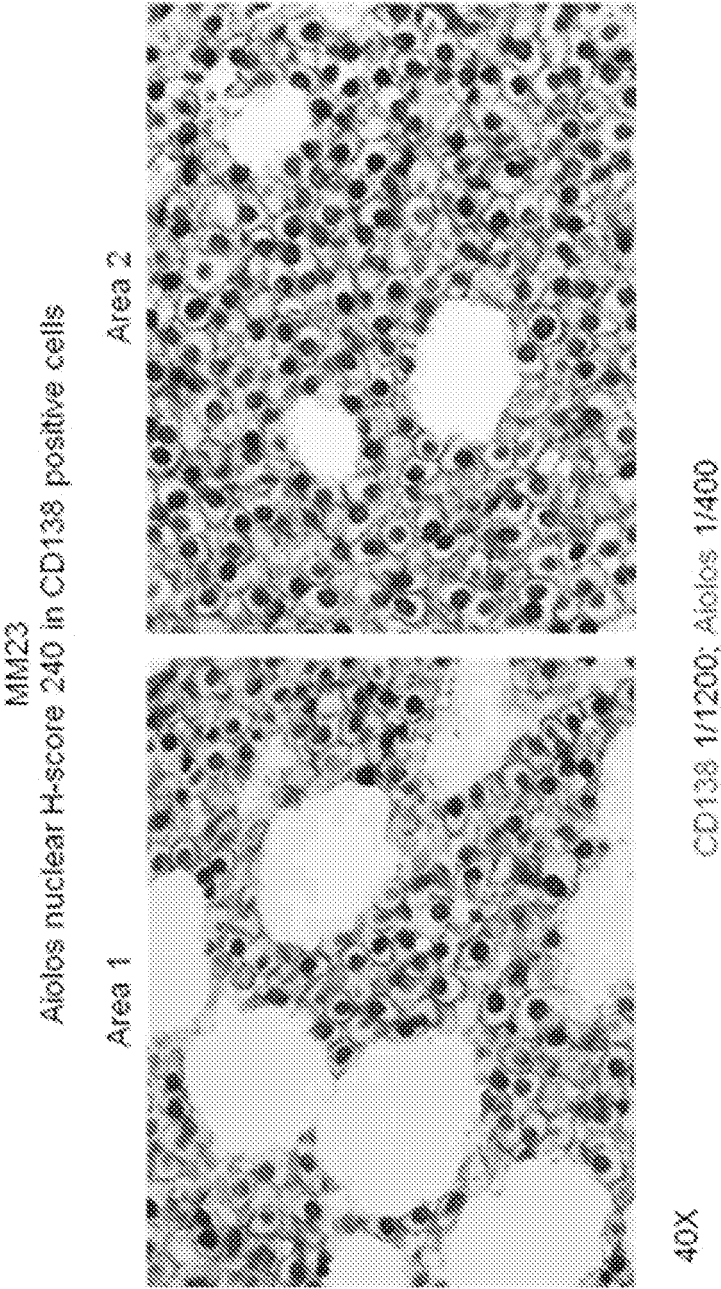


Figure 20

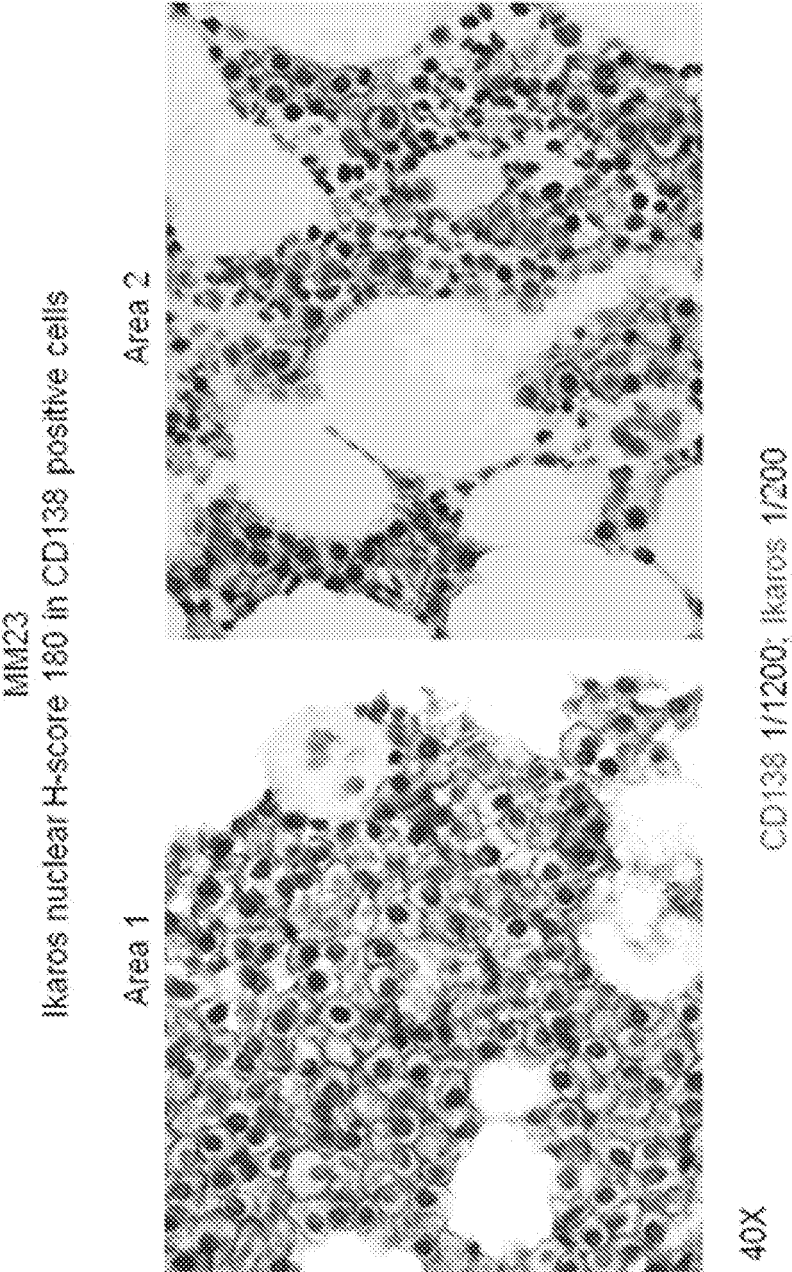


Figure 21

Cell proliferation after 4d treatment (% control)	
	10µM CC-5013
AML-193	102.13 +/- 12.18
F-36P	55.13 +/- 26.95
HL-60	91.97 +/- 8.2
HNT-34	15.06 +/- 1.08
K-562	101.65 +/- 6.8
KASUMI-1	67.95 +/- 5.3
KASUMI-3	65.05 +/- 2.21
KG-1	73.78 +/- 8.63
KG-1a	91.53 +/- 2.76
MOLM-13	107.23 +/- 9.01
OCI-AML3	77.28 +/- 11.8
THP-1	114.85 +/- 5.56
MDS-L	25.15 +/- 5.75
U266	21.28 +/- 3.76

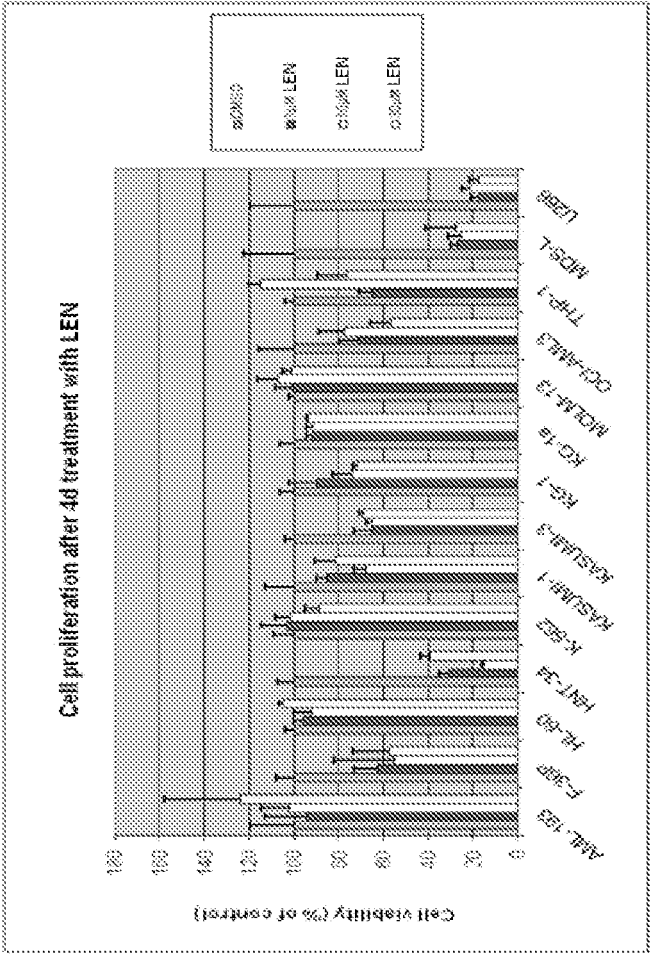


Figure 22A

Cell line	BrdU assay,		3H-thymidine assay	
	% viable +/- range		EC ₅₀ , μM	
	LEN (10 μM)	LEN	Compound A	
HNT-34	15.06 +/- 1.08	0.64	>10	
MDS-L	25.15 +/- 5.75	1.50	0.66	
KG-1	73.78 +/- 8.63	>10	>10	
HL-60	91.97 +/- 8.2	>10	>10	
THP-1	114.85 +/- 5.56	>10	>10	
MOLM-13	107.23 +/- 9.01	>10	>10	

AML, acute myeloid leukemia; APL, acute promyelocytic leukemia; BrdU, bromodeoxyuridine; Compound A, cerebion-binding analog; CML, chronic myeloid leukemia; del, deletion; EC₅₀, half maximal effective concentration; LEN, lenalidomide; MDS, myelodysplastic syndromes.

Figure 22C

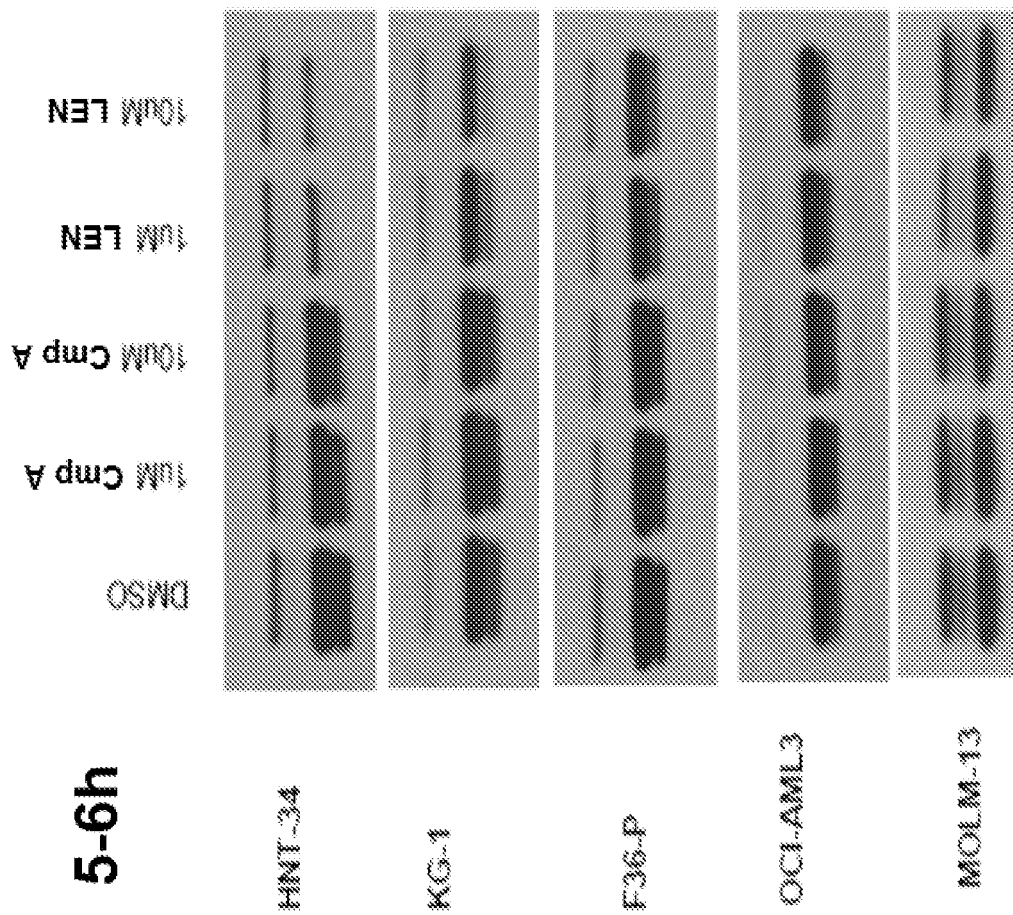
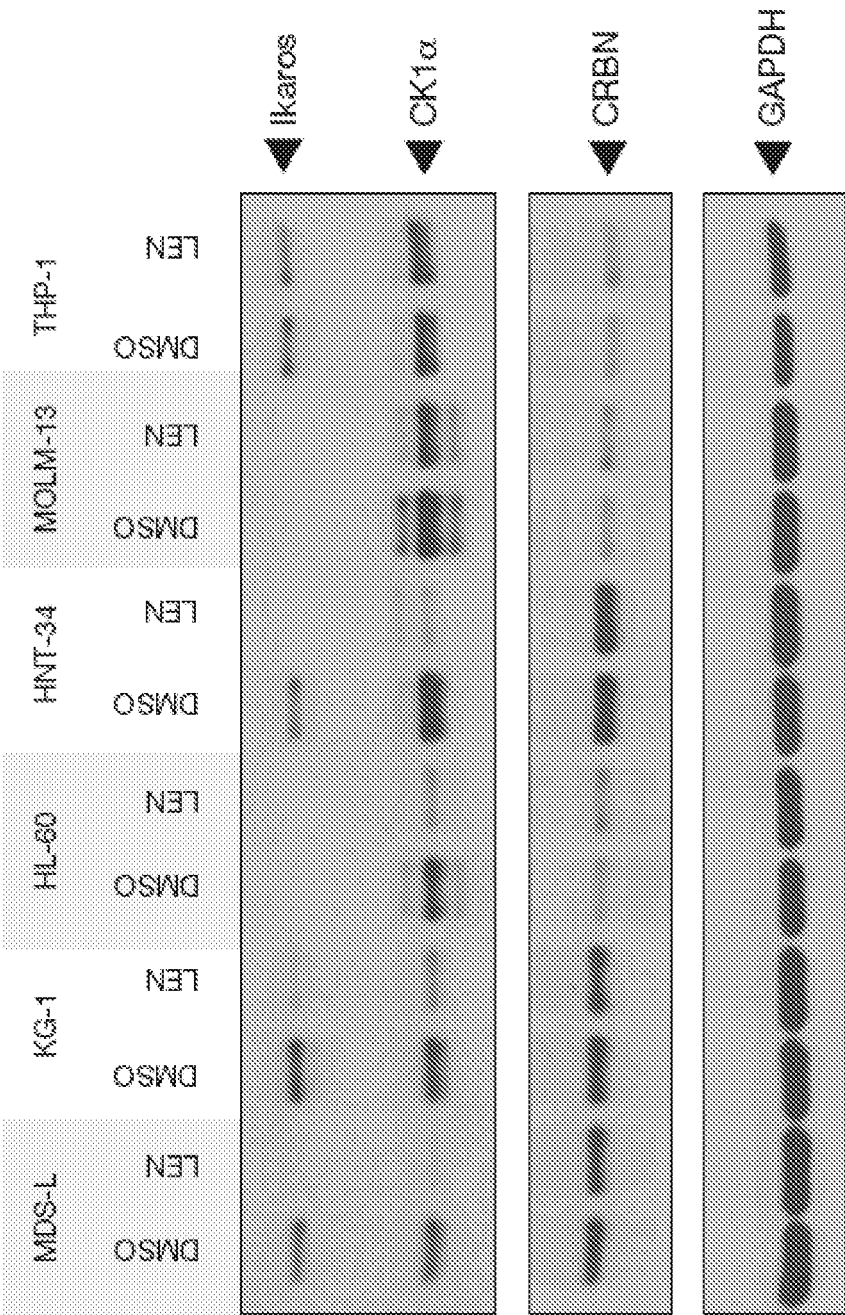


Figure 22D



CK1α, casein kinase 1α; CRBN, cereblon; DMSO, dimethyl sulfoxide; GAPDH, glyceraldehyde 3-phosphate dehydrogenase; LEN, lenalidomide.

Figure 22E

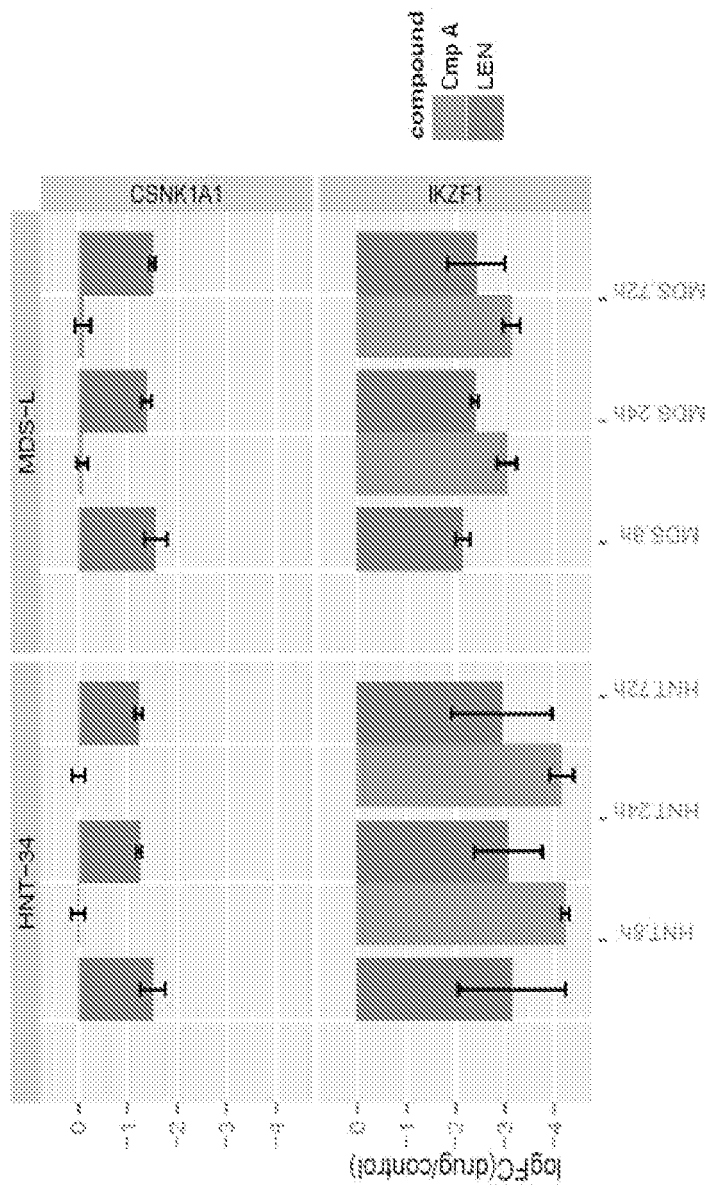


Figure 23A

Protein Id		Gene symbol	Protein description	# of quantified peptides	BH adjusted p value	Len/DMSO	CC122/DMSO	Log2(Ratio)
sp Q13422 IKZF1_HUMAN	IKZF1	IKZF1	HUMAN DNA-binding protein Itkaros	10	8.09E-08	-2.4063	-3.1211	
sp P48729-2 KC1A_HUMAN	CSNK1A1	KC1A	HUMAN Isoform 2 of Casein kinase1 isoform alpha	11	2.48E-06	-1.4921	-0.0826	

Figure 23B

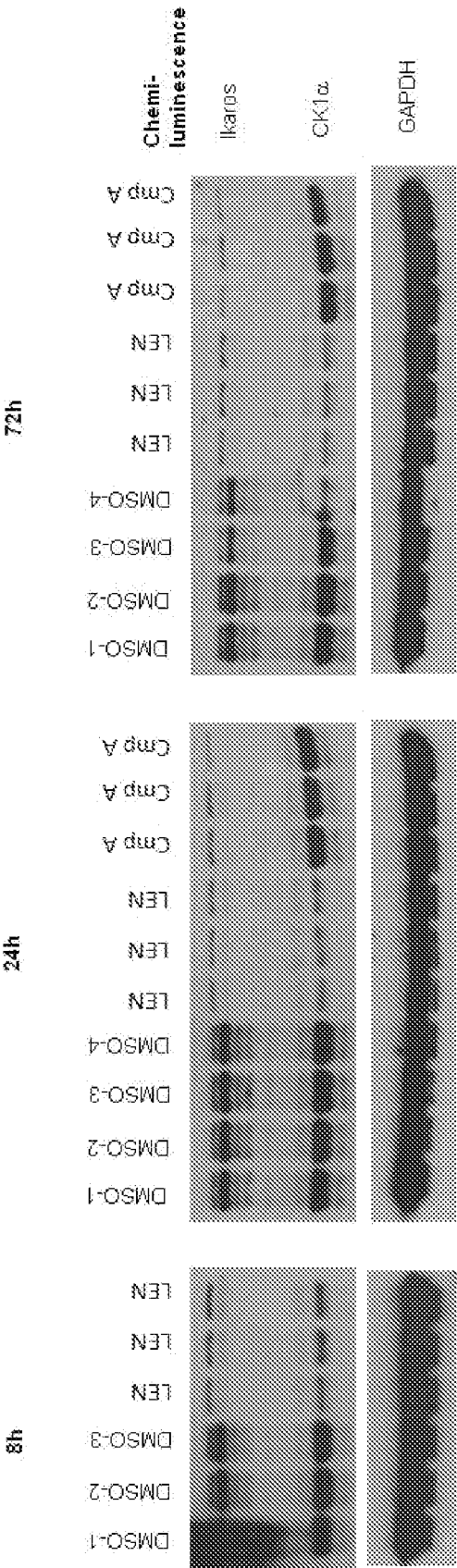


Figure 23C

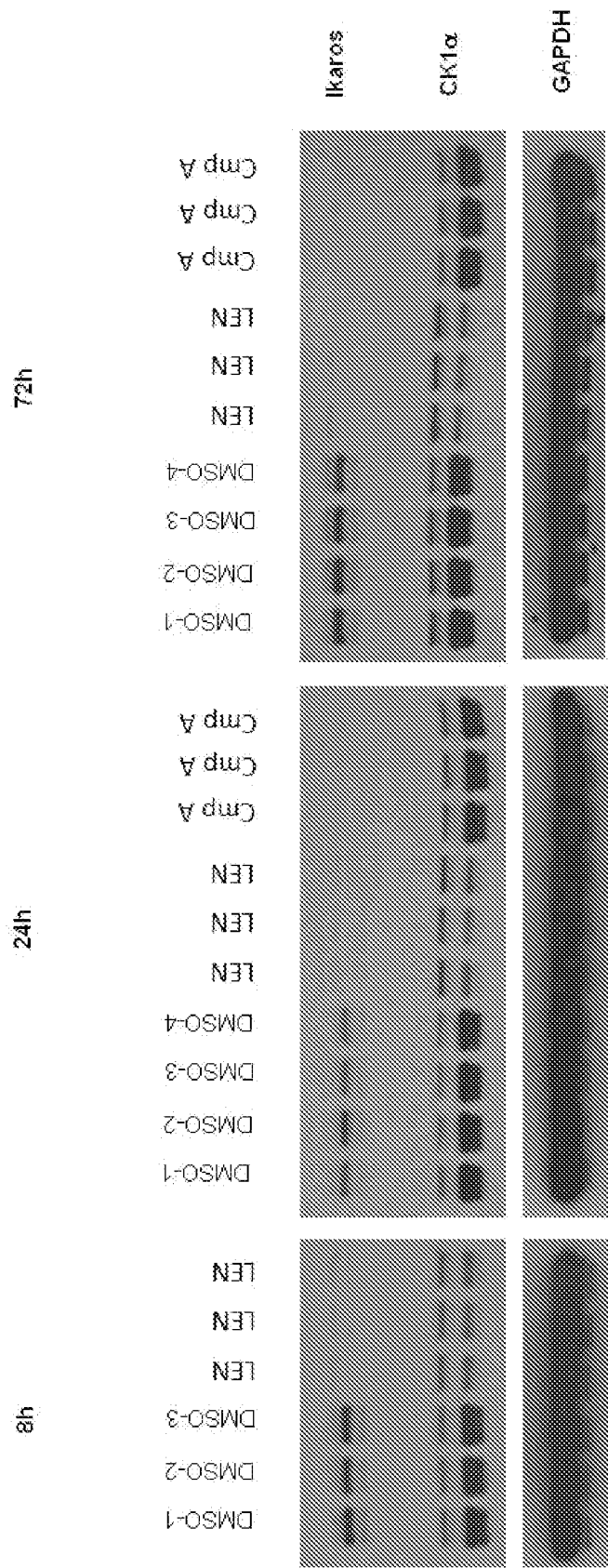


Figure 23D

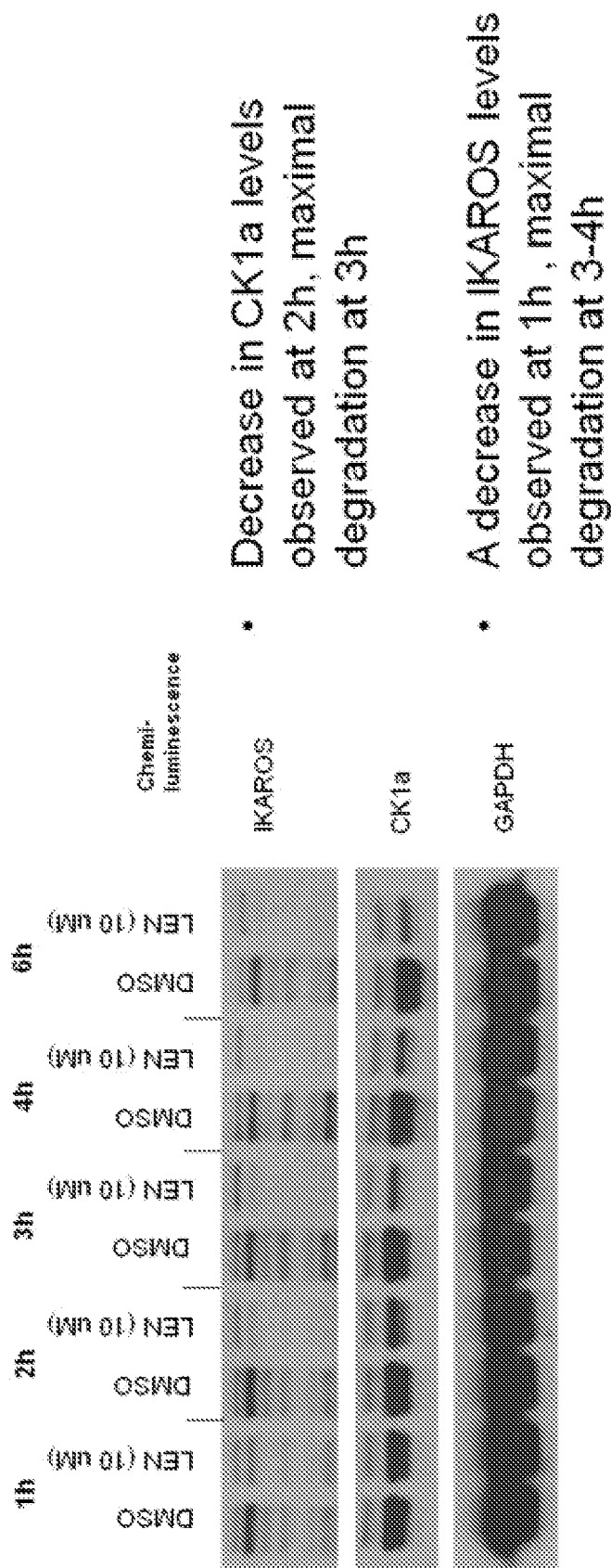


Figure 24A

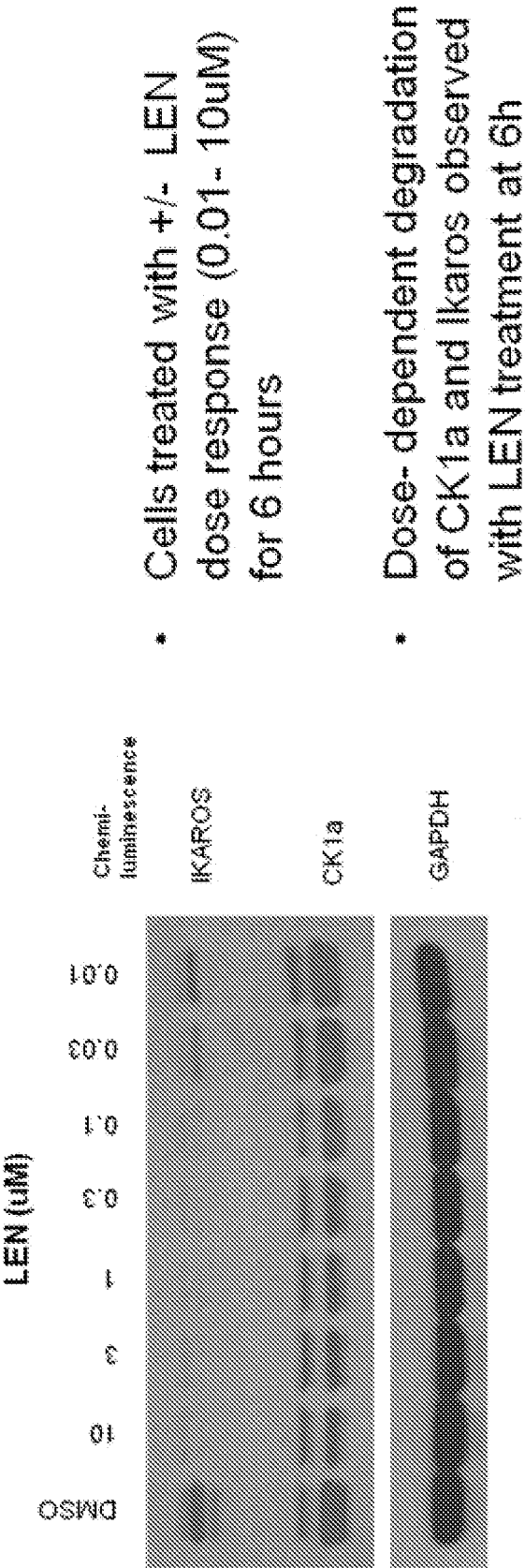


Figure 24B

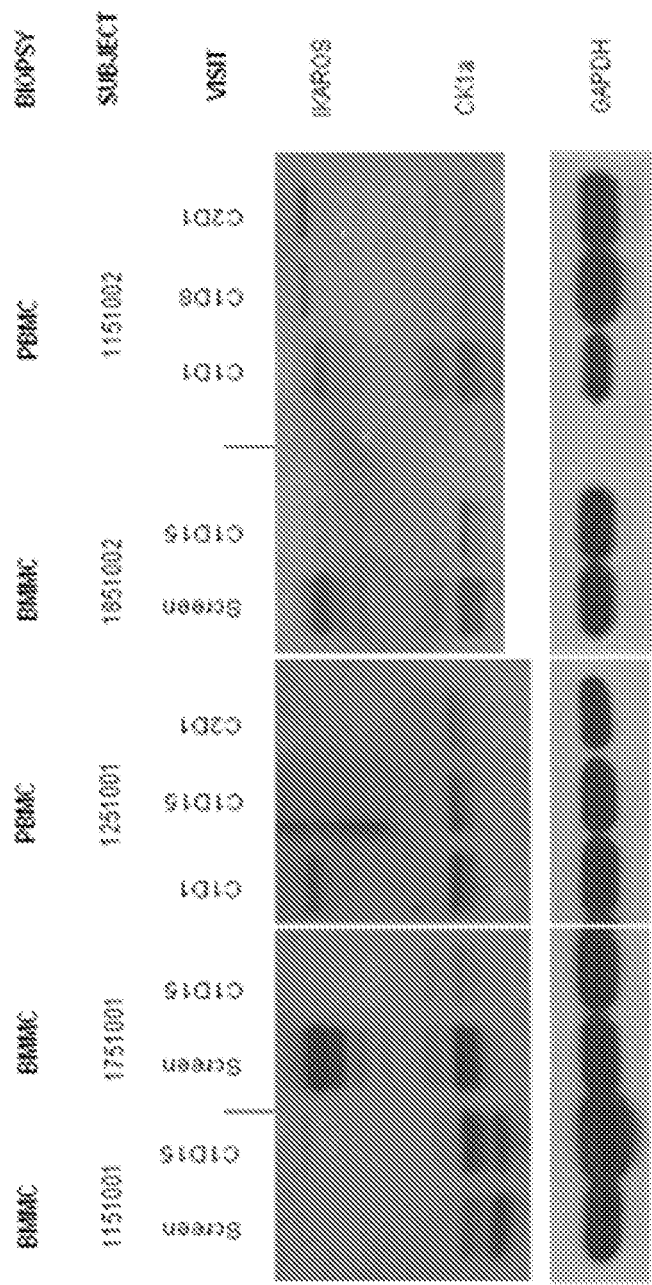


Figure 25A

	HNT-34	MDS-L	KG-1	HL-60	MOLM-13	THP-1
Sensitivity to LEN	Yes	Yes	No	No	No	No
del(5q)	No	Yes	Yes	Yes	No	No
CRBN expression	Yes	Yes	Yes	Low	Low	Low
CK1 α expression	Yes	Yes	Yes	Yes	Yes	Yes
CK1 α regulation by LEN	Yes	Yes	Yes	Yes	No	No
Ikaros expression	Yes	Yes	Yes	No	No	Yes
Ikaros regulation by LEN	Yes	Yes	Yes	NA	NA	No

CK1 α , casein kinase 1 α ; CRBN, cereblon; del(5q), deletion 5q; LEN, lenalidomide; NA, not applicable.

Figure 25B

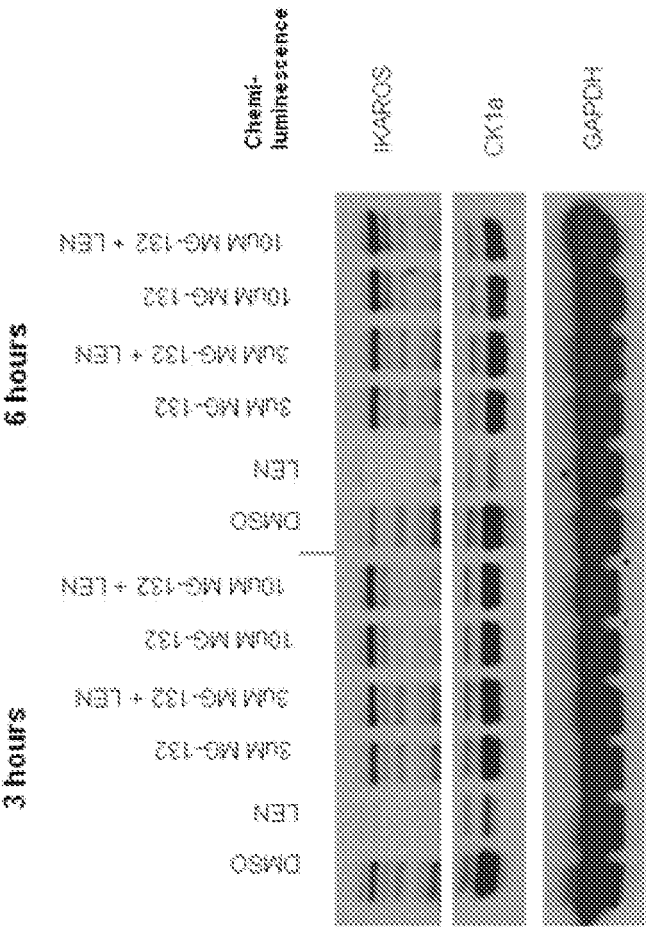


Figure 26

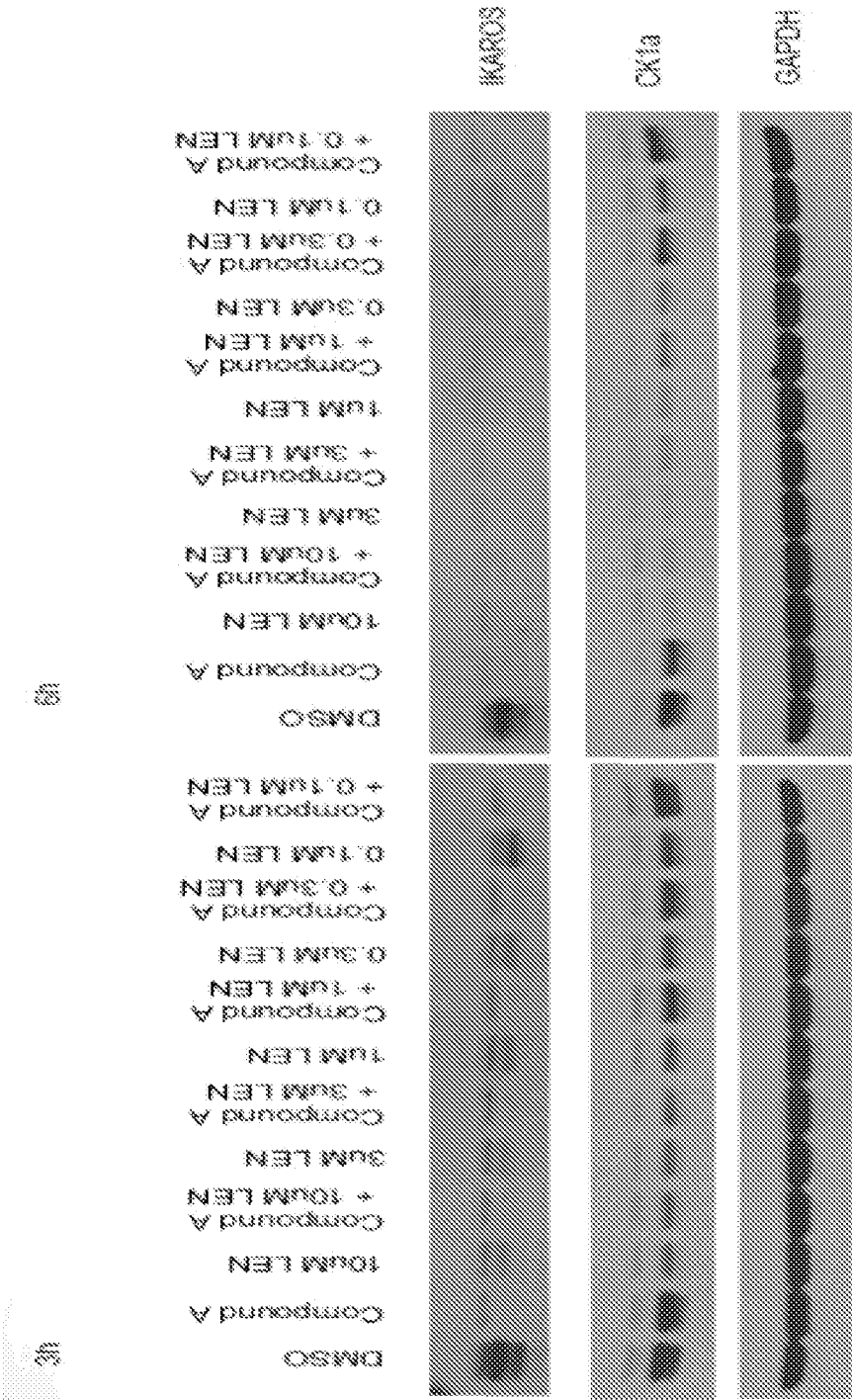


Figure 27A

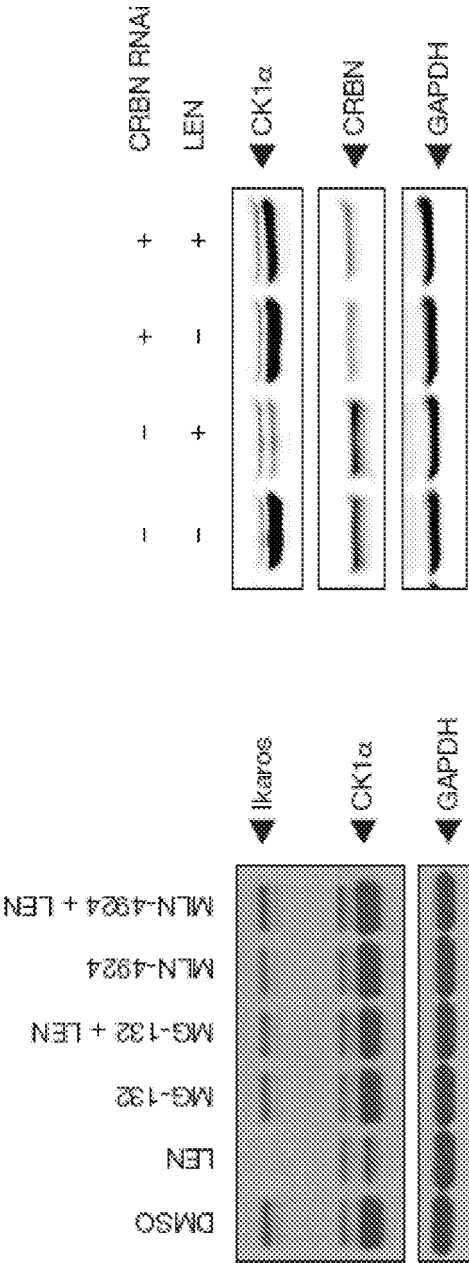


Figure 27B