

	aP2 Humano	aP2 de ratón
	KD (M)	KD (M)
CA33	2.831E-06	4.131E-06
CA13	1.37E-09	1.12E-09
CA15	2.43E-09	1.84E-09
CA23	7.48E-10	7.51E-10
H3	1.10E-09	1.78E-09

FIG. 1A

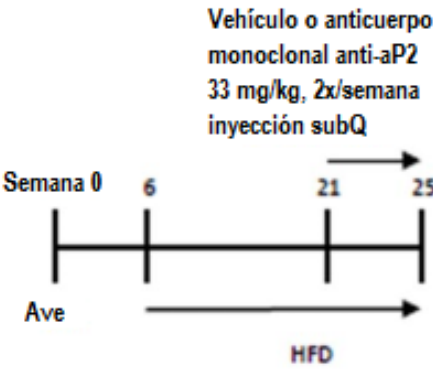


FIG. 1B

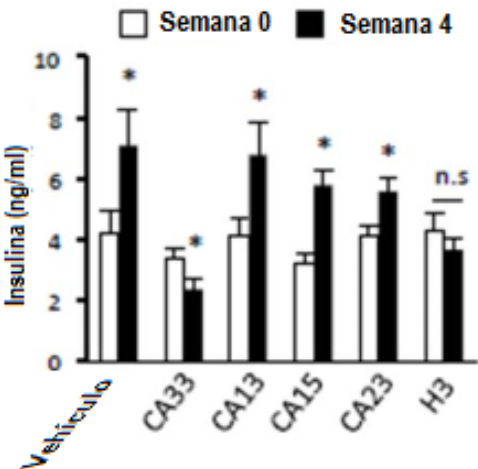


FIG. 1C

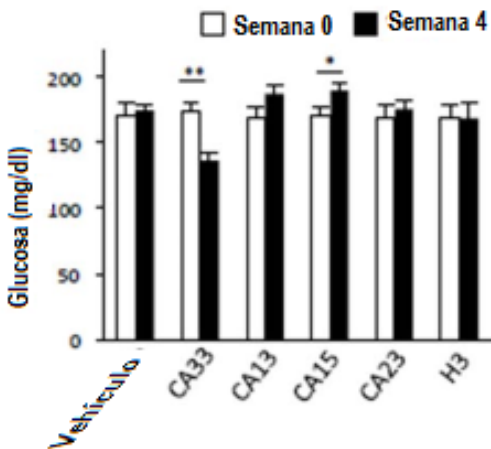


FIG. 1D

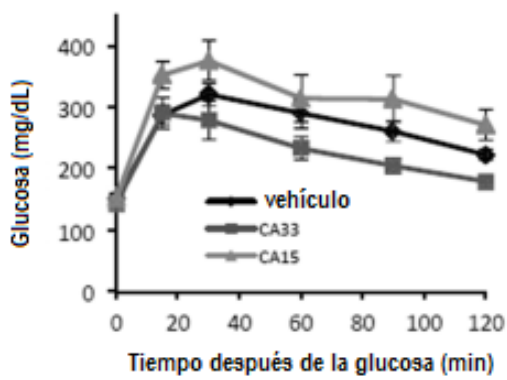


FIG. 1E

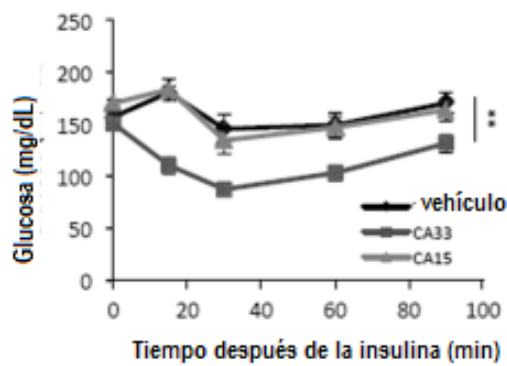


FIG. 1F

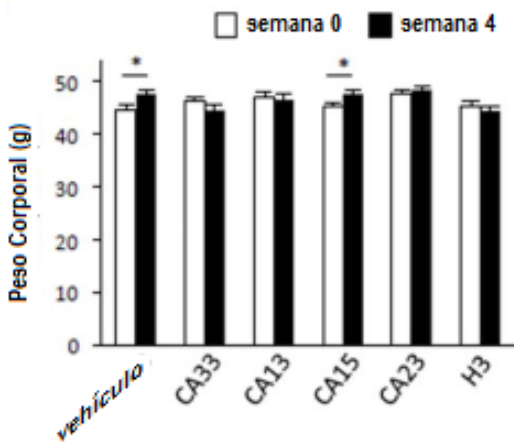


FIG. 1G

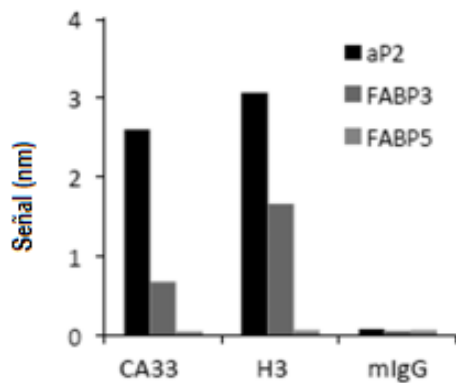


FIG. 2A

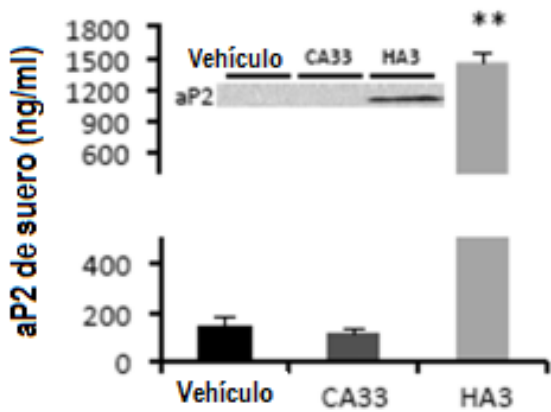


FIG. 2B

	H3
CA33	+
CA13	++
CA15	++
CA23	-

FIG. 2C

1MCDAFVGTWKLVSSENF
DDYMKEVGVGFATRKV....
118 CVMKGVTSRVERA 132

epítopo
CA33
Seq. Id. No.
2

1MCDAFVGTWKLVSSENF
DDYMKEVGVGFATRKVAG
MAKPNMIISVNG...

epítopo
H3
Seq. Id. No.
2

FIG. 2D

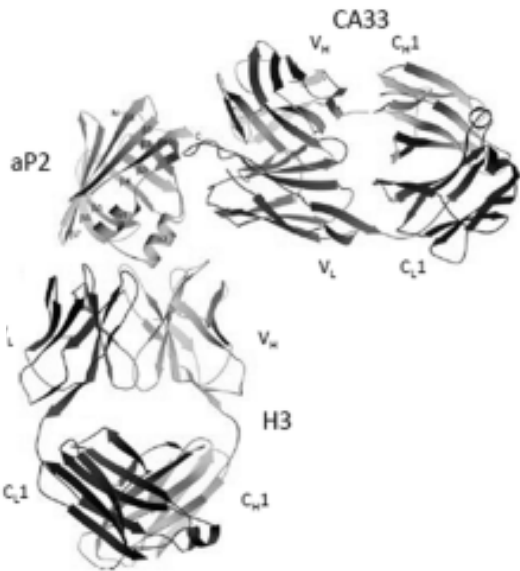


FIG. 2E

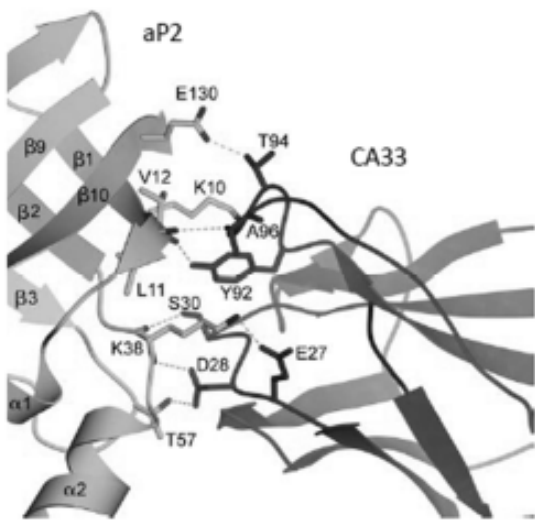


FIG. 2F

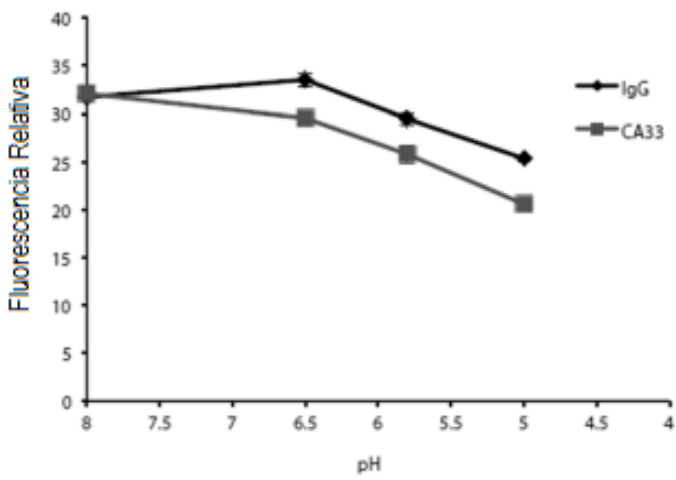


FIG. 2G

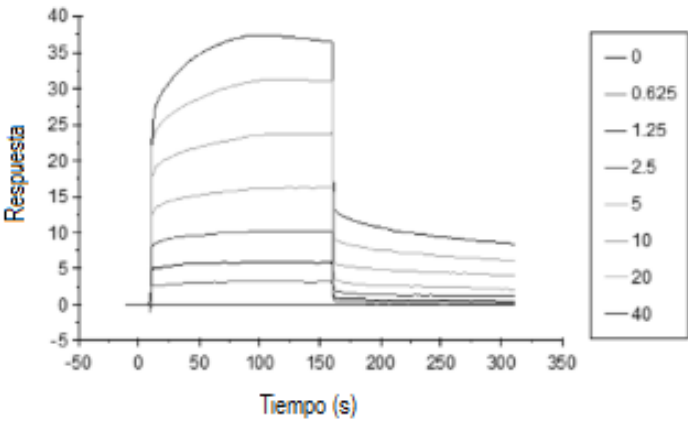


FIG. 2H

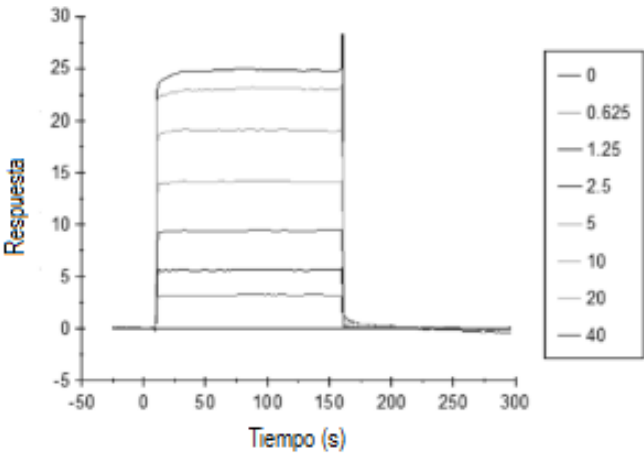


FIG. 2I

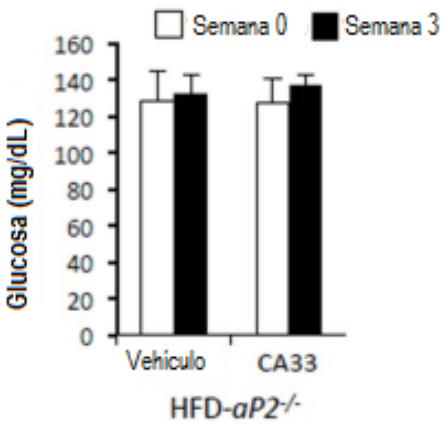


FIG. 3A

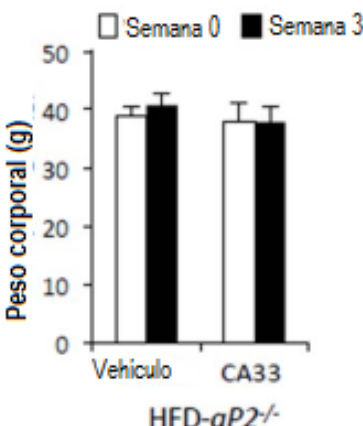


FIG. 3B

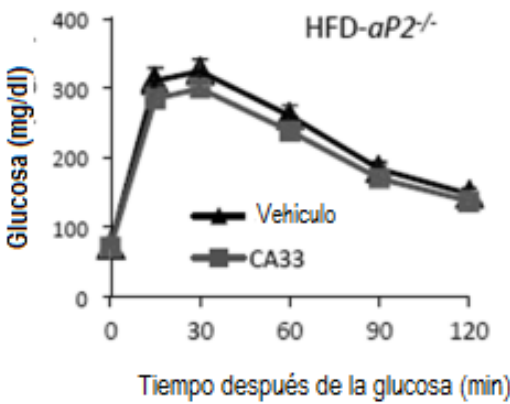


FIG. 3C

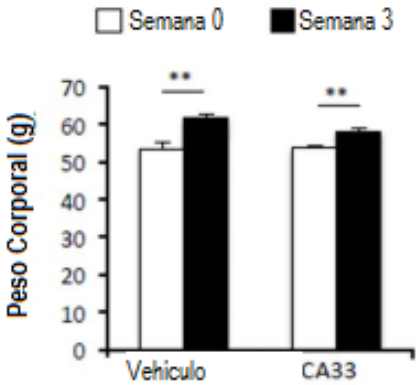


FIG. 3D

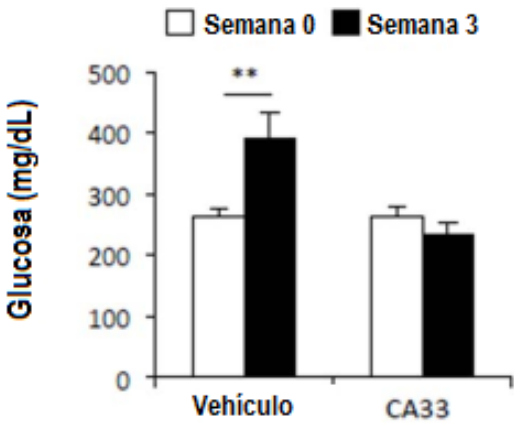


FIG. 3E

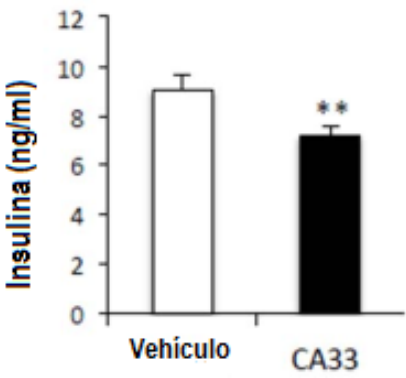


FIG. 3F

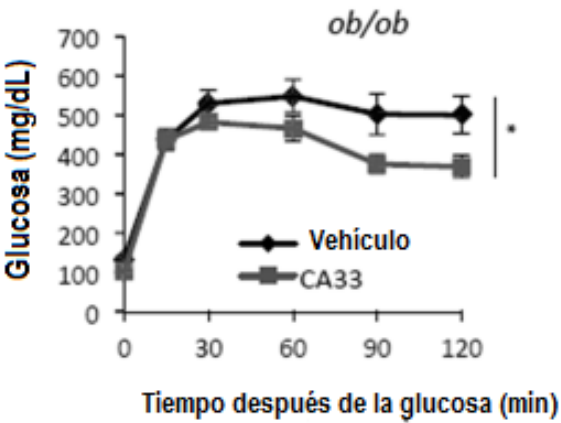


FIG. 3G

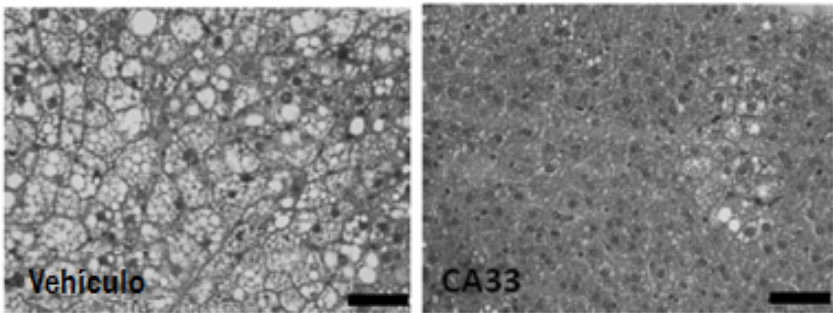


FIG. 4A

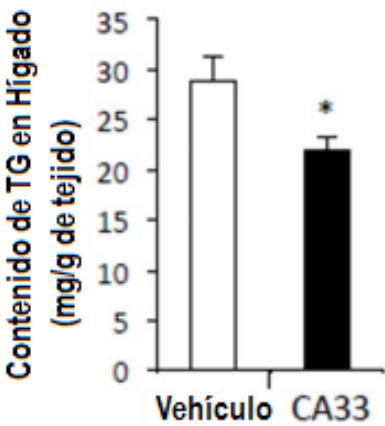


FIG. 4B

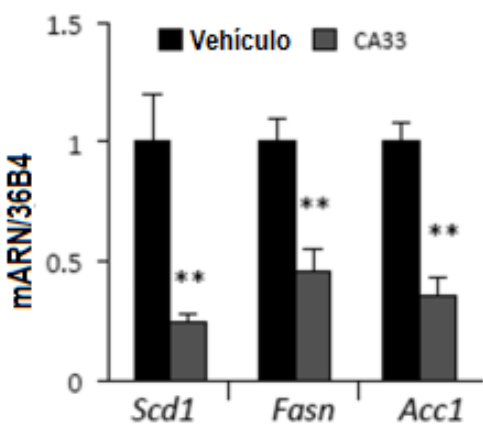


FIG. 4C

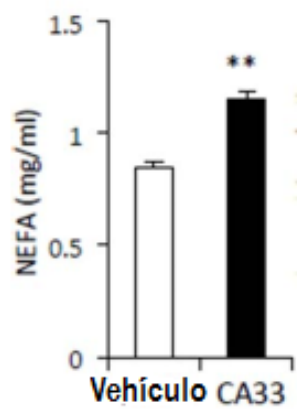


FIG. 4D

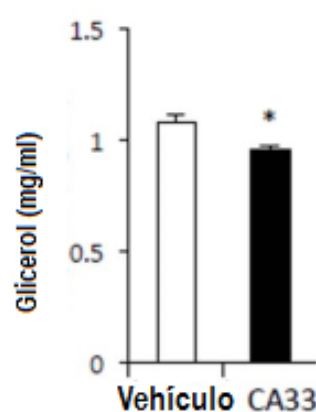


FIG. 4E

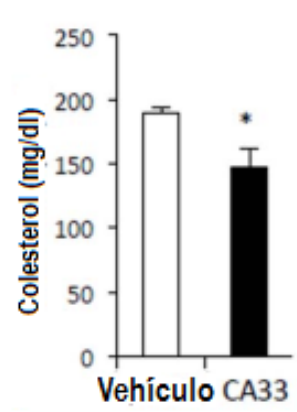


FIG. 4F

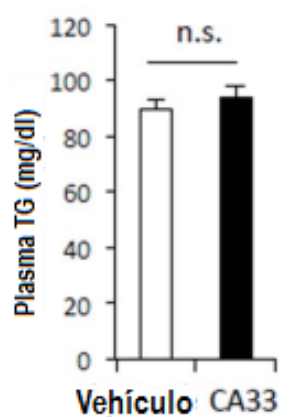


FIG. 4G

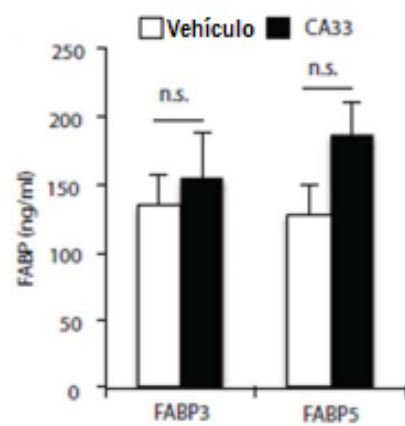


FIG. 4H

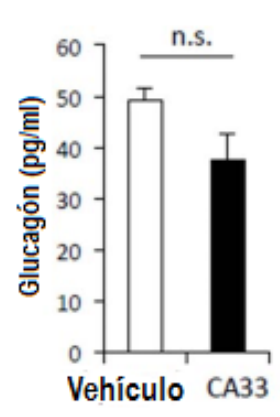


FIG. 4I

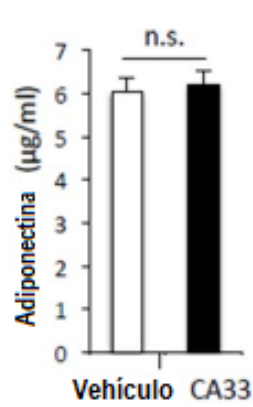


FIG. 4J

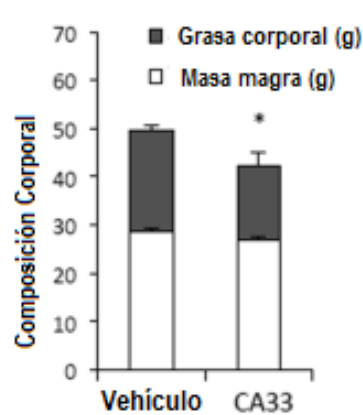


FIG. 5A

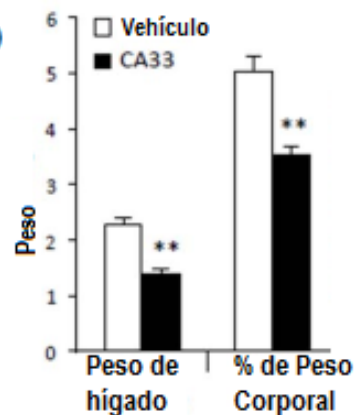


FIG. 5B

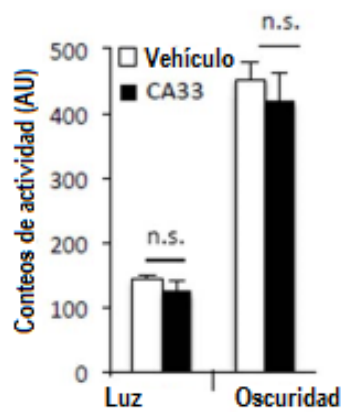


FIG. 5C

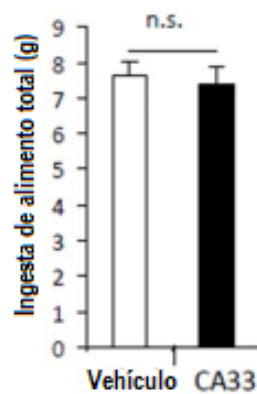


FIG. 5D

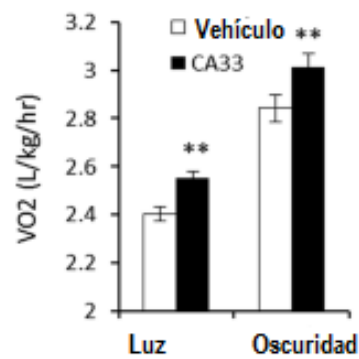


FIG. 5E

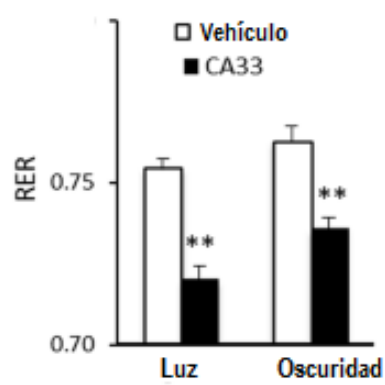


FIG. 5F

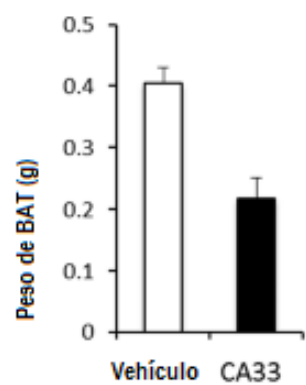


FIG. 5G

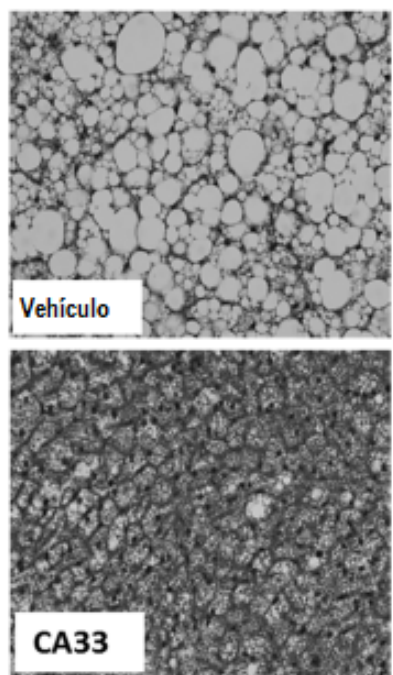


FIG. 5H

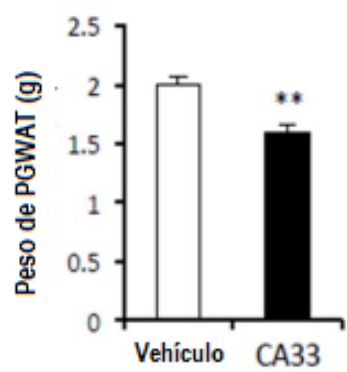


FIG. 5I

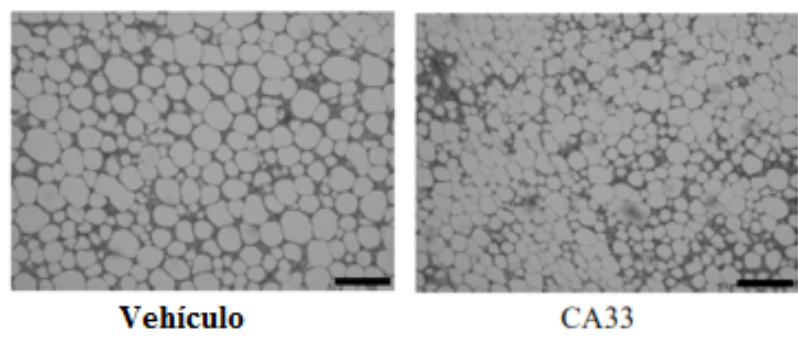


FIG. 5J

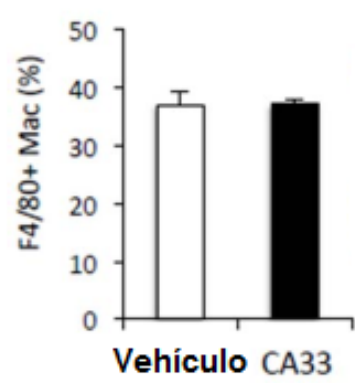


FIG. 5K

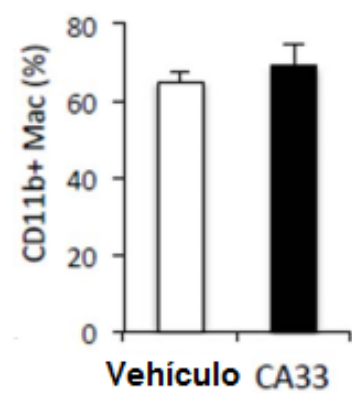


FIG. 5L

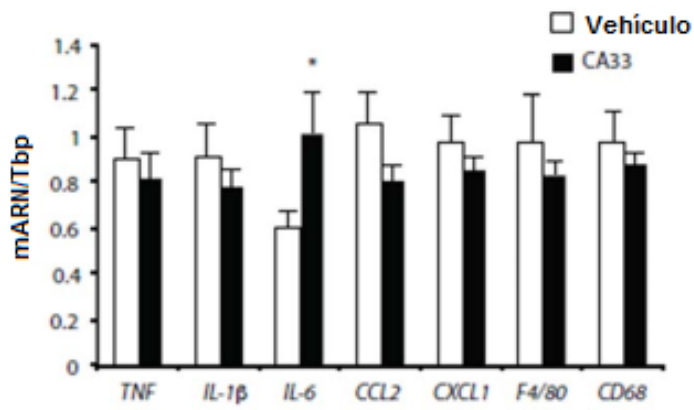


FIG. 5M

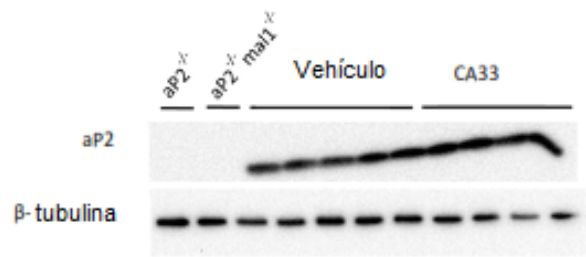


FIG. 5N

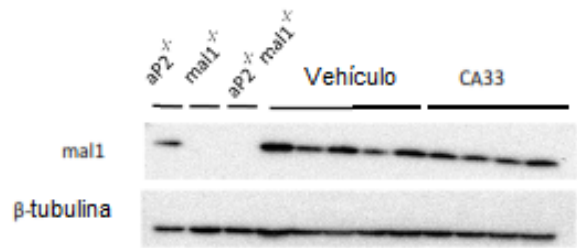


FIG. 5O

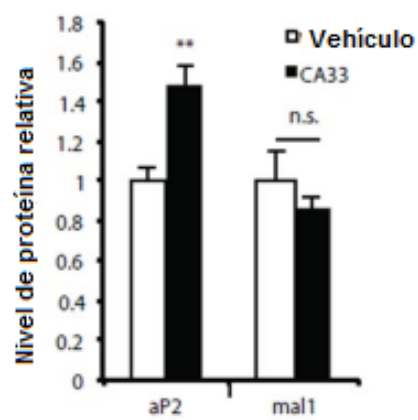


FIG. 5P

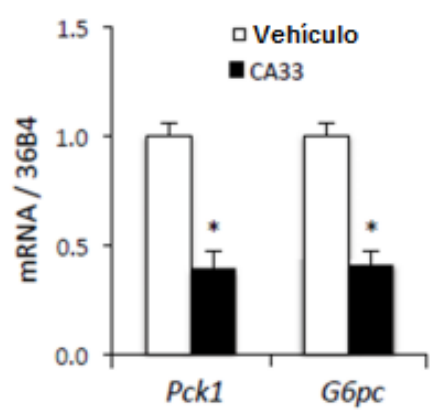


FIG. 6A

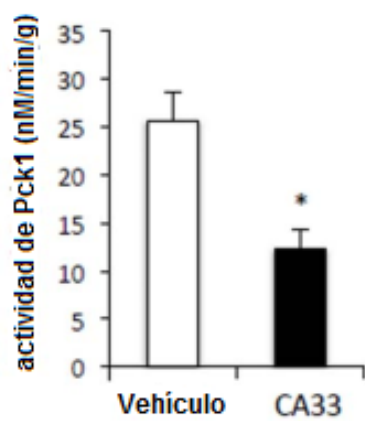


FIG. 6B

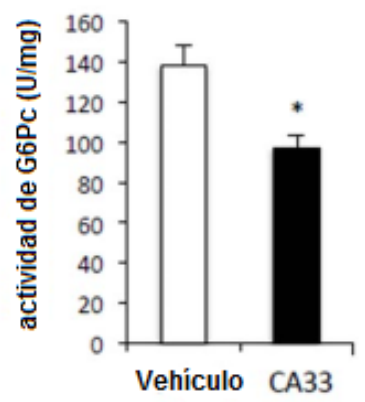


FIG. 6C

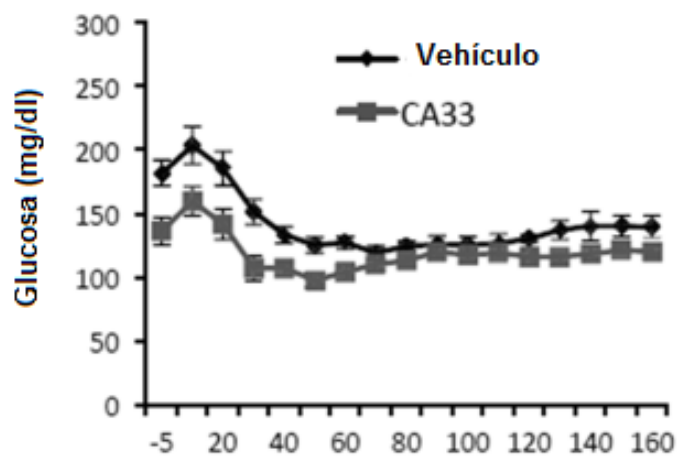


FIG. 6D

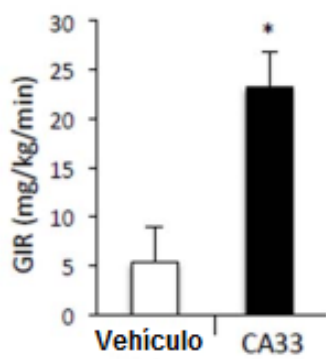


FIG. 6E

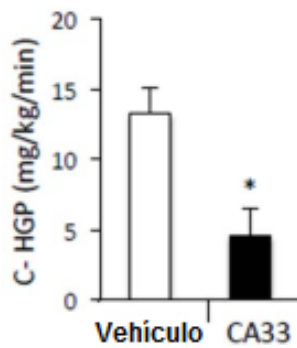


FIG. 6F

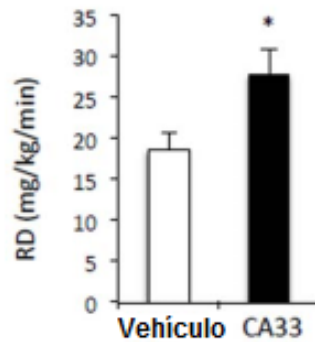


FIG. 6G

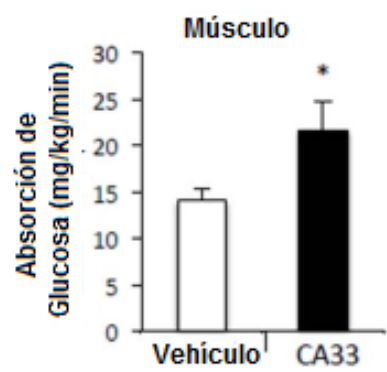


FIG. 6H

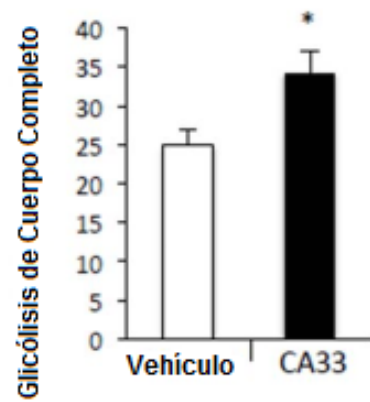


FIG. 6I

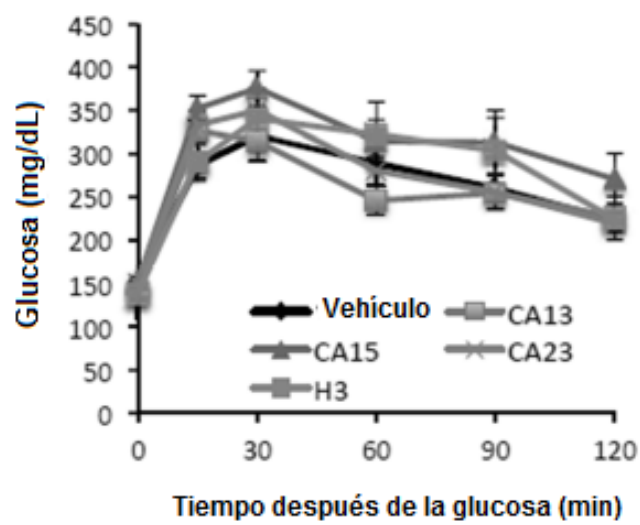


FIG. 7A

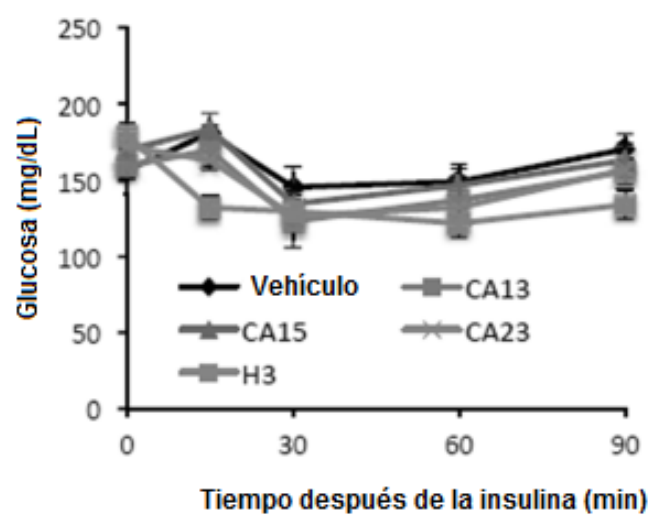


FIG. 7B

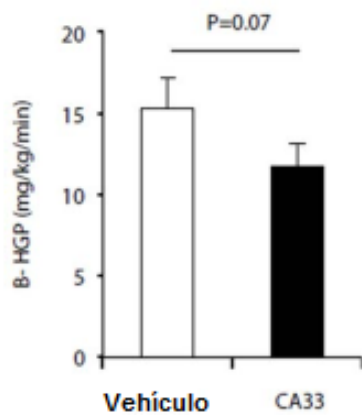


FIG. 8A

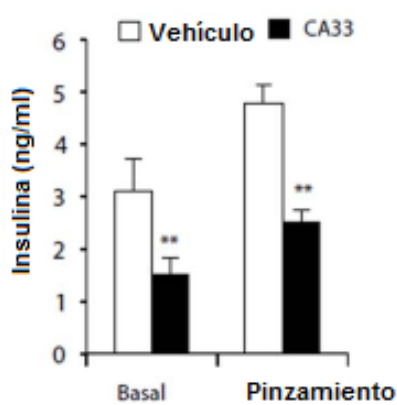


FIG. 8B

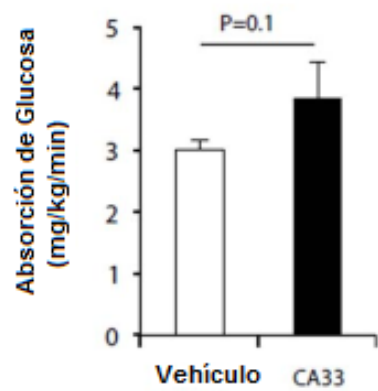


FIG. 8C

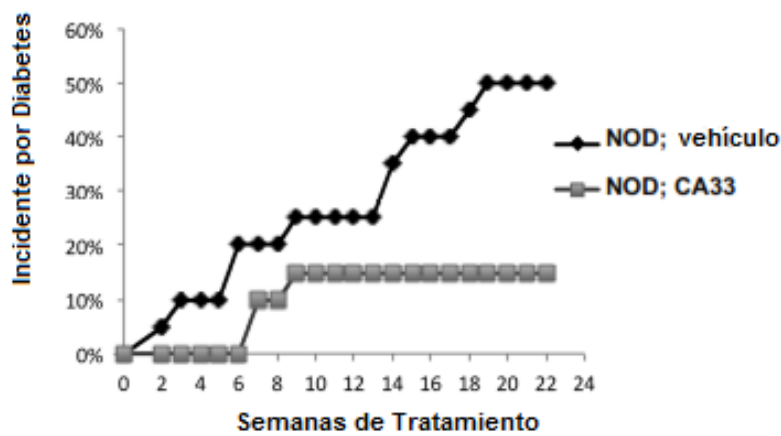


FIG. 9

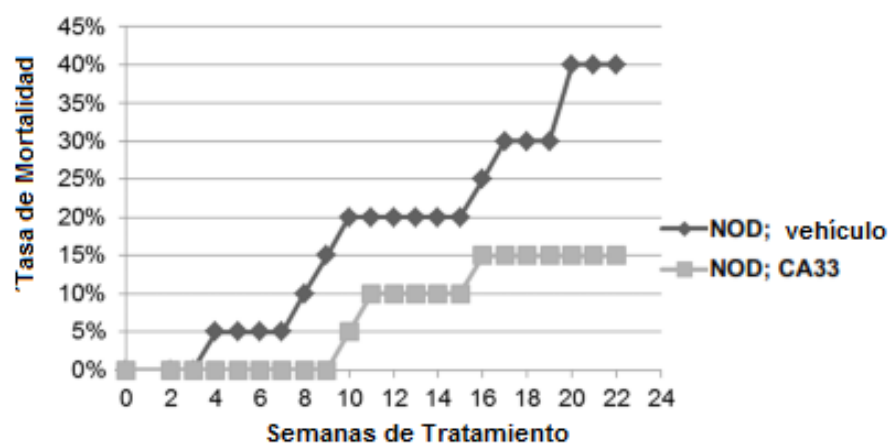


FIG. 10A

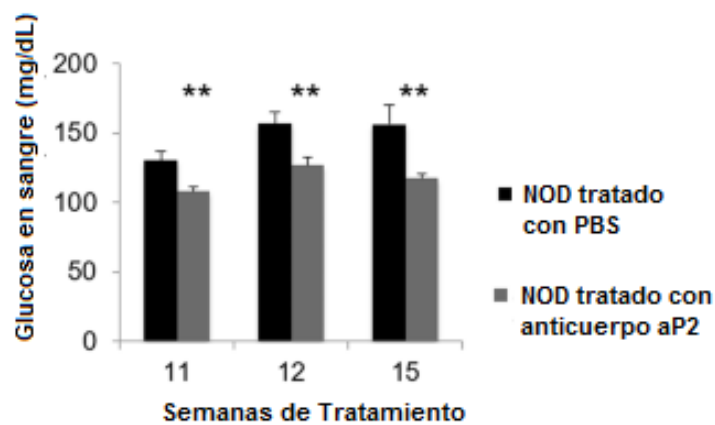


FIG. 10B

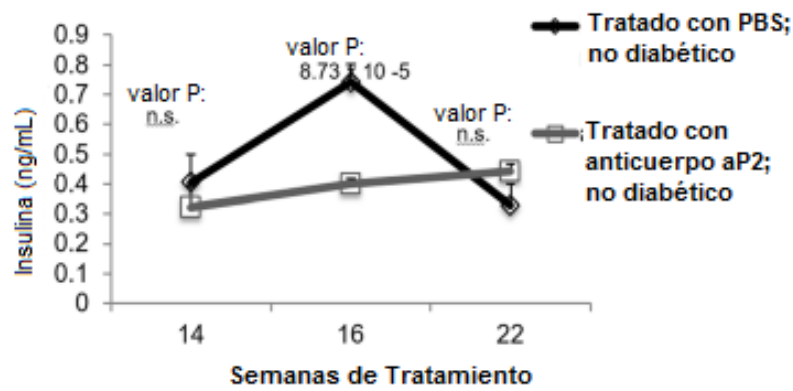


FIG. 10C

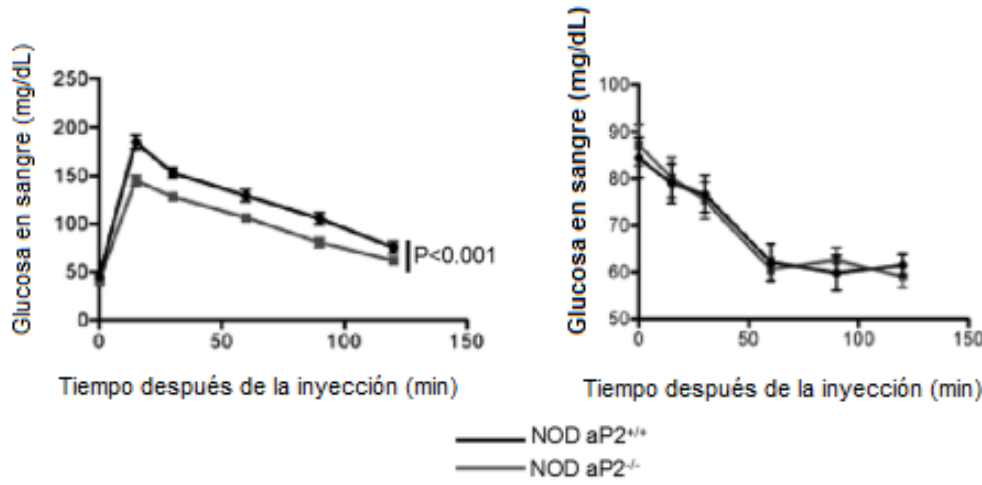


FIG. 11A

FIG. 11B

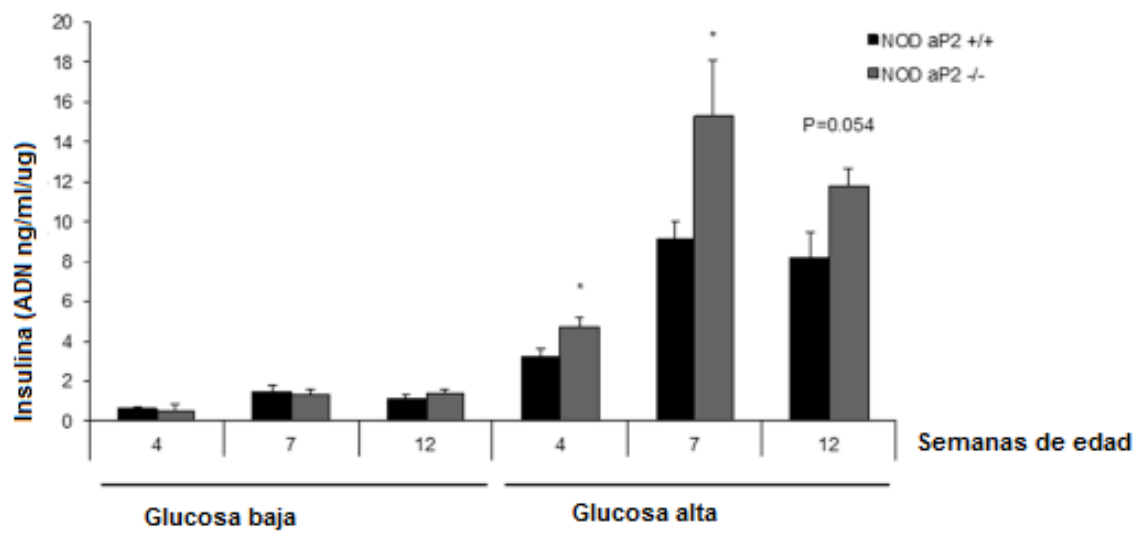


FIG. 12A

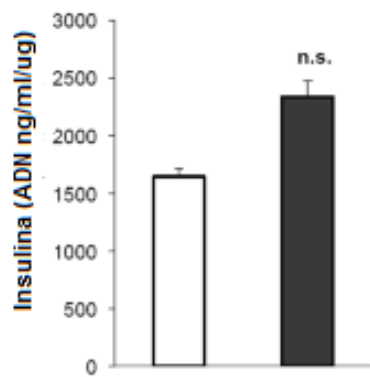


FIG. 12B

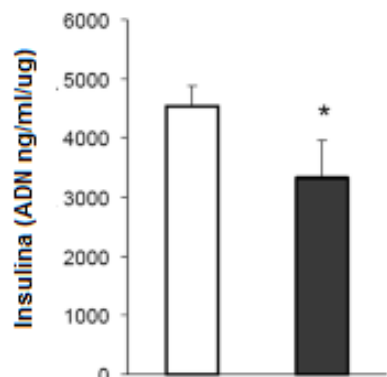


FIG. 12C

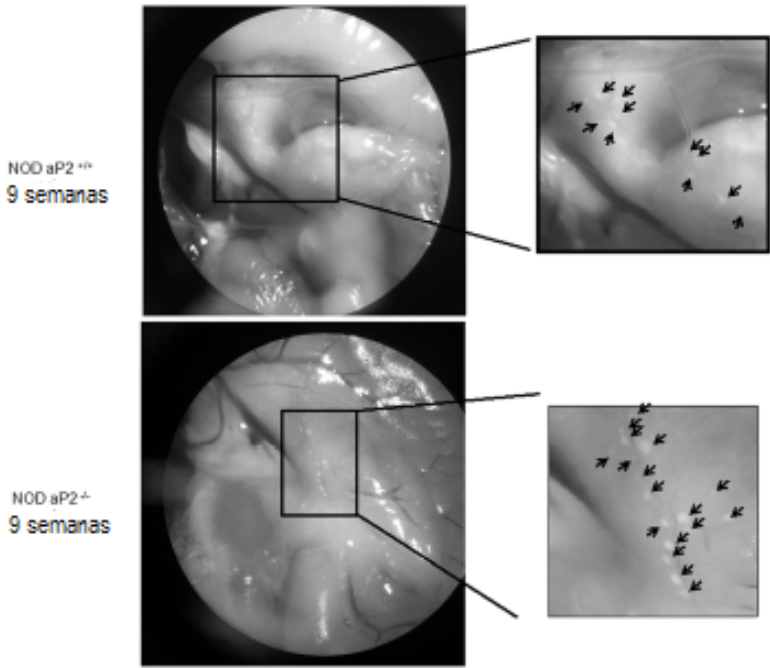


FIG.13

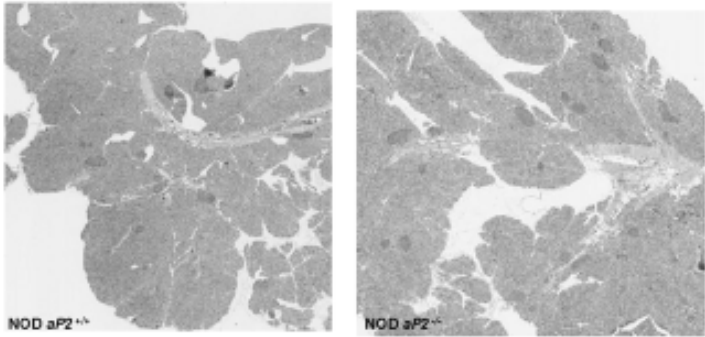


FIG. 14A

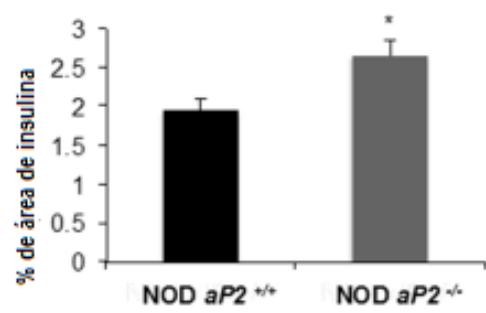


FIG. 14B

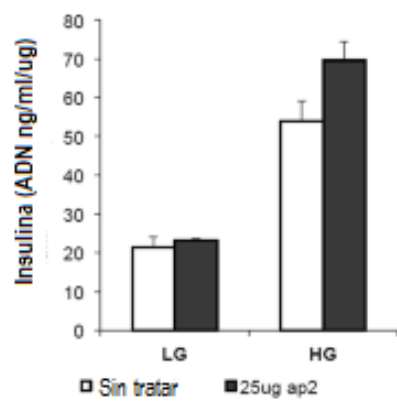


FIG. 15A

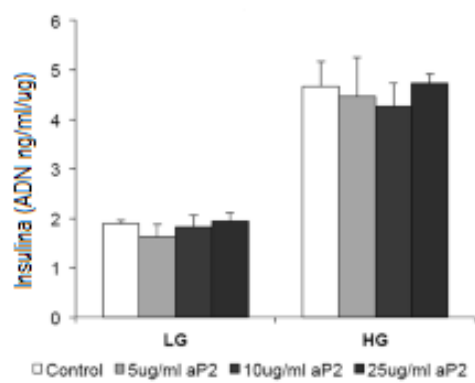


FIG. 15B

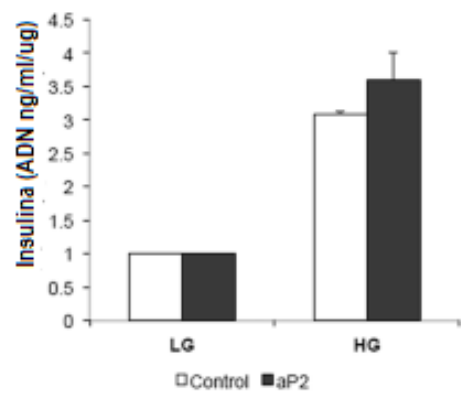


FIG. 15C

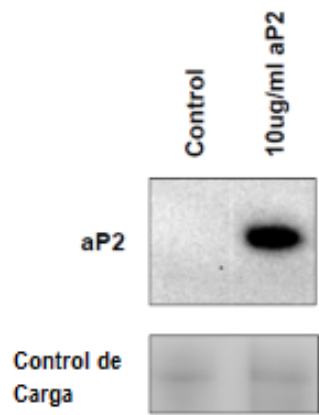


FIG. 15D

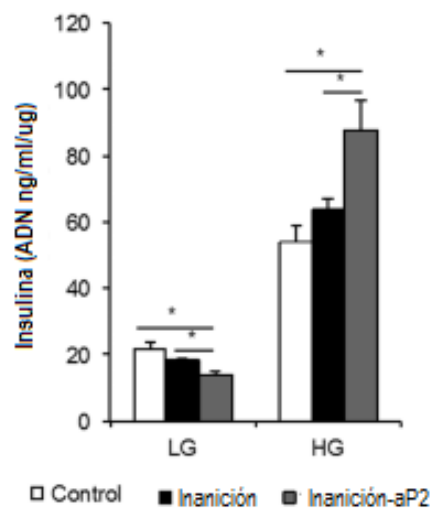


FIG.15E

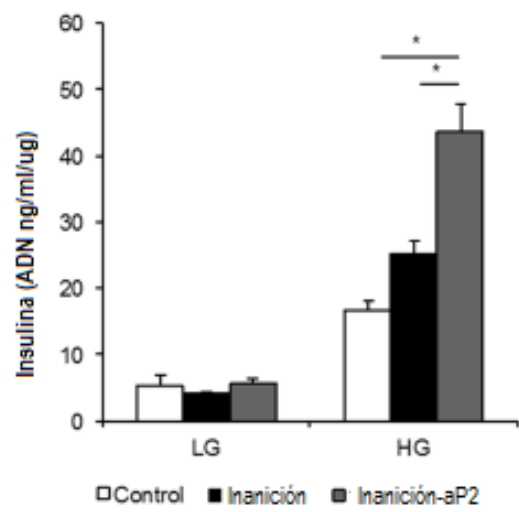


FIG. 15F

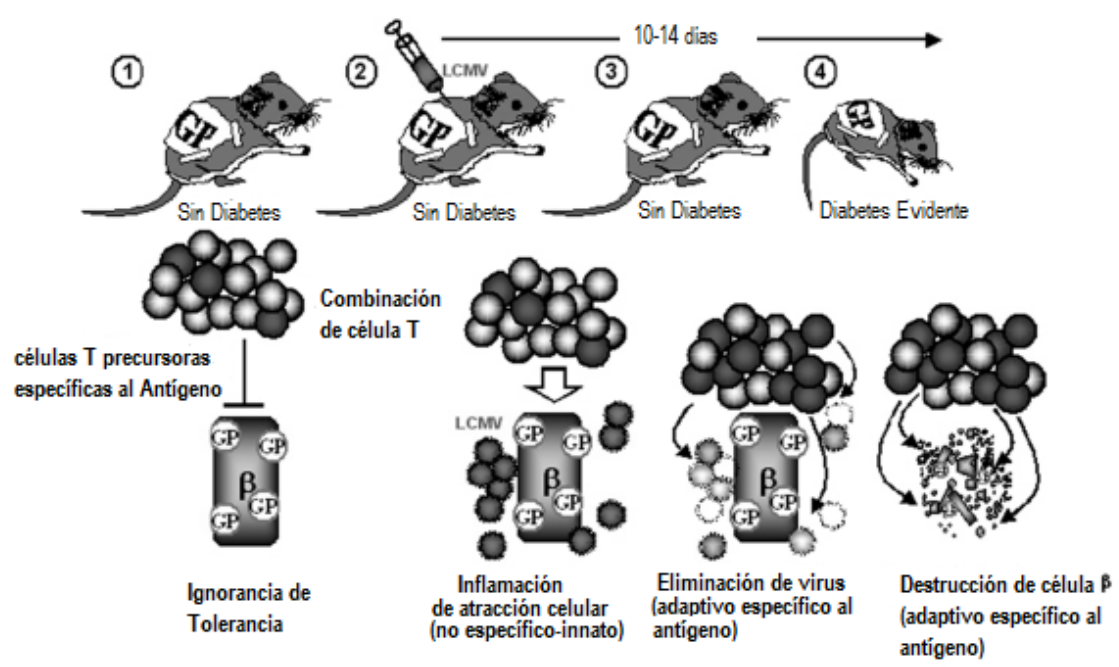


FIG. 16

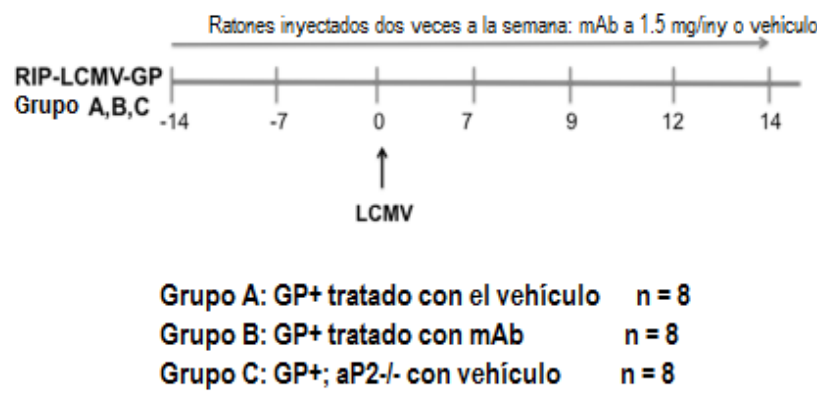


FIG. 17

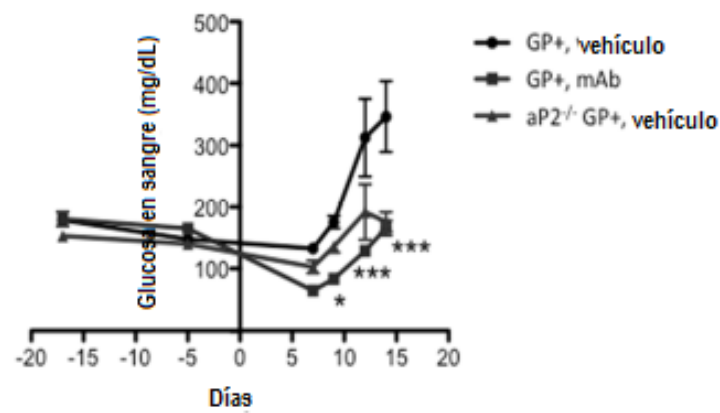


FIG. 18

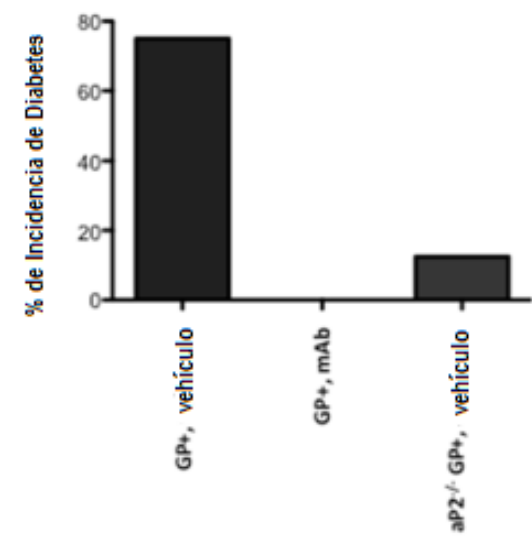


FIG. 19

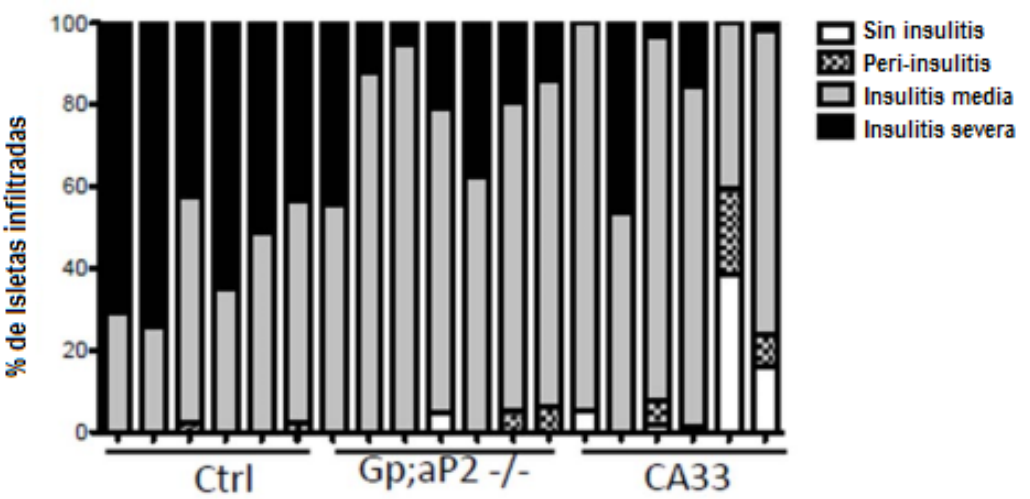


FIG. 20A

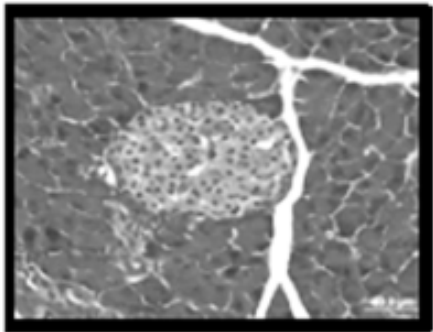


FIG. 20B

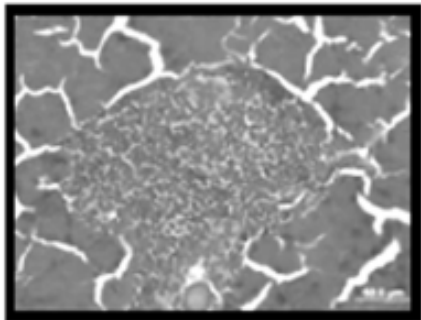


FIG. 20C

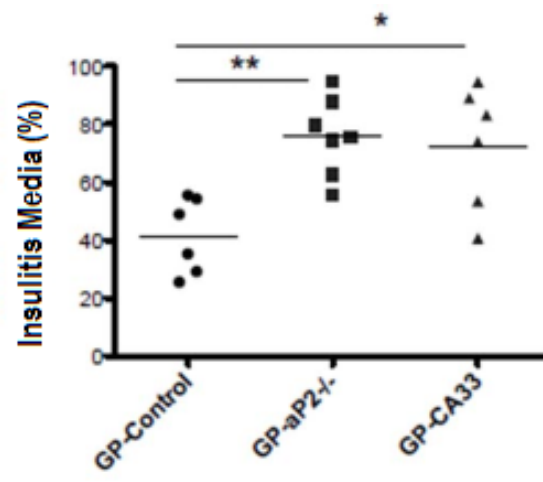
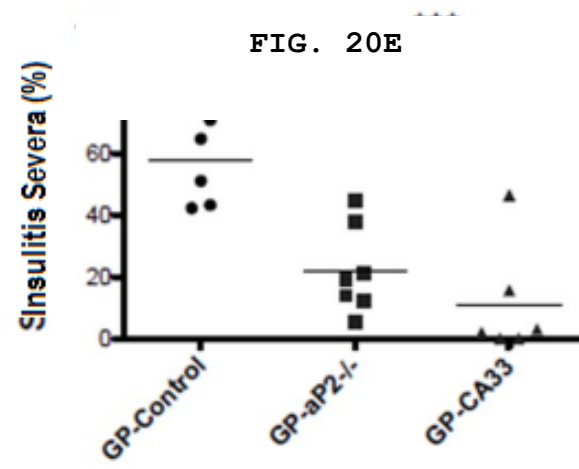


FIG. 20D



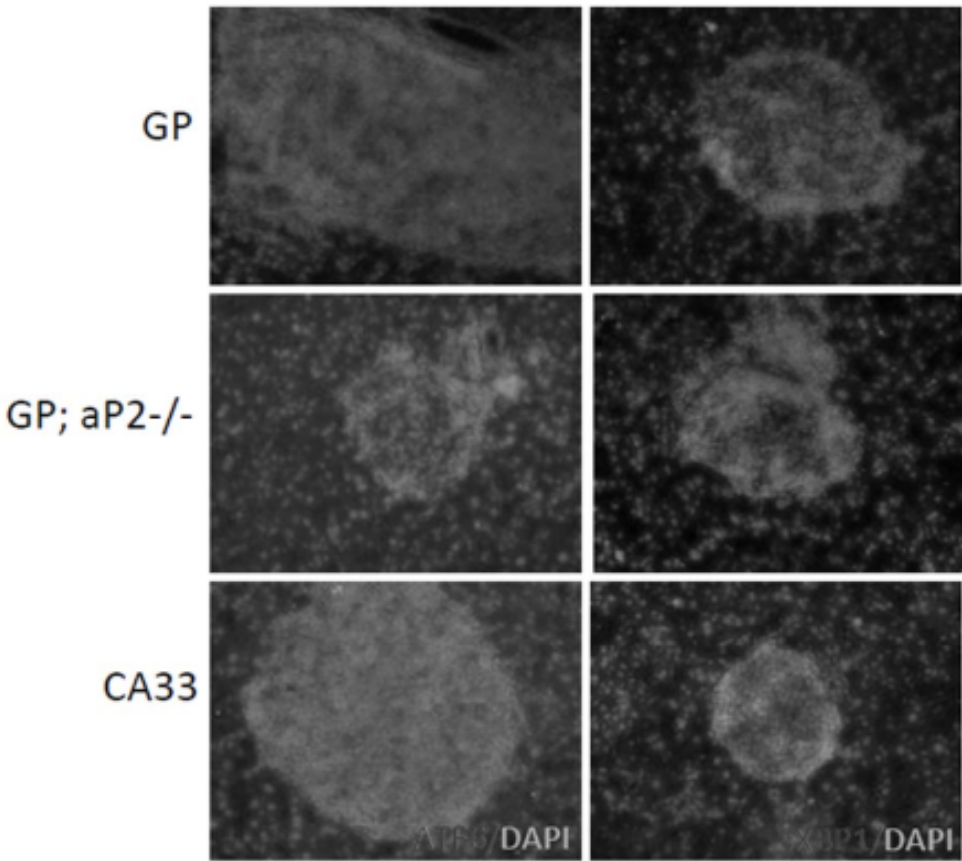


FIG. 21A

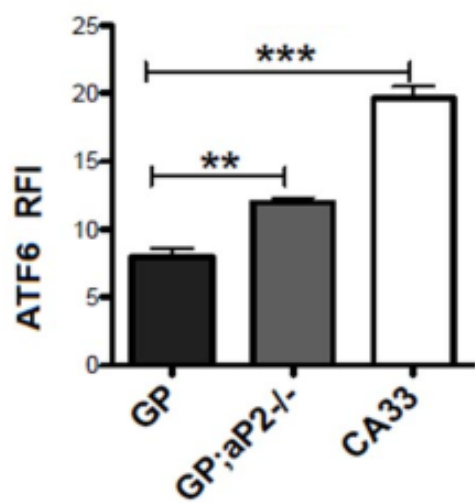


FIG. 21B

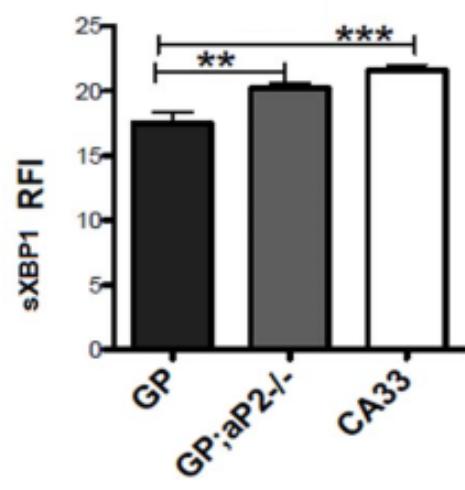


FIG. 21C

Edad (sems)	5	6	7	8	9	10	11	12	13	14	15	16	17	18
	Peso corporal Promedio (g)													
PBS	19.8	22.0	24.7	25.6	27.8	29.0	29.6	30.7	30.8	32.0	32.8	33.5	33.6	33.7
CA33	20.0	22.0	23.3	24.2	26.2	27.6	28.4	29.1	28.9	29.8	30.4	30.7	30.9	31.3
CA15	20.1	22.1	24.3	25.3	27.1	28.3	29.3	30.3	29.9	31.1	31.8	32.7	32.7	33.0
dosis de anticuerpo (ug)	660	728	795	826	892	934	960	991	986	1022	1045	1066	1070	1078
Concentración	5 mg/ml										10 mg/ml			
Volumen inyectado (ul)	132	146	159	165	178	187	192	198	197	102	104	107	107	108

FIG. 22A

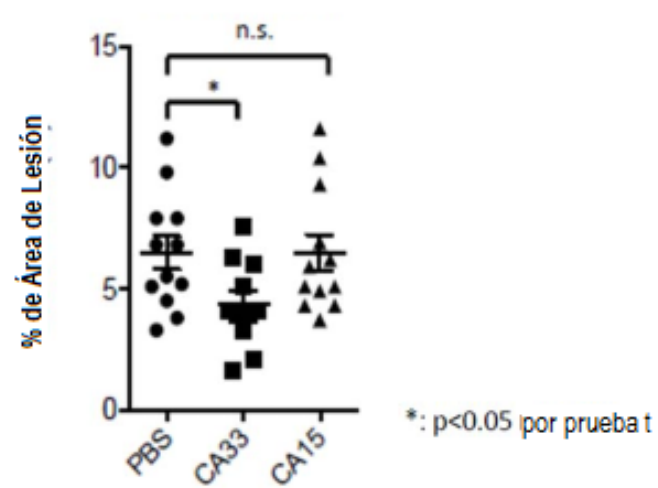


FIG. 22B

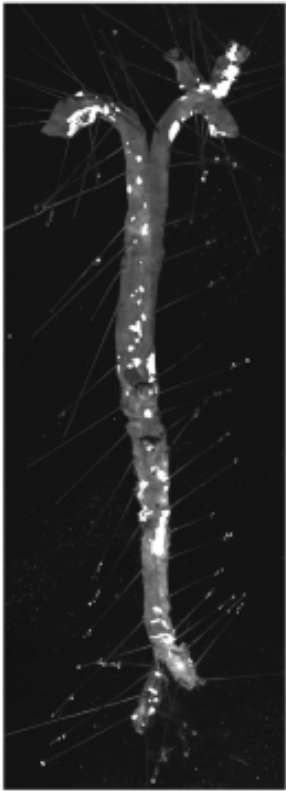


FIG. 22C

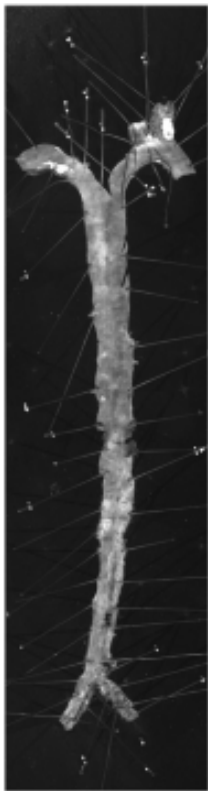


FIG. 22D

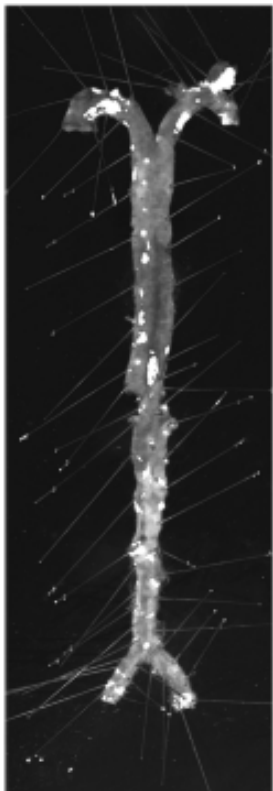


FIG. 22E

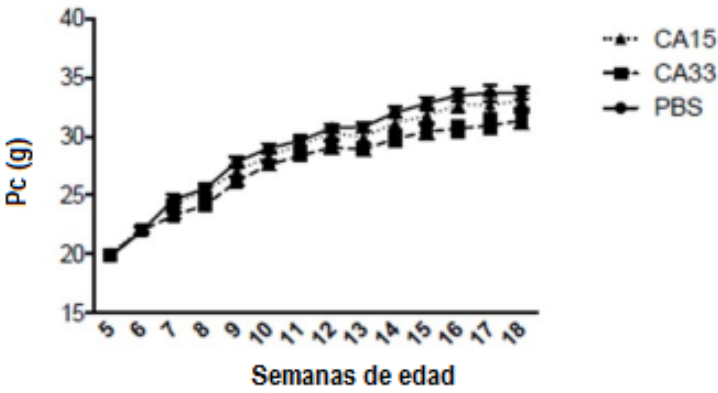


FIG. 22F

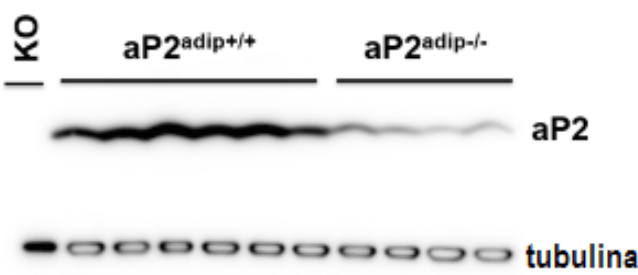


FIG. 22G

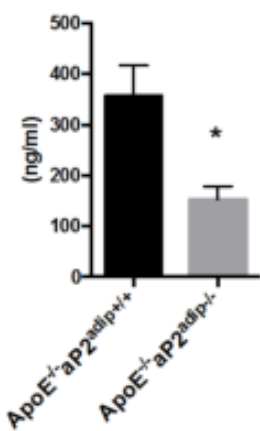


FIG. 22H

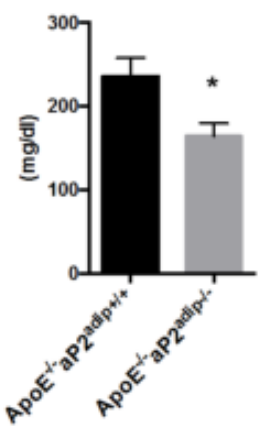


FIG. 22I

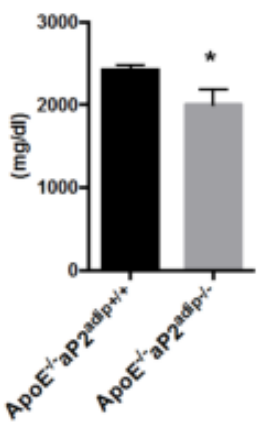


FIG. 22J

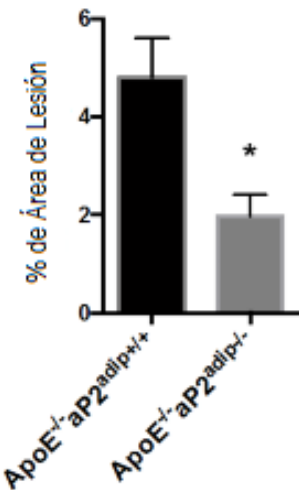


FIG. 22K

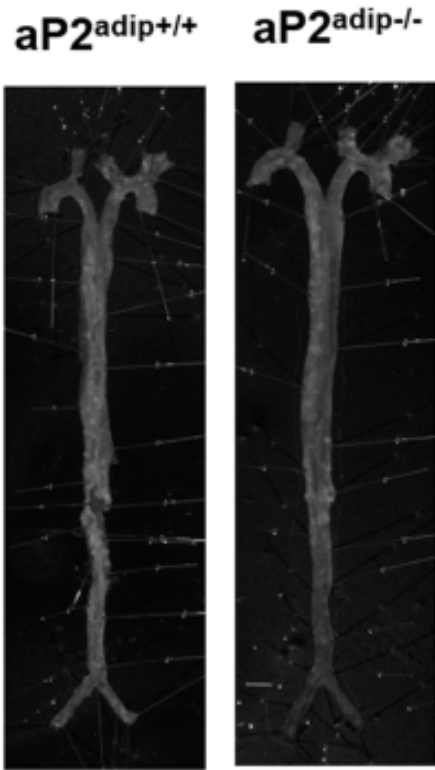


FIG. 22L

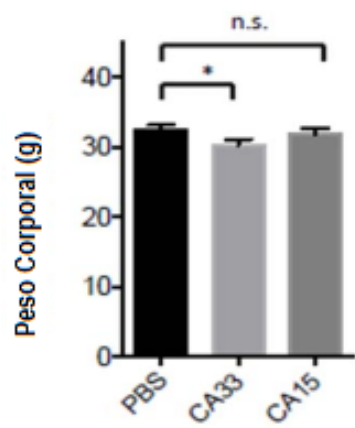


FIG. 23A

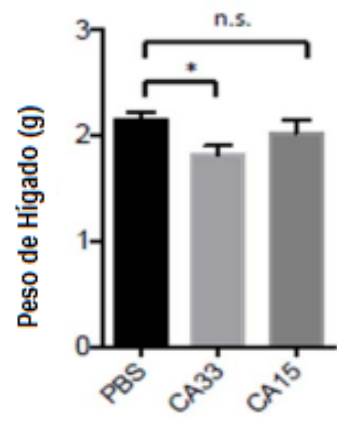


FIG. 23B

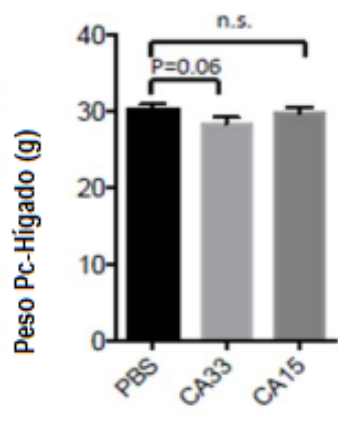


FIG. 23C

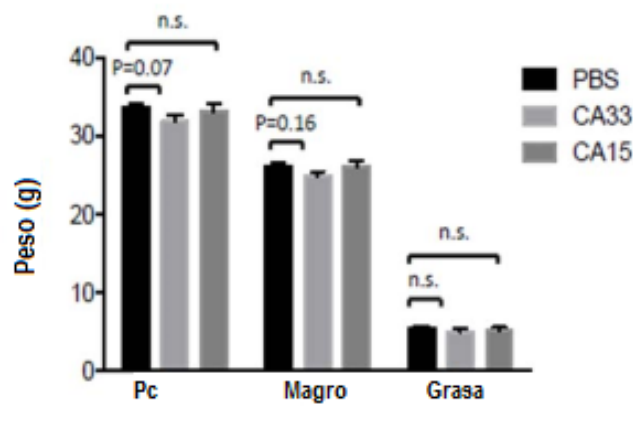


FIG. 23D

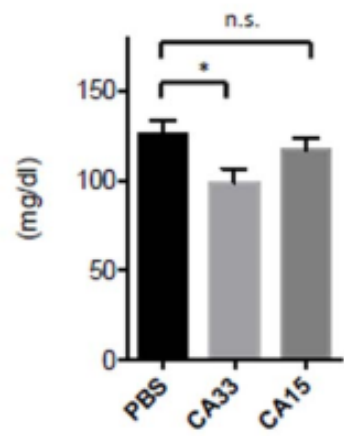


FIG. 24A

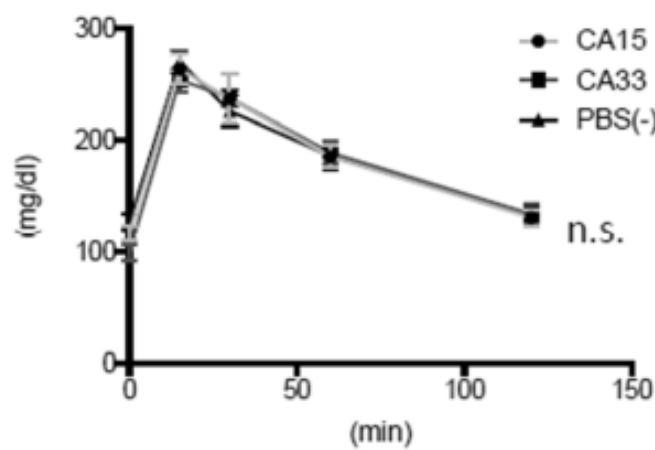


FIG. 24B

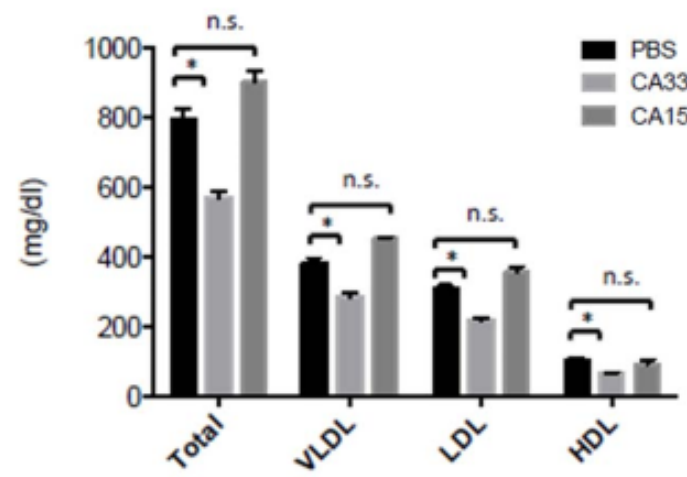


FIG. 25A

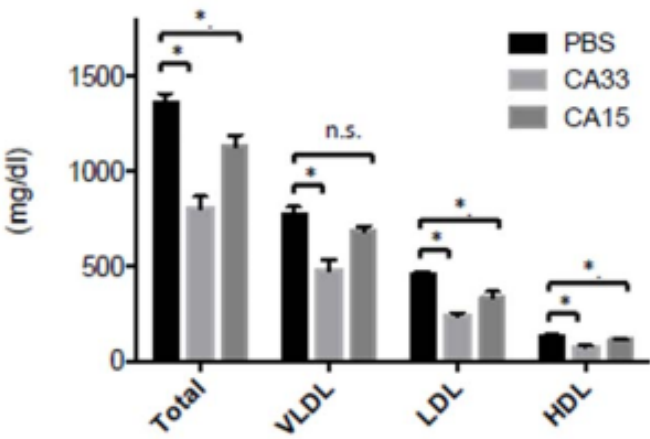


FIG. 25B

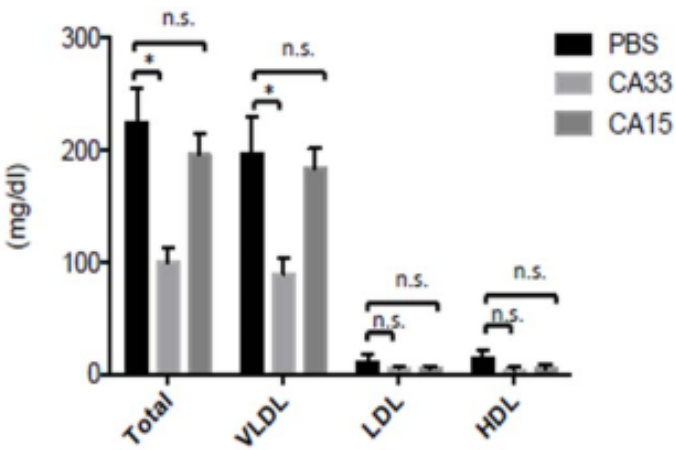


FIG. 26A

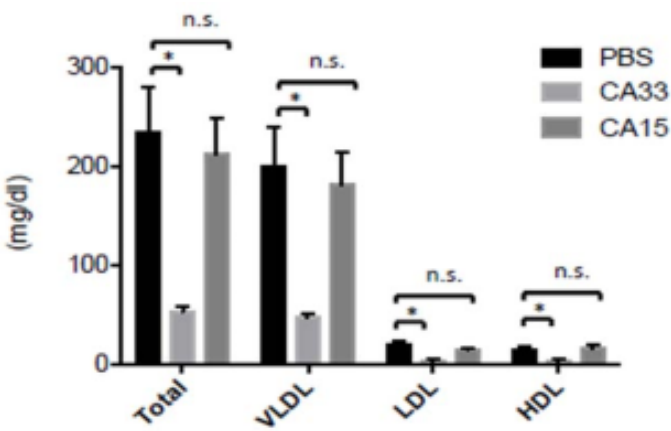


FIG. 26B

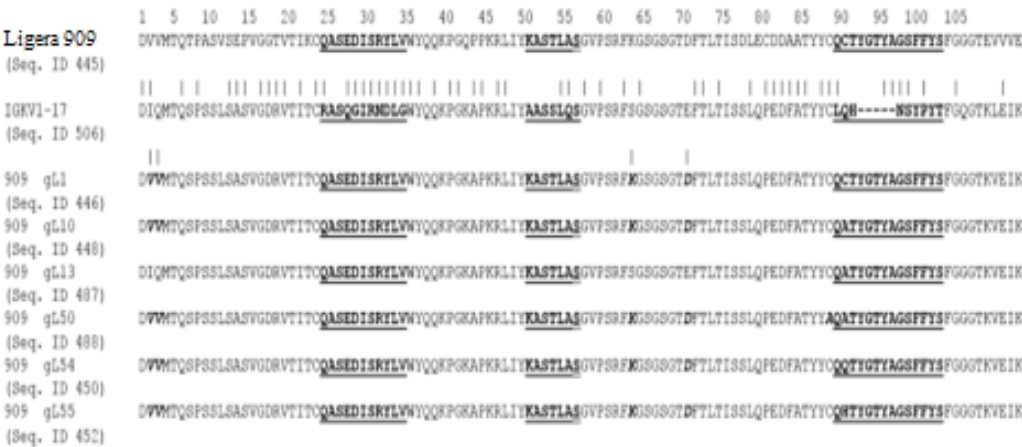


FIG. 27

Pesada 909
 (Seq. ID 454)

1 5 10 15 20 25 30 a 35 40 45 50 55 60 65 70 75 80 abc 85 90 95 100 105 110
 -QSEVESGGGLVTPGTLTLCTVSGFSLST-YDMSWVQPPGNGLEWIGIITPGSGSTYCASMAHGFITISKAST--TVLQKITSPPTTEDATATYFCARFONDGTSGYLSGFLWGQGLNTLVSS
 (Seq. ID 454)

10974-4
 (Seq. ID 481)

1 5 10 15 20 25 30 a 35 40 45 50 55 60 65 70 75 80 abc 85 90 95 100 105 110
 QVQLQESGPGLVKPGTGLSLTCAVSGGSISSSNWVQPPGNGLEWIGIITPGSGSTYTPSLASHVTISVRSKQFSLKLSVTAADATATYFCARY-----FDYWGQGLNTLVSS
 (Seq. ID 481)

909gH1
 (Seq. ID 455)

1 5 10 15 20 25 30 a 35 40 45 50 55 60 65 70 75 80 abc 85 90 95 100 105 110
 EVQLQESGPGLVKPGTGLSLTCTVSGFSLST-YDMSWVQPPGNGLEWIGIITPGSGSTYCASMAHGFITISKAST--TVLQKITSPPTTEDATATYFCARFONDGTSGYLSGFLWGQGLNTLVSS
 (Seq. ID 455)

909gH5
 (Seq. ID 459)

1 5 10 15 20 25 30 a 35 40 45 50 55 60 65 70 75 80 abc 85 90 95 100 105 110
 EVQLQESGPGLVKPGTGLSLTCTVSGFSLST-YDMSWVQPPGNGLEWIGIITPGSGSTYCASMAHGFITISKAST--TVLQKITSPPTTEDATATYFCARFONDGTSGYLSGFLWGQGLNTLVSS
 (Seq. ID 459)

909gH4
 (Seq. ID 457)

1 5 10 15 20 25 30 a 35 40 45 50 55 60 65 70 75 80 abc 85 90 95 100 105 110
 EVQLQESGPGLVKPGTGLSLTCAVSGFSLST-YDMSWVQPPGNGLEWIGIITPGSGSTYCASMAHGFITISKAST--TVLQKITSPPTTEDATATYFCARFONDGTSGYLSGFLWGQGLNTLVSS
 (Seq. ID 457)

909gH61
 (Seq. ID 461)

1 5 10 15 20 25 30 a 35 40 45 50 55 60 65 70 75 80 abc 85 90 95 100 105 110
 EVQLQESGPGLVKPGTGLSLTCAVSGFSLST-YDMSWVQPPGNGLEWIGIITPGSGSTYCASMAHGFITISKAST--TVLQKITSPPTTEDATATYFCARFONDGTSGYLSGFLWGQGLNTLVSS
 (Seq. ID 461)

909gH62
 (Seq. ID 463)

1 5 10 15 20 25 30 a 35 40 45 50 55 60 65 70 75 80 abc 85 90 95 100 105 110
 EVQLQESGPGLVKPGTGLSLTCAVSGFSLST-YDMSWVQPPGNGLEWIGIITPGSGSTYCASMAHGFITISKAST--TVLQKITSPPTTEDATATYFCARFONDGTSGYLSGFLWGQGLNTLVSS
 (Seq. ID 463)

FIG. 28

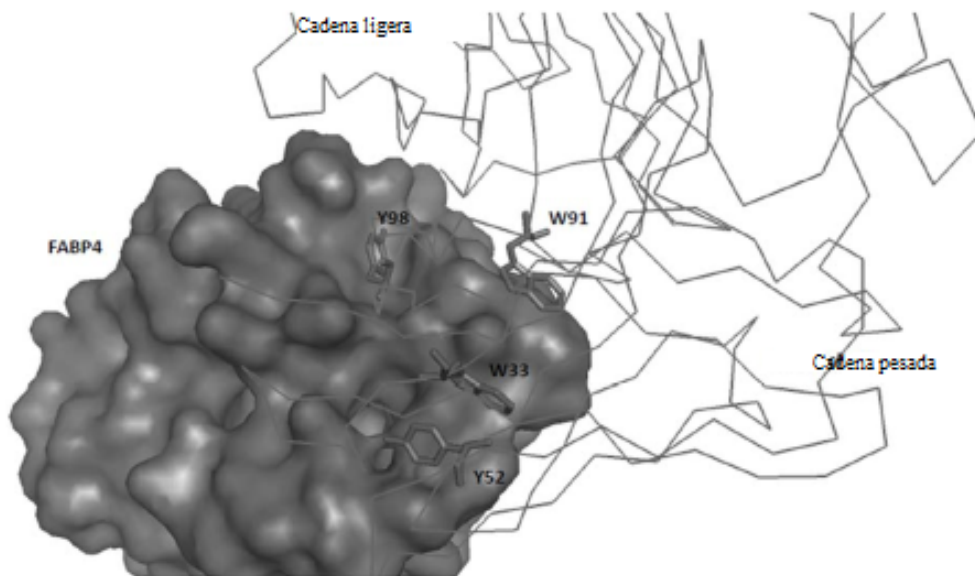


FIG. 29

		<u>Cadena Ligera</u>	<u>Cadena Pesada</u>	<u>Afinidad</u>
CA33				6.5 μM
APP5168	PPP4048	g11 = W91A	g19 = W33A, Y52S	6.03 μM
APP5169	PPP4049	g1 = precursor	g20 = W33A, Y52S, Y98F	5.82 μM

FIG. 30A

Cadena Pesada

	CDR1										CDR2										CDR3									
	1	5	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	abc	85	90	95	100	105							
g1	QVQLQQPGAEIVKPGASVKLSCKASGYTFTSNWITWVQKRPQGLEWIGDIYFGSGSTTNMEKFKSKATLTVDTSSTANMQLSSLTSEDSAVYYCARGYYDYFFIEWQQGTTLTSS																													
(Seq. ID No. 482)																														
g19	QVQLQQPGAEIVKPGASVKLSCKASGYTFTSNWITWVQKRPQGLEWIGDIYFGSGSTTNMEKFKSKATLTVDTSSTANMQLSSLTSEDSAVYYCARGYYDYFFIEWQQGTTLTSS																													
(Seq. ID No. 483)																														
g20	QVQLQQPGAEIVKPGASVKLSCKASGYTFTSNWITWVQKRPQGLEWIGDIYFGSGSTTNMEKFKSKATLTVDTSSTANMQLSSLTSEDSAVYYCARGYYDYFFIEWQQGTTLTSS																													
(Seq. ID No. 484)																														

FIG. 30B

Cadena Ligera

	CDR1										CDR2										CDR3									
	1	5	10	15	20	25	30	35	40	45	50	55	60	65	70	75	80	85	90	95	100	105								
g1	EVVLTQSPALMAASPGEKVTITCSVSSSISSSNLHWYQQKSETSPKFWIYGTSNLASGVPRFSGSGSGTSYSLTISMEAEADAATYYCQASQSHYPLTFGAGTKLELK																													
(Seq. ID No. 485)																														
g11	EVVLTQSPALMAASPGEKVTITCSVSSSISSSNLHWYQQKSETSPKFWIYGTSNLASGVPRFSGSGSGTSYSLTISMEAEADAATYYCQASQSHYPLTFGAGTKLELK																													
(Seq. ID No. 486)																														

FIG. 30C

Humano				Ratón		
Anti-aP2	Resp. de Unión	KD (M)	KD (μM)	Resp. de Unión	KD (M)	KD (μM)
BSN	a 40uM			a 40uM		
5251.mIgG1.168 (PB1172)	30.6	5.62E-06	5.62	31.4	4.14E-06	4.14
	28.7	6.44E-06	6.44	32.7	4.99E-06	4.99
Promedio			6.03			4.57
5252.mIgG1.169 (PB1171)	33.4	6.13E-06	6.13	36.5	5.53E-06	5.53
	30.5	5.51E-06	5.51	35.5	4.71E-06	4.71
Promedio			5.82			5.12

FIG. 31

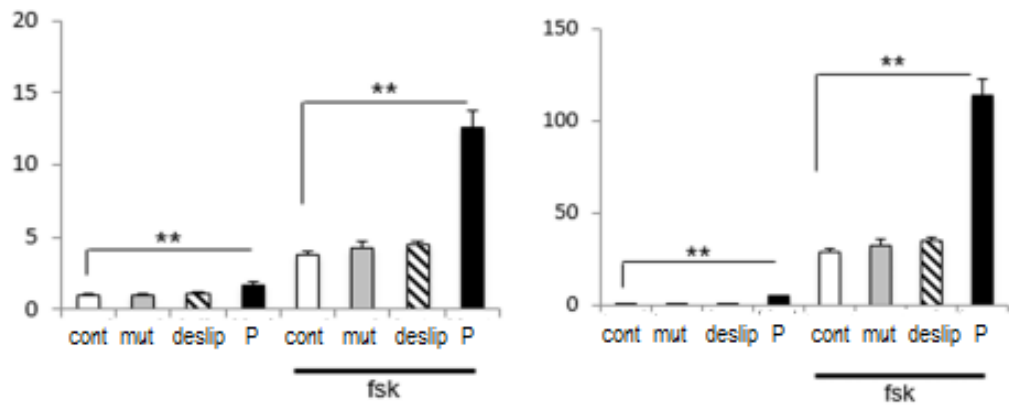


FIG. 32A

FIG. 32B

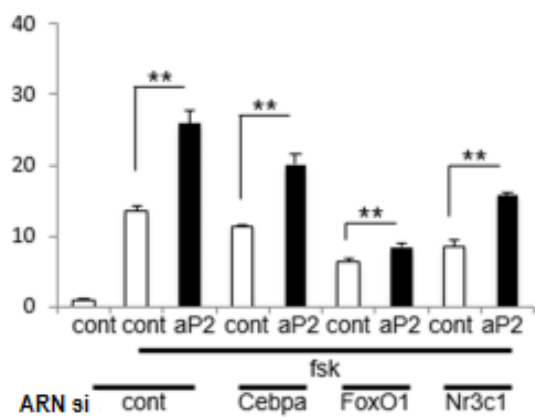


FIG. 32C

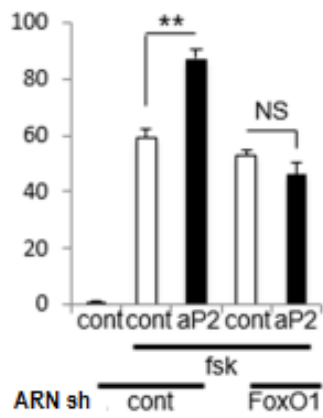


FIG. 32D

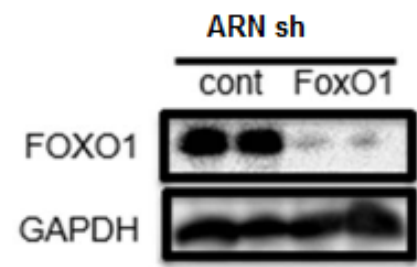


FIG. 32E

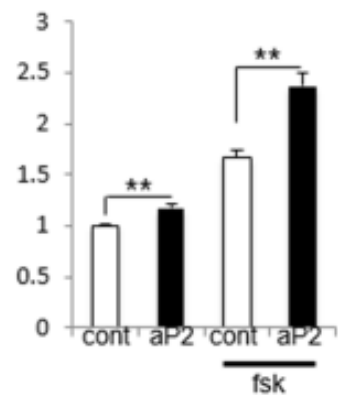


FIG. 32F

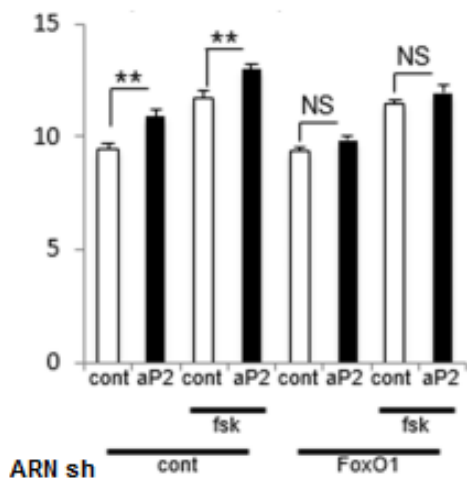


FIG. 32G

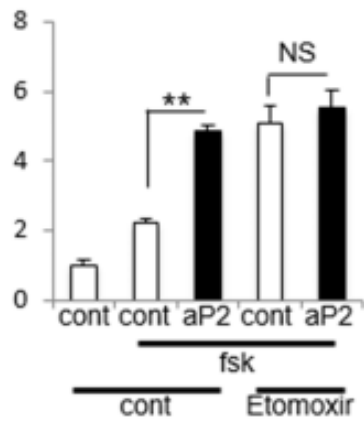


FIG. 33A

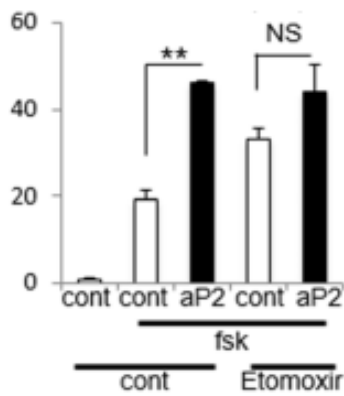


FIG. 33B

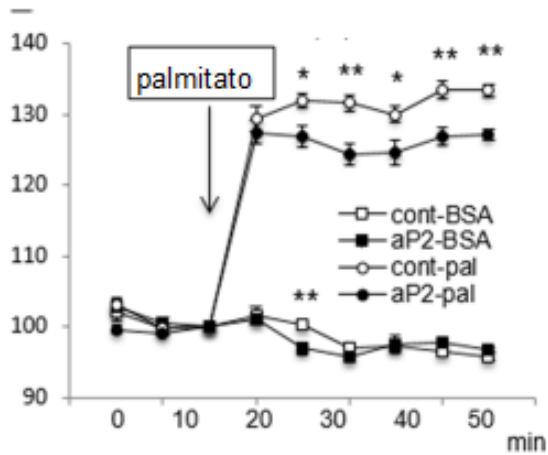


FIG. 33C

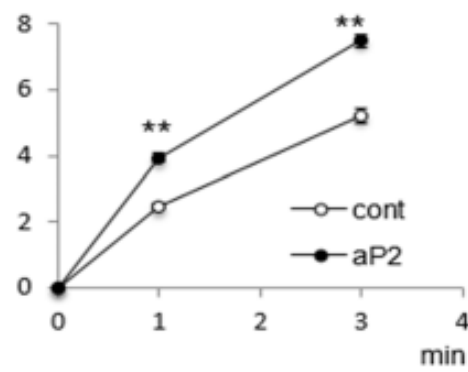


FIG. 33D

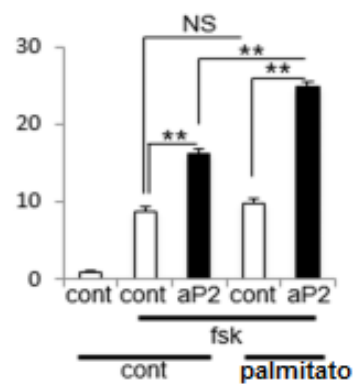


FIG. 33E

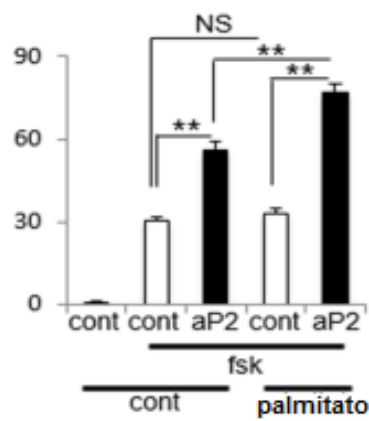


FIG. 33F

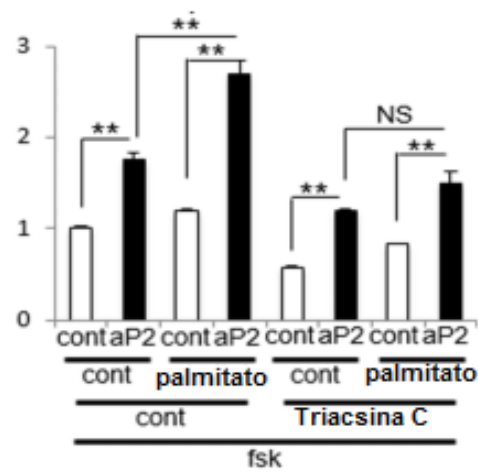


FIG. 33G

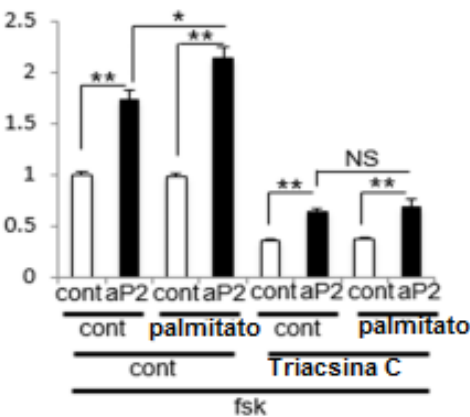


FIG. 33H

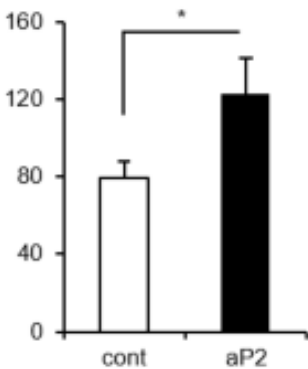


FIG. 33I

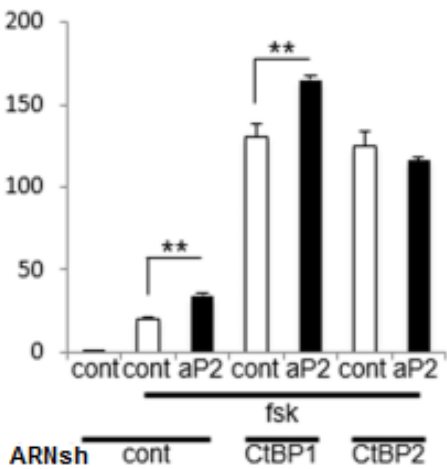


FIG. 34A

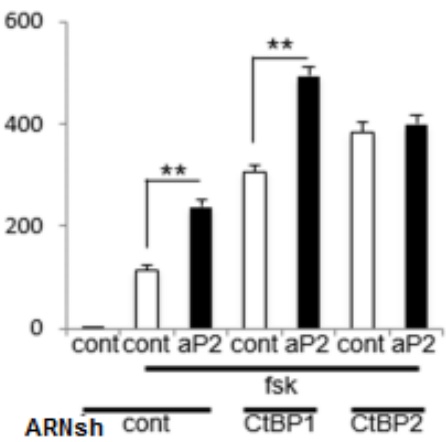


FIG. 34B

FOXO1 571	de Ratón	algsyssvss cngygrmgvl hqekpsdldgmfierldcd mesiiirndlm 610	Seq. ID. No.603
FOXO3 581	de Ratón	tlstdslsgss lysasanlpv mghdkpsdl ddmfngsle cdmesiirse 620	Seq. ID. No.604
FOXO4 441	de Ratón	magapipkvl gtpvlaspte dsshdrmpqd lldmymenl ecdmdniisd 480	Seq. ID. No.605
FOXO6 481	de Ratón	lpgpyaaaaa gplgagpdrfpadldmfs gslecdvesi ilndfmdsde 520	Seq. ID. No.606
FOXO1 581	Humano	vsscngygrm gllhqekps dldgmfierl dcdmesiirn dldmgdtldf 620	Seq. ID. No.607
FOXO3 591	Humano	slystsanlp vmghekpsd lldmfngsl ecdmesiirs elmdadglfd 630	Seq. ID. No.608
FOXO4 451	Humano	tpvltptea asqdrmpqd lldmymenle cdmndiisd mdegegldfn 490	Seq. ID. No.609
FOXO6 411	Humano	ldalpgpyaa aaagplgaap drfpadld mfgslecdrv esiilndfmd 451	Seq. ID. No.610

FIG. 34C

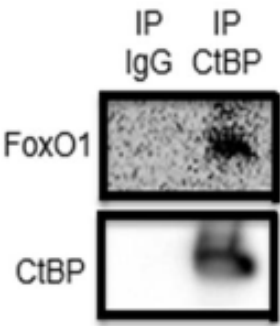


FIG. 34D

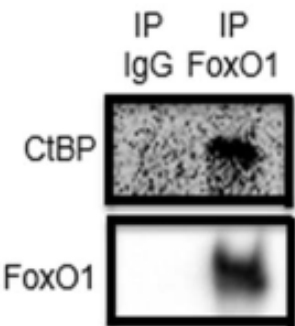


FIG. 34E

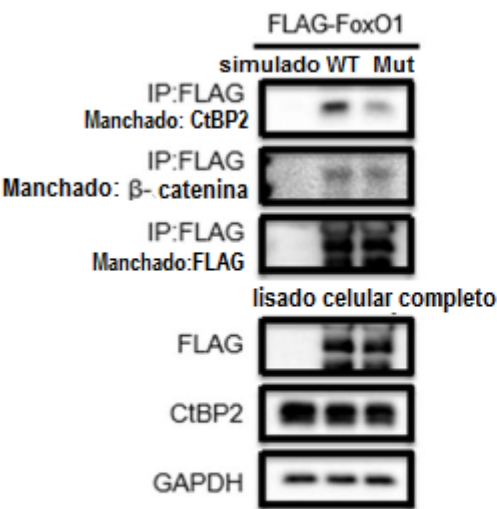


FIG. 34F

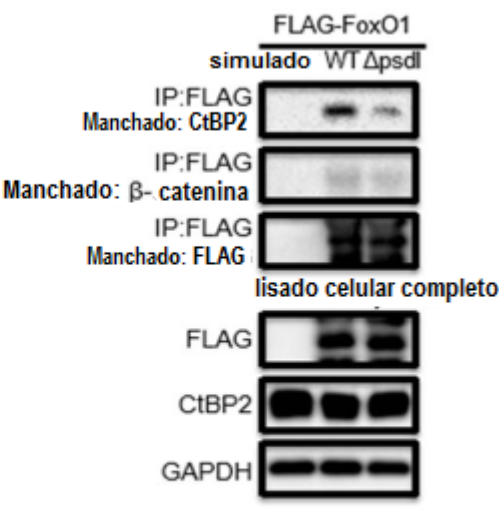


FIG. 34G

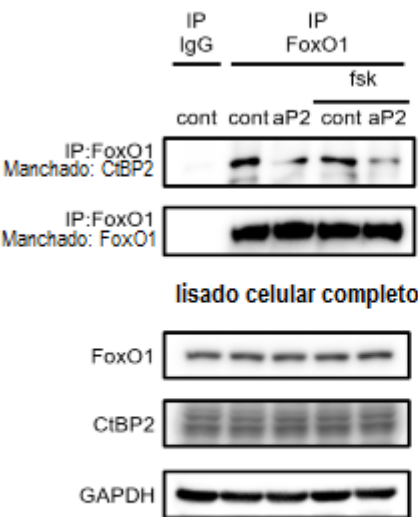


FIG. 34H

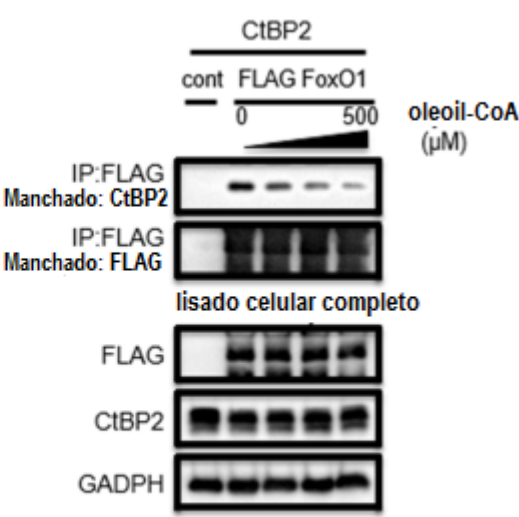


FIG. 34I

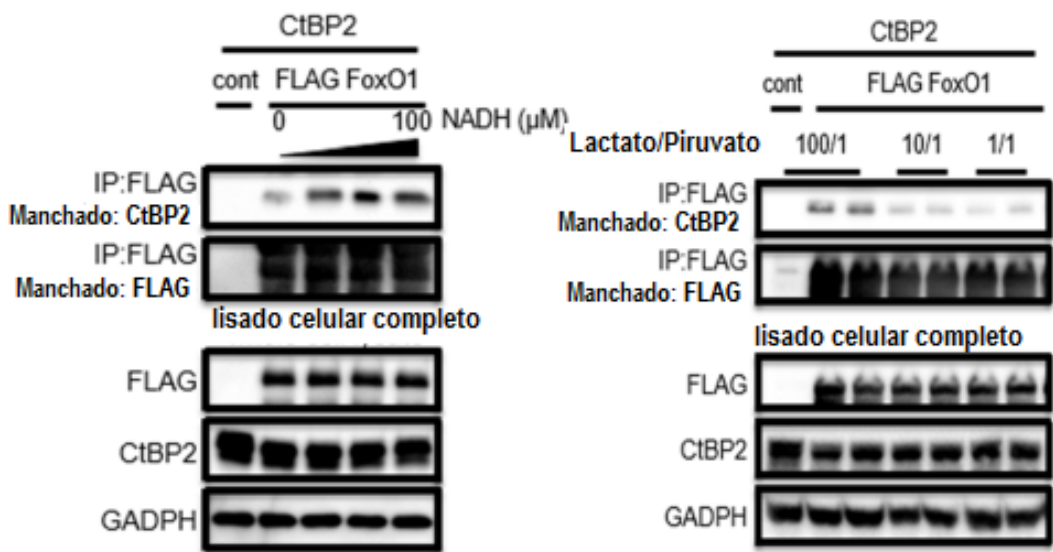


FIG. 34J

FIG. 34K

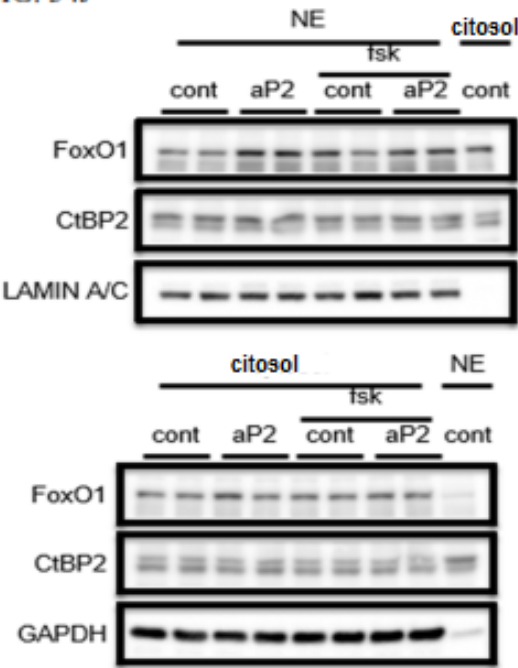


FIG. 34L

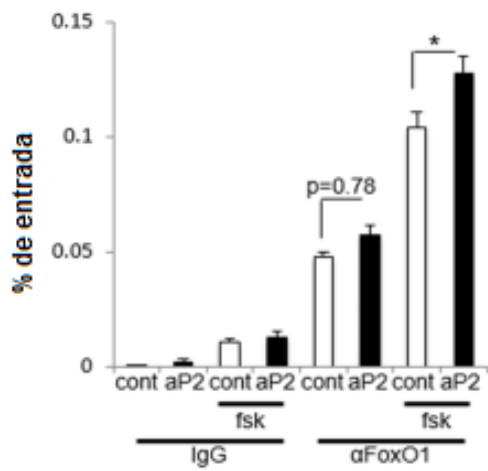


FIG. 34M

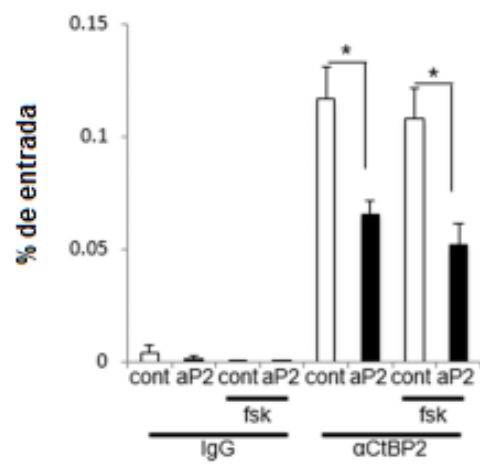


FIG. 34N

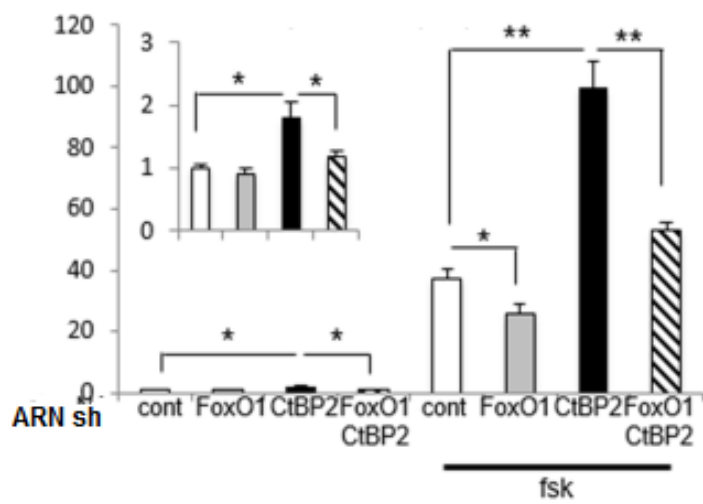


FIG. 35A

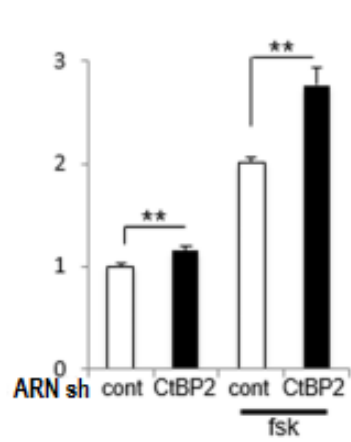


FIG. 35B

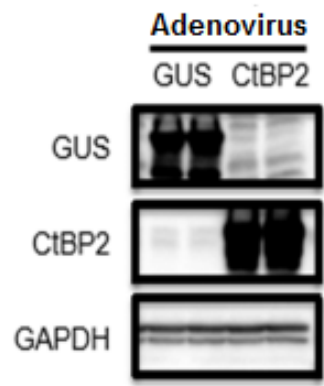


FIG. 35C

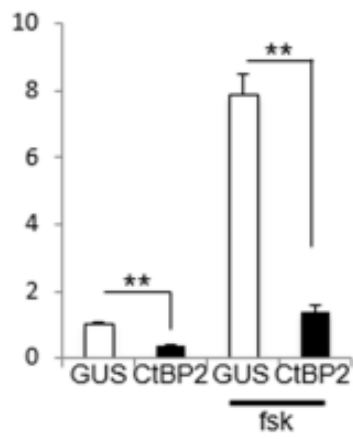


FIG. 35D

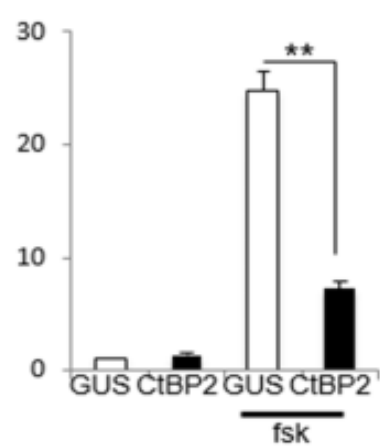


FIG. 35E

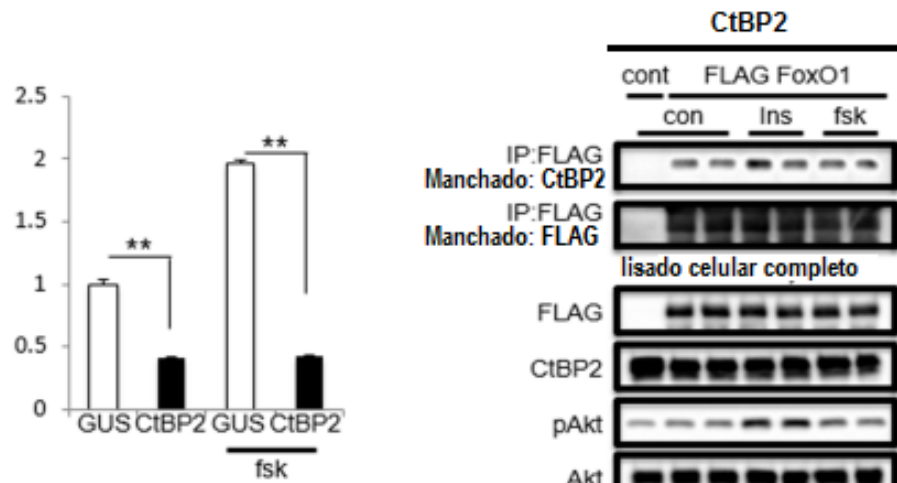


FIG. 35F

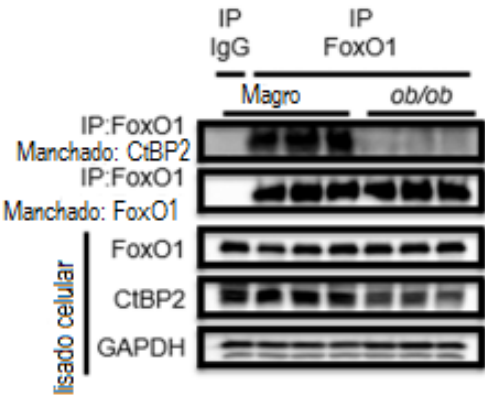


FIG. 36A

FIG. 35G

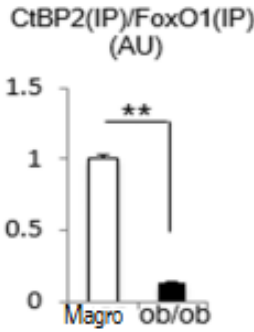


FIG. 36B

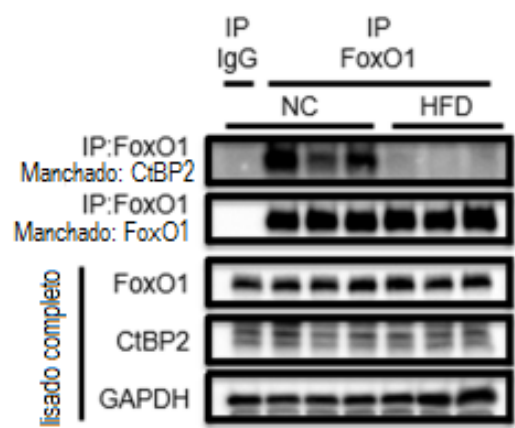


FIG. 36C

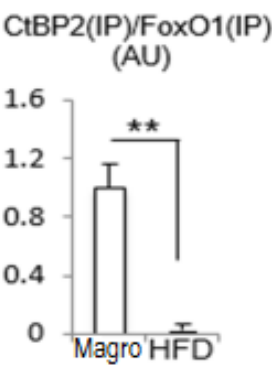


FIG. 36D

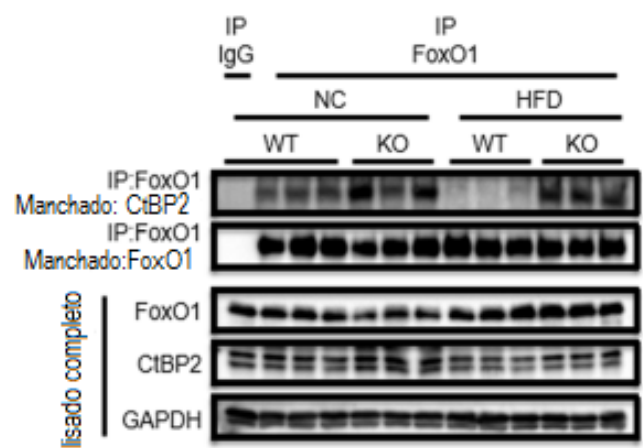


FIG. 36E

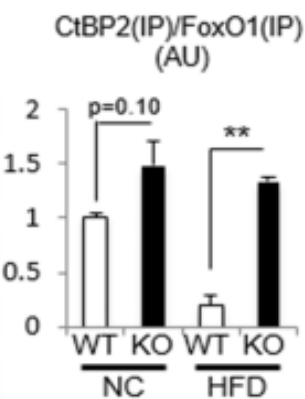


FIG. 36F

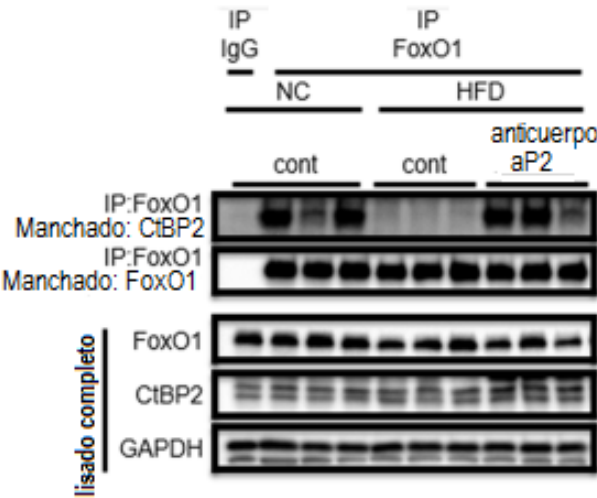


FIG. 36G

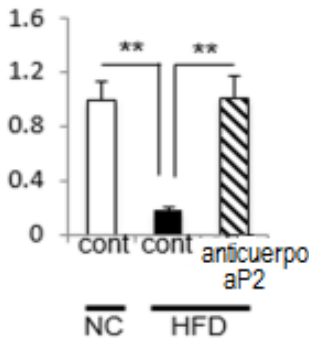


FIG. 36H

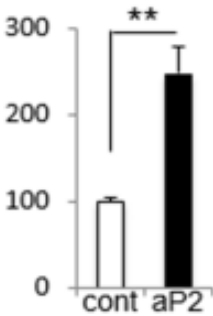


FIG. 36I

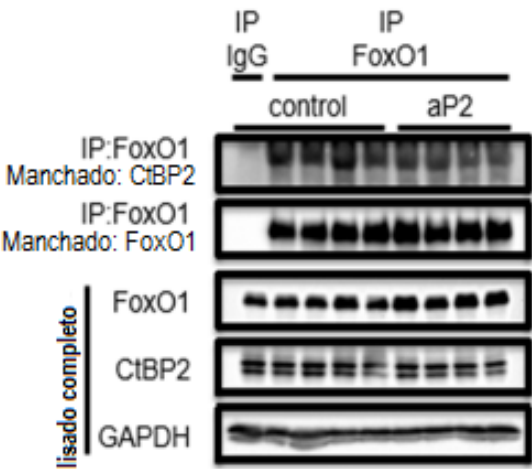


FIG. 36J

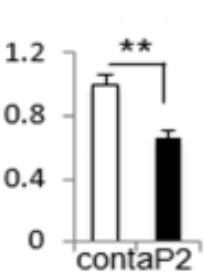


FIG. 36K

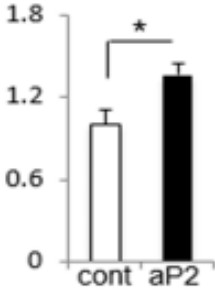


FIG. 36L

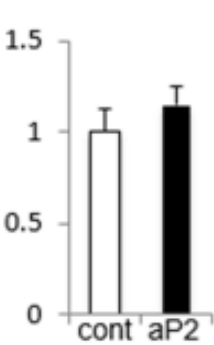


FIG. 36M

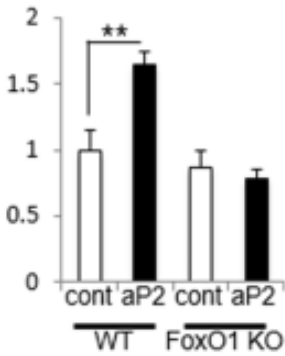


FIG. 36N

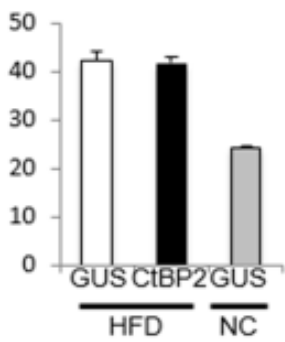


FIG. 37A

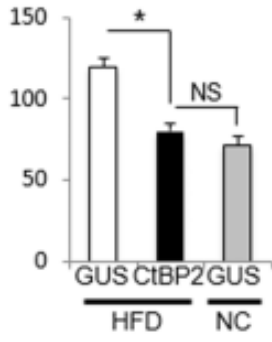


FIG. 37B

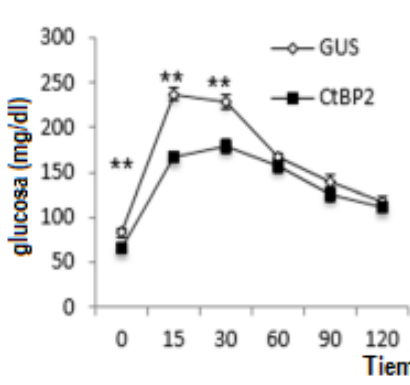


FIG. 37C

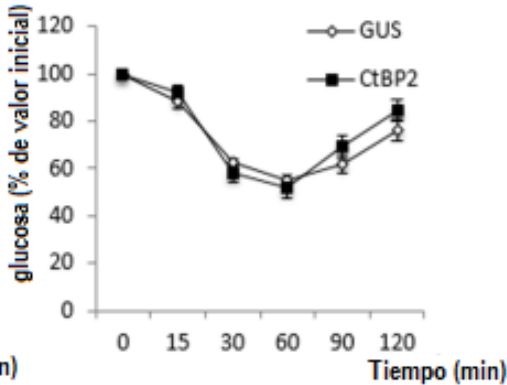


FIG. 37D

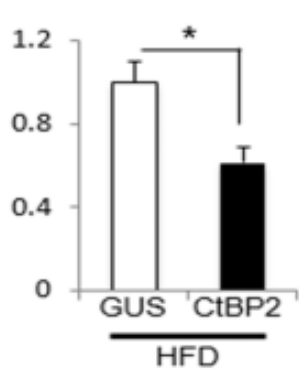


FIG. 37E

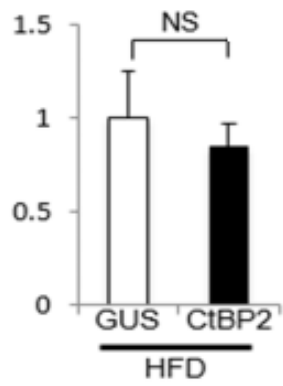


FIG. 37F

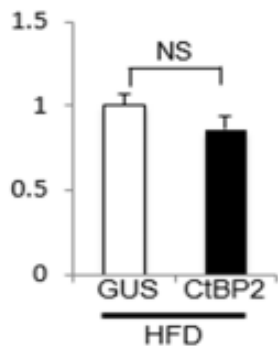


FIG. 37G

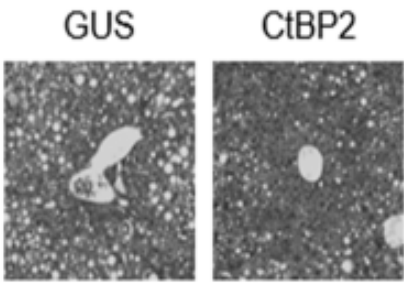


FIG. 37H

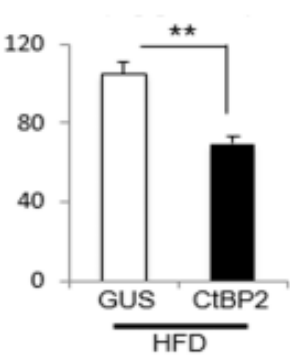


FIG. 37I

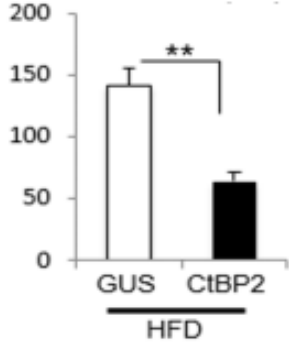


FIG. 37J

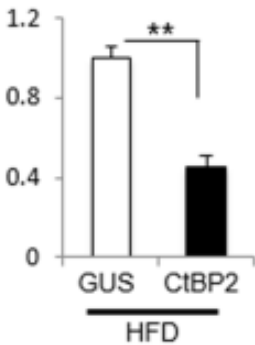


FIG. 37K

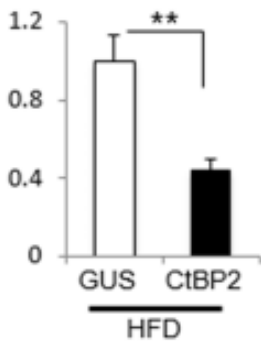


FIG. 37L

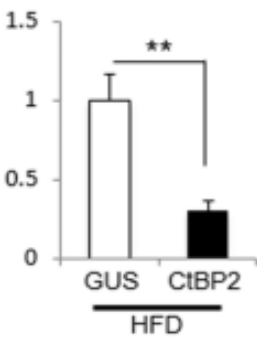


FIG. 37M

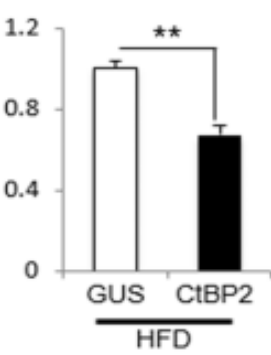


FIG. 37N

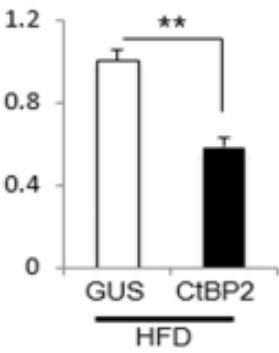


FIG. 37O

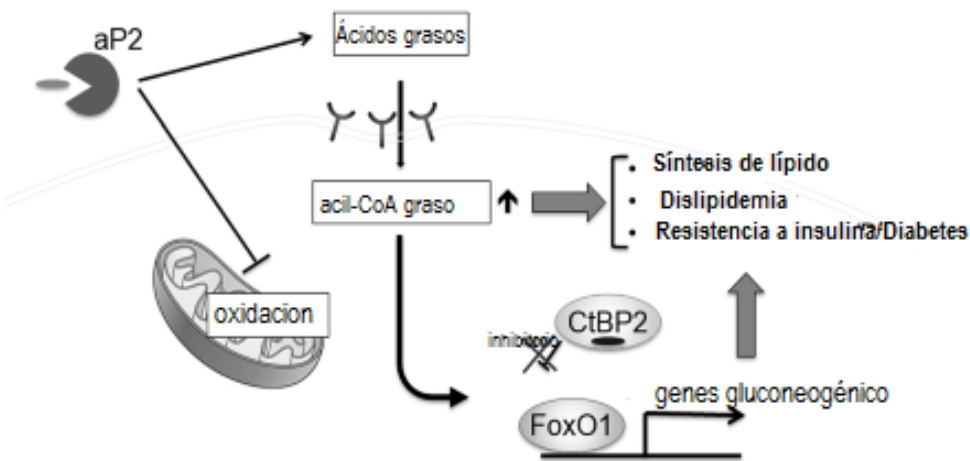


FIG. 37P

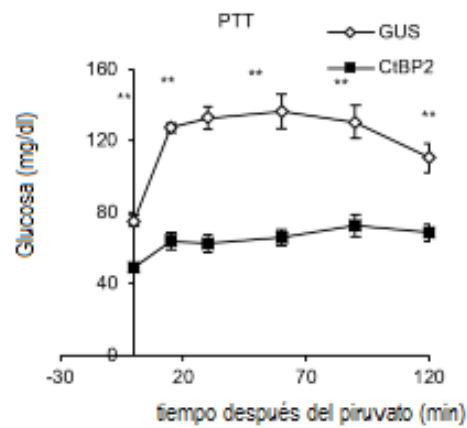


FIG. 37Q

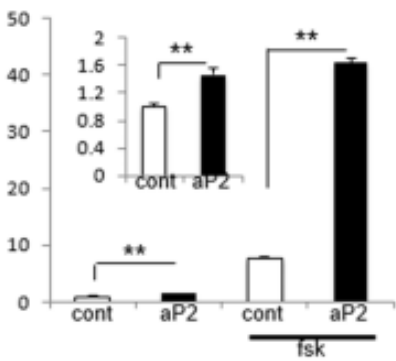


FIG. 38A

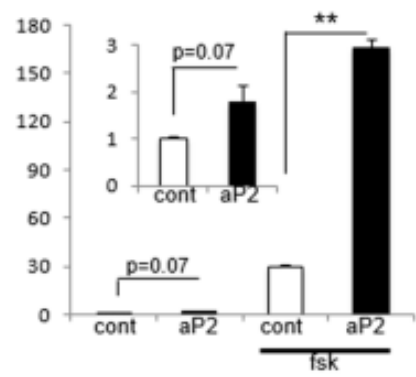


FIG. 38B

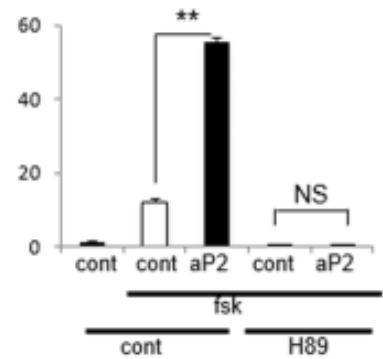


FIG. 38C

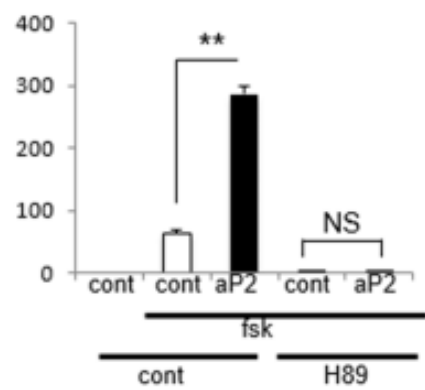


FIG. 38D

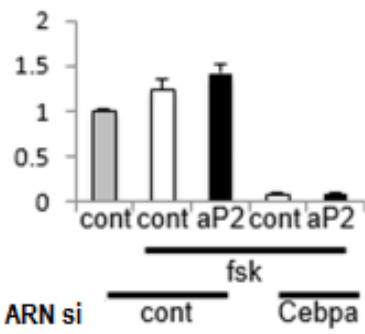


FIG. 39A

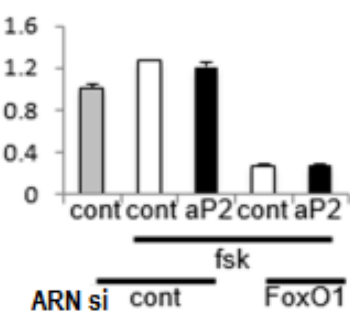


FIG. 39B

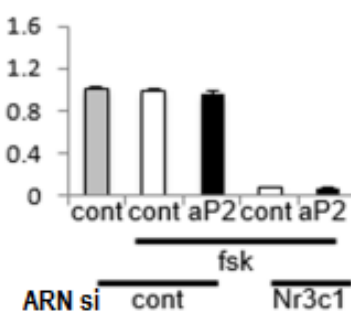


FIG. 39C

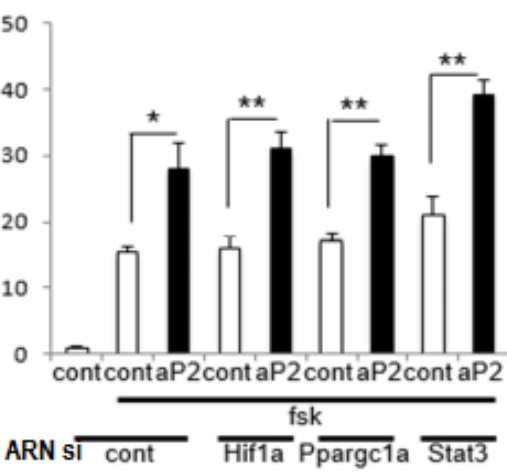


FIG. 39D

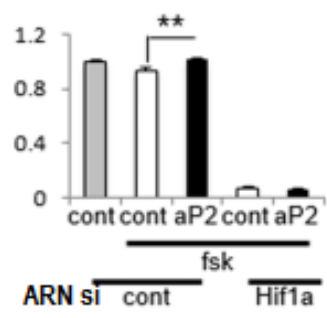


FIG. 39E

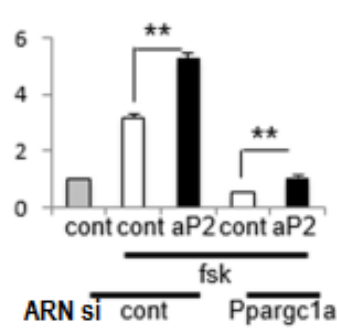


FIG. 39F

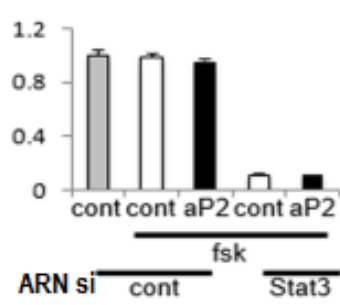


FIG. 39G

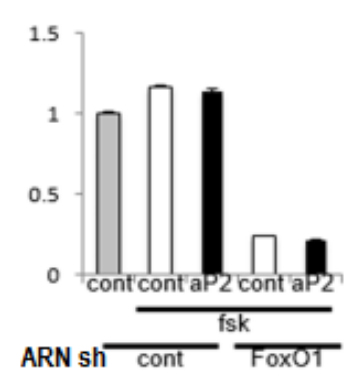


FIG. 39H

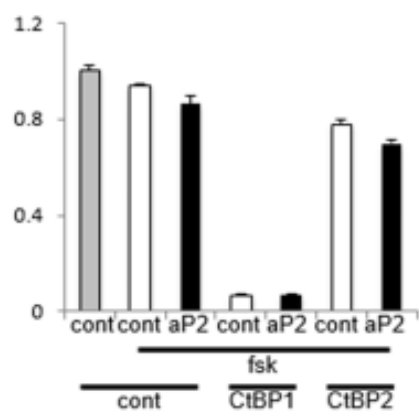


FIG. 40A

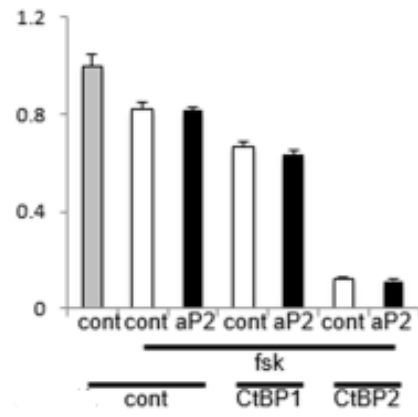


FIG. 40B

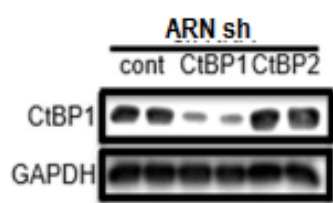


FIG. 40C

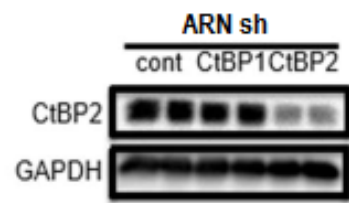


FIG. 40D

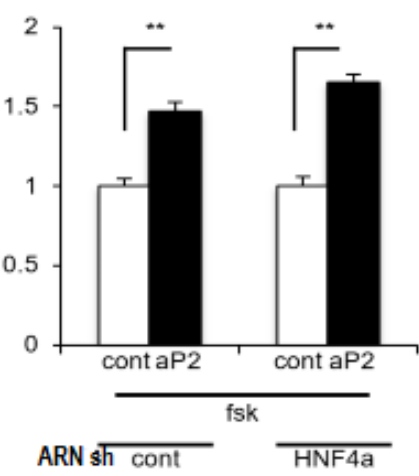


FIG. 40E

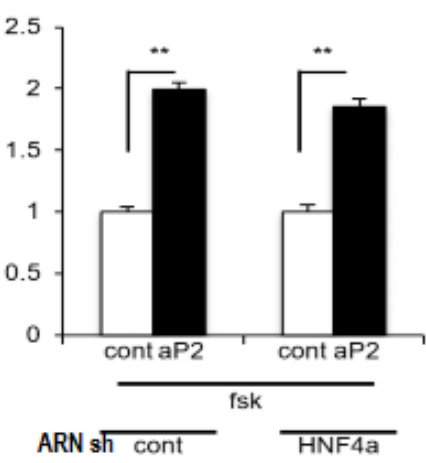


FIG. 40F

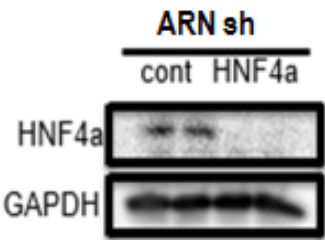
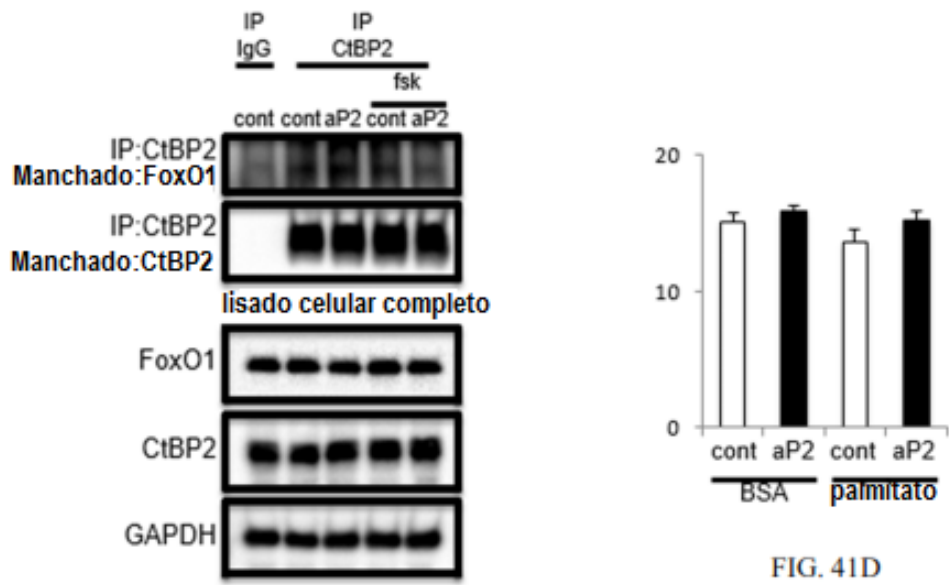
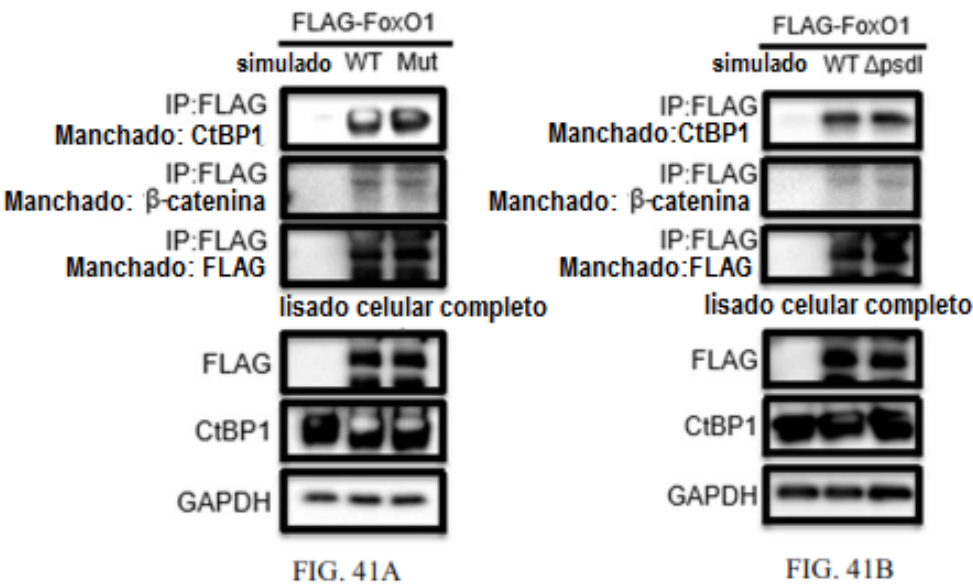


FIG. 40G



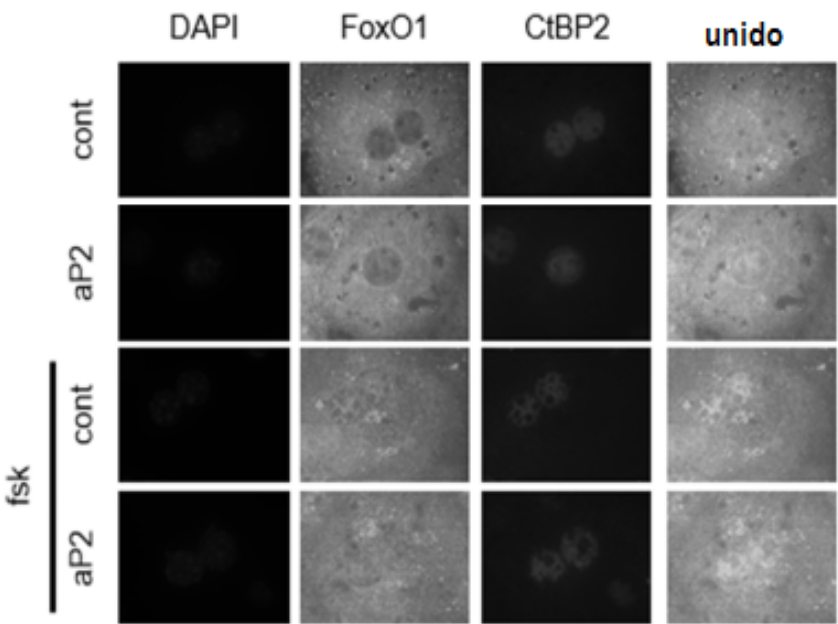


FIG. 41E

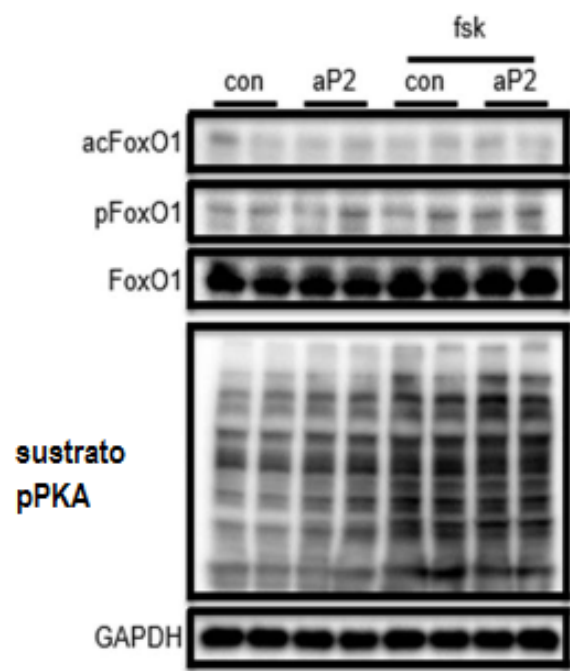


FIG. 41F

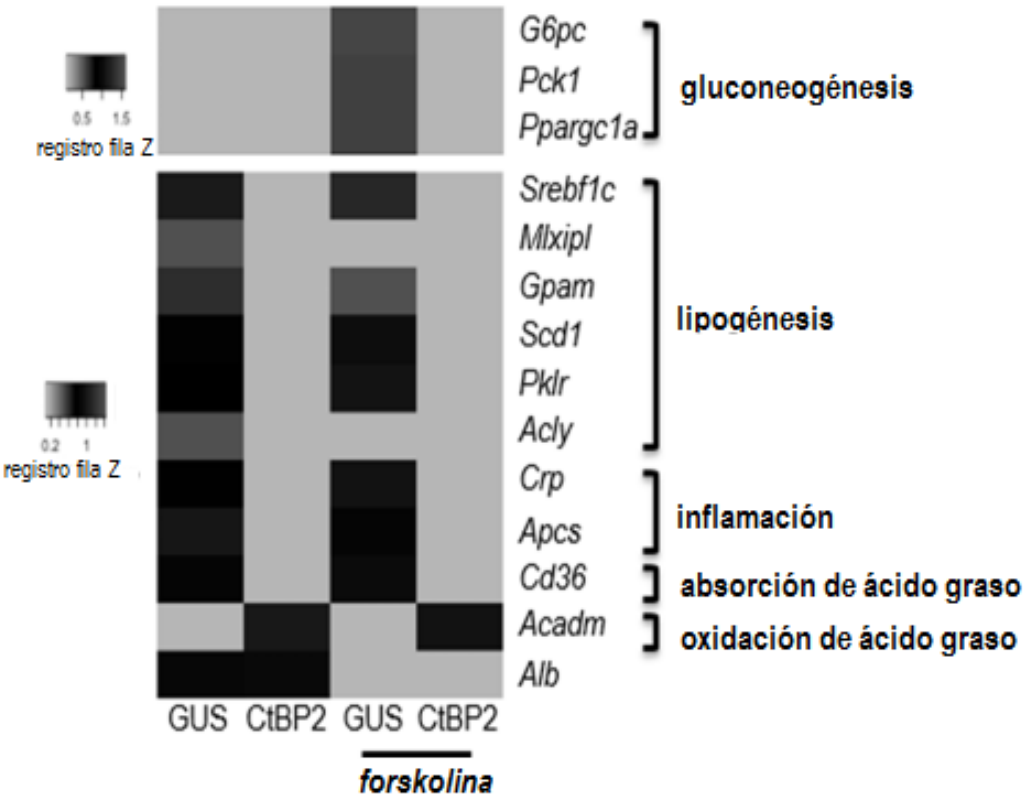


FIG. 42

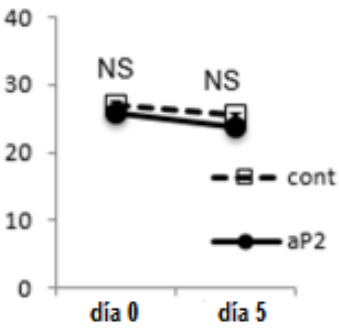


FIG. 43A

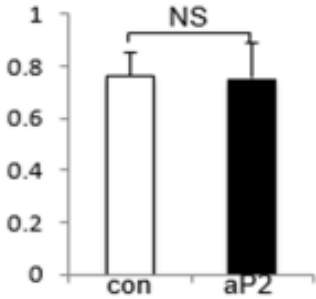


FIG. 43B

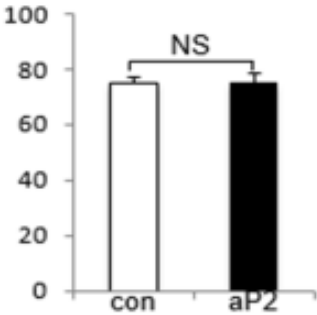


FIG. 43C

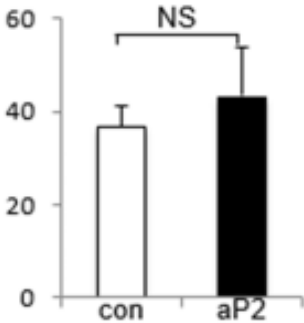


FIG. 43D

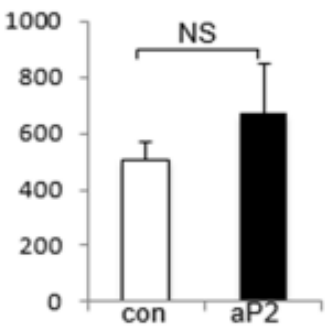


FIG. 43E

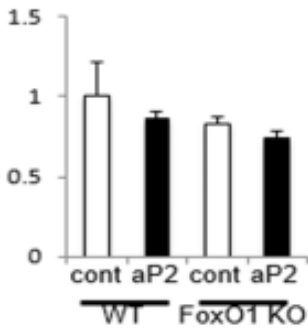


FIG. 43F

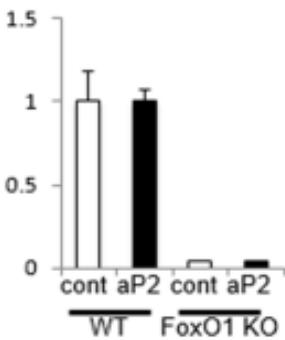


FIG. 43G

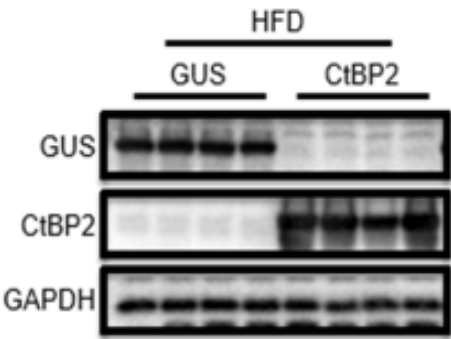


FIG. 44A

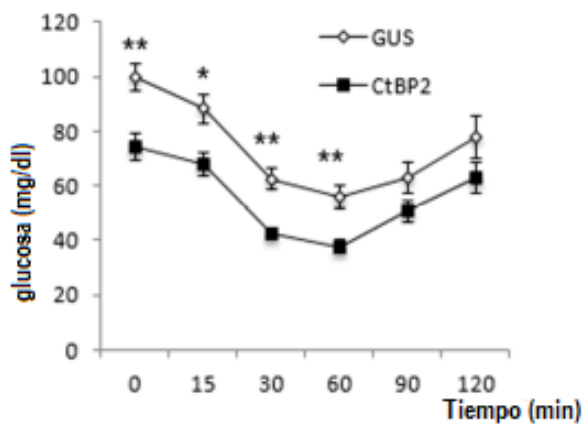


FIG. 44B

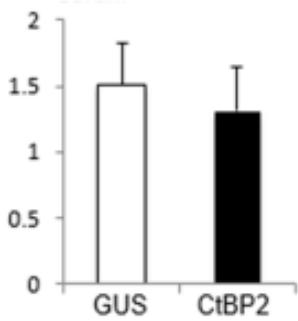


FIG. 44C

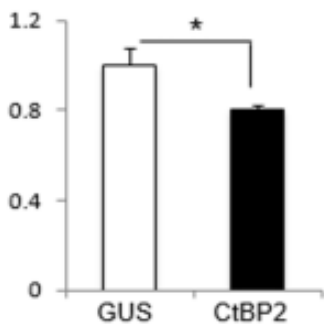


FIG. 45A

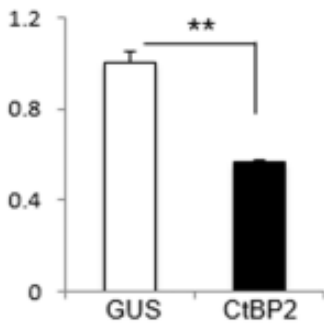


FIG. 45B

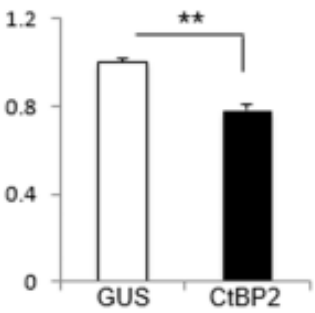


FIG. 45C

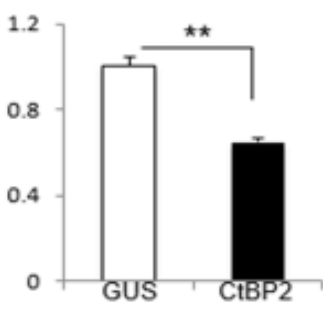


FIG. 45D

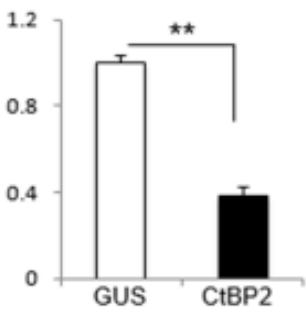


FIG. 45E

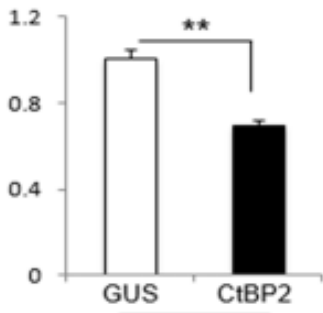


FIG. 45F

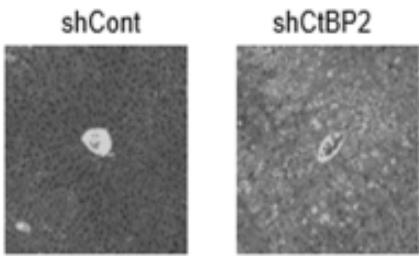


FIG. 45G

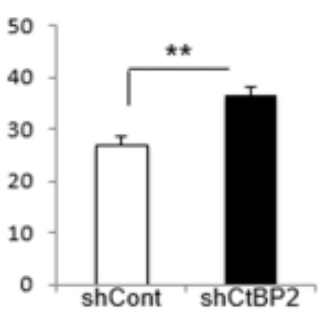


FIG. 45H

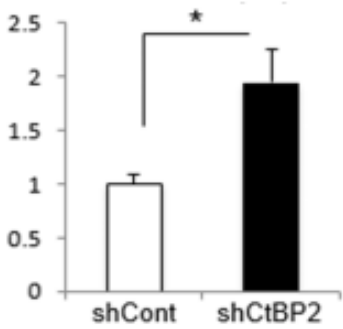


FIG. 45I

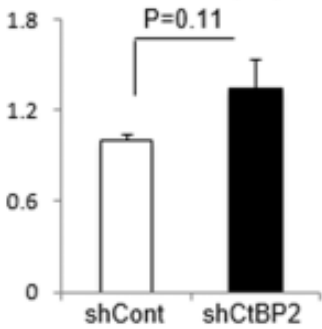


FIG. 45J

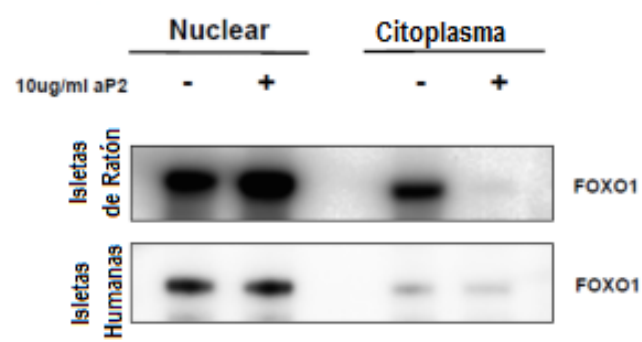


FIG. 46A

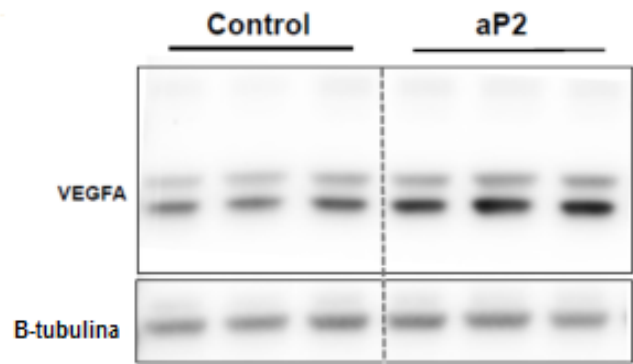


FIG. 46B

Expresión del gen objetivo FOXO1

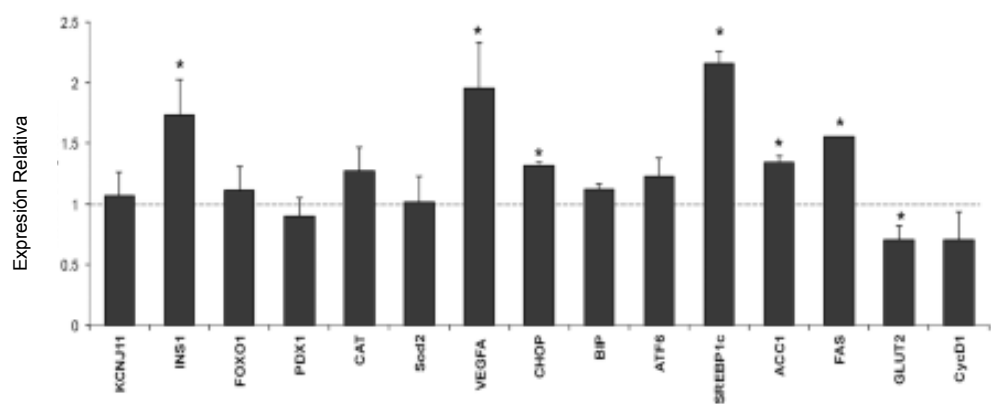


FIG. 46C

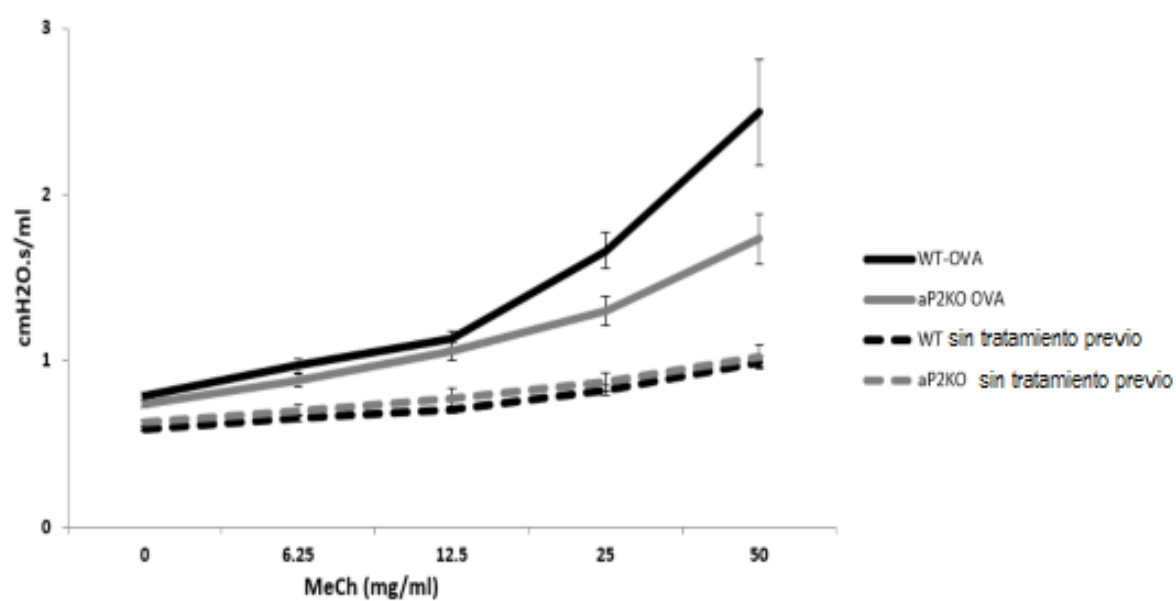


FIG. 47