FIG. 1A

SEQ ID NO: 1 (SLC25A13; Citrin, wt, isoform 1)

MAAAKVALTKRADPAELRTIFLKYASIEKNGEFFMSPNDFVTRYLNIFGESQPNPKTVE
LLSGVVDQTKDGLISFQEFVAFESVLCAPDALFMVAFQLFDKAGKGEVTFEDVKQVFGQ
TTIHQHIPFNWDSEFVQLHFGKERKRHLTYAEFTQFLLEIQLEHAKQAFVQRDNARTGR
VTAIDFRDIMVTIRPHVLTPFVEECLVAAAGGTTSHQVSFSYFNGFNSLLNNMELIRKI
YSTLAGTRKDVEVTKEEFVLAAQKFGQVTPMEVDILFQLADLYEPRGRMTLADIERIAP
LEEGTLPFNLAEAQRQKASGDSARPVLLQVAESAYRFGLGSVAGAVGATAVYPIDLVKT
RMQNQRSTGSFVGELMYKNSFDCFKKVLRYEGFFGLYRGLLPQLLGVAPEKAIKLTVND
FVRDKFMHKDGSVPLAAEILAGGCAGGSQVIFTNPLEIVKIRLQVAGEITTGPRVSALS
VVRDLGFFGIYKGAKACFLRDIPFSAIYFPCYAHVKASFANEDGQVSPGSLLLAGAIAG
MPAASLVTPADVIKTRLQVAARAGQTTYSGVIDCFRKILREEGPKALWKGAGARVFRSS
PQFGVTLLTYELLQRWFYIDFGGVKPMGSEPVPKSRINLPAPNPDHVGGYKLAVATFAG
IENKFGLYLPLFKPSVSTSKAIGGGP

See Calcium-binding mitochondrial carrier protein Aralar2, Uniprot Acc. No. Q9UJS0. This is the 'canonical' sequence. All positional information in related variants and isoforms refer to it.

FIG. 1B

Feature	Position	Length	Description
Initiator Methionine	1	1	Removed
Calcium binding	66 – 77	12	Calcium binding site 1
Calcium binding	100 – 111	12	Calcium binding site 2
Calcium binding	171 – 182	12	Calcium binding site 3
Transmembrane	332 – 349	18	Helical
Transmembrane	393 – 412	20	Helical
Transmembrane	436 – 449	14	Helical
Transmembrane	485 – 504	20	Helical
Transmembrane	524 – 541	18	Helical
Transmembrane	581 – 600	20	Helical
Domain	51 – 86	36	EF-hand 1
Domain	87 – 122	36	EF-hand 2
Domain	125 – 157	33	EF-hand 3
Domain	158 – 193	36	EF-hand 4
Repeat	326 – 418	93	Solcar 1
Repeat	426 – 510	85	Solcar 2
Repeat	518 – 606	89	Solcar 3

All positional information refers to the 'canonical' sequence

FIG. 1C

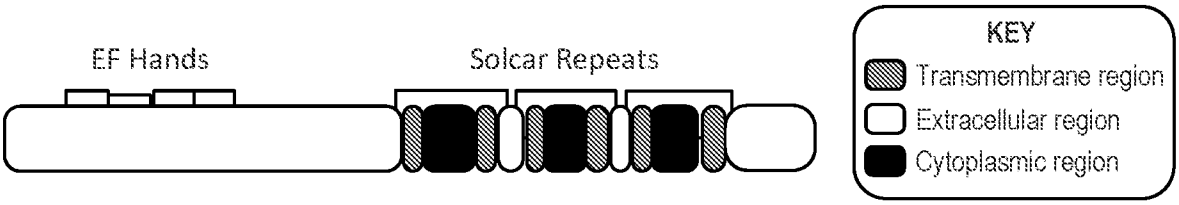


FIG. 1D

D. SEQ ID NO: 2

ATGGCGGCCGCCAAGGTGGCTTTAACCAAGAGAGCAGATCCAGCTGAGCTTAGAACAATATTTTTGA
AGTATGCAAGCATTGAGAAAAACGGTGAATTTTTCATGTCCCCCAATGACTTTGTCACTCGATACTT
GAACATTTTTGGAGAAAGCCAGCCTAATCCAAAGACTGTGGAACTTTTAAGTGGAGTGGTGGATCAG
ACCAAAGATGGATTAATATCTTTTCAAGAATTTGTTGCCTTTGAATCTGTCCTGTGTGCCCCTGATG
CTTTGTTTATGGTAGCCTTTCAGCTGTTTGACAAAGCTGGCAAAGGAGAAGTAACTTTTGAGGATGT
TAAGCAAGTTTTTGGACAGACCACAATTCATCAACATATTCCATTTAACTGGGATTCAGAATTTGTG
CAACTACATTTTGGAAAAGAAAGAAAAAGACACCTGACATATGCGGAATTTACTCAGTTTTTATTGG
AAATACAACTGGAGCACGCAAAGCAAGCCTTTGTGCAACGGGACAATGCTAGGACTGGGAGAGTCAC
AGCCATCGACTTCCGAGACATCATGGTCACCATCCGCCCCCATGTCTTGACTCCTTTTGTAGAAGAA
TGTCTAGTAGCTGCTGCTGGAGGTACCACATCCCATCAAGTTAGTTTCTCCTATTTTAATGGATTTA
ATTCGCTCCTTAACAACATGGAACTCATTAGAAAGATCTATAGCACTCTGGCTGGCACCAGGAAAGA
TGTTGAAGTGACTAAGGAGGAGTTTGTTCTGGCAGCTCAGAAATTTGGTCAGGTTACACCCATGGAA
GTTGACATCTTGTTTCAGTTAGCAGATTTATATGAGCCAAGGGGACGTATGACCTTAGCAGACATTG
AACGGATTGCTCCTCTGGAAGAGGGAACTCTGCCCTTTAACTTGGCTGAGGCCCAGAGGCAGAAGGC
CTCAGGTGATTCAGCTCGACCAGTTCTTCTACAAGTTGCAGAGTCGGCCTACAGGTTTGGTCTGGGT
TCTGTTGCTGGAGCTGTTGGAGCCACTGCTGTGTATCCTATCGATCTTGTAAAAACTCGAATGCAGA
ACCAACGATCAACTGGCTCTTTTGTGGGAGAACTCATGTATAAAAACAGCTTTGACTGTTTTAAGAA
AGTGCTACGCTATGAAGGCTTCTTTGGACTGTATAGAGGTCTGTTGCCACAGTTATTGGGAGTTGCC
CCAGAGAAGGCCATAAAACTTACAGTGAACGATTTTGTGAGGGATAAATTTATGCACAAAGATGGTT
CGGTCCCACTTGCAGCAGAAATTCTTGCTGGAGGCTGCGCTGGAGGCTCCCAGGTGATTTTCACAAA
TCCTTTAGAAATCGTCAAGATCCGTTTGCAAGTGGCAGGAGAAATCACCACTGGTCCTCGAGTCAGT
GCTCTGTCTGTCGTGCGGGACCTGGGGTTTTTTGGGATCTACAAGGGTGCCAAAGCATGCTTTCTGC
GGGACATTCCTTTCTCGGCCATCTACTTTCCGTGCTATGCTCATGTGAAGGCTTCCTTTGCAAATGA
AGATGGGCAGGTTAGCCCAGGAAGCCTGCTCTTAGCTGGTGCCATAGCTGGTATGCCTGCAGCATCT
TTAGTGACCCCTGCTGATGTTATCAAGACGAGATTACAGGTGGCTGCCCGGGCTGGCCAAACCACTT
ACAGCGGAGTGATAGACTGCTTTAGAAAGATACTGCGTGAAGAAGGACCAAAAGCTCTGTGGAAGGG
AGCTGGTGCTCGTGTATTTCGATCCTCACCCCAGTTTGGTGTAACTTTGCTGACTTACGAATTGCTA
CAGCGATGGTTCTACATTGATTTTGGAGGAGTAAAACCCATGGGATCAGAGCCAGTTCCTAAATCCA
GGATCAACCTGCCTGCCCCGAATCCTGATCACGTTGGGGGCTACAAACTGGCAGTTGCTACATTTGC
AGGGATTGAAAACAAATTTGGACTTTACCTACCTCTCTTCAAGCCATCAGTATCTACCTCAAAGGCT
ATTGGTGGAGGCCCA

FIG. 2A

SEQ ID NO: 3 (SLC25A13 ; Citrin, wt, isoform 2)

MAAAKVALTKRADPAELRTIFLKYASIEKNGEFFMSPNDFVTRYLNIFGESQPNPKTVE
LLSGVVDQTKDGLISFQEFVAFESVLCAPDALFMVAFQLFDKAGKGEVTFEDVKQVFGQ
TTIHQHIPFNWDSEFVQLHFGKERKRHLTYAEFTQFLLEIQLEHAKQAFVQRDNARTGR
VTAIDFRDIMVTIRPHVLTPFVEECLVAAAGGTTSHQVSFSYFNGFNSLLNNMELIRKI
YSTLAGTRKDVEVTKEEFVLAAQKFGQVTPMEVDILFQLADLYEPRGRMTLADIERIAP
LEEGTLPFNLAEAQRQQKASGDSARPVLLQVAESAYRFGLGSVAGAVGATAVYPIDLVK
TRMQNQRSTGSFVGELMYKNSFDCFKKVLRYEGFFGLYRGLLPQLLGVAPEKAIKLTVN
DFVRDKFMHKDGSVPLAAEILAGGCAGGSQVIFTNPLEIVKIRLQVAGEITTGPRVSAL
SVVRDLGFFGIYKGAKACFLRDIPFSAIYFPCYAHVKASFANEDGQVSPGSLLLAGAIA
GMPAASLVTPADVIKTRLQVAARAGQTTYSGVIDCFRKILREEGPKALWKGAGARVFRS
SPQFGVTLLTYELLQRWFYIDFGGVKPMGSEPVPKSRINLPAPNPDHVGGYKLAVATFA
GIENKFGLYLPLFKPSVSTSKAIGGGP

See Calcium-binding mitochondrial carrier protein Aralar2, Uniprot Acc. No. Q9UJS0-2. The sequence of this isoform differs from the canonical sequence as follows: 311-311: Q → QQ

FIG. 2B

Feature	Position	Length	Description
Initiator Methionine	1	1	Removed
Calcium binding	66 – 77	12	Calcium binding site 1
Calcium binding	100 – 111	12	Calcium binding site 2
Calcium binding	171 – 182	12	Calcium binding site 3
Transmembrane	332 – 349	18	Helical
Transmembrane	393 – 412	20	Helical
Transmembrane	436 – 449	14	Helical
Transmembrane	485 – 504	20	Helical
Transmembrane	524 – 541	18	Helical
Transmembrane	581 – 600	20	Helical
Domain	51 – 86	36	EF-hand 1
Domain	87 – 122	36	EF-hand 2
Domain	125 – 157	33	EF-hand 3
Domain	158 – 193	36	EF-hand 4
Repeat	326 – 418	93	Solcar 1
Repeat	426 – 510	85	Solcar 2
Repeat	518 – 606	89	Solcar 3

FIG. 2C

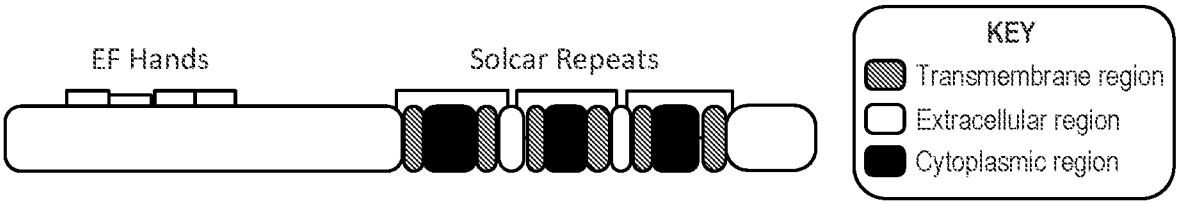


FIG. 2D

D. SEQ ID NO: 4

ATGGCGGCCGCCAAGGTGGCTTTAACCAAGAGAGCAGATCCAGCTGAGCTTAGAACAATATTTTTGA
AGTATGCAAGCATTGAGAAAAACGGTGAATTTTTCATGTCCCCCAATGACTTTGTCACTCGATACTT
GAACATTTTTGGAGAAAGCCAGCCTAATCCAAAGACTGTGGAACTTTTAAGTGGAGTGGTGGATCAG
ACCAAAGATGGATTAATATCTTTTCAAGAATTTGTTGCCTTTGAATCTGTCCTGTGTGCCCCTGATG
CTTTGTTTATGGTAGCCTTTCAGCTGTTTGACAAAGCTGGCAAAGGAGAAGTAACTTTTGAGGATGT
TAAGCAAGTTTTTGGACAGACCACAATTCATCAACATATTCCATTTAACTGGGATTCAGAATTTGTG
CAACTACATTTTGGAAAAGAAAGAAAAAGACACCTGACATATGCGGAATTTACTCAGTTTTTATTGG
AAATACAACTGGAGCACGCAAAGCAAGCCTTTGTGCAACGGGACAATGCTAGGACTGGGAGAGTCAC
AGCCATCGACTTCCGAGACATCATGGTCACCATCCGCCCCCATGTCTTGACTCCTTTTGTAGAAGAA
TGTCTAGTAGCTGCTGCTGGAGGTACCACATCCCATCAAGTTAGTTTCTCCTATTTTAATGGATTTA
ATTCGCTCCTTAACAACATGGAACTCATTAGAAAGATCTATAGCACTCTGGCTGGCACCAGGAAAGA
TGTTGAAGTGACTAAGGAGGAGTTTGTTCTGGCAGCTCAGAAATTTGGTCAGGTTACACCCATGGAA
GTTGACATCTTGTTTCAGTTAGCAGATTTATATGAGCCAAGGGGACGTATGACCTTAGCAGACATTG
AACGGATTGCTCCTCTGGAAGAGGGAACTCTGCCCTTTAACTTGGCTGAGGCCCAGAGGCAGCAGAA
GGCCTCAGGTGATTCAGCTCGACCAGTTCTTCTACAAGTTGCAGAGTCGGCCTACAGGTTTGGTCTG
GGTTCTGTTGCTGGAGCTGTTGGAGCCACTGCTGTGTATCCTATCGATCTTGTAAAAACTCGAATGC
AGAACCAACGATCAACTGGCTCTTTTGTGGGAGAACTCATGTATAAAAACAGCTTTGACTGTTTTAA
GAAAGTGCTACGCTATGAAGGCTTCTTTGGACTGTATAGAGGTCTGTTGCCACAGTTATTGGGAGTT
GCCCCAGAGAAGGCCATAAAACTTACAGTGAACGATTTTGTGAGGGATAAATTTATGCACAAAGATG
GTTCGGTCCCACTTGCAGCAGAAATTCTTGCTGGAGGCTGCGCTGGAGGCTCCCAGGTGATTTTCAC
AAATCCTTTAGAAATCGTCAAGATCCGTTTGCAAGTGGCAGGAGAAATCACCACTGGTCCTCGAGTC
AGTGCTCTGTCTGTCGTGCGGGACCTGGGGTTTTTTGGGATCTACAAGGGTGCCAAAGCATGCTTTC
TGCGGGACATTCCTTTCTCGGCCATCTACTTTCCGTGCTATGCTCATGTGAAGGCTTCCTTTGCAAA
TGAAGATGGGCAGGTTAGCCCAGGAAGCCTGCTCTTAGCTGGTGCCATAGCTGGTATGCCTGCAGCA
TCTTTAGTGACCCCTGCTGATGTTATCAAGACGAGATTACAGGTGGCTGCCCGGGCTGGCCAAACCA
CTTACAGCGGAGTGATAGACTGCTTTAGAAAGATACTGCGTGAAGAAGGACCAAAAGCTCTGTGGAA
GGGAGCTGGTGCTCGTGTATTTCGATCCTCACCCCAGTTTGGTGTAACTTTGCTGACTTACGAATTG
CTACAGCGATGGTTCTACATTGATTTTGGAGGAGTAAAACCCATGGGATCAGAGCCAGTTCCTAAAT
CCAGGATCAACCTGCCTGCCCCGAATCCTGATCACGTTGGGGGCTACAAACTGGCAGTTGCTACATT
TGCAGGGATTGAAAACAAATTTGGACTTTACCTACCTCTCTTCAAGCCATCAGTATCTACCTCAAAG
GCTATTGGTGGAGGCCCA

Protein	Length	Theoretical Minimum U (%)	Theoretical Minimum U (abs)							
Citrin Protein	675	14.22%	288							
Nucleic Acid	Length	U Content (abs)	U Content (%)	U Content v WT (%)	U Content v Theoretical Minimum (%)	UU pairs	UU pairs v WT (%)	UUU	UUUU	UUUUU
Citrin-WT	2025	562	27.75%	100.00%	195.14%	61	100.00%	37	11	5
Citrin-CO01	2025	343	16.94%	61.03%	119.10%	43	70.49%	10	3	0
Citrin-CO02	2025	342	16.89%	60.85%	118.75%	47	77.05%	6	1	0
Citrin-CO03	2025	352	17.38%	62.63%	122.22%	41	67.21%	13	0	0
Citrin-CO04	2025	346	17.09%	61.57%	120.14%	45	73.77%	10	1	0
Citrin-CO05	2025	346	17.09%	61.57%	120.14%	42	68.85%	12	0	2
Citrin-CO06	2025	348	17.19%	61.92%	120.83%	42	68.85%	10	1	1
Citrin-CO07	2025	347	17.14%	61.74%	120.49%	43	70.49%	12	1	0
Citrin-CO08	2025	359	17.73%	63.88%	124.65%	42	68.85%	11	0	1
Citrin-CO09	2025	356	17.58%	63.35%	123.61%	42	68.85%	9	2	1
Citrin-CO10	2025	356	17.58%	63.35%	123.61%	34	55.74%	12	4	2
Citrin-CO11	2025	339	16.74%	60.32%	117.71%	40	65.57%	7	2	1
Citrin-CO12	2025	363	17.93%	64.59%	126.04%	52	85.25%	8	1	0
Citrin-CO13	2025	355	17.53%	63.17%	123.26%	45	73.77%	10	0	1
Citrin-CO14	2025	343	16.94%	61.03%	119.10%	48	78.69%	7	1	0
Citrin-CO15	2025	339	16.74%	60.32%	117.71%	48	78.69%	1	3	2
Citrin-CO16	2025	357	17.63%	63.52%	123.96%	49	80.33%	11	1	0
Citrin-CO17	2025	349	17.23%	62.10%	121.18%	45	73.77%	8	2	0
Citrin-CO18	2025	350	17.28%	62.28%	121.53%	40	65.57%	14	1	2
Citrin-CO19	2025	342	16.89%	60.85%	118.75%	46	75.41%	8	1	0
Citrin-CO20	2025	342	16.89%	60.85%	118.75%	40	65.57%	14	1	0
Citrin-CO21	2025	344	16.99%	61.21%	119.44%	42	68.85%	9	0	0
Citrin-CO22	2025	348	17.19%	61.92%	120.83%	50	81.97%	5	1	0
Citrin-CO23	2025	339	16.74%	60.32%	117.71%	43	70.49%	11	1	0
Citrin-CO24	2025	344	16.99%	61.21%	119.44%	45	73.77%	10	0	1
Citrin-CO25	2025	345	17.04%	61.39%	119.79%	41	67.21%	13	1	0
	MAX	363	17.93%	64.59%	126.04%	52	85.25%	14	4	2
	MIN	339	16.74%	60.32%	117.71%	34	55.74%	1	0	0
	AVERAGE	347.76	17.17%	61.88%	120.75%	43.8	71.80%	9.64	1.16	0.56
	MEDIAN	346	17.09%	61.57%	120.14%	43	70.49%	10	1	0
	STD DEV	6.69	0.33%	1.19%	2.32%	3.88	6.37%			

FIG. 3

Protein	Length	Theoretical Maximum G (%)	Theoretical Maximum G (abs)		
Citrin Protein	675	42.27%	856		
Nucleic Acid	Length	G Content(abs)	G Content(%)	G Content v WT (%)	G Content v Theoretical Maximum (%)
Citrin-WT	2025	499	24.64%	100.00%	58.29%
Citrin-CO01	2025	634	31.31%	127.05%	74.07%
Citrin-CO02	2025	610	30.12%	122.24%	71.26%
Citrin-CO03	2025	620	30.62%	124.25%	72.43%
Citrin-CO04	2025	605	29.88%	121.24%	70.68%
Citrin-CO05	2025	614	30.32%	123.05%	71.73%
Citrin-CO06	2025	611	30.17%	122.44%	71.38%
Citrin-CO07	2025	627	30.96%	125.65%	73.25%
Citrin-CO08	2025	619	30.57%	124.05%	72.31%
Citrin-CO09	2025	612	30.22%	122.65%	71.50%
Citrin-CO10	2025	619	30.57%	124.05%	72.31%
Citrin-CO11	2025	622	30.72%	124.65%	72.66%
Citrin-CO12	2025	627	30.96%	125.65%	73.25%
Citrin-CO13	2025	631	31.16%	126.45%	73.71%
Citrin-CO14	2025	626	30.91%	125.45%	73.13%
Citrin-CO15	2025	611	30.17%	122.44%	71.38%
Citrin-CO16	2025	626	30.91%	125.45%	73.13%
Citrin-CO17	2025	612	30.22%	122.65%	71.50%
Citrin-CO18	2025	647	31.95%	129.66%	75.58%
Citrin-CO19	2025	619	30.57%	124.05%	72.31%
Citrin-CO20	2025	614	30.32%	123.05%	71.73%
Citrin-CO21	2025	620	30.62%	124.25%	72.43%
Citrin-CO22	2025	620	30.62%	124.25%	72.43%
Citrin-CO23	2025	625	30.86%	125.25%	73.01%
Citrin-CO24	2025	619	30.57%	124.05%	72.31%
Citrin-CO25	2025	643	31.75%	128.86%	75.12%
	MAX	647	31.95%	129.66%	75.58%
	MIN	605	29.88%	121.24%	70.68%
	MEAN	621.32	30.68%	124.51%	72.58%
	MEDIAN	620	30.62%	124.25%	72.43%
	STD DEV	10.04	0.50%	2.01%	1.17%

FIG. 4

Protein	Length	Theoretical Maximum C	Theoretical Maximum C (abs)		
Citrin Protein	675	44.49%	901		
Nucleic Acid	Length	C Content(abs)	C Content(%)	C Content v WT (%)	C Content v Theoretical Maximum (%)
Citrin-WT	2025	432	21.33%	100.00%	47.95%
Citrin-CO01	2025	652	32.20%	150.93%	72.36%
Citrin-CO02	2025	657	32.44%	152.08%	72.92%
Citrin-CO03	2025	640	31.60%	148.15%	71.03%
Citrin-CO04	2025	671	33.14%	155.32%	74.47%
Citrin-CO05	2025	671	33.14%	155.32%	74.47%
Citrin-CO06	2025	656	32.40%	151.85%	72.81%
Citrin-CO07	2025	639	31.56%	147.92%	70.92%
Citrin-CO08	2025	656	32.40%	151.85%	72.81%
Citrin-CO09	2025	652	32.20%	150.93%	72.36%
Citrin-CO10	2025	648	32.00%	150.00%	71.92%
Citrin-CO11	2025	657	32.44%	152.08%	72.92%
Citrin-CO12	2025	642	31.70%	148.61%	71.25%
Citrin-CO13	2025	628	31.01%	145.37%	69.70%
Citrin-CO14	2025	647	31.95%	149.77%	71.81%
Citrin-CO15	2025	668	32.99%	154.63%	74.14%
Citrin-CO16	2025	628	31.01%	145.37%	69.70%
Citrin-CO17	2025	647	31.95%	149.77%	71.81%
Citrin-CO18	2025	625	30.86%	144.68%	69.37%
Citrin-CO19	2025	646	31.90%	149.54%	71.70%
Citrin-CO20	2025	648	32.00%	150.00%	71.92%
Citrin-CO21	2025	650	32.10%	150.46%	72.14%
Citrin-CO22	2025	658	32.49%	152.31%	73.03%
Citrin-CO23	2025	655	32.35%	151.62%	72.70%
Citrin-CO24	2025	647	31.95%	149.77%	71.81%
Citrin-CO25	2025	628	31.01%	145.37%	69.70%
	MAX	671	33.14%	155.32%	74.47%
	MIN	625	30.86%	144.68%	69.37%
	AVERAGE	648.64	32.03%	150.15%	71.99%
	MEDIAN	648	32.00%	150.00%	71.92%
	STD DEV	12.65	0.62%	2.93%	1.40%

FIG. 5

Protein	Length	Theoretical Maximum GC	Theoretical Maximum GC (abs)		
Citrin Protein	675	67.70%	1371		
Nucleic Acid	Length	GC Content(abs)	GC Content(%)	GC Content v WT (%)	GC Content v Theoretical Maximum (%)
Citrin-WT	2025	931	45.98%	100.00%	67.81%
Citrin-CO01	2025	1286	63.51%	138.13%	93.80%
Citrin-CO02	2025	1267	62.57%	136.09%	92.41%
Citrin-CO03	2025	1260	62.22%	135.34%	91.90%
Citrin-CO04	2025	1276	63.01%	137.06%	93.07%
Citrin-CO05	2025	1285	63.46%	138.02%	93.73%
Citrin-CO06	2025	1267	62.57%	136.09%	92.41%
Citrin-CO07	2025	1266	62.52%	135.98%	92.34%
Citrin-CO08	2025	1275	62.96%	136.95%	93.00%
Citrin-CO09	2025	1264	62.42%	135.77%	92.20%
Citrin-CO10	2025	1267	62.57%	136.09%	92.41%
Citrin-CO11	2025	1279	63.16%	137.38%	93.29%
Citrin-CO12	2025	1269	62.67%	136.31%	92.56%
Citrin-CO13	2025	1259	62.17%	135.23%	91.83%
Citrin-CO14	2025	1273	62.86%	136.73%	92.85%
Citrin-CO15	2025	1279	63.16%	137.38%	93.29%
Citrin-CO16	2025	1254	61.93%	134.69%	91.47%
Citrin-CO17	2025	1259	62.17%	135.23%	91.83%
Citrin-CO18	2025	1272	62.81%	136.63%	92.78%
Citrin-CO19	2025	1265	62.47%	135.88%	92.27%
Citrin-CO20	2025	1262	62.32%	135.55%	92.05%
Citrin-CO21	2025	1270	62.72%	136.41%	92.63%
Citrin-CO22	2025	1278	63.11%	137.27%	93.22%
Citrin-CO23	2025	1280	63.21%	137.49%	93.36%
Citrin-CO24	2025	1266	62.52%	135.98%	92.34%
Citrin-CO25	2025	1271	62.77%	136.52%	92.71%
	MAX	1286	63.51%	138.13%	93.80%
	MIN	1254	61.93%	134.69%	91.47%
	AVERAGE	1269.96	62.71%	136.41%	92.63%
	MEDIAN	1269	62.67%	136.31%	92.56%
	STD DEV	8.33	0.41%	0.89%	0.61%

FIG. 6

FIG. 7

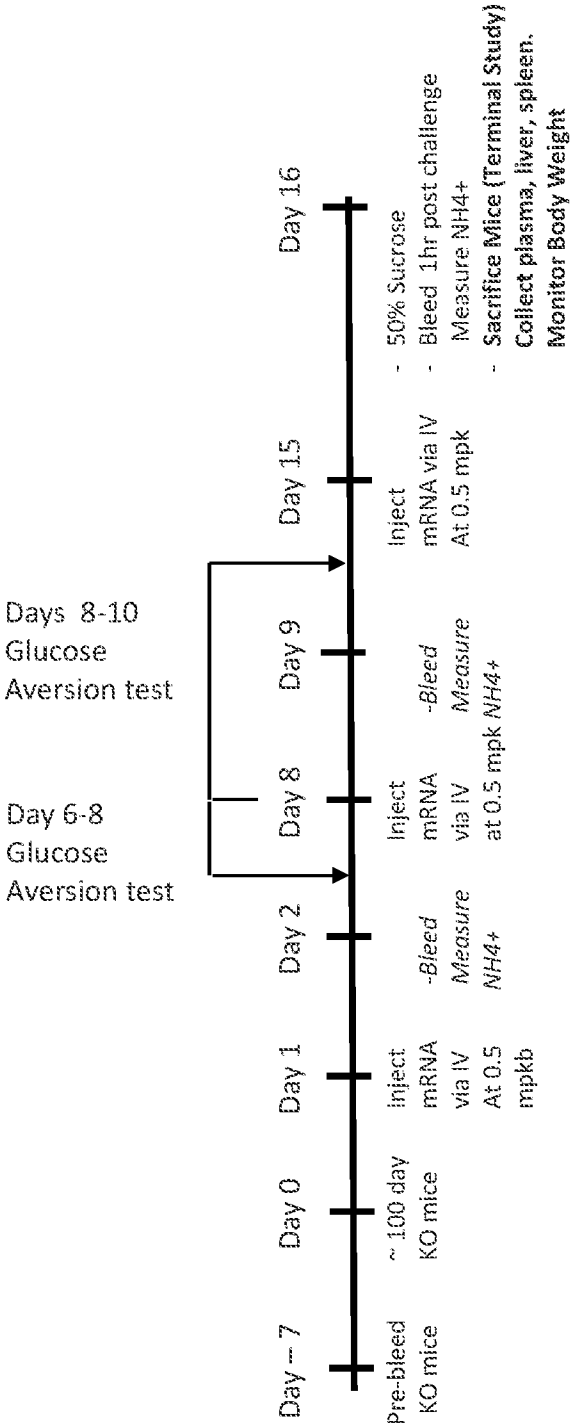

Day -- 7
Day 0
Day 1
Day 2
Day 8
Day 9
Day 15
Day 16
Pre-bleed KO mice
~ 100 day KO mice
Inject mRNA via IV At 0.5 mpkb
-Bleed Measure NH4+
Inject mRNA via IV at 0.5 mpk
-Bleed Measure NH4+
Inject mRNA via IV At 0.5 mpk
- 50% Sucrose
- Bleed 1hr post challenge
- Measure NH4+
- Sacrifice Mice (Terminal Study) Collect plasma, liver, spleen. Monitor Body Weight
Days 8-10 Glucose Aversion test
Day 6-8 Glucose Aversion test

FIG. 8

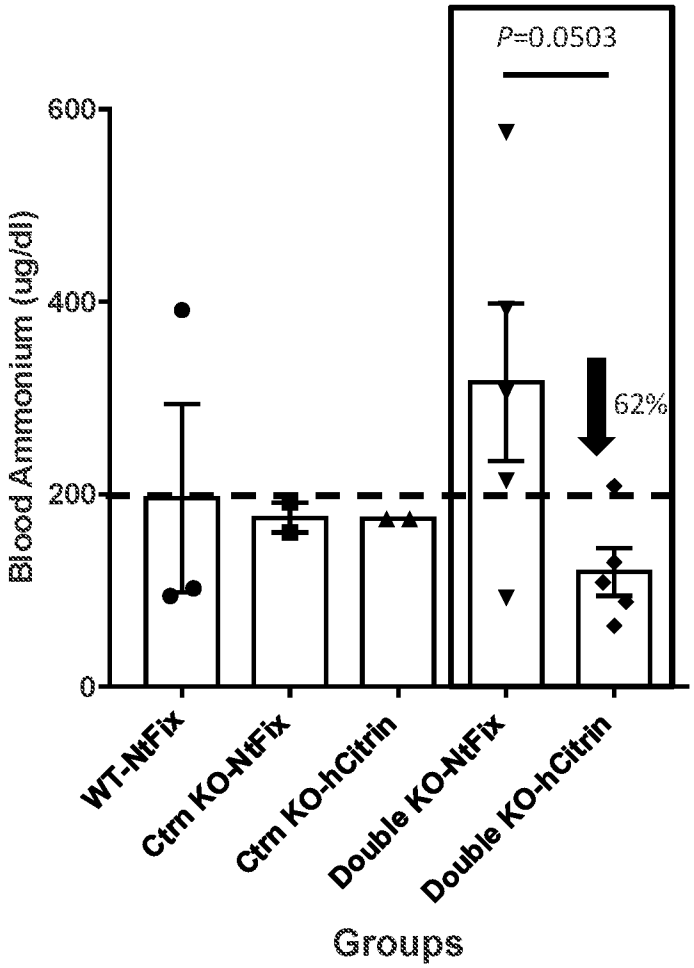
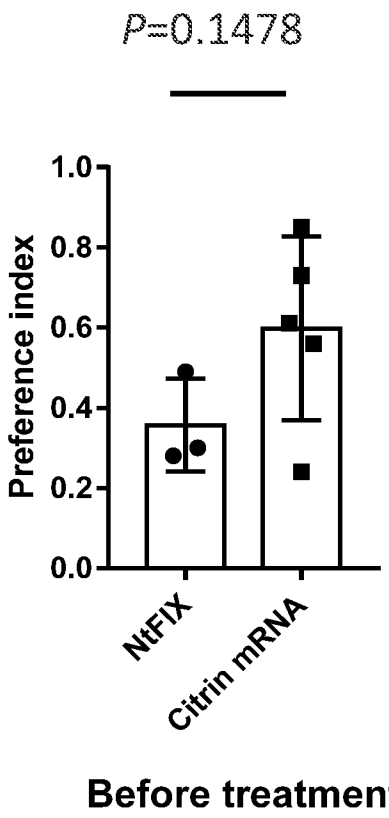
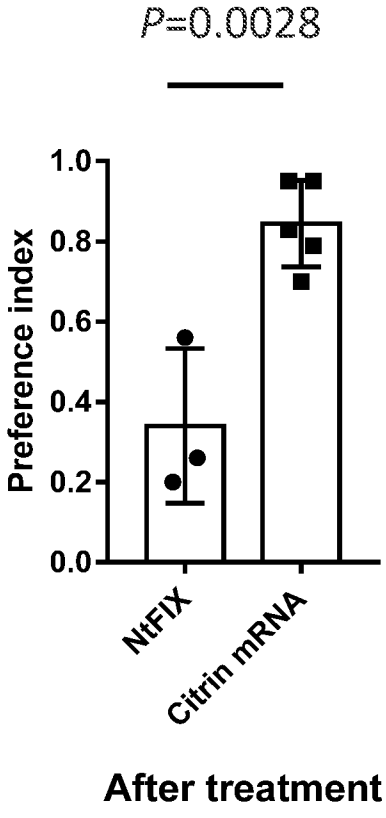

P=0.0503
600
400
200
0
Blood Ammonium (ug/dl)
62%
WT-NtFix
Ctrn KO-NtFix
Ctrn KO-hCitrin
Double KO-NtFix
Double KO-hCitrin
Groups

FIG. 9A



Before treatment

FIG. 9B



After treatment

FIG. 10

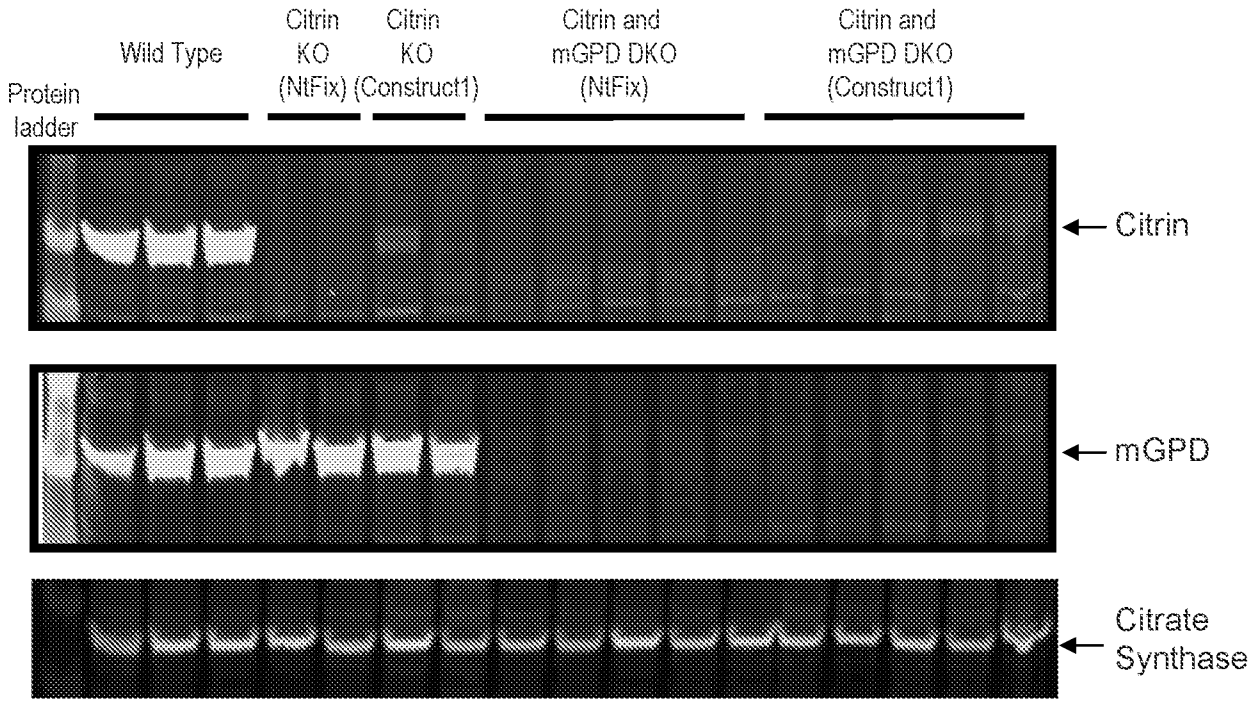

Protein ladder
Wild Type
Citrin KO (NtFix)
Citrin KO (Construct1)
Citrin and mGPD DKO (NtFix)
Citrin and mGPD DKO (Construct1)
Citrin
mGPD
Citrate Synthase

FIG. 11

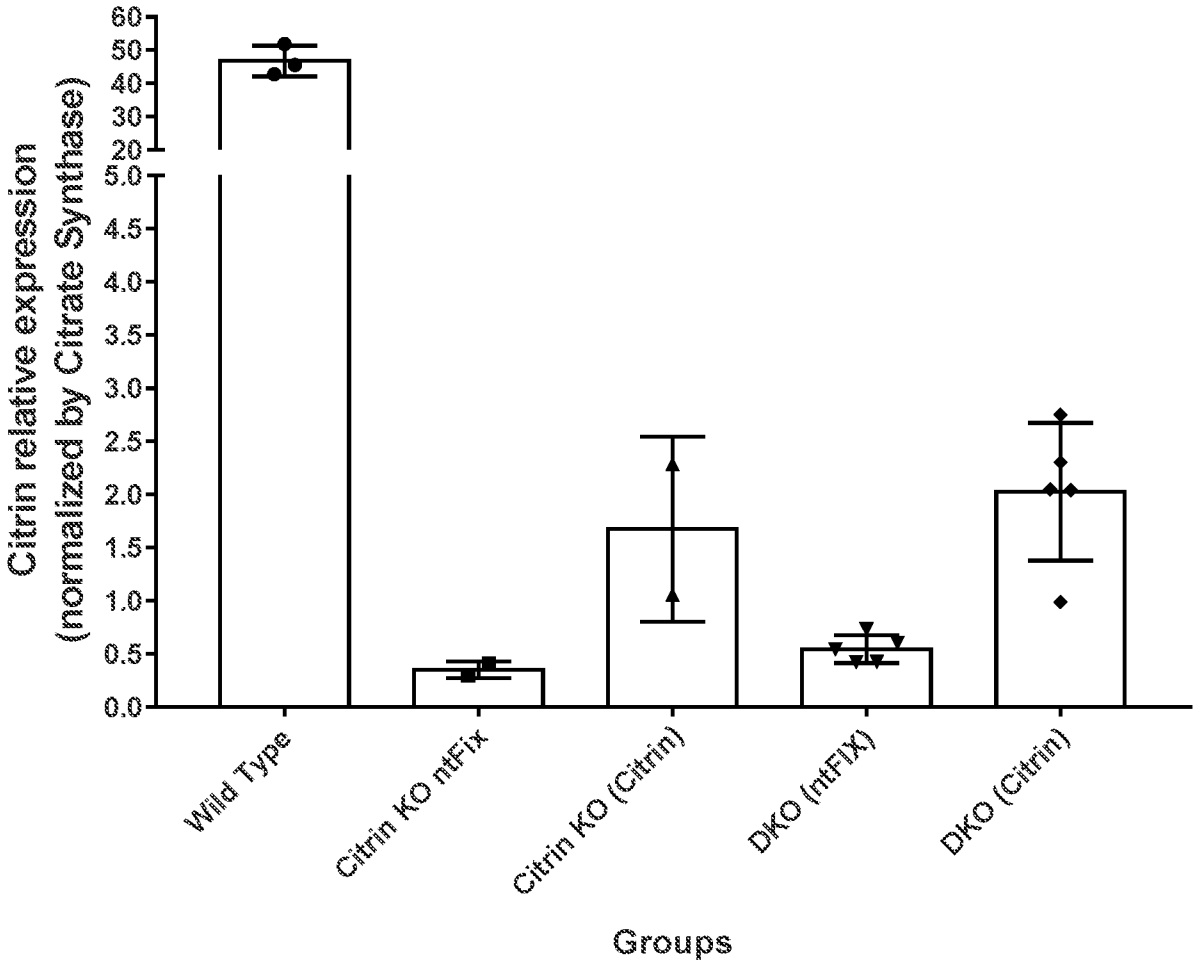

Citrin relative expression
(normalized by Citrate Synthase)
60
50
40
30
20
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
Wild Type
Citrin KO ntFix
Citrin KO (Citrin)
DKO (ntFIX)
DKO (Citrin)
Groups

FIG. 12

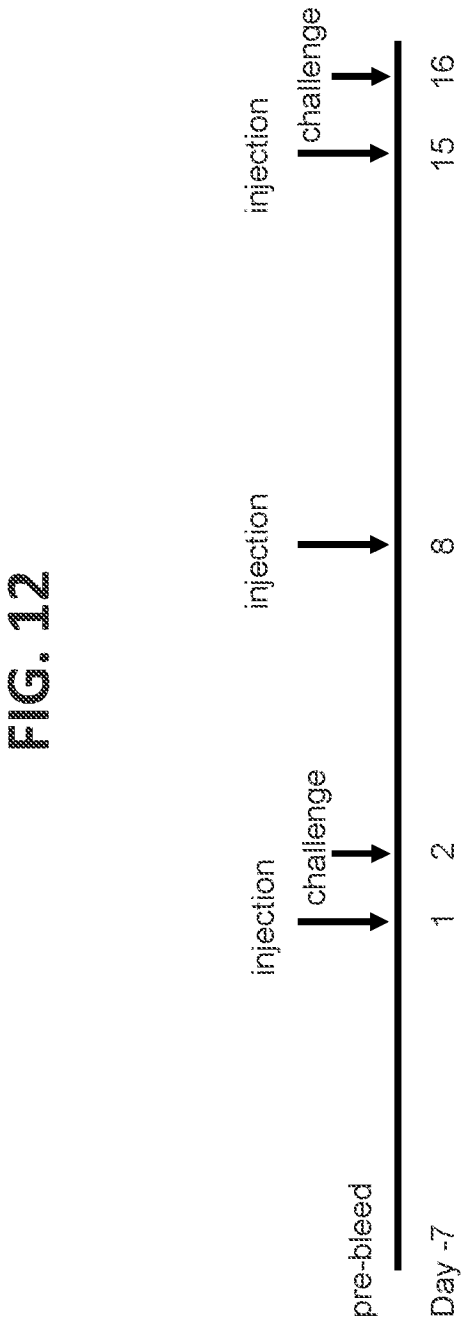

pre-bleed
injection
challenge
injection
injection
challenge
Day -7
1
2
8
15
16

FIG. 13A

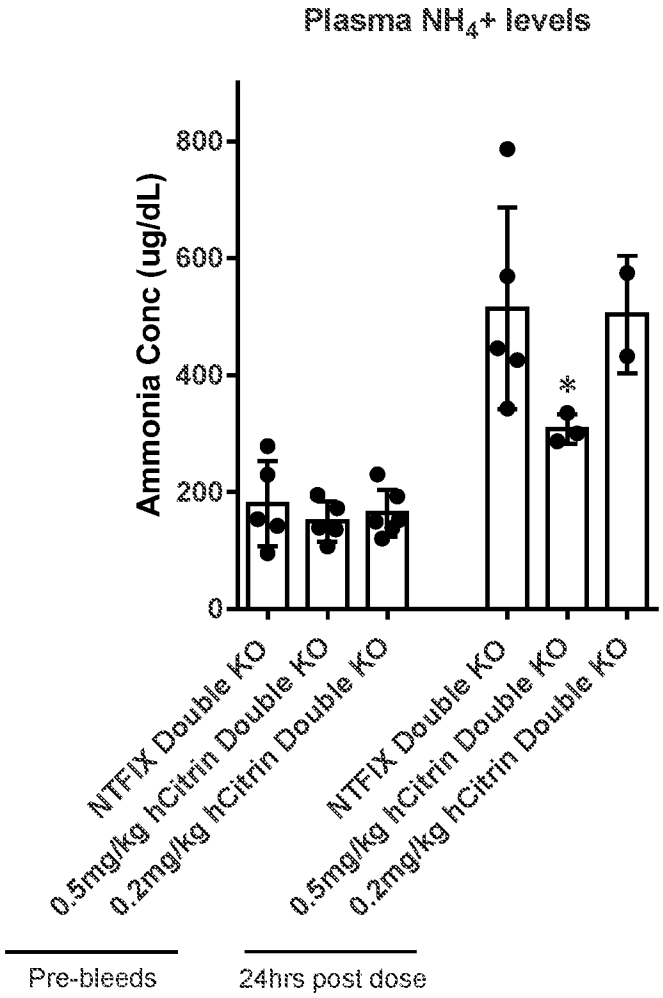


FIG. 13B

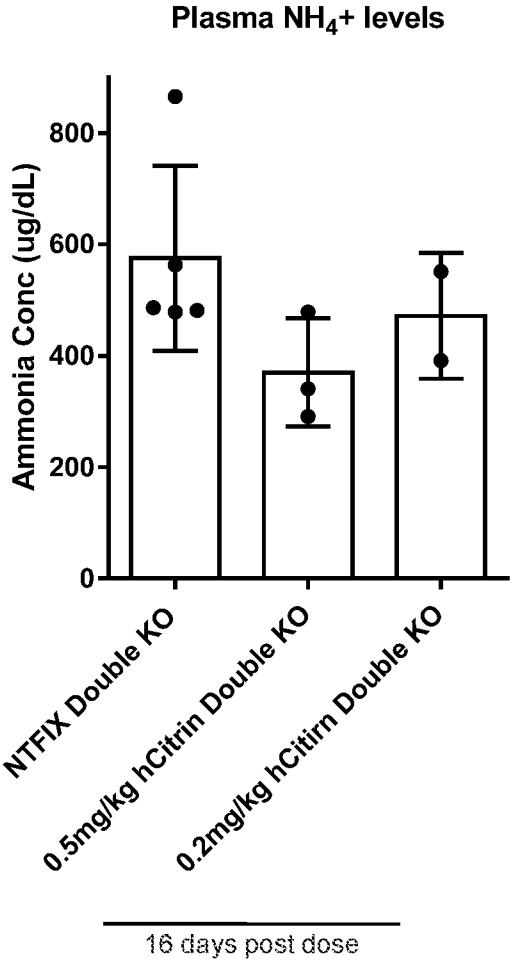


FIG. 14A

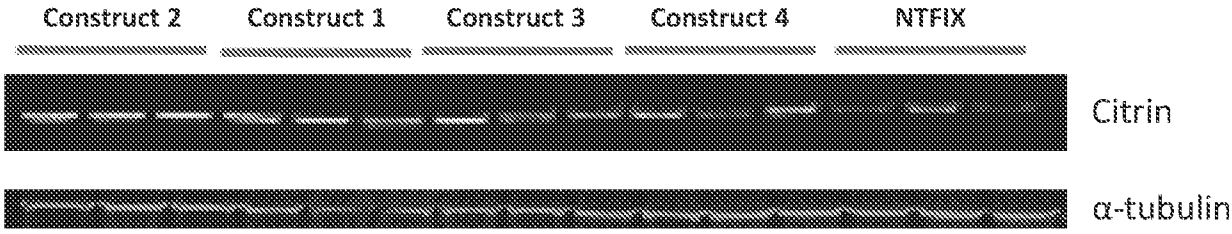
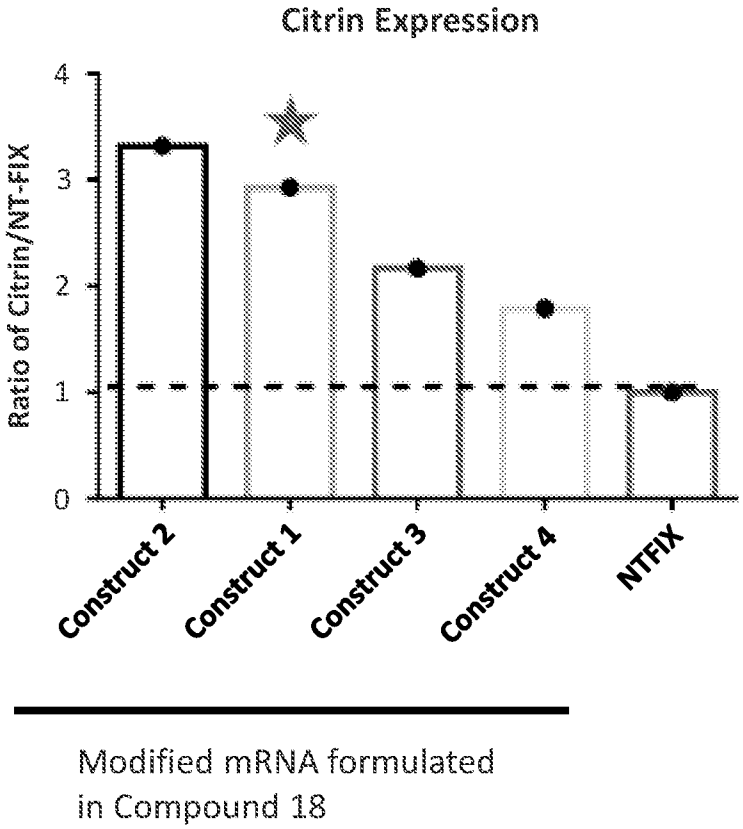


FIG. 14B



Modified mRNA formulated in Compound 18