

[図1]

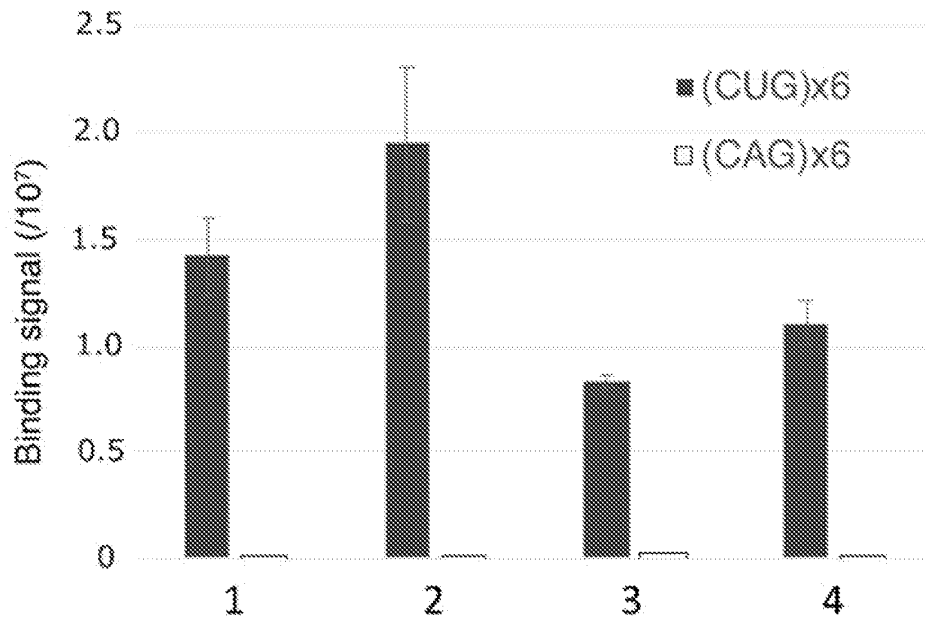


図1：CUG結合PPRタンパク質の結合実験

1: Luc-CUG-PPR1, 2: Luc-CUG-PPR2, 3: Luc-CUG-PPR3, 4: Luc-CUG-PPR4

[図2]

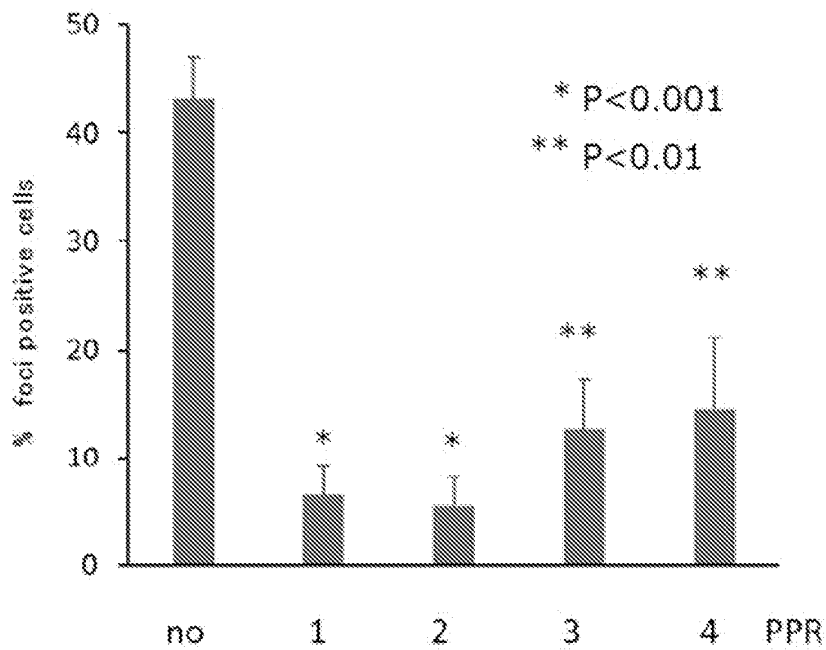


図2：RNA-foci形成抑制効果

1: mCLe-CUG-PPR1, 2: mCLe-CUG-PPR2, 3: mCLe-CUG-PPR3, 4: mCLe-CUG-PPR4

[図3]

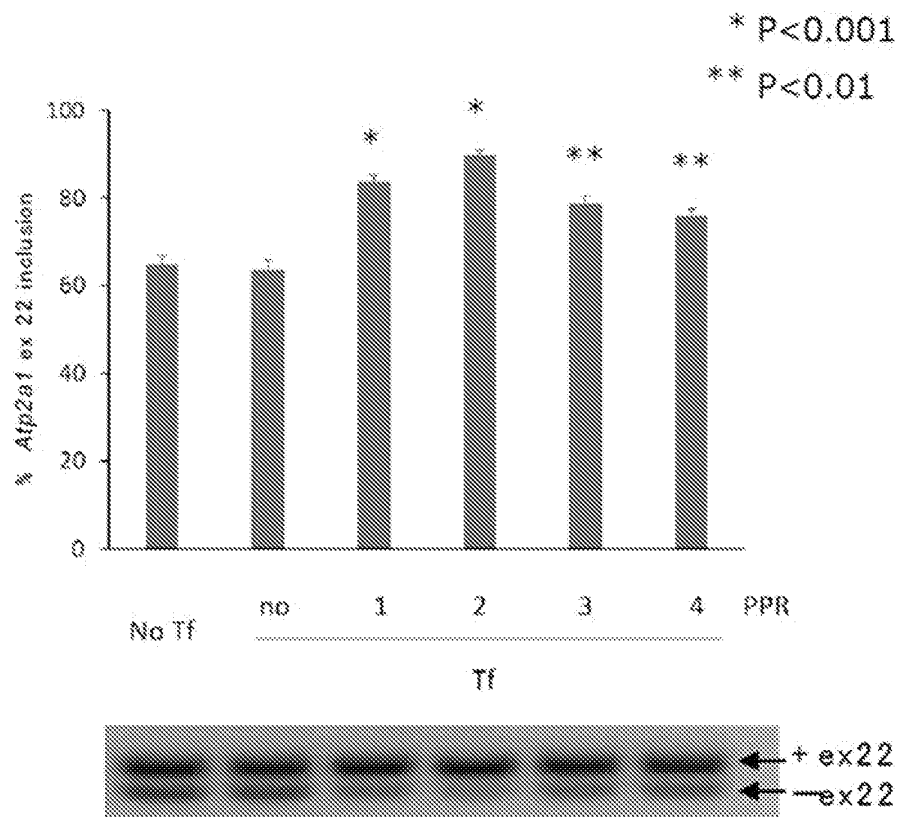


図3：A t p 2 a 1 の異常スプライシングの P P R 作用効果

1: mCLO-CUG-PPR1, 2: mCLO-CUG-PPR2, 3: mCLO-CUG-PPR3, 4: mCLO-CUG-PPR4

[図4]

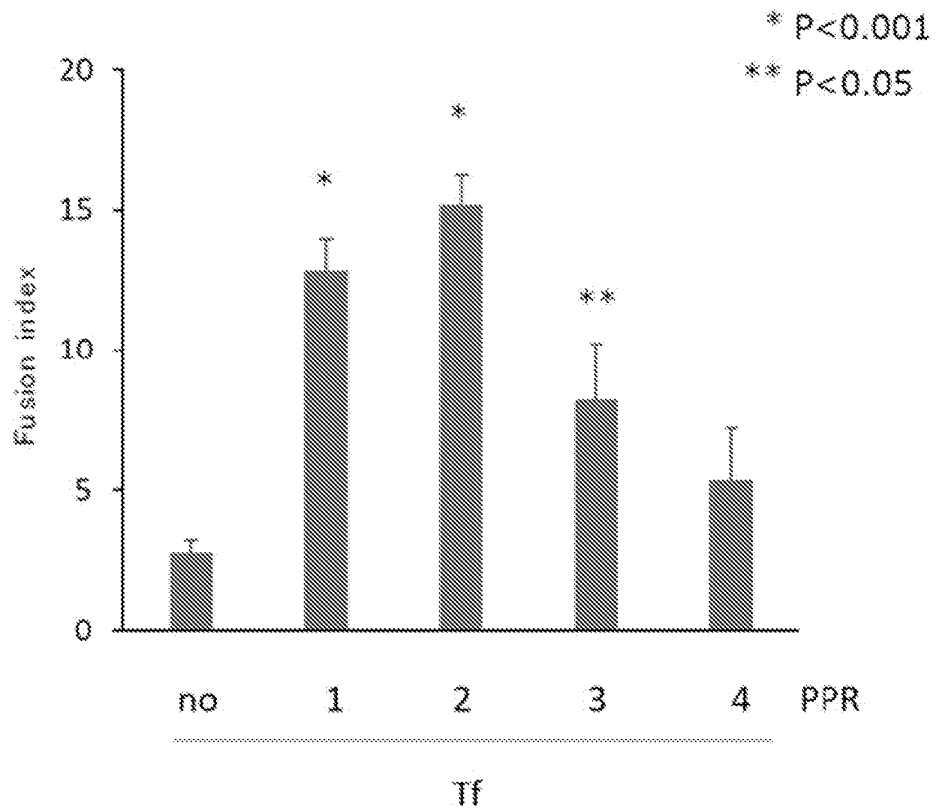


図4：筋分化効率の検証

1: mCLo-CUG-PPR1, 2: mCLo-CUG-PPR2, 3: mCLo-CUG-PPR3, 4: mCLo-CUG-PPR4

[図5]

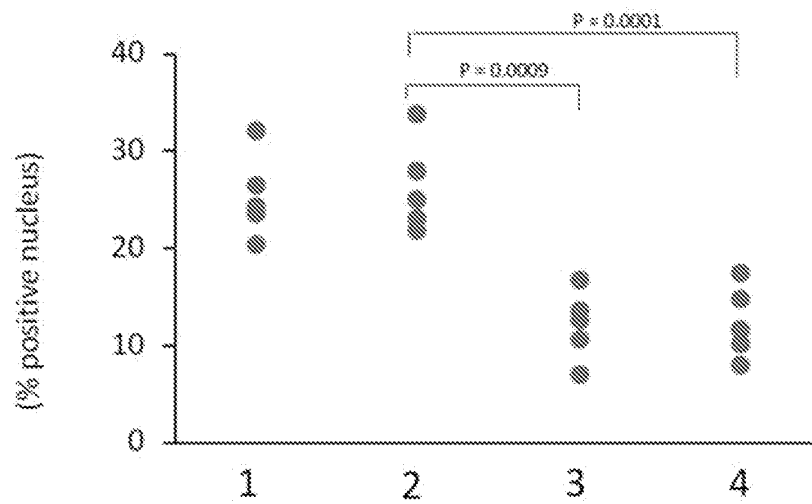


図5：RNA-foci形成抑制効果の検証

1: PBS, 2: AAV6-CMV-mCLo-empty, 3: AAV6-CMV-mCLo-CUG-PPR1, 4: AAV6-CMV-mCLo-CUG-PPR2

[図6]

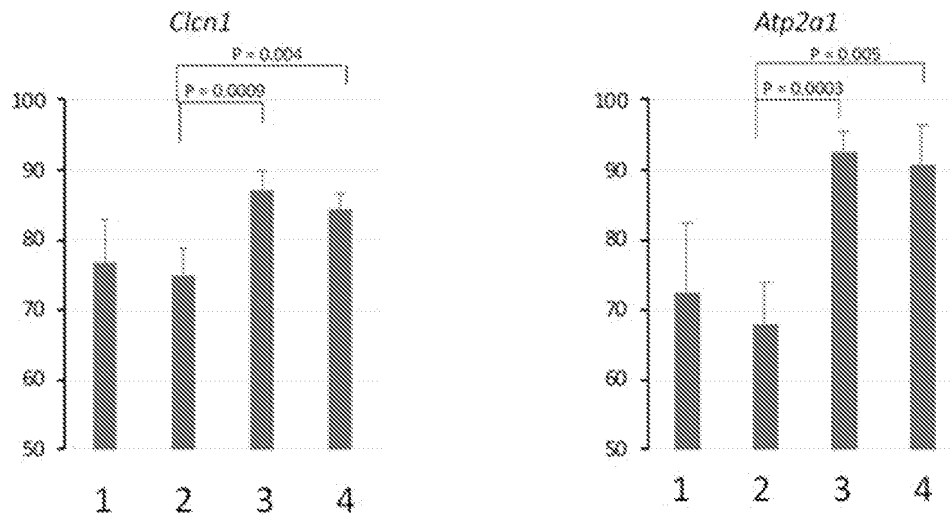


図6：異常スプライシング効果の検証

1: PBS, 2: AAV6-CMV-mCLO-empty, 3: AAV6-CMV-mCLO-CUG-PPR1, 4: AAV6-CMV-mCLO-CUG-PPR2

[図7]

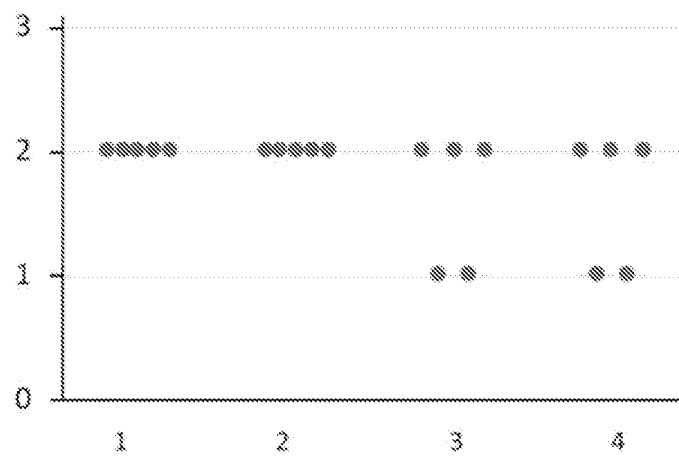
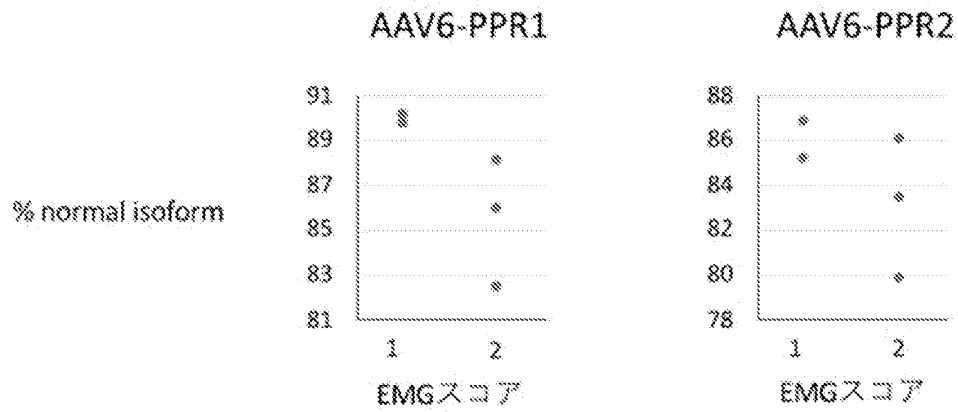


図7：筋強直放電に関するPPRの効果

1: PBS, 2: AAV6-CMV-mCLO-empty, 3: AAV6-CMV-mCLO-CUG-PPR1, 4: AAV6-CMV-mCLO-CUG-PPR2

[図8]

図8: *Cttn*遺伝子の異常スプライシング改善効果とEMGスコアの相関

左図: AAV6-CMV-mCLO-CUG-PPR1, 右図: AAV6-CMV-mCLO-CUG-PPR2

[図9]

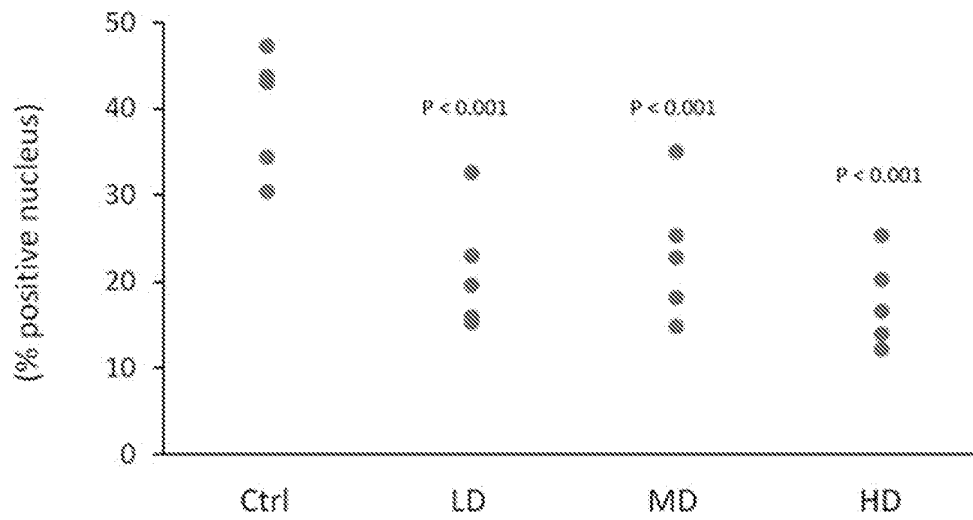


図9: AAV9-CUG-PPR1 の用量依存的な RNA-foci 形成抑制効果

[図10]

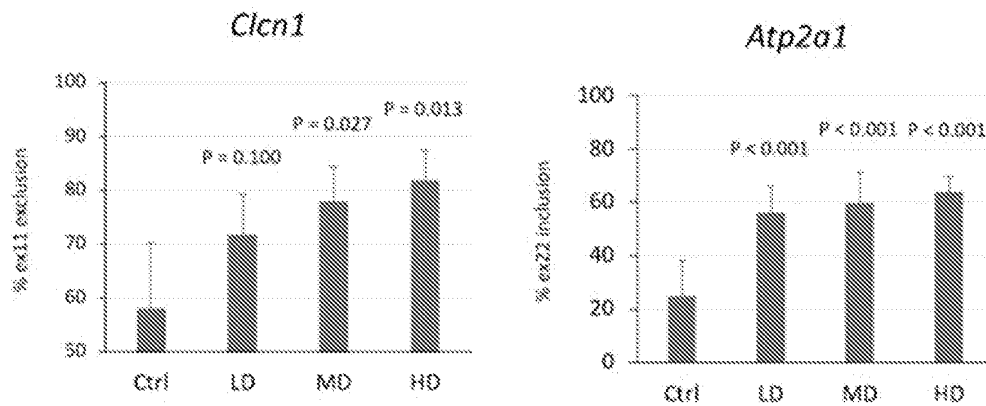


図 10: AAV9-CUG-PPR1 の用量依存的な異常スプライシング改善効果

[図11]

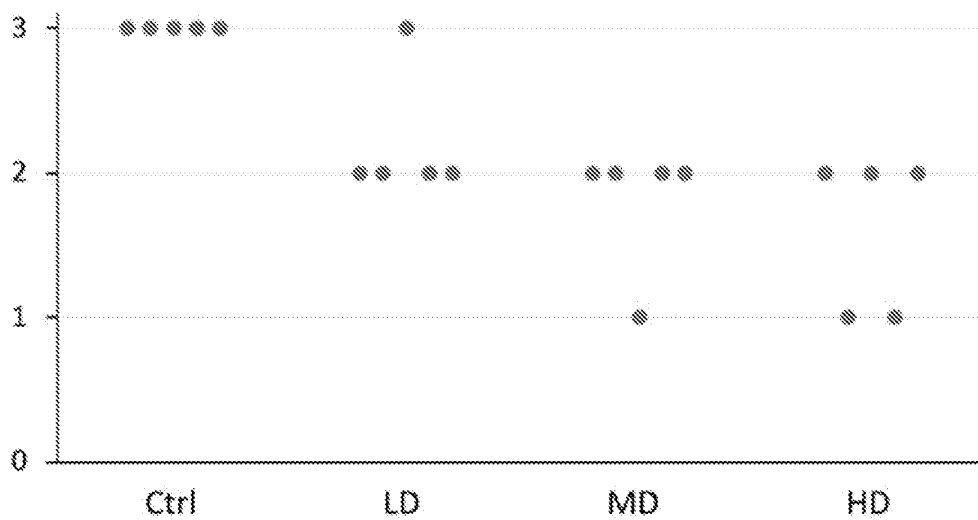


図 11: AAV9-CUG-PPR1 の用量依存的な筋強直放電抑制効果

[図12]

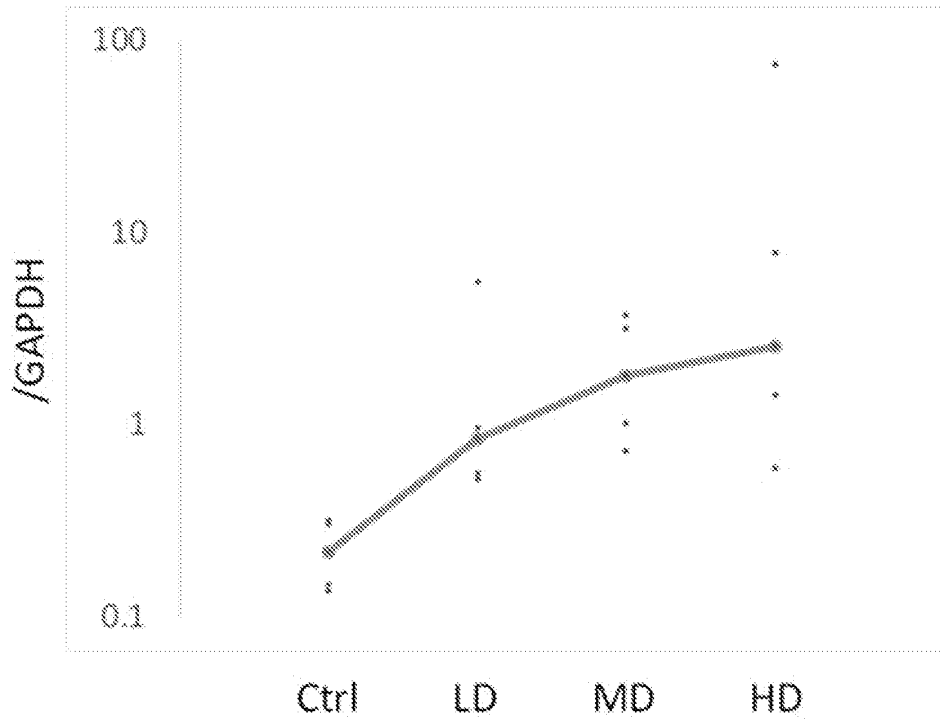


図 12: AAV9-CUG-PPR1 の投与用量と PPR mRNA 発現量との関係

[図13]

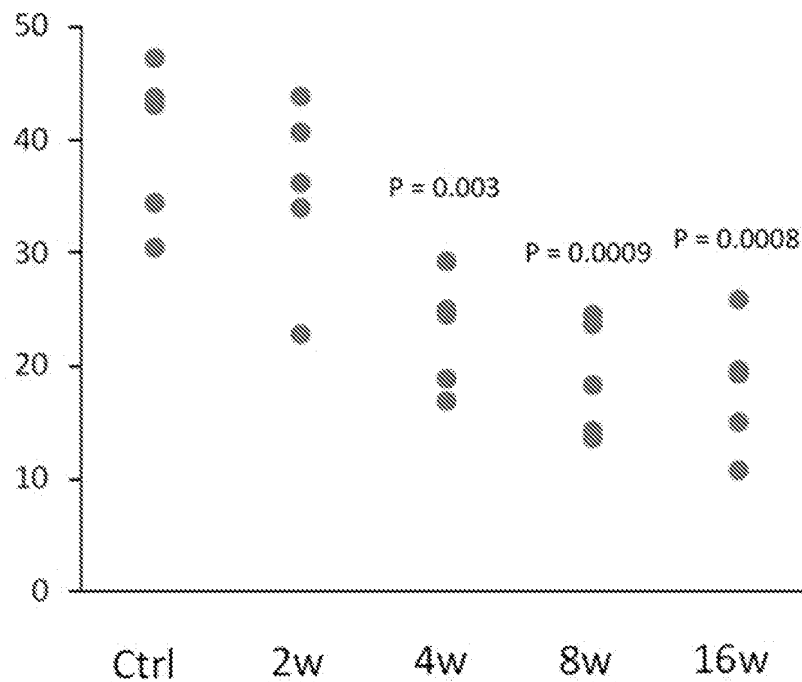


図 13: AAV9-CUG-PPR1 の時間依存的な RNA-foci 形成抑制効果

[図14]

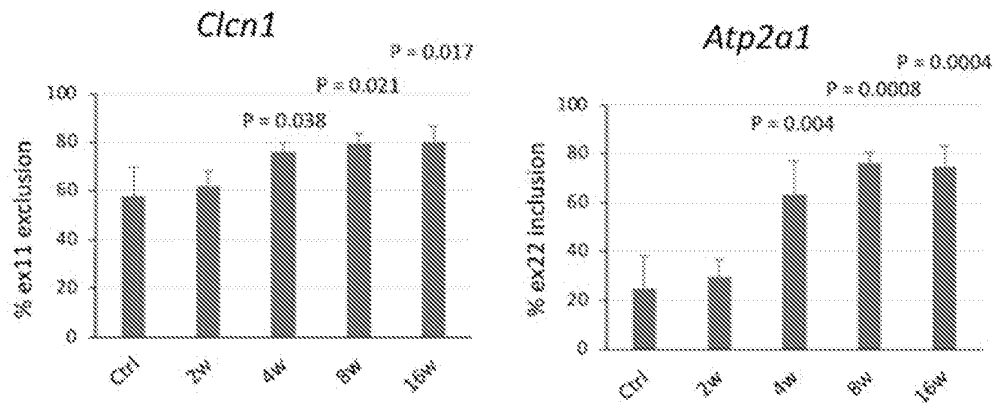


図 14: AAV9-CUG-PPR1 の時間依存的な異常スプライシング改善効果

[図15]

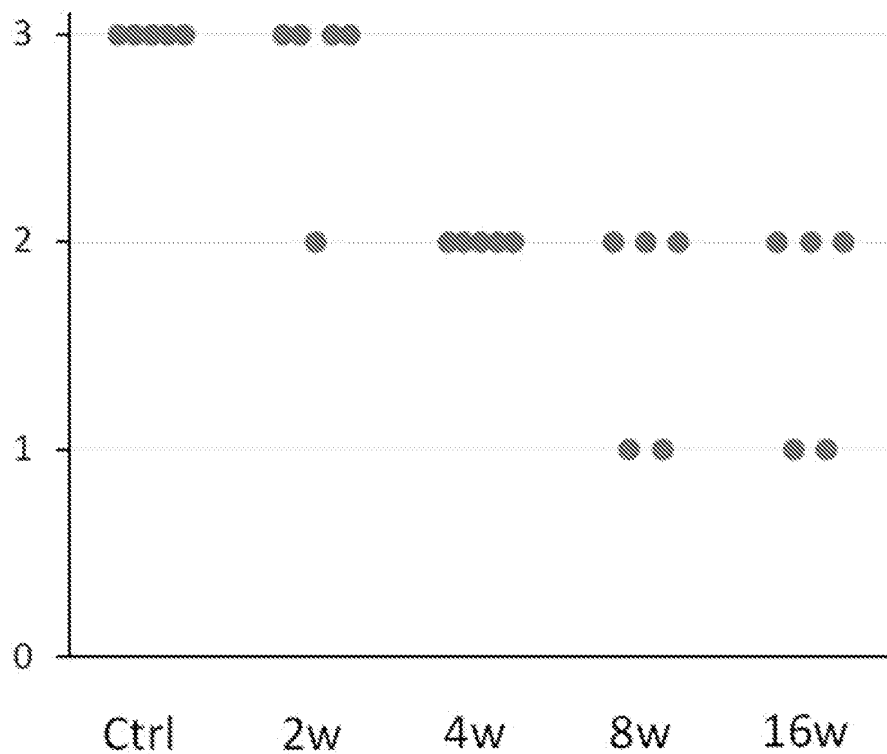
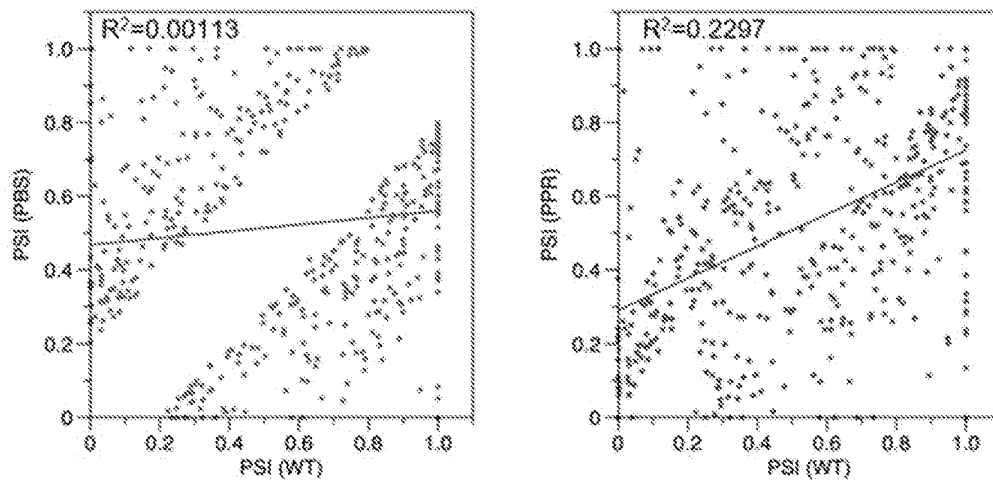


図 15: AAV9-CUG-PPR1 の時間依存的な筋強直放電抑制効果

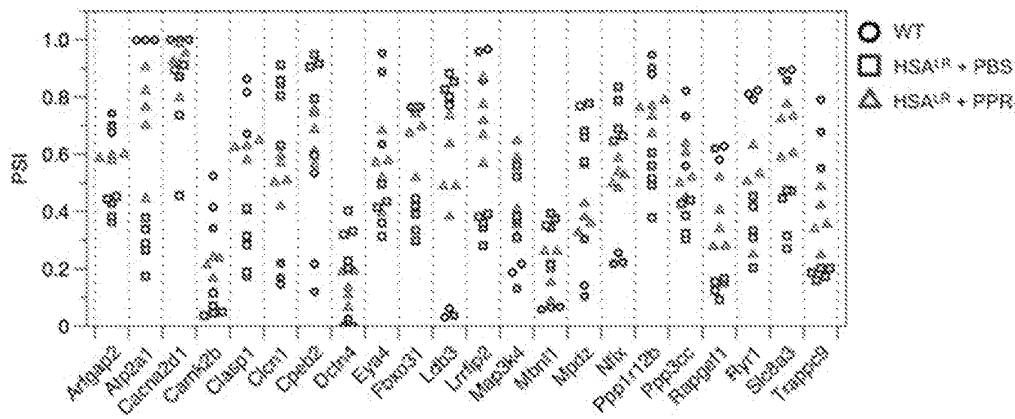
[図16a]

a



[図16b]

b



[図16c]

c

	log(P-value)	Number of gene		
		> 50%	50%, ≥20%	<20%
GO:0097435 supramolecular fiber organizat	-6.82	12	16	4
R-MMU-397014 Muscle contraction	-5.62	14	17	3
GO:0010256 endomembrane system organizati	-4.77	6	12	1
GO:0120035 regulation of plasma membrane	-4.66	19	12	2
GO:0031116 positive regulation of microtu	-4.22	14	17	1
GO:0031032 actomyosin structure organizat	-3.86	12	7	5
GO:0000381 regulation of alternative mRNA	-3.84	4	8	1
GO:0006468 protein phosphorylation	-3.80	9	12	1
GO:0008347 glial cell migration	-3.50	4	9	0
GO:0034453 microtubule anchoring	-3.44	5	5	1
GO:0030100 regulation of endocytosis	-3.44	7	8	2
GO:0032989 cellular component morphogenes	-3.38	13	14	3
GO:0048312 intracellular distribution of	-3.33	2	4	0
GO:0016482 cytosolic transport	-3.32	4	7	0
GO:0032469 endoplasmic reticulum calcium	-3.31	2	3	0
R-MMU-445355 Smooth Muscle Contraction	-3.31	7	4	3
GO:0008088 axo-dendritic transport	-3.18	6	6	0
GO:2001222 regulation of neuron migration	-3.09	3	2	0
R-MMU-9013424 RHOV GTPase cycle	-2.98	9	5	3
GO:0034822 cellular protein-containing co	-2.93	7	10	3

[図17]

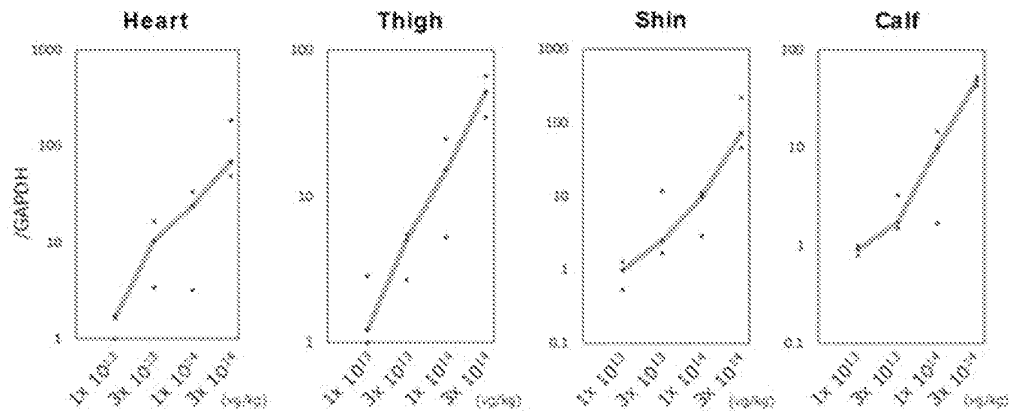


図17: AAV9-CUG-PPR1 投与マウスの各臓器における PPR mRNA 発現量

[図18]

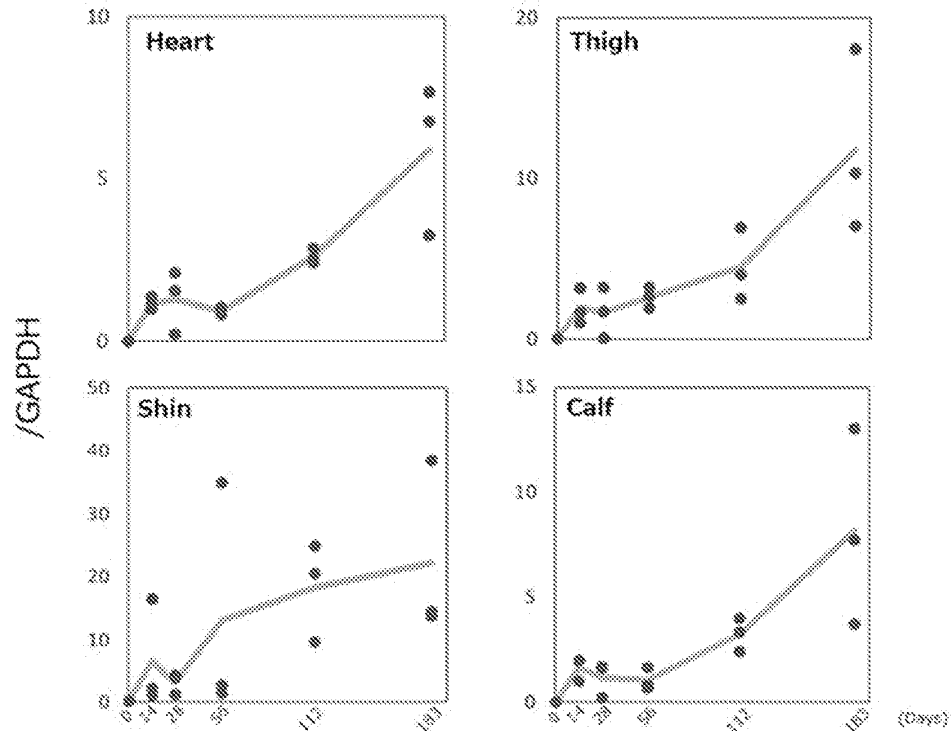


図18: AAV9-CUG-PPR1投与マウスの各臓器におけるPPR mRNAの発現持続性