

Supplemental Table 1. Frequencies of expansion and contraction events in cell models.

MRC-5 800R (conditional model)		% expanded alleles <sup>a</sup>	% contracted alleles <sup>a</sup>	Sum (%)	Estimated mutation rate	Number of alleles
Clone A	Initial growth	2.5	2.5	5.0	0.28%	40
	20d no prolif.	0	5.0	5.0		40
	20d prolif.	0	11.9	11.9		42
	42d no transcription	14.6	14.6	29.3		41
	42d transcription	31.1	27.0	58.1		74
Clone B	Initial growth	2.5	5.0	7.5		40
	20d no prolif.	4.3	4.3	8.7		46
	20d prolif.	11.1	11.1	22.3		45
	42d no transcription	12.2	22.0	34.1		41
	42d transcription	17.3	42.3	59.6		52
Clone C	Initial growth	2.5	0	2.5		40
	20d no prolif.	0	5.0	5.0		40
	20d prolif.	6.8	2.3	9.1		44
	42d no transcription	2.0	12.2	14.3		49
	42d transcription	17.0	21.2	38.3		47
Sum	Initial growth	2.5	2.5	5.0	0.28%	120
	20d no prolif.	1.6	4.8	6.3	0.78%	126
	20d prolif.	6.1	8.4	14.5		131
	42d no transcription	9.2	16.0	25.2		131
	42d transcription	23.1	30.1	53.2	3.7%	173
<b>MRC-5 800R (constitutive model)</b>						
MRC-5 800R (constitutive model)		% expanded alleles <sup>a</sup>	% contracted alleles <sup>a</sup>	Sum (%)	Estimated mutation rate	Number of alleles
Unidirectional transcription (forward)	Clone 1	8.0	38.0	46.0	2.8%	50
	Clone 2	26.0	24.0	50.0		50
	Clone 3	4.0	32.0	36.0		50
	Clone 4	6.0	24.0	30.0		50
	Sum	11.0	29.5	40.5		200
Unidirectional transcription (reverse)	Clone 1	0	18.0	18.0	1.4%	50
	Clone 2	6.0	20.0	26.0		50
	Clone 3	0	22.0	22.0		50
	Clone 4	2.0	24.0	26.0		50
	Sum	2.0	21.0	23.0		200
Bidirectional transcription	Clone 1	44.0	38.0	82.0	8.3%	50
	Clone 2	44.0	26.0	70.0		50
	Clone 3	42.0	46.0	88.0		50
	Clone 4	38.0	38.0	76.0		50
	Sum	42.0	37.0	79.0		200

<sup>a</sup> A cut-off point of  $\pm 25$  repeats was used for counting as unstable.

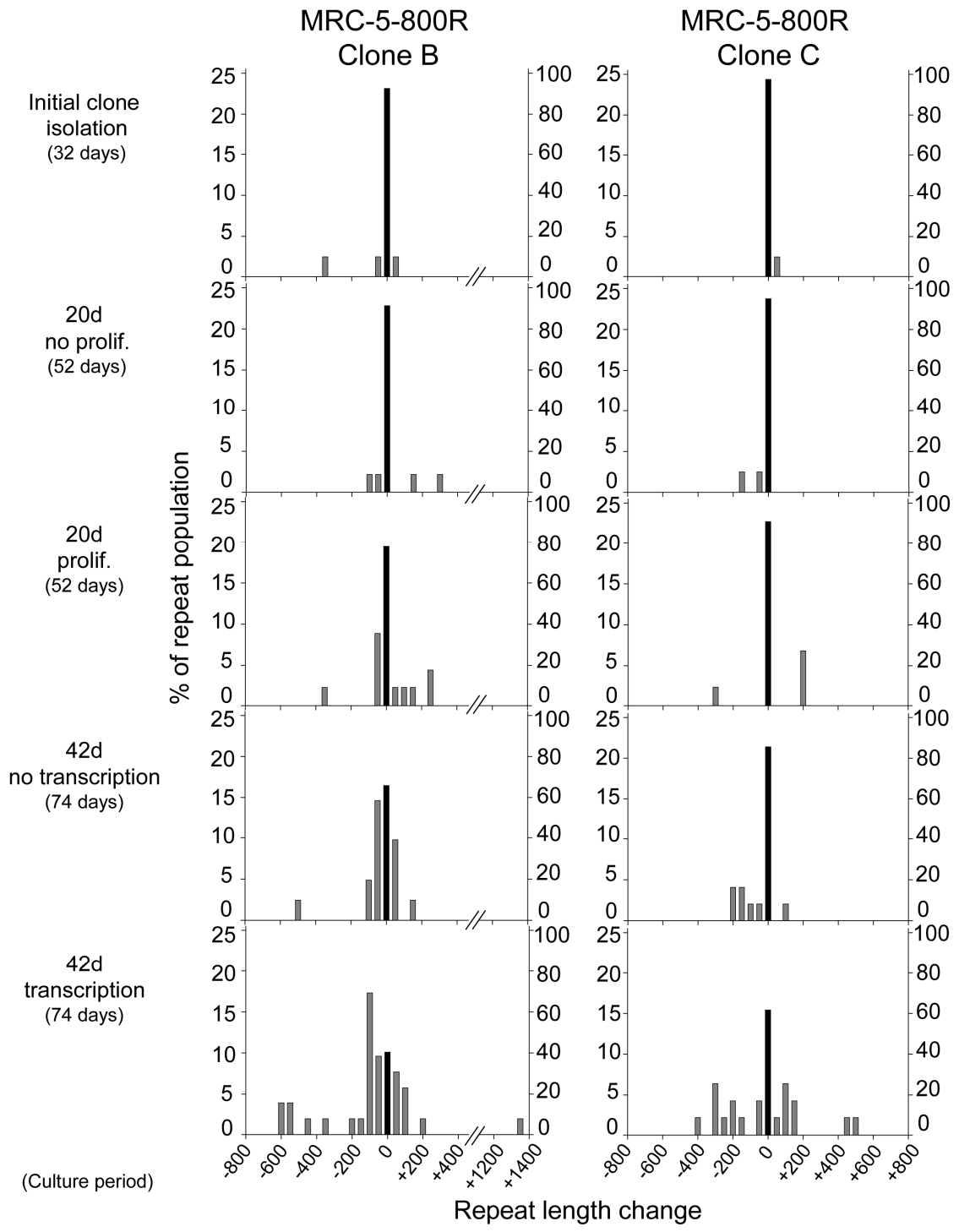
### Supplemental Figure 1

Histograms of repeat length distributions in two different clones (conditional expression of expanded repeat). The distribution of unstable allele is shown by gray bars (left vertical axis). The frequency of stable allele is shown by black bars (right vertical axis). Allele lengths have been grouped into bins spanning 50 repeats.

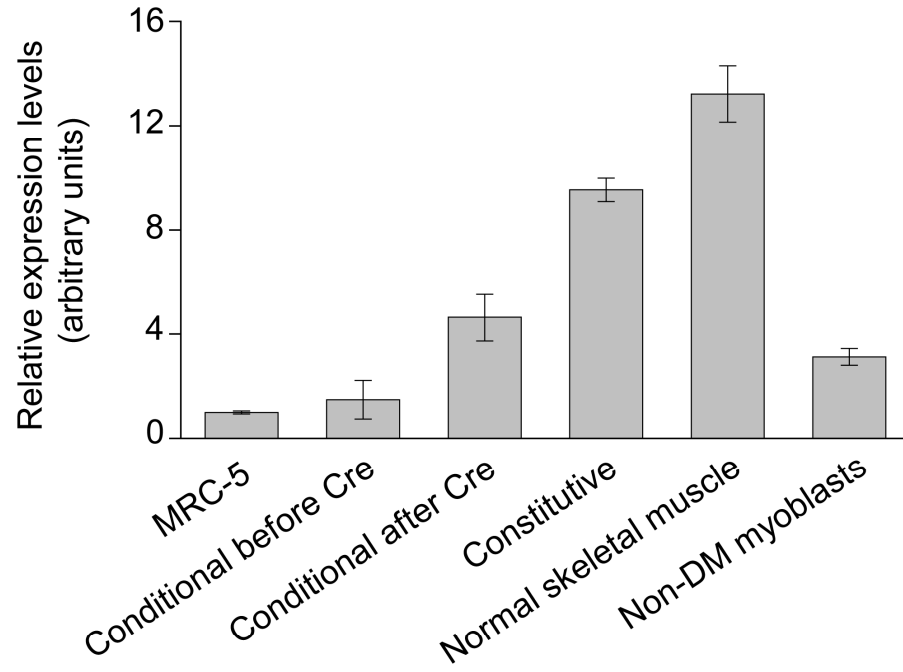
### Supplemental Figure 2

**A** The level of transgene expression in conditional and constitutive model was similar to native *DMPK* in normal human skeletal muscle. *DMPK* 3' UTR expression was analyzed by qRT-PCR. Identical sequence was detected in the transgene mRNA. For comparison across different cells and tissues, results were normalized to the mean expression level of two housekeeping transcripts, 18S rRNA and RNA polymerase II polypeptide A (*POLR2A*). Data are indicated as the mean  $\pm$  SD of triplicates.

**B** FISH analysis for RNA containing an expanded CUG repeat (CUG<sup>exp</sup>). Cells and tissue were processed in parallel and then imaged and displayed under identical exposure and threshold settings. DM1 heart tissue and myoblasts shows many large nuclear foci, whereas smaller foci are observed in MRC-5 clones that have constitutive expression of expanded repeats.



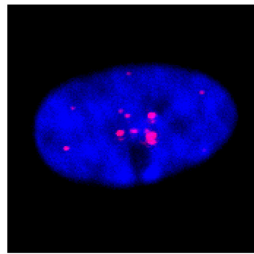
**A**



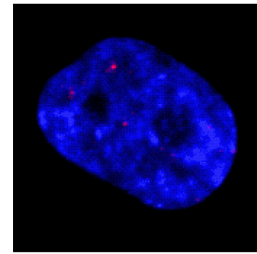
**B**



DM1 heart



DM1 myoblast



MRC-5 with (CTG)<sub>800</sub>