**Supplementary Figure 1: Expression of total *SMN2* and *LT-SMN2* transcripts in tissues derived from adult *Smn*^{-/-} *SMN2*^{+/+} transgenic mice.** Comparision of *SMN2* **(A)** and *LT-SMN2* **(B)** transcript levels in two neuronal and three nonneuronal tissues derived from adult *Smn*^{-/-} *SMN2*^{+/+} mice. In both analyses, *SMN2* **(A)** and *LT-SMN2* **(B)** transcript levels in skeletal muscle were set to 100%.

Supplementary Figure 2: The *SMN1* methylation patterns in blood samples derived from *SMN2*-deleted and unaffected individuals. (A) Bar chart shows the mean methylation levels (± SEM) of each CpG dinucleotide within the respective ^{SMN1}CGIs in DNA isolated from blood samples drawn from 6 unaffected, *SMN2*-deleted individuals carrying 2 *SMN1* copies (4 female, 2 male). The mean methylation levels of each ^{SMN1}CGI (see frequency plot) are as follows: ^{SMN1}CGI 1: 87.0%, ^{SMN1}CGI 2: 54.0%, ^{SMN1}CGI 3: 8.2%, ^{SMN1}CGI 4: 77.6%; **(B)** Bar chart shows the difference of DNA methylation levels at each CpG dinucleotide within CGI 2 in unaffected *SMN2*-deleted individuals compared with *SMN1*-deleted type I and type III SMA patients. At nt position -330, *SMN1* shows significantly higher methylation levels compared with type I *SMN2* and type III *SMN2* epialleles, while the *SMN1* methylation at nt position -258 is significantly lower. At nt position -296, *SMN1* shows lower methylation levels compared with type I *SMN2*, and higher levels compared with type III *SMN2* epialleles. Three levels of statistical significance were discriminated: * = $p < 0.05$, ** = $p < 0.01$, *** = $p < 0.001$ (*t*-test).

A

B

Supplementary Figure 1

A

SMN1

mean methylation [%]

CGI 1   CGI 2   CGI 3   CGI 4

SMN1

CGI   1   2   3   4

B

SMN2 (type I) versus SMN1

methylation differences [%]

- 290 nt
- 296 nt
- 258 nt
**
**
- 330 nt
***

CGI 2
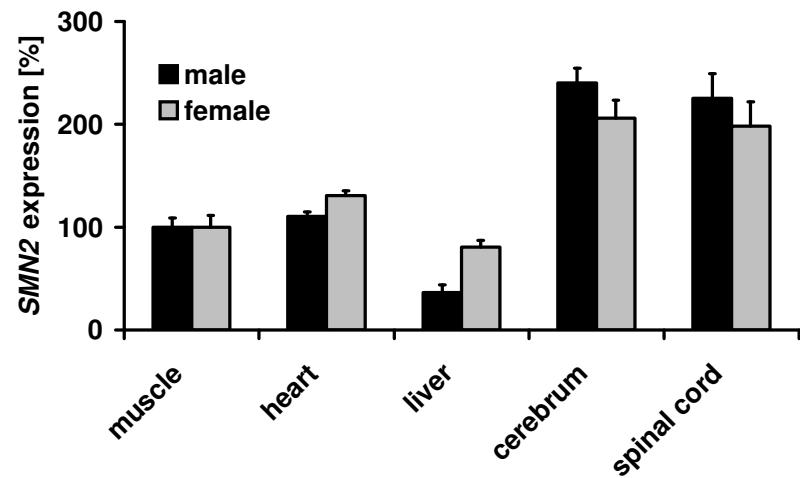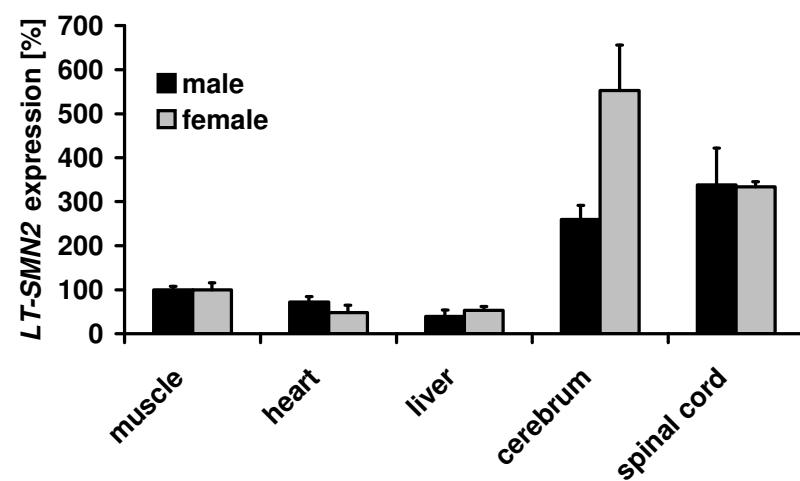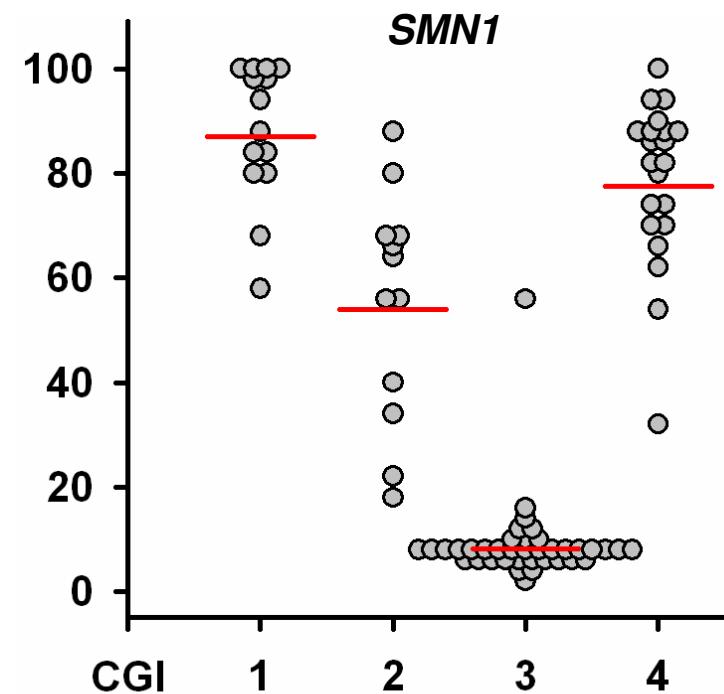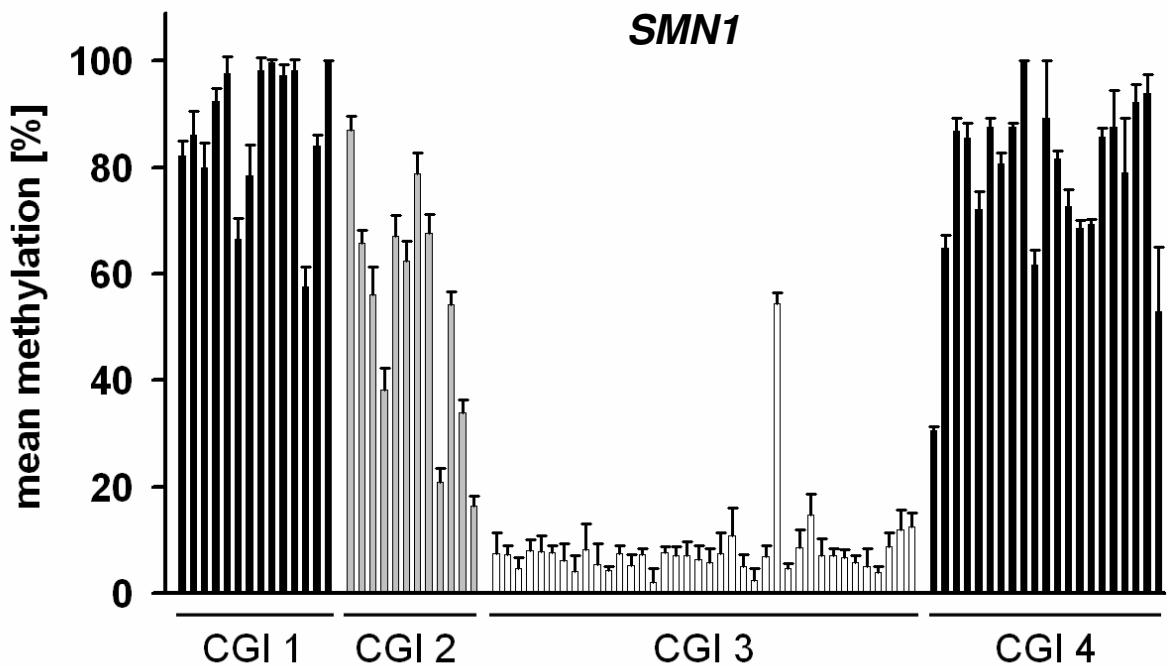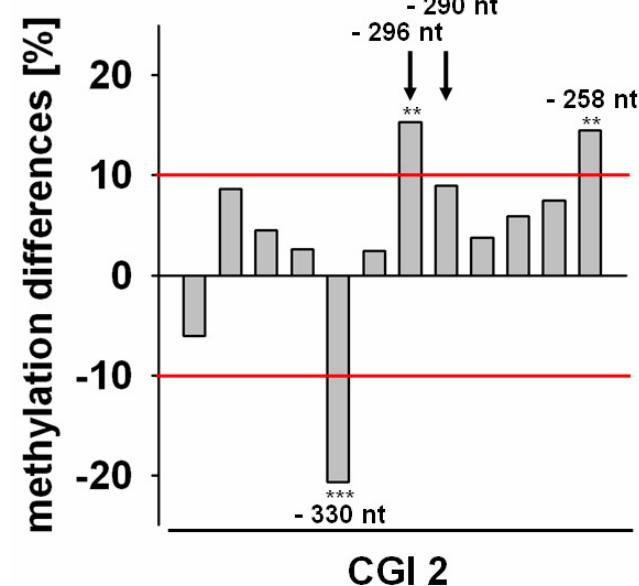
SMN2 (type III) versus SMN1

- 258 nt
**
- 330 nt
*
- 296 nt
*
- 290 nt

CGI 2
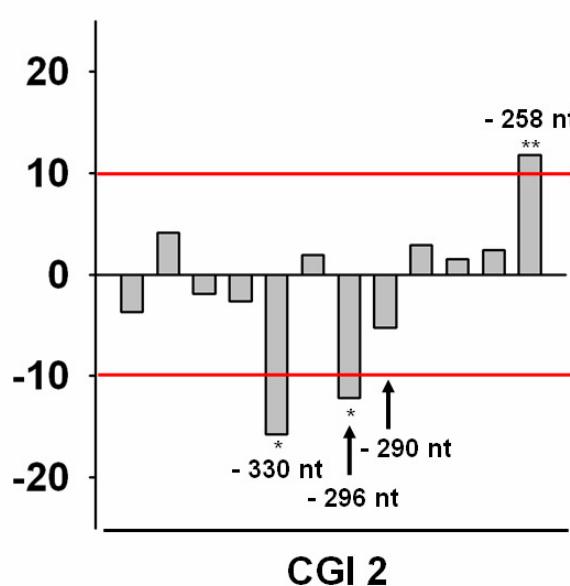
Supplementary Figure 2

Primers used for bisulfite genomic sequencing

	name	sequence
CGI 1	CGI 1 outer fwd	5'-GAT GTT TAA TAA AGA ATA TTG GAG-3'
	CGI 1 outer rev	5'-AAA TAT TTA ATC CCC CAA CCT TA-3'
	CGI 1 inner 1 fwd	5'-GTT TAA TAA AGA ATA TTG GAG GTT-3'
	CGI 1 inner 1 rev Bio	5'-Bio-CTC TAT CAC CCA AAC TAA AAT AC-3'
	CGI 1 inner 2 fwd	5'-GTA TTT TAG TTT GGG TGA TAG AG-3'
	CGI 1 inner 2 rev Bio	5'-Bio-TTA ATC CCC CAA CCT TAT TTA TTA-3'
	seqprimer CGI 1 1.1 fwd	5'-GTT TAA TAA AGA ATA TTG GAG GTT-3'
	seqprimer CGI 1 1.2 fwd	5'-GGT TTG GTG TGG TGG TTT ATA TT-3'
	seqprimer CGI 1 1.3 fwd	5'-TTA AAA ATA TAA AAA TTA GT-3'
	seqprimer CGI 1 2.1 fwd	5'-GTA TTT TAG TTT GGG TGA TAG AG-3'
	seqprimer CGI 1 2.2 fwd	5'-AGT ATT TTG GGA TGT TAG AG-3'
	seqprimer CGI 1 2.3 fwd	5'-GGA ATA TTT TGA GTT TAG GAG TT-3'
	seqprimer CGI 1 2.4 fwd	5'-GTG TTT TTG TGG TTT TAG TTA-3'
	seqprimer CGI 1 2.5 fwd	5'-ATG GTG TTA TTG TAT TTT G-3'
CGI 2	CGI 2 outer fwd	5'-TAA GGG GGA GGG GGA ATA AA-3'
	CGI 2 outer rev	5'-ATA ATT ATC RCC CTC CCA CAT TTA-3'
	CGI 2 inner1 fwd	5'-AGA YGA GGT TTA AGT AAT ATG T-3'
	CGI 2 inner2 rev Bio	5'-Bio-CTC AAT CCT TTC ATT TCA CTA TA-3'
	seqprimer CGI 2 1.1 fwd	5'-AGA YGA GGT TTA AGT AAT ATG T-3'
	seqprimer CGI 2 1.2 fwd	5'-AAA TAG TTG AGY GTG GTG-3'
	seqprimer CGI 2 1.3 fwd	5'-AGG TTG AGG TGG GAG GAT-3'
	seqprimer CGI 2 1.4 fwd	5'-AAG TYG AGG TTG TAG TGA GT-3'
	seqprimer CGI 2 1.5 fwd	5'-TTG TAT TTT AGT TTG AG-3'
CGI 3	CGI 3 outer fwd	5'-GTG AAA TGA AAG GAT TGA GAG A-3'
	CGI 3 outer rev	5'-CTC CCC CAC ACC AAC CAA AA-3'
	CGI 3 inner1 fwd	5'-Bio-TAA ATG TGG GAG GGY GAT AAT TAT-3'
	CGI 3 inner1 rev	5'-CTA CRA CCT CAC CTA ACC TAT A-3'
	CGI 3 inner2A fwd	5'-GTA TAG GTT AGG TGA GGT YGT AG-3'
	CGI 3 inner2A rev Bio	5'-Bio-ATA AAC AAA ATA AAC TAC TA-3'
	CGI 3 inner2B fwd Bio	5'-Bio-GTA TAG GTT AGG TGA GGT YGT AG-3'
	CGI 3 inner2B rev	5'-ATA AAC AAA ATA AAC TAC TA-3'
	seqprimer CGI 3 1.1 fwd	5'-TAA ATG TGG GAG GGT GAT-3'
	seqprimer CGI 3 1.2 fwd	5'-GTA GAA AGC GTG AGA AGT TAT TAT-3'
	seqprimer CGI 3 1.3 fwd	5'-GTT TYG TTT TTA GAA GTT T-3'
	seqprimer CGI 3 1.4 fwd	5'-GTY GTT ATT TTT AAG AAG GG-3'
	seqprimer CGI 3 1.5 fwd	5'-TTG TTA TGG YGA TGA GTA-3'
	seqprimer CGI 3 1.6 fwd	5'-GAG TAG GAG GAT TTY GTG TT-3'
	seqprimer CGI 3 2.1 fwd	5'-GTG TAG TTT TTT TAT TA-3'
	seqprimer CGI 3 2.2 rev	5'-AAC CAC AAC TCC AAT AAA-3'
	seqprimer CGI 3 2.3 fwd	5'-TTT ATT GGA GTT GTG GTT-3'
	seqprimer CGI 3 2.4 rev	5'-CTA TCA AAA AAC CCA AAC TA-3'
	seqprimer CGI 3 2.5 rev	5'-ATA AAC AAA ATA AAC TAC TA-3'
CGI 4	CGI 4 outer fwd	5'-GTG GTT TTA GTT ATT TGG AAG-3'
	CGI 4 outer rev	5'-CTA CCA TAA ACT AAA ATC ATA CC-3'
	CGI 4 inner1A fwd	5'-GTT TAG GGA GGT GGA GGT TGT-3'

CGI 4 inner1A rev Bio	5'-Bio-TAT TAA CCA AAA TAA TCT-3'	
CGI 4 inner1B fwd Bio	5'-Bio-GTT TAG GGA GGT GGA GGT TGT-3'	
CGI 4 inner1B rev	5'-TAT TAA CCA AAA TAA TCT-3'	
CGI 4 inner2A fwd	5'-AGA TTA TTT TGG TTA ATA-3'	
CGI 4 inner2A rev Bio	5'-Bio-CCA CTA TAC TCC AAC CTA AAC C-3'	
CGI 4 inner2B fwd Bio	5'-Bio-AGA TTA TTT TGG TTA ATA-3'	
CGI 4 inner2B rev	5'-CCA CTA TAC TCC AAC CTA AAC C-3'	
seqprimer CGI 4 1.1 fwd	5'-GTT TAG GGA GGT GGA GGT TGT-3'	
seqprimer CGI 4 1.2 fwd	5'-TGT TTT AAA ATA AAA TAA-3'	
seqprimer CGI 4 1.3 fwd	5'-AAG TTT GTA ATT TTA GTA-3'	
seqprimer CGI 4 2.1 fwd	5'-AGA TTA TTT TGG TT-3'	
seqprimer CGI 4 2.2 rev	5'-CTT CAT AAC ATT CTC CTA-3'	
seqprimer CGI 4 2.3 fwd	5'-TAG GAG AAT GTT ATG AAG-3'	
seqprimer CGI 4 2.4 fwd	5'-TTA TTG TAT TTT AGT TTG GG-3'	
seqprimer CGI 4 2.5 rev	5'-ATT CCT TAA AAT ATA CCTA-3'	
seqprimer CGI 4 2.6 rev	5'-CTA TAC TCC AAC CTA AAC CAC AA-3'	

Primers used for *SMN2* CGI cloning (results shown in Figure 2 C)

	name	sequence
CGI 1	CGI1 cloning fwd	5'-TGT AAT TTT AGT ATT TTG GGA GGT-3'
	CGI1 cloning rev	5'-TTA ATC CCC CAA CCT TAT TTA TTA-3'
CGI 2	CGI2 cloning fwd	5'-GAG TTY GAG AYG AGG TTT AAG T-3'
	CGI2 cloning rev	5'-CTA CGA CCT CAC CTA ACC TAT A-3'
CGI 3	CGI3 cloning fwd	5'-TAA ATG TGG GAG GGC GAT AAT TAT-3'
	CGI3 cloning rev	5'-AAA AAT AAA CAA AAT AAA CTA CTA-3'
CGI 4	CGI4 cloning outer fwd	5'-TAG TTA TTT GGA AGG TTT AGG TT-3'
	CGI4 cloning outer rev	5'-ATA ACT CAC TCC TTT AAA CCC AA-3'
	CGI4 cloning inner fwd	5'-GTT TAG GGA GGT GGA GGT TGT-3'
	CGI4 cloning inner rev	5'-CCA CTA TAC TCC AAC CTA AAC C-3'

Primers used for ChIP analyses (results shown in Figure 7 E, F, G)

name	sequence
-631 to -524 fwd	5'-GTG TTT AAG GAT CTG CCG CCT-3'
-631 to -524 rev	5'-GTA AAT GTA AGC TCC TAC TAG GAA-3'
-609 to -487 fwd	5'-CCT TCC TGC CCC CAT GTT TGT-3'
-609 to -487 rev	5'-TGT GTG TAG ATA TTT ATT CCC C-3'
-449 to -349 fwd	5'-GTT CGA GAC GAG GCC TAA GCA-3'

-449 to -349 rev	5'-CCC CAG TAG CTA GGA CTA TAG GCG-3'
-372 to -266 fwd	5'-CGC CTA TAG TCC TAG CTA CTG GG-3'
-372 to -266 rev	5'-GCT CAG GCT GGA GTG CAG C-3'
-167 to -43 fwd	5'-CAC GCC ACA AAT GTG GGA GG-3'
-167 to -43 rev	5'-AAG AGT GAC GAC TTC CGC CG-3'
-63 to +59 fwd	5'-CGG CGG AAG TCG TCA CTC TT-3'
-63 to +59 rev	5'-CAG CAC GGA ATC CTC CTG CT-3'