Supplemental Figure 1. Sequence logos for the predicted motifs.

Supplemental Figure 2. Comparison of predicted modules with experimentally defined modules for the entire set of genes.

Supplemental Figure 3. ROC curves of muscle gene prediction with different non-muscle-specific motifs added to the set of muscle-specific motifs. Genomic genes are ranked by their muscle-specificity score. We plotted the ROC curves of the set of well-characterized muscle-specific genes that were not used for motif identification (44 test set). The diagonal line represents the result of random guessing. The y-axis is the fraction of true positives exceeding the cutoff for every cutoff value. The x-axis is the fraction of true negatives that exceed the same cutoff.

Supplemental Table 1. 122 *C. elegans* muscle specific genes

B0228.4	F32A6.4	R11G10.1
B0304.1	F34D6.3	T01D1.2
B0513.1	F40E10.3	T01H3.3
C02D4.2	F41C3.2	T02C5.5
C02F4.2	F41E7.6	T04C12.4
C04D8.1	F42A10.2	T04C12.5
C09D1.1	F42A10.3	T04C12.6
C16C2.2	F42G10.2	T08G11.5
C29F9.7	F42E11.4	T14A8.1
C33G3.1	F43D9.1	T14B1.1
C36B7.7	F44B9.2	T14B1.2
C36E6.3	F44A6.1	T18D3.4
C38C3.5	F47G6.1	T21C12.1
C37H5.8	F47F6.1	T22C1.7
C40C9.1	F49B2.5	T22E5.5
C46F11.1	F49E2.5	T23D8.8
C47C12.6	F49E12.5	T26H10.1
C47E8.7	F52A8.2	T28B4.1
C48A7.1	F54C1.7	W02D3.3
C52E4.2	F55B12.1	W05F4.2
D1081.2	F58A3.2	W08D2.1
F02A9.4	F59C12.2	W09B12.1
F07C3.4	F59F3.1	Y38C1AA.4
F07A5.7	F59F5.6	Y48A6C.5
F08B6.2	H10E21.3	Y48B6A.8
F08B6.4	K03E6.5	Y51A2D.19
F08C6.7	K08C7.3	Y71G12B.14
F09F7.2	K08F4.7	Y60A3A.1
F11C3.3	K09H11.3	Y105E8B.1

F12F3.1	K10B3.7	Y113G7A.8
F12F3.2	K10B3.8	ZC21.2
F13G3.9	K11C4.5	ZC101.2
F14D12.2	K12F2.1	ZK617.1
F15D3.1	M01D7.7	ZK643.1
F17C8.1	M03F4.2	ZK643.3
F18G5.3	R06A10.2	ZK673.7
F23H11.5	R06C7.10	ZK721.2
F25F8.2	R09A8.5	ZK899.8
F29F11.5	R09G11.1	ZK1058.2
F30A10.8	R10H10.5	ZK1086.1
F30H5.1	R11A5.2	

Supplemental Table 2. 78 pairs of *C. elegans* and *C. briggsae* orthologous genes.

C. elegans	*C. briggsae*
B0513.1	CBG22449
C04D8.1	CBG18119
C29F9.7	CBG15792
C36B7.7	CBG10976
C37H5.8	CBG08827
C40C9.1	CBG07401
C46F11.1	CBG09771
C47C12.6	CBG16785
C47E8.7	CBG04558
C52E4.2	CBG23344
D1081.2	CBG12542
F07C3.4	CBG19235
F07A5.7	CBG11932
F08B6.2	CBG04053
F08C6.7	CBG16732
F11C3.3	CBG19730
F13G3.9	CBG11909
F14D12.2	CBG14705
F17C8.1	CBG18000
F18G5.3	CBG16182
F23H11.5	CBG15171
F25F8.2	CBG20504
F29F11.5	CBG09671
F30H5.1	CBG15283
F34D6.3	CBG19563
F40E10.3	CBG07571
F41C3.2	CBG20625
F41E7.6	CBG17205
F42A10.3	CBG21119
F42G10.2	CBG01940
F42E11.4	CBG17351
F43D9.1	CBG18375
F44B9.2	CBG22957
F47F6.1	CBG07212
F47G6.1	CBG22285
F49B2.5	CBG08738
F52A8.2	CBG11904
F54C1.7	CBG10771
F55B12.1	CBG11477
F59C12.2	CBG16350
F59F3.1	CBG17535
F59F5.6	CBG04493

K03E6.5	CBG08066
K08F4.7	CBG03452
K10B3.7	CBG14137
K10B3.8	CBG14136
K11C4.5	CBG19042
K12F2.1	CBG23416
R06A10.2	CBG22078
R06C7.10	CBG21911
R09A8.5	CBG00099
R09G11.1	CBG01870
R10H10.5	CBG08377
R11A5.2	CBG23735
T01H3.3	CBG03300
T04C12.4	CBG23091
T04C12.5	CBG23090
T08G11.5	CBG12389
T14A8.1	CBG17683
T14B1.1	CBG16058
T14B1.2	CBG16060
T18D3.4	CBG00120
T22C1.7	CBG08257
T22E5.5	CBG05057
T23D8.8	CBG03778
T26H10.1	CBG23195
W02D3.3	CBG12712
W05F2.4	CBG14950
W08D2.1	CBG03476
W09B12.1	CBG16374
Y38C1AA.4	CBG01660
Y113G7A.8	CBG12934
ZC21.2	CBG18103
ZK643.1	CBG06858
ZK643.3	CBG06860
ZK673.7	CBG03100
ZK721.2	CBG15446
ZK1058.2	CBG03601

Supplemental Table 3. Performance test with different non-muscle-specific motifs added to the set of muscle-specific motifs. The results for each set of motif and distance constraint were ranked by sensitivity. Motif set 0 is the motif set with only muscle-specific motifs.

Motif Set	Motifs Added	Distance	Sensitivity	PPV
0		70	76.0	70.3
1	6, 10, 14	100	96.0	72.2
2	6, 7, 12	100	92.0	65.8
3	6, 10, 14	90	92.0	67.6
4	6, 11, 14	100	92.0	67.6
5	6, 10, 14	80	92.0	66.7
6	6, 12, 14	50	92.0	70.5

Supplemental Table 4. The effect of distance on prediction sensitivity and positive predictive value. c.p. : number of correctly predicted modules, t.p.: total number of predicted modules

distance	c.p./25	sensitivity	c.p./t.p.	PPV
20	20	80.0	33/ 46	71.7
25	20	80.0	32/ 45	71.1
30	21	84.0	33/ 46	71.7
35	22	88.0	31/ 47	66.0
40	22	88.0	30/ 46	65.2
45	21	84.0	29/ 47	61.7
50	22	88.0	30/ 48	62.5
55	22	88.0	27/ 44	61.4
60	22	88.0	27/ 44	61.4
65	21	84.0	27/ 44	61.4
70	21	84.0	26/ 43	60.5
75	21	84.0	26/ 43	60.5
80	23	92.0	27/ 40	67.5
85	24	96.0	26/ 35	74.3
90	24	96.0	26/ 35	74.3
95	24	96.0	25/ 34	73.5
100	24	96.0	24/ 31	77.4

Supplemental Table 5. Primers used in this study to amplify the predicted modules.

C02D4.2a

Forward
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCGCTGCCACTCTTTATGACTGACGAG
Reverse
CTTTGGGTCCTTTGGCCAATCCCGGGGATCCTGCACCGAATCAGTGTAATTTCGGAACATG

C33G3.1a
Forward
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCGCAGACGTAGCACATACACATCCAAGAG
Reverse
CTTTGGGTCCTTTGGCCAATCCCGGGGATCCTCGGGATCGAACCGAATCATTTTG

F08B6.2
Forward
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCGCTGTCTGTCCTTTGTATATAAGCTCCACAC
Reverse
CTTTGGGTCCTTTGGCCAATCCCGGGGATCCCGTTGCATGTCAGATTTATCCATC

C01B7.1b
Forward
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCGCCTTCTTCCATCATCGTTTG
reverse
CTTTGGGTCCTTTGGCCAATCCCGGGGATCCCTGATGCTCATCAGGTGATCTG

C01B7.3
Forward
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCCGCTCCATTTGTCAAGTGTCTTTG
Reverse
CTTTGGGTCCTTTGGCCAATCCCGGGGATCCACCACATCATTCATCCACATCTC

C10G11.7
Forward
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCGCCTTCTAGTACTCTACCTTC
Reverse
CTTTGGGTCCTTTGGCCAATCCCGGGGATCCTTGATTTCCTCAGACATAGTTGATG

F45D3.2
Forward
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCGGCATCCGATCTTCCTTAAATCCTC
Reverse
CTTTGGGTCCTTTGGCCAATCCCGGGGATCCTGGGAAGTCAGTTGGTCCATTTC

W06H8.6
Forward
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCCTTCGTCAGCCCCCATTCTATTTC
Reverse
CTTTGGGTCCTTTGGCCAATCCCGGGGATCCAACACCATTTTTTGACCCGGGG

T28B8.1
Forward
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCGTGTCAACTAGGTCTATTGGGACTG
Reverse
CTTTGGGTCCTTTGGCCAATCCCGGGGATCCCGGCGGAACATGATGACTGCTG

K10G6.3
Forward_large
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCCATTTTTCCAACTTTTTAGGCCCCC
Forward_small
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCCGACGACGAGCAGTCACGTAAG
Reverse
CTTTGGGTCCTTTGGCCAATCCCGGGGATCCCCCTCCATCGACTCTACTGGCG

F27D4.2
Forward_large
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCGGAAGATGGGGATGCACAATTTG
Forward_small
GGAACAAAAGCTGGAGCTCCACCGCGGTGGCGGCCGCCTTTTTTGCAGCTCATTGCTCCGTG
Reverse
CTTTGGGTCCTTTGGCCAATCCCGGGGATCCGCTAGTGACATTCCGCTGGCTG

PEST-10 CLONING OLIGOS
W06H8.6
FORWARD CCGGAAGCTTCTGAGATTCCAGAGAACAGG
Reverse GGCCTCTAGAGAAATGGAGAAACCGAGAGGG

Supplemental Table 6. Position weight matrices for the identified motifs.

Matrix:1

	C	T	C	T	C	T	C	T	C	T	C
A |	0	4	1	0	1	6	4	1	2	1	0
C |	56	1	54	7	53	7	51	4	58	17	56
G |	5	0	2	1	4	9	3	7	0	4	5
T |	3	59	7	56	6	42	6	52	4	42	3

Matrix:2

	C	T	T	C	T	T	C	T	T	C	T	T	C
A |	0	2	1	0	1	2	4	7	1	0	4	4	1
C |	53	5	3	50	4	9	42	10	1	49	1	11	46
G |	0	8	1	1	10	2	2	7	1	1	1	2	1
T |	1	39	49	3	39	41	6	30	51	4	48	37	6

Matrix:3

	C	G	C	C	R	C	C	G	C	C	K	C	C
A |	3	1	2	4	13	2	9	1	3	3	1	1	4
C |	29	7	36	36	5	35	27	8	38	30	1	43	31
G |	6	38	4	6	25	6	6	32	3	6	21	1	4
T |	8	0	4	0	3	3	4	5	2	7	23	1	7

Matrix:4

	R	C	A	C	A	C	A	C
A |	13	1	34	0	38	1	36	4
C |	4	36	4	37	0	37	0	29
G |	17	0	0	0	0	0	1	3
T |	4	1	0	1	0	0	1	2

Matrix:5

	G	C	A	A	A	N	A	A	R	G	C
A |	0	0	10	13	16	3	10	15	8	2	0
C |	0	15	4	0	0	2	0	0	0	0	14
G |	16	0	2	3	0	5	4	0	8	14	1
T |	0	1	0	0	0	6	2	1	0	0	1

Matrix:6

	W	C	T	T	T	G	M
A |	10	0	0	0	0	2	18
C |	1	32	1	0	0	0	10
G |	2	0	1	0	0	28	3
T |	19	0	30	32	32	2	1

Matrix:7

	Y	C	A	W	T	T	T	T	C

```
A |   0   1  30  11   0   0   0   0   0
C |  10  29   0   2   0   0   0   0  30
G |   4   0   0   2   6   0   0   0   0
T |  16   0   0  15  24  30  30  30   0

Matrix:8
      A   C   T   G   C   A   G
A |  20   0   2   0   1  25   0
C |   1  22   1   1  28   1   0
G |   2   5   0  25   0   0  30
T |   7   3  27   4   1   4   0

Matrix:9
      C   G   T   T   T   C   G
A |   0   1   5   1   0   0   4
C |  27   1   3   0   3  27   0
G |   1  26   1   0   4   1  22
T |   0   0  19  27  21   0   2

Matrix:10
      T   T   C   C   A   G   A
A |   2   0   0   0  28   0  19
C |   0   0  28  23   0   0   1
G |   0   0   0   0   0  28   5
T |  26  28   0   5   0   0   3

Matrix:11
      S   A   C   G   T   G   G
A |   1  25   0   2   1   0   2
C |  14   0  26   0   0   3   0
G |  10   1   0  18   0  22  24
T |   1   0   0   6  25   1   0

Matrix:12
      C   C   M   A   A   A   M   C
A |   1   0  11  21  22  22   9   1
C |  22  20  13   3   0   1  12  16
G |   1   0   0   0   0   0   1   1
T |   0   4   0   0   2   1   2   6

Matrix:13
      T   C   T   G   G   T   T
A |   4   0   0   0   1   0   0
C |   0  22   0   0   0   0   2
G |   3   0   0  20  20   0   0
T |  15   0  22   2   1  22  20
```

```
Matrix:14
     C   T   G   A   C   C   G
A |   5   1   0  18   1   1   0
C |  20   0   1   1  25  28   3
G |   1   1  27   7   2   0  27
T |   4  28   2   4   2   1   0
```

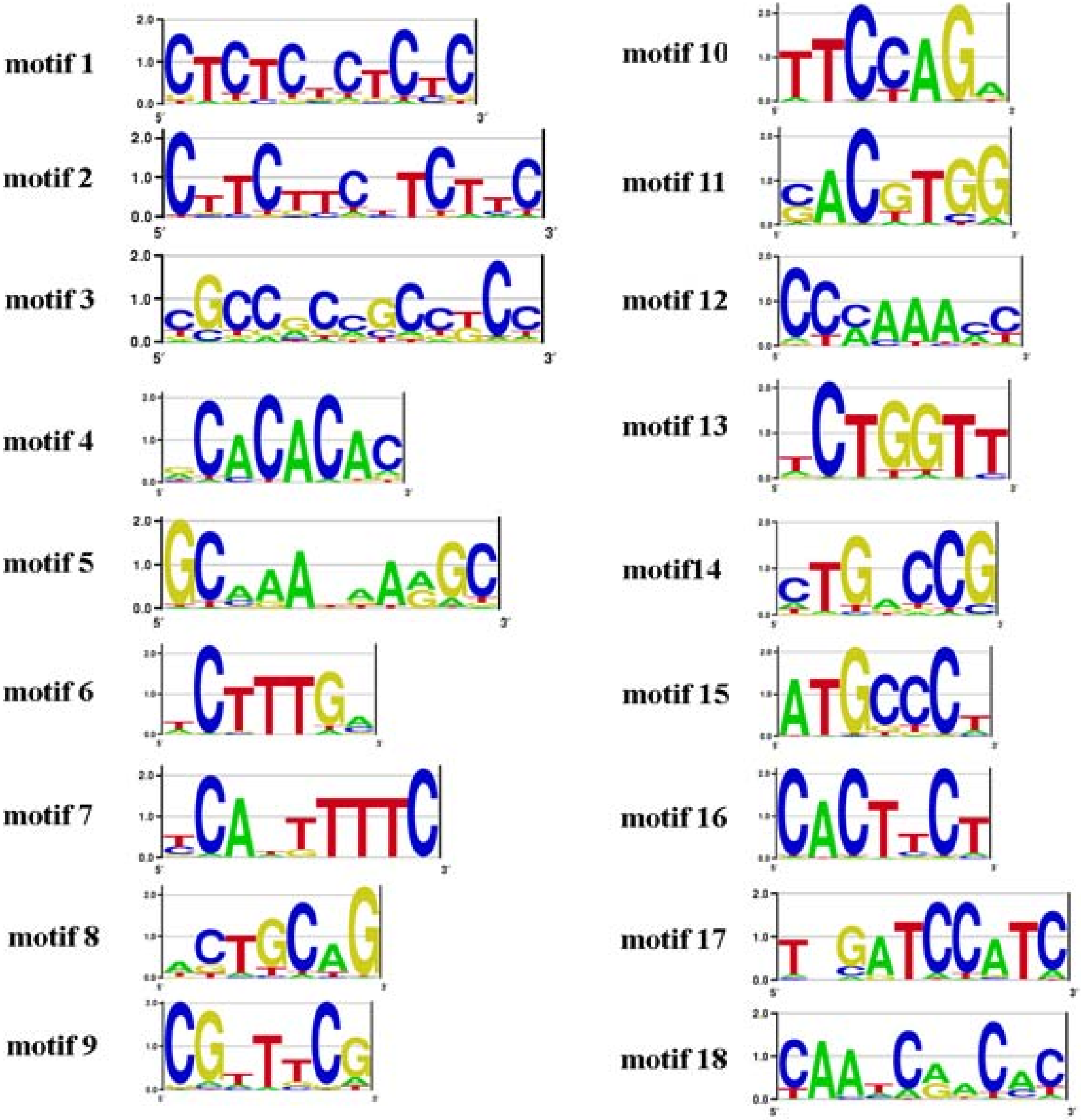
```
Matrix:15
     A   T   G   C   C   C   T
A |  20   0   0   0   0   0   4
C |   0   0   0  17  17  20   2
G |   0   0  20   2   1   0   0
T |   0  20   0   1   2   0  14
```

```
Matrix:16
     C   A   C   T   T   C   T
A |   0  20   0   0   1   0   1
C |  20   0  20   0   3  20   1
G |   0   0   0   0   1   0   0
T |   0   0   0  20  15   0  18
matrices same to it:
```

```
Matrix:17
     T   N   G   A   T   C   C   A   T   C
A |   1   5   1  16   0   1   0  16   0   2
C |   1   3   3   0   0  17  17   1   0  16
G |   0   5  14   2   0   0   0   1   0   0
T |  16   5   0   0  18   0   1   0  18   0
```

```
Matrix:18
     C   A   A   T   C   R   A   C   A   C
A |   0  18  17   4   2  10  12   0  12   1
C |  15   0   1   3  16   0   1  17   5  14
G |   0   0   0   0   0   8   3   0   1   0
T |   3   0   0  11   0   0   2   1   0   3
```

Supplemental Figure 1



Supplemental Figure 2

Supplemental Figure 3