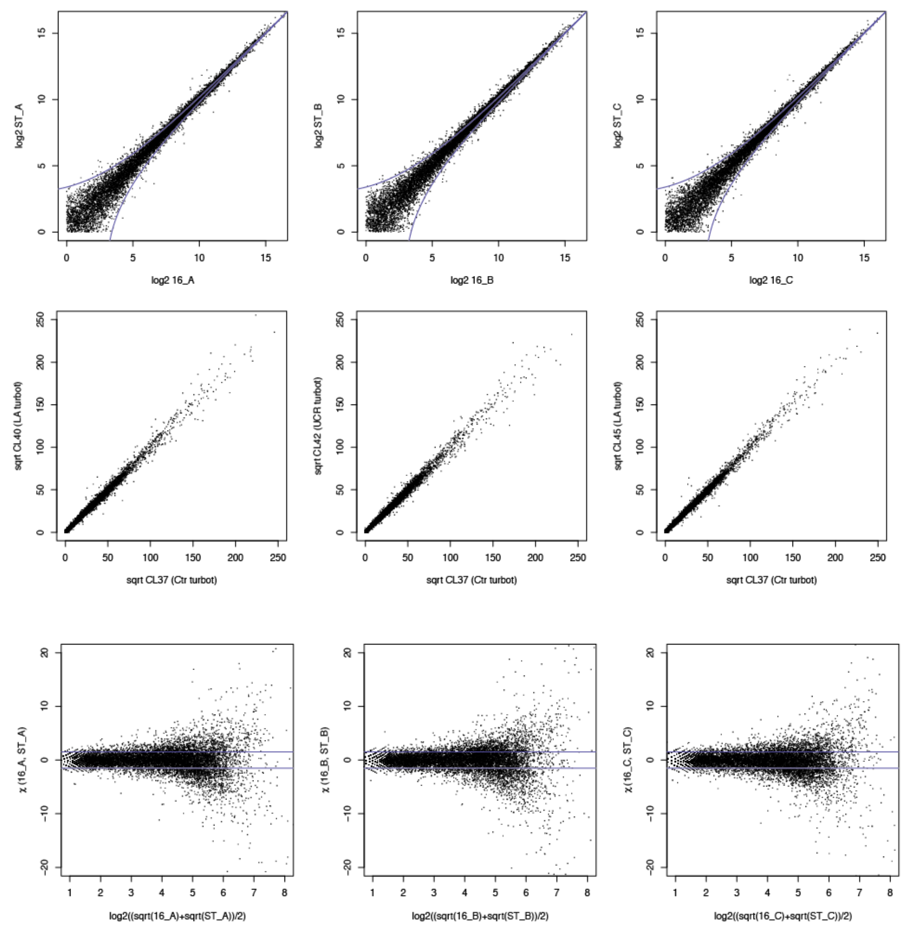
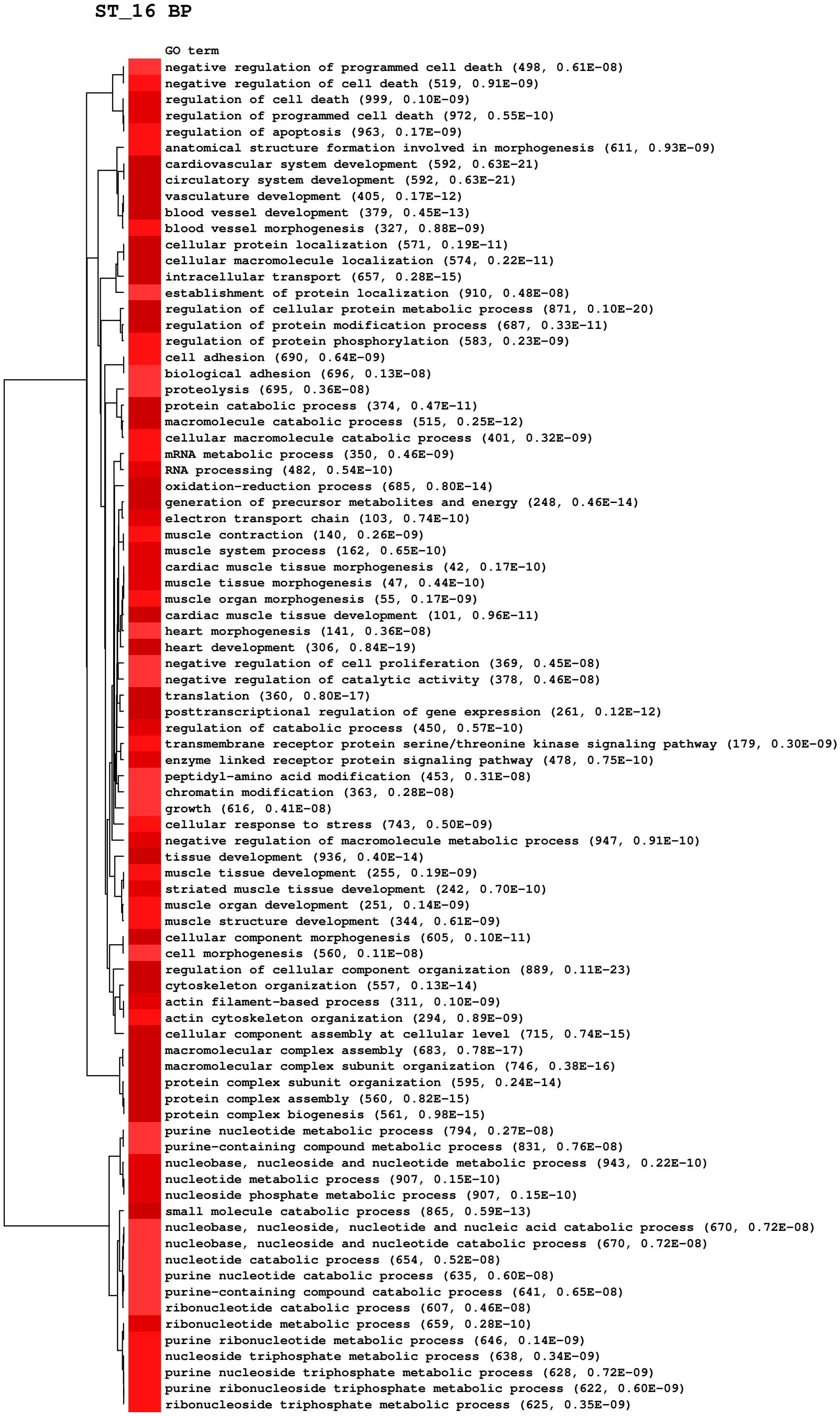


Supplemental Figure 1. Scatter plots comparing the RNA-Seq data from stretched and static samples The blue lines denote 3 standard deviations of Poisson noise away from perfect identity. ST represents static samples. 16 denotes data from samples exposed to 16% cyclic stretch.



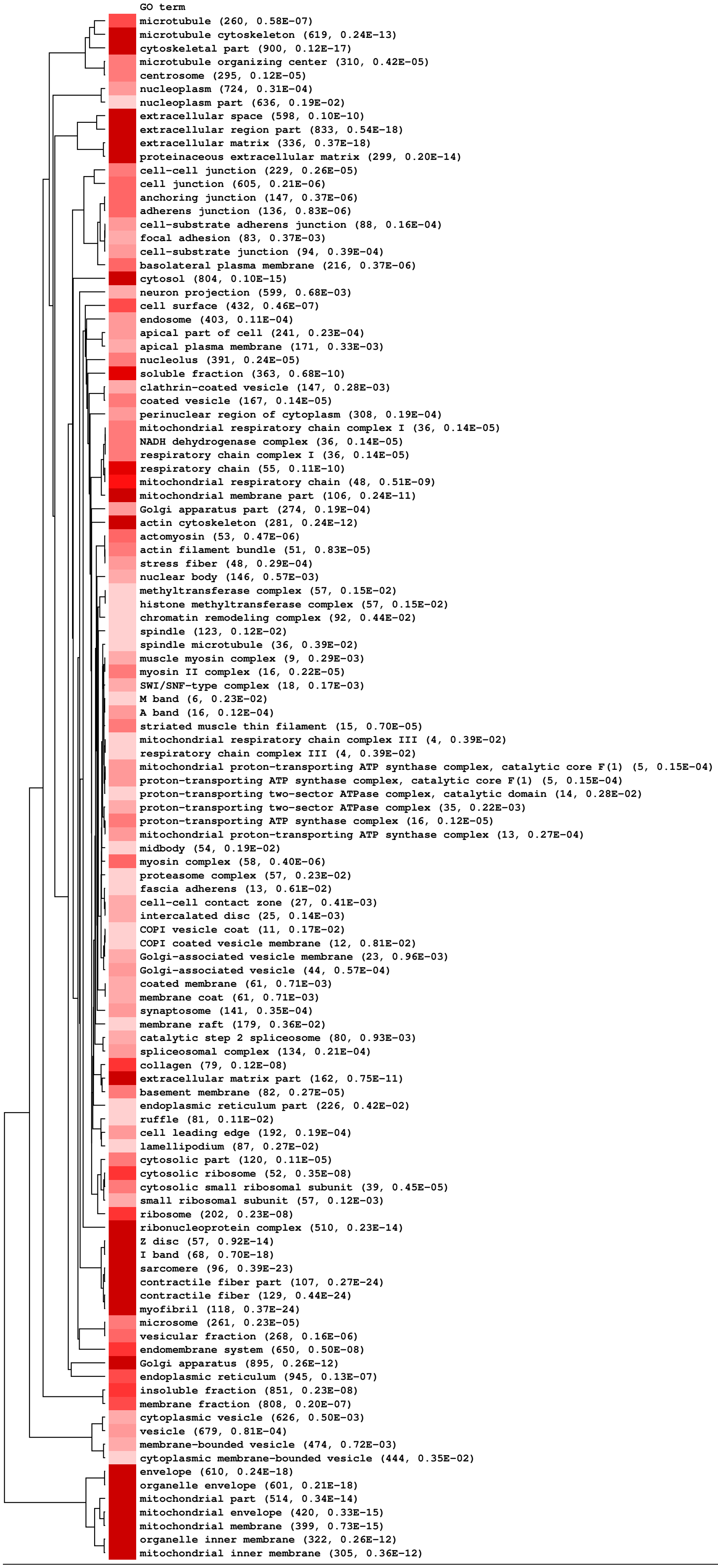
ST_16 BP

GO term
negative regulation of programmed cell death (498, 0.61E-08)
negative regulation of cell death (519, 0.91E-09)
regulation of cell death (999, 0.10E-09)
regulation of programmed cell death (972, 0.55E-10)
regulation of apoptosis (963, 0.17E-09)
anatomical structure formation involved in morphogenesis (611, 0.93E-09)
cardiovascular system development (592, 0.63E-21)
circulatory system development (592, 0.63E-21)
vasculature development (405, 0.17E-12)
blood vessel development (379, 0.45E-13)
blood vessel morphogenesis (327, 0.88E-09)
cellular protein localization (571, 0.19E-11)
cellular macromolecule localization (574, 0.22E-11)
intracellular transport (657, 0.28E-15)
establishment of protein localization (910, 0.48E-08)
regulation of cellular protein metabolic process (871, 0.10E-20)
regulation of protein modification process (687, 0.33E-11)
regulation of protein phosphorylation (583, 0.23E-09)
cell adhesion (690, 0.64E-09)
biological adhesion (696, 0.13E-08)
proteolysis (695, 0.36E-08)
protein catabolic process (374, 0.47E-11)
macromolecule catabolic process (515, 0.25E-12)
cellular macromolecule catabolic process (401, 0.32E-09)
mRNA metabolic process (350, 0.46E-09)
RNA processing (482, 0.54E-10)
oxidation-reduction process (685, 0.80E-14)
generation of precursor metabolites and energy (248, 0.46E-14)
electron transport chain (103, 0.74E-10)
muscle contraction (140, 0.26E-09)
muscle system process (162, 0.65E-10)
cardiac muscle tissue morphogenesis (42, 0.17E-10)
muscle tissue morphogenesis (47, 0.44E-10)
muscle organ morphogenesis (55, 0.17E-09)
cardiac muscle tissue development (101, 0.96E-11)
heart morphogenesis (141, 0.36E-08)
heart development (306, 0.84E-19)
negative regulation of cell proliferation (369, 0.45E-08)
negative regulation of catalytic activity (378, 0.46E-08)
translation (360, 0.80E-17)
posttranscriptional regulation of gene expression (261, 0.12E-12)
regulation of catabolic process (450, 0.57E-10)
transmembrane receptor protein serine/threonine kinase signaling pathway (179, 0.30E-09)
enzyme linked receptor protein signaling pathway (478, 0.75E-10)
peptidyl-amino acid modification (453, 0.31E-08)
chromatin modification (363, 0.28E-08)
growth (616, 0.41E-08)
cellular response to stress (743, 0.50E-09)
negative regulation of macromolecule metabolic process (947, 0.91E-10)
tissue development (936, 0.40E-14)
muscle tissue development (255, 0.19E-09)
striated muscle tissue development (242, 0.70E-10)
muscle organ development (251, 0.14E-09)
muscle structure development (344, 0.61E-09)
cellular component morphogenesis (605, 0.10E-11)
cell morphogenesis (560, 0.11E-08)
regulation of cellular component organization (889, 0.11E-23)
cytoskeleton organization (557, 0.13E-14)
actin filament-based process (311, 0.10E-09)
actin cytoskeleton organization (294, 0.89E-09)
cellular component assembly at cellular level (715, 0.74E-15)
macromolecular complex assembly (683, 0.78E-17)
macromolecular complex subunit organization (746, 0.38E-16)
protein complex subunit organization (595, 0.24E-14)
protein complex assembly (560, 0.82E-15)
protein complex biogenesis (561, 0.98E-15)
purine nucleotide metabolic process (794, 0.27E-08)
purine-containing compound metabolic process (831, 0.76E-08)
nucleobase, nucleoside and nucleotide metabolic process (943, 0.22E-10)
nucleotide metabolic process (907, 0.15E-10)
nucleoside phosphate metabolic process (907, 0.15E-10)
small molecule catabolic process (865, 0.59E-13)
nucleobase, nucleoside, nucleotide and nucleic acid catabolic process (670, 0.72E-08)
nucleobase, nucleoside and nucleotide catabolic process (670, 0.72E-08)
nucleotide catabolic process (654, 0.52E-08)
purine nucleotide catabolic process (635, 0.60E-08)
purine-containing compound catabolic process (641, 0.65E-08)
ribonucleotide catabolic process (607, 0.46E-08)
ribonucleotide metabolic process (659, 0.28E-10)
purine ribonucleotide metabolic process (646, 0.14E-09)
nucleoside triphosphate metabolic process (638, 0.34E-09)
purine nucleoside triphosphate metabolic process (628, 0.72E-09)
purine ribonucleoside triphosphate metabolic process (622, 0.60E-09)
ribonucleoside triphosphate metabolic process (625, 0.35E-09)

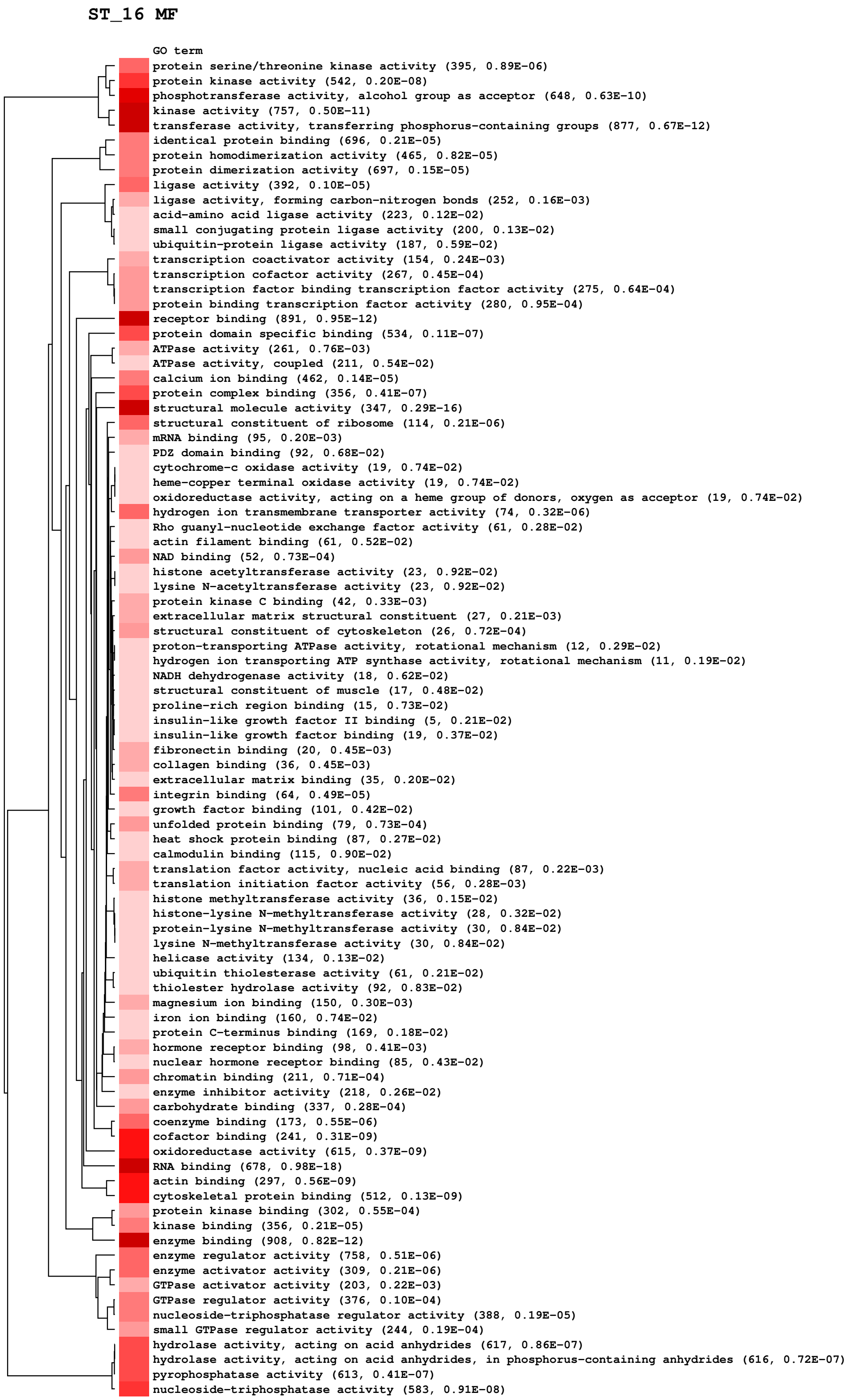
Supplemental Figure 2. Information clustering of stretch-modulated biologic process GO-terms

Clustering of GO-terms associated with biologic processes is presented. Numbers in parentheses are number of expressed genes in the process and adjusted p-value. Hue of the red color is proportional to (log) p-value; darker color means higher significance.

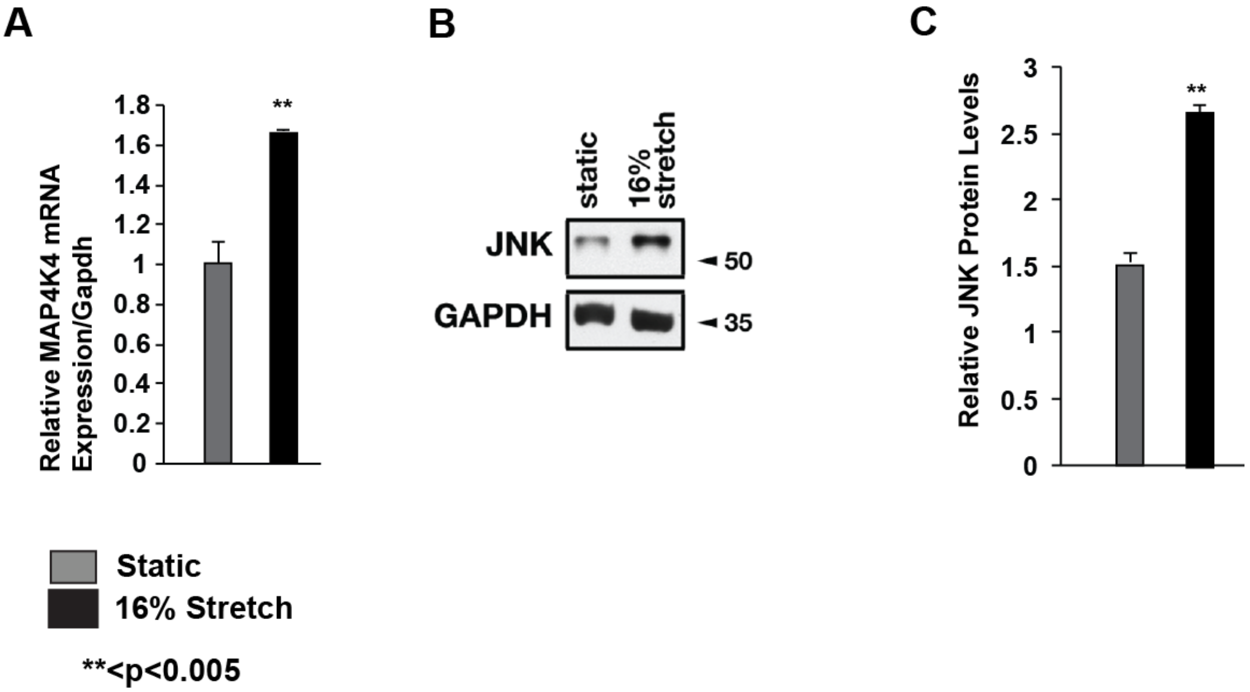
ST_16 CC


GO term
microtubule (260, 0.58E-07)
microtubule cytoskeleton (619, 0.24E-13)
cytoskeletal part (900, 0.12E-17)
microtubule organizing center (310, 0.42E-05)
centrosome (295, 0.12E-05)
nucleoplasm (724, 0.31E-04)
nucleoplasm part (636, 0.19E-02)
extracellular space (598, 0.10E-10)
extracellular region part (833, 0.54E-18)
extracellular matrix (336, 0.37E-18)
proteinaceous extracellular matrix (299, 0.20E-14)
cell-cell junction (229, 0.26E-05)
cell junction (605, 0.21E-06)
anchoring junction (147, 0.37E-06)
adherens junction (136, 0.83E-06)
cell-substrate adherens junction (88, 0.16E-04)
focal adhesion (83, 0.37E-03)
cell-substrate junction (94, 0.39E-04)
basolateral plasma membrane (216, 0.37E-06)
cytosol (804, 0.10E-15)
neuron projection (599, 0.68E-03)
cell surface (432, 0.46E-07)
endosome (403, 0.11E-04)
apical part of cell (241, 0.23E-04)
apical plasma membrane (171, 0.33E-03)
nucleolus (391, 0.24E-05)
soluble fraction (363, 0.68E-10)
clathrin-coated vesicle (147, 0.28E-03)
coated vesicle (167, 0.14E-05)
perinuclear region of cytoplasm (308, 0.19E-04)
mitochondrial respiratory chain complex I (36, 0.14E-05)
NADH dehydrogenase complex (36, 0.14E-05)
respiratory chain complex I (36, 0.14E-05)
respiratory chain (55, 0.11E-10)
mitochondrial respiratory chain (48, 0.51E-09)
mitochondrial membrane part (106, 0.24E-11)
Golgi apparatus part (274, 0.19E-04)
actin cytoskeleton (281, 0.24E-12)
actomyosin (53, 0.47E-06)
actin filament bundle (51, 0.83E-05)
stress fiber (48, 0.29E-04)
nuclear body (146, 0.57E-03)
methyltransferase complex (57, 0.15E-02)
histone methyltransferase complex (57, 0.15E-02)
chromatin remodeling complex (92, 0.44E-02)
spindle (123, 0.12E-02)
spindle microtubule (36, 0.39E-02)
muscle myosin complex (9, 0.29E-03)
myosin II complex (16, 0.22E-05)
SWI/SNF-type complex (18, 0.17E-03)
M band (6, 0.23E-02)
A band (16, 0.12E-04)
striated muscle thin filament (15, 0.70E-05)
mitochondrial respiratory chain complex III (4, 0.39E-02)
respiratory chain complex III (4, 0.39E-02)
mitochondrial proton-transporting ATP synthase complex, catalytic core F(1) (5, 0.15E-04)
proton-transporting ATP synthase complex, catalytic core F(1) (5, 0.15E-04)
proton-transporting two-sector ATPase complex, catalytic domain (14, 0.28E-02)
proton-transporting two-sector ATPase complex (35, 0.22E-03)
proton-transporting ATP synthase complex (16, 0.12E-05)
mitochondrial proton-transporting ATP synthase complex (13, 0.27E-04)
midbody (54, 0.19E-02)
myosin complex (58, 0.40E-06)
proteasome complex (57, 0.23E-02)
fascia adherens (13, 0.61E-02)
cell-cell contact zone (27, 0.41E-03)
intercalated disc (25, 0.14E-03)
COPI vesicle coat (11, 0.17E-02)
COPI coated vesicle membrane (12, 0.81E-02)
Golgi-associated vesicle membrane (23, 0.96E-03)
Golgi-associated vesicle (44, 0.57E-04)
coated membrane (61, 0.71E-03)
membrane coat (61, 0.71E-03)
synaptosome (141, 0.35E-04)
membrane raft (179, 0.36E-02)
catalytic step 2 spliceosome (80, 0.93E-03)
spliceosomal complex (134, 0.21E-04)
collagen (79, 0.12E-08)
extracellular matrix part (162, 0.75E-11)
basement membrane (82, 0.27E-05)
endoplasmic reticulum part (226, 0.42E-02)
ruffle (81, 0.11E-02)
cell leading edge (192, 0.19E-04)
lamellipodium (87, 0.27E-02)
cytosolic part (120, 0.11E-05)
cytosolic ribosome (52, 0.35E-08)
cytosolic small ribosomal subunit (39, 0.45E-05)
small ribosomal subunit (57, 0.12E-03)
ribosome (202, 0.23E-08)
ribonucleoprotein complex (510, 0.23E-14)
Z disc (57, 0.92E-14)
I band (68, 0.70E-18)
sarcomere (96, 0.39E-23)
contractile fiber part (107, 0.27E-24)
contractile fiber (129, 0.44E-24)
myofibril (118, 0.37E-24)
microsome (261, 0.23E-05)
vesicular fraction (268, 0.16E-06)
endomembrane system (650, 0.50E-08)
Golgi apparatus (895, 0.26E-12)
endoplasmic reticulum (945, 0.13E-07)
insoluble fraction (851, 0.23E-08)
membrane fraction (808, 0.20E-07)
cytoplasmic vesicle (626, 0.50E-03)
vesicle (679, 0.81E-04)
membrane-bounded vesicle (474, 0.72E-03)
cytoplasmic membrane-bounded vesicle (444, 0.35E-02)
envelope (610, 0.24E-18)
organelle envelope (601, 0.21E-18)
mitochondrial part (514, 0.34E-14)
mitochondrial envelope (420, 0.33E-15)
mitochondrial membrane (399, 0.73E-15)
organelle inner membrane (322, 0.26E-12)
mitochondrial inner membrane (305, 0.36E-12)

Supplemental Figure 3. Information clustering of stretch-modulated cellular component GO-terms Clustering of GO-terms associated with cellular component is presented. Numbers in parentheses are number of expressed genes in the process and adjusted p-value. Hue of the red color is proportional to (log) p-value; darker color means higher significance.

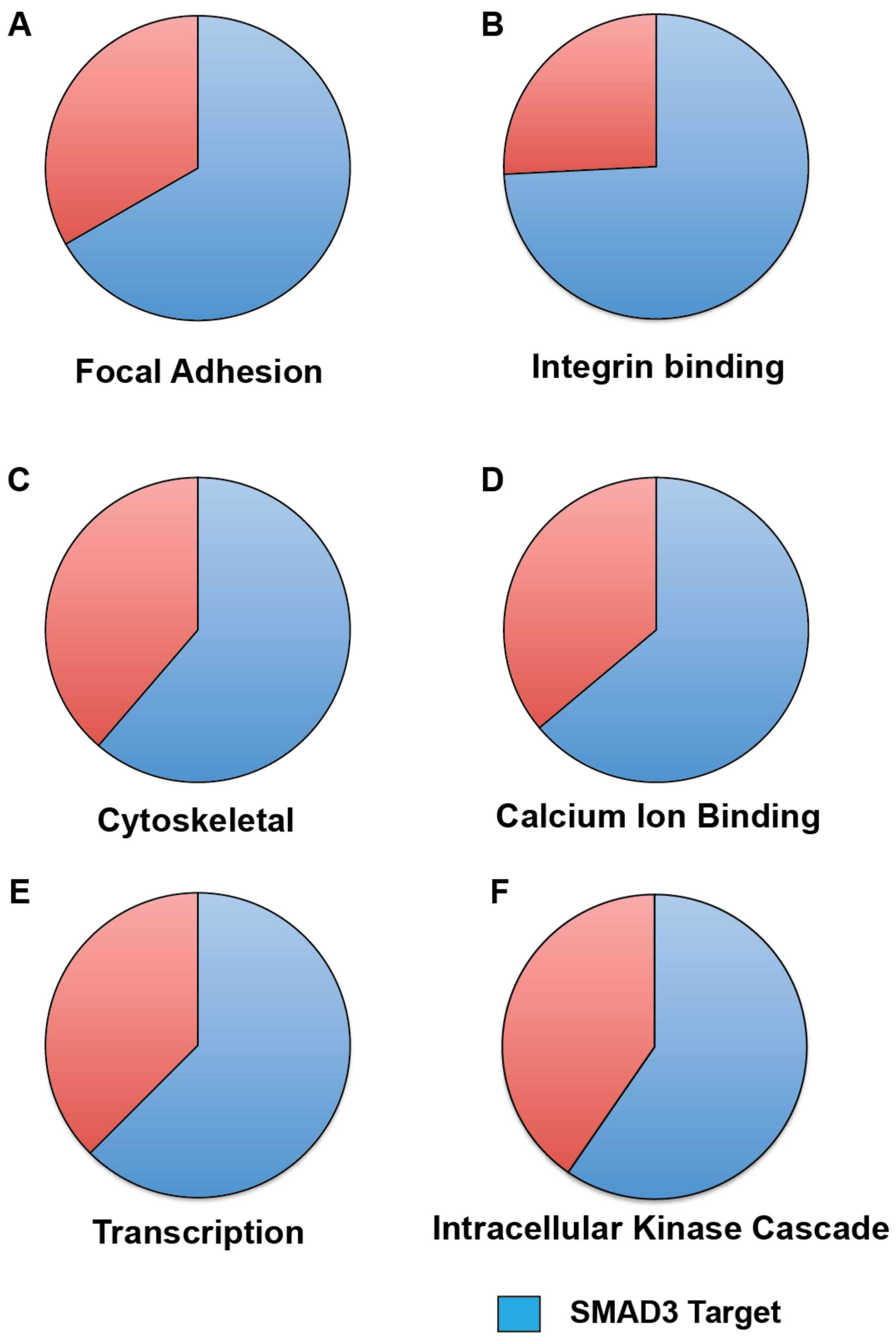


Supplemental Figure 4. Information clustering of stretch-modulated molecular function GO-terms
Clustering of GO-terms associated with Molecular Function is presented. Numbers in parentheses are number of expressed genes in the process and adjusted p-value. Hue of the red color is proportional to (log) p-value; darker color means higher significance.



Supplemental

Figure 5. Stretch increases of *MAP4K4* expression and JNK protein levels. A. qPCR demonstrating that stretch is sufficient to increase the expression of *MAP4K4*, which is an activator of the JNK pathway (1 +/- 11.3% for static and 1.67 +/- 1.0%; n=4). B. and C. Cyclic stretch is sufficient to increase the protein levels of JNK. (1 +/- 14% for static and 2.66 +/- 12.4% for stretch; n=4).



Supplemental Figure 6. rVISTA analysis of selected stretch responsive GO-terms. rVISTA analysis was performed for stretch responsive GO-terms (see section 3.1). Myofibrillar and cardiac development rVISTA results are in Fig 2F. A. 66.7% of stretch responsive genes in the focal adhesion GO are predicted to contain a conserved Smad3 site within 5 kb of the proximal promoter region ($p<0.05$). B. 74.2% of stretch responsive genes in the integrin binding GO-group have conserved Smad3 binding sites ($p=3.98\times10^{-6}$). C. 61.3% of cytoskeletal GO-members that are stretch responsive have conserved Smad3 binding sites ($p=9.77 \times 10^{-4}$). D. 63.9% of calcium binding genes that were stretch responsive have Smad3 binding sites ($p=3.98\times10^{-7}$). E. 62.5% of genes in the transcription GO-term are predicted to have Smad3 binding sites within the proximal promoter region ($p=1.62 \times 10^{-15}$). F. 59.6% of genes in the intracellular kinase cascade GO-term modulated by stretch contain a conserved Smad3 site ($p=1.43 \times 10^{-10}$). Of note, GTPase, oxidoreductase activity, and translation GO-terms did not show significant SMAD3 enrichment using rVISTA.

Supplemental Videos

Supplemental Video 1. Video demonstrating Dynamic Monolayer Force Microscopy (DMFM)
Supplemental Video 2. Video demonstrating DMFM in EMCMs treated with Tgf-β2
Supplemental Video 3. Video demonstrating DMFM in control EMCMs

Supplemental Data files

Supplemental File 1. Excel file of RNA-Seq data
Table of the 4900 genes modulated by stretch with a FDR<0.05 are listed.

Supplemental File 2. Excel file of Biologic Process GO-terms modulated by stretch

Supplemental File 3. Excel file of Cellular Components GO-terms modulated by stretch

Supplemental File 4. Excel file of Molecular Process GO-terms modulated by stretch

Biologic Process GO Terms Modulated by Stretch

GO ID	Biological Process	Bonferroni p-value
51128	regulation of cellular component organization	1.08E-24
72358	cardiovascular system development	6.33E-22
72359	circulatory system development	6.33E-22
32268	regulation of cellular protein metabolic process	1.03E-21
7507	heart development	8.37E-20
65003	macromolecular complex assembly	7.75E-18
6412	translation	7.97E-18
43933	macromolecular complex subunit organization	3.83E-17
46907	intracellular transport	2.82E-16
71844	cellular component assembly at cellular level	7.36E-16
6461	protein complex assembly	8.18E-16
70271	protein complex biogenesis	9.85E-16
7010	cytoskeleton organization	1.31E-15
71822	protein complex subunit organization	2.44E-15
9888	tissue development	3.97E-15
6091	generation of precursor metabolites and energy	4.56E-15
55114	oxidation-reduction process	7.95E-15
1568	blood vessel development	4.47E-14
44282	small molecule catabolic process	5.93E-14
10608	posttranscriptional regulation of gene expression	1.17E-13
1944	vasculature development	1.66E-13
9057	macromolecule catabolic process	2.52E-13
32989	cellular component morphogenesis	1.04E-12
34613	cellular protein localization	1.94E-12
70727	cellular macromolecule localization	2.16E-12
31399	regulation of protein modification process	3.31E-12
30163	protein catabolic process	4.65E-12
48738	cardiac muscle tissue development	9.57E-12
6753	nucleoside phosphate metabolic process	1.50E-11
9117	nucleotide metabolic process	1.50E-11
55008	cardiac muscle tissue morphogenesis	1.67E-11
55086	nucleobase, nucleoside and nucleotide metabolic proces	2.23E-11
9259	ribonucleotide metabolic process	2.77E-11
60415	muscle tissue morphogenesis	4.44E-11
6396	RNA processing	5.42E-11
43067	regulation of programmed cell death	5.45E-11
9894	regulation of catabolic process	5.68E-11
3012	muscle system process	6.53E-11
14706	striated muscle tissue development	7.05E-11
22900	electron transport chain	7.39E-11
7167	enzyme linked receptor protein signaling pathway	7.46E-11
10605	negative regulation of macromolecule metabolic proces	9.13E-11
10941	regulation of cell death	1.01E-10
30029	actin filament-based process	1.02E-10
7517	muscle organ development	1.42E-10
9150	purine ribonucleotide metabolic process	1.43E-10
48644	muscle organ morphogenesis	1.70E-10

42981	regulation of apoptosis	1.75E-10
60537	muscle tissue development	1.91E-10
1932	regulation of protein phosphorylation	2.30E-10
6936	muscle contraction	2.60E-10
7178	transmembrane receptor protein serine/threonine kinas	3.04E-10
44265	cellular macromolecule catabolic process	3.23E-10
9141	nucleoside triphosphate metabolic process	3.43E-10
9199	ribonucleoside triphosphate metabolic process	3.52E-10
16071	mRNA metabolic process	4.59E-10
33554	cellular response to stress	5.01E-10
9205	purine ribonucleoside triphosphate metabolic process	6.04E-10
61061	muscle structure development	6.09E-10
7155	cell adhesion	6.36E-10
9144	purine nucleoside triphosphate metabolic process	7.20E-10
48514	blood vessel morphogenesis	8.81E-10
30036	actin cytoskeleton organization	8.91E-10
60548	negative regulation of cell death	9.07E-10
48646	anatomical structure formation involved in morphogene	9.35E-10
902	cell morphogenesis	1.10E-09
22610	biological adhesion	1.30E-09
6163	purine nucleotide metabolic process	2.66E-09
16568	chromatin modification	2.82E-09
18193	peptidyl-amino acid modification	3.08E-09
3007	heart morphogenesis	3.58E-09
6508	proteolysis	3.64E-09
40007	growth	4.13E-09
8285	negative regulation of cell proliferation	4.53E-09
9261	ribonucleotide catabolic process	4.61E-09
43086	negative regulation of catalytic activity	4.63E-09
45184	establishment of protein localization	4.80E-09
9166	nucleotide catabolic process	5.22E-09
6195	purine nucleotide catabolic process	5.95E-09
43069	negative regulation of programmed cell death	6.10E-09
72523	purine-containing compound catabolic process	6.48E-09
34655	nucleobase, nucleoside, nucleotide and nucleic acid cata	7.23E-09
34656	nucleobase, nucleoside and nucleotide catabolic process	7.23E-09
72521	purine-containing compound metabolic process	7.59E-09
6325	chromatin organization	1.04E-08
48729	tissue morphogenesis	1.14E-08
9203	ribonucleoside triphosphate catabolic process	1.17E-08
31329	regulation of cellular catabolic process	1.23E-08
43066	negative regulation of apoptosis	1.39E-08
6417	regulation of translation	1.42E-08
34621	cellular macromolecular complex subunit organization	1.49E-08
9154	purine ribonucleotide catabolic process	1.52E-08
9143	nucleoside triphosphate catabolic process	1.59E-08
55010	ventricular cardiac muscle tissue morphogenesis	1.62E-08
6397	mRNA processing	1.66E-08
44270	cellular nitrogen compound catabolic process	1.66E-08

9207	purine ribonucleoside triphosphate catabolic process	1.73E-08
8015	blood circulation	1.74E-08
3013	circulatory system process	1.83E-08
19752	carboxylic acid metabolic process	1.84E-08
43436	oxoacid metabolic process	1.84E-08
34622	cellular macromolecular complex assembly	1.98E-08
16192	vesicle-mediated transport	2.33E-08
60070	canonical Wnt receptor signaling pathway	2.54E-08
46700	heterocycle catabolic process	2.74E-08
3229	ventricular cardiac muscle tissue development	2.90E-08
44092	negative regulation of molecular function	3.23E-08
9146	purine nucleoside triphosphate catabolic process	3.28E-08
51726	regulation of cell cycle	3.50E-08
6082	organic acid metabolic process	4.46E-08
30239	myofibril assembly	5.06E-08
43408	regulation of MAPKKK cascade	5.08E-08
6084	acetyl-CoA metabolic process	5.39E-08
51276	chromosome organization	5.50E-08
22402	cell cycle process	6.57E-08
904	cell morphogenesis involved in differentiation	7.83E-08
55001	muscle cell development	7.93E-08
44262	cellular carbohydrate metabolic process	8.05E-08
31324	negative regulation of cellular metabolic process	9.28E-08
51603	proteolysis involved in cellular protein catabolic process	9.36E-08
42325	regulation of phosphorylation	9.40E-08
42127	regulation of cell proliferation	1.03E-07
42180	cellular ketone metabolic process	1.21E-07
51248	negative regulation of protein metabolic process	1.29E-07
51259	protein oligomerization	1.40E-07
165	MAPKKK cascade	1.59E-07
3015	heart process	1.63E-07
60047	heart contraction	1.63E-07
3208	cardiac ventricle morphogenesis	1.65E-07
6886	intracellular protein transport	1.69E-07
55002	striated muscle cell development	1.96E-07
33275	actin-myosin filament sliding	2.01E-07
19220	regulation of phosphate metabolic process	2.16E-07
51174	regulation of phosphorus metabolic process	2.16E-07
44257	cellular protein catabolic process	2.21E-07
15031	protein transport	2.26E-07
6928	cellular component movement	2.30E-07
51146	striated muscle cell differentiation	2.72E-07
9790	embryo development	2.80E-07
44093	positive regulation of molecular function	2.90E-07
60429	epithelium development	3.18E-07
16569	covalent chromatin modification	3.26E-07
70647	protein modification by small protein conjugation or ren	3.42E-07
30198	extracellular matrix organization	3.83E-07
43062	extracellular structure organization	3.83E-07

31032	actomyosin structure organization	3.87E-07
16049	cell growth	3.88E-07
16570	histone modification	4.46E-07
32270	positive regulation of cellular protein metabolic process	4.81E-07
70252	actin-mediated cell contraction	5.26E-07
51336	regulation of hydrolase activity	5.34E-07
278	mitotic cell cycle	6.30E-07
9887	organ morphogenesis	6.72E-07
45859	regulation of protein kinase activity	7.26E-07
30030	cell projection organization	7.74E-07
33365	protein localization to organelle	7.83E-07
1558	regulation of cell growth	8.35E-07
61024	membrane organization	8.38E-07
6099	tricarboxylic acid cycle	8.57E-07
16044	cellular membrane organization	1.04E-06
22008	neurogenesis	1.09E-06
31175	neuron projection development	1.12E-06
30111	regulation of Wnt receptor signaling pathway	1.15E-06
45333	cellular respiration	1.19E-06
30855	epithelial cell differentiation	1.20E-06
9060	aerobic respiration	1.21E-06
10648	negative regulation of cell communication	1.60E-06
30199	collagen fibril organization	1.66E-06
46356	acetyl-CoA catabolic process	1.71E-06
3231	cardiac ventricle development	1.79E-06
5975	carbohydrate metabolic process	1.84E-06
6457	protein folding	1.90E-06
6605	protein targeting	1.96E-06
6066	alcohol metabolic process	2.12E-06
9967	positive regulation of signal transduction	2.19E-06
43085	positive regulation of catalytic activity	2.21E-06
8380	RNA splicing	2.28E-06
60828	regulation of canonical Wnt receptor signaling pathway	2.50E-06
35295	tube development	2.72E-06
7265	Ras protein signal transduction	2.75E-06
3206	cardiac chamber morphogenesis	2.94E-06
44087	regulation of cellular component biogenesis	3.18E-06
7243	intracellular protein kinase cascade	3.63E-06
23057	negative regulation of signaling	3.65E-06
15985	energy coupled proton transport, down electrochemical	3.74E-06
15986	ATP synthesis coupled proton transport	3.74E-06
1701	in utero embryonic development	3.77E-06
32269	negative regulation of cellular protein metabolic proces	4.06E-06
48699	generation of neurons	4.10E-06
51346	negative regulation of hydrolase activity	4.29E-06
3205	cardiac chamber development	4.77E-06
43549	regulation of kinase activity	4.86E-06
10627	regulation of intracellular protein kinase cascade	4.87E-06
51338	regulation of transferase activity	5.43E-06

30811	regulation of nucleotide catabolic process	6.35E-06
33121	regulation of purine nucleotide catabolic process	6.35E-06
51247	positive regulation of protein metabolic process	6.70E-06
6413	translational initiation	6.85E-06
43632	modification-dependent macromolecule catabolic proces	7.11E-06
45595	regulation of cell differentiation	7.22E-06
48584	positive regulation of response to stimulus	7.48E-06
19941	modification-dependent protein catabolic process	7.52E-06
33673	negative regulation of kinase activity	8.53E-06
30182	neuron differentiation	9.94E-06
6913	nucleocytoplasmic transport	1.00E-05
48585	negative regulation of response to stimulus	1.16E-05
2000026	regulation of multicellular organismal development	1.17E-05
6941	striated muscle contraction	1.27E-05
22604	regulation of cell morphogenesis	1.32E-05
9968	negative regulation of signal transduction	1.32E-05
40008	regulation of growth	1.33E-05
51169	nuclear transport	1.41E-05
44283	small molecule biosynthetic process	1.47E-05
6511	ubiquitin-dependent protein catabolic process	1.57E-05
42692	muscle cell differentiation	1.68E-05
30048	actin filament-based movement	1.68E-05
51130	positive regulation of cellular component organization	1.73E-05
7266	Rho protein signal transduction	1.99E-05
51260	protein homooligomerization	1.99E-05
30177	positive regulation of Wnt receptor signaling pathway	2.09E-05
7264	small GTPase mediated signal transduction	2.12E-05
32446	protein modification by small protein conjugation	2.22E-05
51056	regulation of small GTPase mediated signal transductior	2.32E-05
90092	regulation of transmembrane receptor protein serine/th	2.34E-05
51186	cofactor metabolic process	2.65E-05
6184	GTP catabolic process	2.76E-05
22411	cellular component disassembly	2.89E-05
30518	steroid hormone receptor signaling pathway	2.89E-05
71901	negative regulation of protein serine/threonine kinase a	2.99E-05
6469	negative regulation of protein kinase activity	3.21E-05
23056	positive regulation of signaling	3.33E-05
48666	neuron development	3.44E-05
51187	cofactor catabolic process	3.67E-05
22603	regulation of anatomical structure morphogenesis	3.75E-05
10629	negative regulation of gene expression	3.87E-05
46039	GTP metabolic process	3.89E-05
7179	transforming growth factor beta receptor signaling path	3.95E-05
1525	angiogenesis	4.55E-05
43623	cellular protein complex assembly	4.78E-05
46578	regulation of Ras protein signal transduction	4.84E-05
9890	negative regulation of biosynthetic process	5.44E-05
9109	coenzyme catabolic process	5.47E-05
16055	Wnt receptor signaling pathway	5.52E-05

10647	positive regulation of cell communication	5.60E-05
19318	hexose metabolic process	5.87E-05
2000113	negative regulation of cellular macromolecule biosynthe	5.94E-05
51129	negative regulation of cellular component organization	5.97E-05
42592	homeostatic process	6.27E-05
40012	regulation of locomotion	6.33E-05
90263	positive regulation of canonical Wnt receptor signaling p	6.52E-05
51493	regulation of cytoskeleton organization	7.05E-05
40011	locomotion	7.41E-05
51348	negative regulation of transferase activity	7.50E-05
45214	sarcomere organization	8.03E-05
8284	positive regulation of cell proliferation	8.15E-05
8016	regulation of heart contraction	8.17E-05
31327	negative regulation of cellular biosynthetic process	8.36E-05
16477	cell migration	8.39E-05
6259	DNA metabolic process	8.49E-05
35023	regulation of Rho protein signal transduction	8.86E-05
48870	cell motility	8.87E-05
51674	localization of cell	8.87E-05
30049	muscle filament sliding	8.88E-05
71845	cellular component disassembly at cellular level	8.92E-05
48858	cell projection morphogenesis	9.50E-05
6897	endocytosis	9.55E-05
10324	membrane invagination	9.55E-05
31401	positive regulation of protein modification process	9.89E-05
10927	cellular component assembly involved in morphogenesis	1.10E-04
15980	energy derivation by oxidation of organic compounds	1.13E-04
6172	ADP biosynthetic process	1.15E-04
9136	purine nucleoside diphosphate biosynthetic process	1.15E-04
9180	purine ribonucleoside diphosphate biosynthetic process	1.15E-04
6974	response to DNA damage stimulus	1.20E-04
16567	protein ubiquitination	1.26E-04
10558	negative regulation of macromolecule biosynthetic proc	1.27E-04
32386	regulation of intracellular transport	1.27E-04
43087	regulation of GTPase activity	1.30E-04
32990	cell part morphogenesis	1.32E-04
70887	cellular response to chemical stimulus	1.40E-04
71843	cellular component biogenesis at cellular level	1.58E-04
43009	chordate embryonic development	1.62E-04
30334	regulation of cell migration	1.67E-04
31668	cellular response to extracellular stimulus	1.68E-04
48812	neuron projection morphogenesis	1.71E-04
42176	regulation of protein catabolic process	1.79E-04
51301	cell division	1.85E-04
30522	intracellular receptor mediated signaling pathway	1.86E-04
6916	anti-apoptosis	1.89E-04
9792	embryo development ending in birth or egg hatching	1.93E-04
45786	negative regulation of cell cycle	2.00E-04
46034	ATP metabolic process	2.13E-04

44057	regulation of system process	2.14E-04
34330	cell junction organization	2.14E-04
2000145	regulation of cell motility	2.17E-04
33124	regulation of GTP catabolic process	2.25E-04
50684	regulation of mRNA processing	2.29E-04
22613	ribonucleoprotein complex biogenesis	2.30E-04
31328	positive regulation of cellular biosynthetic process	2.31E-04
10628	positive regulation of gene expression	2.33E-04
51093	negative regulation of developmental process	2.33E-04
43068	positive regulation of programmed cell death	2.38E-04
16126	sterol biosynthetic process	2.52E-04
60284	regulation of cell development	2.53E-04
71496	cellular response to external stimulus	2.56E-04
16579	protein deubiquitination	2.57E-04
5996	monosaccharide metabolic process	2.86E-04
10557	positive regulation of macromolecule biosynthetic proce	2.90E-04
2009	morphogenesis of an epithelium	2.92E-04
51270	regulation of cellular component movement	2.96E-04
87	M phase of mitotic cell cycle	3.05E-04
43547	positive regulation of GTPase activity	3.34E-04
9188	ribonucleoside diphosphate biosynthetic process	3.42E-04
52547	regulation of peptidase activity	3.60E-04
33043	regulation of organelle organization	3.70E-04
48285	organelle fission	3.79E-04
51254	positive regulation of RNA metabolic process	4.22E-04
6006	glucose metabolic process	4.26E-04
43065	positive regulation of apoptosis	4.77E-04
7050	cell cycle arrest	4.83E-04
90257	regulation of muscle system process	5.05E-04
30323	respiratory tube development	5.37E-04
10466	negative regulation of peptidase activity	5.44E-04
17038	protein import	5.59E-04
48667	cell morphogenesis involved in neuron differentiation	6.13E-04
280	nuclear division	6.15E-04
7067	mitosis	6.15E-04
45596	negative regulation of cell differentiation	6.26E-04
7015	actin filament organization	6.34E-04
34329	cell junction assembly	6.52E-04
43648	dicarboxylic acid metabolic process	7.00E-04
60048	cardiac muscle contraction	7.18E-04
55007	cardiac muscle cell differentiation	7.36E-04
46031	ADP metabolic process	7.94E-04
55006	cardiac cell development	8.08E-04
55013	cardiac muscle cell development	8.08E-04
10942	positive regulation of cell death	9.01E-04
71900	regulation of protein serine/threonine kinase activity	9.08E-04
90100	positive regulation of transmembrane receptor protein s	9.36E-04
45893	positive regulation of transcription, DNA-dependent	9.72E-04
1503	ossification	9.92E-04

48771	tissue remodeling	1.13E-03
51253	negative regulation of RNA metabolic process	1.13E-03
16571	histone methylation	1.18E-03
17148	negative regulation of translation	1.26E-03
19725	cellular homeostasis	1.29E-03
30278	regulation of ossification	1.38E-03
51345	positive regulation of hydrolase activity	1.42E-03
30324	lung development	1.42E-03
18209	peptidyl-serine modification	1.45E-03
6357	regulation of transcription from RNA polymerase II pror	1.45E-03
6695	cholesterol biosynthetic process	1.52E-03
9133	nucleoside diphosphate biosynthetic process	1.58E-03
6754	ATP biosynthetic process	1.65E-03
31344	regulation of cell projection organization	1.67E-03
6366	transcription from RNA polymerase II promoter	1.68E-03
30509	BMP signaling pathway	1.84E-03
7017	microtubule-based process	1.98E-03
18105	peptidyl-serine phosphorylation	2.04E-03
15992	proton transport	2.06E-03
6140	regulation of nucleotide metabolic process	2.14E-03
35239	tube morphogenesis	2.16E-03
45732	positive regulation of protein catabolic process	2.22E-03
44275	cellular carbohydrate catabolic process	2.37E-03
43154	negative regulation of caspase activity	2.60E-03
1570	vasculogenesis	2.60E-03
30335	positive regulation of cell migration	2.74E-03
9135	purine nucleoside diphosphate metabolic process	2.82E-03
9179	purine ribonucleoside diphosphate metabolic process	2.82E-03
2027	regulation of heart rate	2.95E-03
6818	hydrogen transport	2.96E-03
31346	positive regulation of cell projection organization	3.03E-03
51173	positive regulation of nitrogen compound metabolic pro	3.08E-03
46777	protein autophosphorylation	3.12E-03
51592	response to calcium ion	3.17E-03
45934	negative regulation of nucleobase, nucleoside, nucleotic	3.20E-03
45892	negative regulation of transcription, DNA-dependent	3.30E-03
45935	positive regulation of nucleobase, nucleoside, nucleotid	3.37E-03
31589	cell-substrate adhesion	3.44E-03
2000147	positive regulation of cell motility	3.49E-03
61077	chaperone-mediated protein folding	3.52E-03
72594	establishment of protein localization to organelle	3.66E-03
70723	response to cholesterol	3.74E-03
43462	regulation of ATPase activity	3.88E-03
10033	response to organic substance	3.99E-03
51172	negative regulation of nitrogen compound metabolic pr	4.03E-03
40017	positive regulation of locomotion	4.04E-03
8217	regulation of blood pressure	4.09E-03
1822	kidney development	4.10E-03
43254	regulation of protein complex assembly	4.14E-03

9206	purine ribonucleoside triphosphate biosynthetic process	4.19E-03
9152	purine ribonucleotide biosynthetic process	4.20E-03
31669	cellular response to nutrient levels	4.30E-03
22403	cell cycle phase	4.30E-03
10975	regulation of neuron projection development	4.33E-03
55003	cardiac myofibril assembly	4.44E-03
32388	positive regulation of intracellular transport	4.51E-03
34968	histone lysine methylation	4.52E-03
9145	purine nucleoside triphosphate biosynthetic process	4.67E-03
72001	renal system development	4.68E-03
34504	protein localization to nucleus	4.80E-03
48193	Golgi vesicle transport	4.81E-03
48878	chemical homeostasis	4.89E-03
43409	negative regulation of MAPKKK cascade	4.97E-03
16337	cell-cell adhesion	5.03E-03
70646	protein modification by small protein removal	5.08E-03
6629	lipid metabolic process	5.15E-03
10740	positive regulation of intracellular protein kinase cascad	5.18E-03
9201	ribonucleoside triphosphate biosynthetic process	5.19E-03
9260	ribonucleotide biosynthetic process	5.19E-03
35051	cardiac cell differentiation	5.28E-03
17015	regulation of transforming growth factor beta receptor	5.32E-03
55085	transmembrane transport	5.58E-03
30155	regulation of cell adhesion	5.61E-03
45664	regulation of neuron differentiation	5.75E-03
3	reproduction	5.81E-03
72593	reactive oxygen species metabolic process	6.35E-03
1655	urogenital system development	6.56E-03
32787	monocarboxylic acid metabolic process	6.72E-03
60541	respiratory system development	6.83E-03
9142	nucleoside triphosphate biosynthetic process	7.05E-03
22414	reproductive process	7.11E-03
90066	regulation of anatomical structure size	7.23E-03
6732	coenzyme metabolic process	7.47E-03
7512	adult heart development	7.48E-03
6979	response to oxidative stress	7.74E-03
32970	regulation of actin filament-based process	7.90E-03
51094	positive regulation of developmental process	8.25E-03
7163	establishment or maintenance of cell polarity	8.28E-03
43281	regulation of caspase activity	8.45E-03
51272	positive regulation of cellular component movement	8.65E-03
6937	regulation of muscle contraction	8.94E-03
14896	muscle hypertrophy	9.40E-03
9896	positive regulation of catabolic process	9.50E-03
7160	cell-matrix adhesion	9.51E-03

Cellular Component GO Terms Modulated by Stretch

GO ID	Cellular Component	Bonferroni p-value
44449	contractile fiber part	2.72E-25
30016	myofibril	3.75E-25
43292	contractile fiber	4.37E-25
30017	sarcomere	3.94E-24
31967	organelle envelope	2.06E-19
31975	envelope	2.39E-19
31012	extracellular matrix	3.74E-19
44421	extracellular region part	5.44E-19
31674	I band	7.02E-19
44430	cytoskeletal part	1.21E-18
5829	cytosol	1.05E-16
5740	mitochondrial envelope	3.35E-16
31966	mitochondrial membrane	7.31E-16
5578	proteinaceous extracellular matrix	2.00E-15
30529	ribonucleoprotein complex	2.34E-15
44429	mitochondrial part	3.36E-15
30018	Z disc	9.23E-15
15630	microtubule cytoskeleton	2.44E-14
15629	actin cytoskeleton	2.36E-13
5794	Golgi apparatus	2.57E-13
19866	organelle inner membrane	2.58E-13
5743	mitochondrial inner membrane	3.60E-13
44455	mitochondrial membrane part	2.37E-12
44420	extracellular matrix part	7.48E-12
5615	extracellular space	1.01E-11
70469	respiratory chain	1.08E-11
5625	soluble fraction	6.76E-11
5746	mitochondrial respiratory chain	5.09E-10
5581	collagen	1.15E-09
5840	ribosome	2.28E-09
5626	insoluble fraction	2.33E-09
22626	cytosolic ribosome	3.48E-09
12505	endomembrane system	5.00E-09
5783	endoplasmic reticulum	1.25E-08
5624	membrane fraction	2.01E-08
9986	cell surface	4.63E-08
5874	microtubule	5.85E-08
42598	vesicular fraction	1.57E-07
30054	cell junction	2.13E-07
70161	anchoring junction	3.69E-07

16323	basolateral plasma membrane	3.70E-07
16459	myosin complex	4.02E-07
42641	actomyosin	4.68E-07
5912	adherens junction	8.30E-07
44445	cytosolic part	1.07E-06
5813	centrosome	1.25E-06
45259	proton-transporting ATP synthase comple	1.25E-06
30135	coated vesicle	1.43E-06
5747	mitochondrial respiratory chain complex	1.43E-06
30964	NADH dehydrogenase complex	1.43E-06
45271	respiratory chain complex I	1.43E-06
16460	myosin II complex	2.23E-06
5792	microsome	2.25E-06
5730	nucleolus	2.40E-06
5911	cell-cell junction	2.62E-06
5604	basement membrane	2.69E-06
5815	microtubule organizing center	4.25E-06
22627	cytosolic small ribosomal subunit	4.51E-06
5865	striated muscle thin filament	6.97E-06
32432	actin filament bundle	8.25E-06
5768	endosome	1.13E-05
31672	A band	1.20E-05
275	mitochondrial proton-transporting ATP sy	1.46E-05
45261	proton-transporting ATP synthase comple	1.46E-05
5924	cell-substrate adherens junction	1.59E-05
44431	Golgi apparatus part	1.85E-05
48471	perinuclear region of cytoplasm	1.88E-05
31252	cell leading edge	1.90E-05
5681	spliceosomal complex	2.06E-05
45177	apical part of cell	2.31E-05
5753	mitochondrial proton-transporting ATP sy	2.71E-05
1725	stress fiber	2.86E-05
5654	nucleoplasm	3.11E-05
19717	synaptosome	3.54E-05
30055	cell-substrate junction	3.86E-05
5798	Golgi-associated vesicle	5.68E-05
31982	vesicle	8.14E-05
15935	small ribosomal subunit	1.19E-04
14704	intercalated disc	1.44E-04
70603	SWI/SNF-type complex	1.74E-04
16469	proton-transporting two-sector ATPase c	2.24E-04
30136	clathrin-coated vesicle	2.81E-04

5859	muscle myosin complex	2.88E-04
16324	apical plasma membrane	3.27E-04
5925	focal adhesion	3.69E-04
44291	cell-cell contact zone	4.13E-04
31410	cytoplasmic vesicle	5.03E-04
16604	nuclear body	5.65E-04
43005	neuron projection	6.79E-04
30117	membrane coat	7.08E-04
48475	coated membrane	7.08E-04
31988	membrane-bounded vesicle	7.22E-04
71013	catalytic step 2 spliceosome	9.27E-04
30660	Golgi-associated vesicle membrane	9.63E-04
1726	ruffle	1.08E-03
5819	spindle	1.19E-03
34708	methyltransferase complex	1.54E-03
35097	histone methyltransferase complex	1.54E-03
30126	COPI vesicle coat	1.67E-03
30496	midbody	1.91E-03
44451	nucleoplasm part	1.94E-03
31430	M band	2.26E-03
502	proteasome complex	2.32E-03
30027	lamellipodium	2.73E-03
33178	proton-transporting two-sector ATPase c	2.76E-03
16023	cytoplasmic membrane-bounded vesicle	3.51E-03
45121	membrane raft	3.57E-03
5876	spindle microtubule	3.90E-03
5750	mitochondrial respiratory chain complex	3.92E-03
45275	respiratory chain complex III	3.92E-03
44432	endoplasmic reticulum part	4.24E-03
16585	chromatin remodeling complex	4.41E-03
5916	fascia adherens	6.08E-03
30663	COPI coated vesicle membrane	8.06E-03

Molecular Function GO Terms Modulated by Stretch

GO ID	Molecular Function	Bonferroni p-value
3723	RNA binding	9.78E-19
5198	structural molecule activity	2.87E-17
16772	transferase activity, transferring pho	6.69E-13
19899	enzyme binding	8.22E-13
5102	receptor binding	9.53E-13
16301	kinase activity	5.04E-12
16773	phosphotransferase activity, alcohol	6.31E-11
8092	cytoskeletal protein binding	1.27E-10
48037	cofactor binding	3.12E-10
16491	oxidoreductase activity	3.65E-10
3779	actin binding	5.59E-10
4672	protein kinase activity	1.95E-09
17111	nucleoside-triphosphatase activity	9.08E-09
19904	protein domain specific binding	1.07E-08
32403	protein complex binding	4.13E-08
16462	pyrophosphatase activity	4.14E-08
16818	hydrolase activity, acting on acid anh	7.16E-08
16817	hydrolase activity, acting on acid anh	8.58E-08
3735	structural constituent of ribosome	2.08E-07
8047	enzyme activator activity	2.11E-07
15078	hydrogen ion transmembrane transp	3.24E-07
30234	enzyme regulator activity	5.07E-07
50662	coenzyme binding	5.54E-07
4674	protein serine/threonine kinase acti	8.89E-07
16874	ligase activity	1.01E-06
5509	calcium ion binding	1.43E-06
46983	protein dimerization activity	1.50E-06
60589	nucleoside-triphosphatase regulator	1.89E-06
42802	identical protein binding	2.14E-06
19900	kinase binding	2.15E-06
5178	integrin binding	4.95E-06
42803	protein homodimerization activity	8.19E-06
30695	GTPase regulator activity	1.04E-05
5083	small GTPase regulator activity	1.85E-05
30246	carbohydrate binding	2.76E-05
3712	transcription cofactor activity	4.51E-05
19901	protein kinase binding	5.49E-05
989	transcription factor binding transcrip	6.45E-05
3682	chromatin binding	7.15E-05
5200	structural constituent of cytoskeleto	7.21E-05

51082	unfolded protein binding	7.29E-05
51287	NAD binding	7.29E-05
988	protein binding transcription factor a	9.52E-05
16879	ligase activity, forming carbon-nitrog	1.63E-04
3729	mRNA binding	1.99E-04
5201	extracellular matrix structural consti	2.10E-04
8135	translation factor activity, nucleic aci	2.16E-04
5096	GTPase activator activity	2.23E-04
3713	transcription coactivator activity	2.44E-04
3743	translation initiation factor activity	2.83E-04
287	magnesium ion binding	2.98E-04
5080	protein kinase C binding	3.27E-04
51427	hormone receptor binding	4.14E-04
5518	collagen binding	4.49E-04
1968	fibronectin binding	4.52E-04
16887	ATPase activity	7.65E-04
16881	acid-amino acid ligase activity	1.24E-03
19787	small conjugating protein ligase activ	1.28E-03
4386	helicase activity	1.31E-03
42054	histone methyltransferase activity	1.46E-03
8022	protein C-terminus binding	1.76E-03
46933	hydrogen ion transporting ATP synth	1.91E-03
50840	extracellular matrix binding	1.97E-03
4221	ubiquitin thiolesterase activity	2.07E-03
31995	insulin-like growth factor II binding	2.09E-03
4857	enzyme inhibitor activity	2.64E-03
31072	heat shock protein binding	2.74E-03
5089	Rho guanyl-nucleotide exchange fac	2.82E-03
46961	proton-transporting ATPase activity,	2.85E-03
18024	histone-lysine N-methyltransferase a	3.22E-03
5520	insulin-like growth factor binding	3.72E-03
19838	growth factor binding	4.23E-03
35257	nuclear hormone receptor binding	4.25E-03
8307	structural constituent of muscle	4.76E-03
51015	actin filament binding	5.21E-03
42623	ATPase activity, coupled	5.43E-03
4842	ubiquitin-protein ligase activity	5.86E-03
3954	NADH dehydrogenase activity	6.25E-03
30165	PDZ domain binding	6.81E-03
70064	proline-rich region binding	7.31E-03
5506	iron ion binding	7.38E-03
4129	cytochrome-c oxidase activity	7.44E-03

15002	heme-copper terminal oxidase activ	7.44E-03
16676	oxidoreductase activity, acting on a l	7.44E-03
16790	thiolester hydrolase activity	8.31E-03
16278	lysine N-methyltransferase activity	8.38E-03
16279	protein-lysine N-methyltransferase a	8.38E-03
5516	calmodulin binding	9.03E-03
4402	histone acetyltransferase activity	9.18E-03
4468	lysine N-acetyltransferase activity	9.18E-03