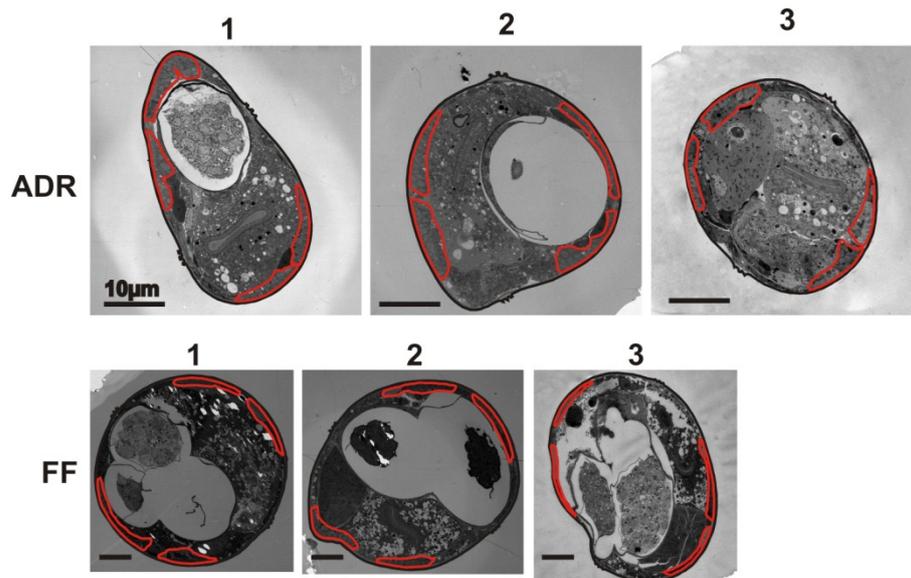
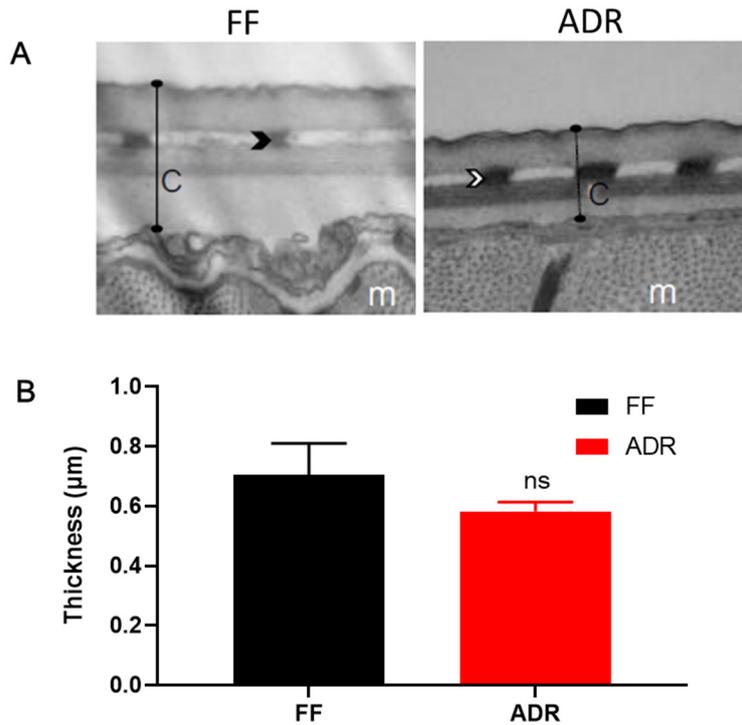


**Figure S1.** Habitus and survival of FF and ADR adult worms. (A) Nomarski DIC microscopy of FF and ADR worms; the average body volume in nL is indicated below the micrographs (mean± s.e.m). Volume was estimated using the cylinder formula and the measurements of worm length ( $1152.97 \pm 5.41$  and  $933 \pm 6.63$  µm for FF and ADR worms respectively) and width ( $40.93 \pm 1.27$  and  $33.8 \pm 0.10$  µm for FF and ADR respectively). (B) Lifespan analysis of FF and ADR worms with mean lifespan,  $16.45 \pm 0.27$  and  $33.23 \pm 0.65$  (mean± s.e.m), respectively. FF = fully fed, ADR = axenic dietary restriction.



**Figure S2.** ADR worms have elevated muscle mass compared to fully-fed controls. Muscle cells were marked as red area of the total cross section of the worm mid-body (TEM images). Muscle surface area (in red) was determined using Image J software and was normalized to total section area.



**Figure S3.** (A) TEM images of cuticles of worms grown in FF (fully fed) and ADR (axenic dietary restriction) conditions. (B) Cuticle thickness in FF (fully fed) and ADR (axenic dietary restriction) worms.  $P=0.1077$ . ns: not significant

**Supplemental Table S1.** Gene ontology information from DAVID bioinformatic resource of DEGs. Reported  $P$  value is the modified Fisher Exact  $P$  value or EASE score.

Representative term (GO, INTERPRO, ...)	Enrichment score	$P$ value
<b>Upregulated in axenically cultured worms</b>		
IPR006210:EGF-like	7.73	1.56E-09
GO:0044421~extracellular region part	6.39	2.26E-07
GO:0031032~actomyosin structure organization	5.87	6.28E-08
IPR018159:Spectrin/alpha-actinin	5.48	1.14E-06
IPR013091:EGF calcium-binding	4.94	1.25E-06
IPR003599:Immunoglobulin subtype	4.59	7.41E-08
GO:0043292~contractile fiber	4.01	4.92E-05
IPR001781:Zinc finger, LIM-type	3.03	7.03E-04
GO:0030182~neuron differentiation	2.91	3.26E-05
IPR004009:Myosin, N-terminal, SH3-like	2.85	6.43E-04
laminin egf-like domain	2.84	1.45E-04
GO:0019098~reproductive behavior	2.80	5.61E-04
IPR002048:Calcium-binding EF-hand	2.76	3.02E-04
GO:0031034~myosin filament assembly	2.73	1.86E-03
GO:0008340~determination of adult life span	2.66	2.20E-03
GO:0006928~cell motion	2.62	1.70E-03
GO:0018988~molting cycle, protein-based cuticle	2.52	2.94E-03

GO:0009791~post-embryonic development	2.28	3.97E-03
IPR001791:Laminin G	2.24	4.18E-03
IPR015650:Heavy chain of Myosin	2.09	1.16E-03
IPR019748:FERM central domain	2.04	1.54E-03
IPR009007:Peptidase aspartic, catalytic domain:Immunoglobulin	2.04	1.54E-03
domain:Immunoglobulin	1.98	1.24E-02
domain:LDL-receptor class A 1	1.95	1.13E-02
IPR003961:Fibronectin, type III	1.82	6.62E-03
IPR004827:Basic-leucine zipper (bZIP) transcription factor	1.82	3.27E-03
GO:0008233~peptidase activity	1.67	1.24E-02
IPR008160:Collagen triple helix repeat	1.63	9.96E-03
GO:0009374~biotin binding	1.62	3.75E-02
IPR017940:ABC transporter integral membrane type 1	1.60	2.12E-03
GO:0034622~cellular macromolecular complex assembly	1.31	2.01E-02
IPR011001:Saposin-like	1.31	3.63E-02
GO:0040008~regulation of growth	1.21	3.48E-02
IPR001192:Phospholipase C, phosphoinositol-specific, C-terminal (PLC)	1.18	3.29E-02
GO:0005874~microtubule	1.17	4.51E-02
GO:0043492~ATPase activity, coupled to movement of substances	1.16	1.33E-02
domain:EF-hand 1	1.12	3.89E-02
GO:0004857~enzyme inhibitor activity	1.08	4.53E-02
binding site:NAD	1.06	4.37E-02
<hr/>		
<b>Downregulated in axenically cultured worms</b>		
GO:0005839~proteasome core complex	10.04	2.55E-12
GO:0000502~proteasome complex	9.32	3.33E-12
GO:0022402~cell cycle process	8.99	4.54E-10
GO:0000279~M phase	7.38	4.74E-09
GO:0007276~gamete generation	6.49	1.80E-07
GO:0030163~protein catabolic process	6.47	1.90E-09
GO:0009791~post-embryonic development	4.16	5.20E-05
IPR003959:ATPase, AAA-type, core	3.78	4.56E-06
GO:0040010~positive regulation of growth rate	3.73	1.21E-04
GO:0040021~hermaphrodite germ-line sex determination	3.71	7.14E-05
IPR006649:Like-Sm ribonucleoprotein, eukaryotic and archaea-type, core	3.52	2.18E-04
GO:0007548~sex differentiation	3.27	1.65E-04
IPR006671:Cyclin, N-terminal	3.22	2.18E-04
IPR016050:Proteasome, beta-type subunit, conserved site	2.92	3.96E-04
GO:0006281~DNA repair	2.81	7.57E-04
IPR016897:E3 ubiquitin ligase, SCF complex	2.65	2.93E-04
GO:0019787~small conjugating protein ligase activity	2.51	1.92E-03
IPR001680:WD40 repeat	2.31	9.73E-04
IPR015880:Zinc finger, C2H2-like	2.17	4.18E-03
GO:0060429~epithelium development	2.14	6.90E-03
GO:0000280~nuclear division	2.02	5.41E-03

IPR012677:Nucleotide-binding, alpha-beta plait	1.82	1.02E-02
GO:0048581~negative regulation of post-embryonic development	1.82	1.00E-02
GO:0032993~protein-DNA complex	1.81	8.36E-04
IPR014400:Cyclin, A/B/D/E	1.66	1.32E-03
GO:0007127~meiosis I	1.40	6.09E-02
IPR017937:Thioredoxin	1.32	7.55E-03
GO:0008406~gonad development	1.20	5.56E-02
GO:0008629~induction of apoptosis by intracellular signals	1.01	3.40E-02

**Supplemental Table S2.** Shortlist of the genes tested in lifespan assays.

Gene names	Gene ontology	Fold change	Mean lifespan (days)	P-value
<b>L4440</b>			<b>40.77±1.43</b>	
<b>Large fold change</b>				
<i>col-94</i>	structural constituent of cuticle	38.91	44.68±1.59	P=0.0141
<i>tbb-6</i>	GTPase activity; microtubule; microtubule-based process; protein polymerization; structural constituent of cytoskeleton	19.77	42.76±1.02	P=0.8521
T11B7.2		14.12	45.59±2.08	P=0.0895
<b>F15D4.5</b>	<b>nucleic acid binding; zinc ion binding</b>	<b>12.88</b>	<b>34.3±2.68</b>	<b>P=0.0368</b>
<b>Lysosomal genes</b>				
<i>hch-1</i>	metalloendopeptidase activity	27.66	49.7±1.55	P=0.0001
<i>asp-5</i>	aspartic peptidase	4.57	39.75±1.37	P=0.9613
<i>asp-8</i>	aspartic peptidase	6.56	37.42±1.33	P=0.0355
<i>asah-1</i>	acylsphingosine amidohydrolase	9.22	42.52±1.64	P=0.5556
<i>pho-8</i>	phosphatase	19.18	50.96±3.74	P=0.0119
<b>Amino acid metabolism</b>				
<i>got-1.2</i>	an ortholog of human glutamic-oxaloacetic transaminase 1	3.97	47.45±2.44	P=0.0316
<i>gln-1</i>	an ortholog of human glutamate-ammonia ligase	3.02	44.45±1.46	P=0.2156
F46H5.3	arginine kinase activity; ATP binding	2.99	42.92±1.35	P=0.3550
<b>Transcription factors and cofactors</b>				
<i>nhr-62</i>	nuclear hormone receptor	9.46	40.65±1.26	P=0.7906
<b><i>nhr-132</i></b>	<b>nuclear hormone receptor</b>	<b>6.73</b>	<b>34.56±1.70</b>	<b>P=0.0013</b>
<i>ceh-37</i>	homobox transcription factor	5.89	38.08±1.45	P=0.2656
<i>nhr-90</i>	nuclear hormone receptor	5.77	43.45±1.21	P=0.3845
<i>nhr-6</i>	nuclear hormone receptor	5.1	44.67±2.52	P=0.1257
<i>lim-7</i>	transcription factor	4.88	47.29±2.11	P=0.0139
<i>nhr-45</i>	nuclear hormone receptor	4.55	43.09±1.04	P=0.1889

<i>nhr-120</i>	nuclear hormone receptor	4.52	40.53±1.41	<i>P</i> =0.9712
<i>nhr-84</i>	nuclear hormone receptor	4.29	41.24±1.18	<i>P</i> =0.9612
<i>xbp-1</i>	ER stress transcription factor	2.4	34.70±1.80	<i>P</i> =0.0129
<i>nhr-97</i>	nuclear hormone receptor	2.17	40.35±2.22	<i>P</i> =0.8427

\* Above RNAi experiment using the *rrf-3* strain. *P*-value compared to L4440.