

Table S4A. Enriched GO terms for upregulated genes				
GO terms	<i>hcf-1(-) / sir-2.1(O/E) -shared</i>	<i>hcf-1(-) / sir-2.1(O/E) / daf-2(-) -shared</i>	<i>daf-2 (-) only</i>	Biological process
Determination of adult lifespan	5.25	5.83		Aging
Glutathione S-transferase	2.93	3.24		Detoxification
Alcohol dehydrogenase	2.35	2.52		Detoxification
Short-chain dehydrogenase	2.20	2.49	2.14	Detoxification
Cytochrome P450	2.10	2.54		Detoxification
Antioxidant/ Oxidoreductase	1.99	2.20	1.73	Detoxification
Cofactor metabolic process	1.96	2.37		
Zinc-finger RING, BBOX	1.85	0.99		
Metal ion binding	1.72	1.19		
Carboxylesterase (type B)	1.60	1.65	1.02	Detoxification
Lysosome	1.52			Detoxification
Endopeptidase inhibitor (cysteine, serpin)	1.44	1.66		Detoxification
G-protein signaling inhibitor	1.10			Signaling
Dauer development		1.06		Development
Phenol metabolic process		1.05		Metabolism
Collagen / cuticle			13.44	
Glycoprotein/ signaling			6.27	Development: pharyngeal, embryonic, neuronal
Neuropeptide signaling			2.63	Development: pharyngeal
EF-hand calcium binding (calmodulin)			2.50	Development: body morphology, locomotion, egg laying
Peptidase/proteolysis			2.32	Metabolism
Cytoskeleton organization			2.12	
UDP-glucuronosyl/UDP-glucosyltransferase			1.99	Detoxification
LIM domain			1.95	Development: muscle, neuron
Patched / hedgehog receptor			1.85	Development : growth, locomotion
Amino acid metabolism (degradation)			1.70	Metabolism
EGF-like domain			1.64	Development: growth
Organismal growth			1.53	
Anion transport			1.48	Cellular homeostasis
Ion homeostasis			1.13	Cellular homeostasis
Glycolysis/Gluconeogenesis			1.12	Metabolism
Sulfur amino acid biosynthesis			1.07	Metabolism
Intermediate filament			1.01	Development: body morphogenesis

Table S4B. Enriched GO terms for downregulated genes				
GO terms	<i>hcf-1(-) / sir-2.1(O/E)</i> -shared	<i>hcf-1(-) / sir-2.1(O/E) / daf-2(-)</i> -shared	<i>daf-2 (-)</i> only	Biological process
Glycoprotein/signaling	3.95	3.76		Cellular signaling
Amino acid biosynthesis	3.14	1.84		Metabolism
Collagen/cuticle	3.00			
SaposinB	2.41			Metabolism: lipid degradation
Acid phosphatase	2.22	1.96		Metabolism: digestion (lysosomal)
Peptidase (serine)	2.18			Metabolism: proteolysis (lysosomal)
Determination of adult lifespan	2.15	2.54		Aging
Lysozyme	1.99	2.24		Immunity
Ribosomal proteins	1.80	2.24	9.96	Translation
Fatty acid biosynthesis	1.60	1.62		Metabolism
Peptidase/proteolysis (C1)	1.51	1.05		Metabolism
UDP-glucuronosyltransferase	1.50	1.76		Detoxification
N-acetyltransferase	1.44			Detoxification
EGF-like domain	1.40			Signaling
C-type lectin	1.31	1.00		Immunity
Carboxylesterase (type B)	1.27			Detoxification
Peptidase/proteolysis (A1)	1.19	1.36		Metabolism
Iron/sulphur/FAD binding	1.18			
FAD-binding	1.15			
Organismal growth (positive)	1.13		14.18	
Peptidase/proteolysis		1.57		
Metal ion transport/binding		1.08		
Larval development			20.93	Development
Hermaphrodite genitalia devel.			7.89	Development
Mitochondrial			6.47	Protein translation/transport
Translation initiation			4.67	Protein biosynthesis
Protein folding/UPR(Chaperone)			4.54	Protein homeostasis
Aminoacyl-tRNA synthetase			4.25	Protein biosynthesis
Protein transport			4.07	Vesicular biogenesis/transport
Endomembrane system			3.59	Protein transport: ER, Golgi, nuclear
Protein targeting/mitochondria			2.99	Protein transport
Organelle lumen			2.94	
WD40 repeat			2.77	
RNA polymerase			2.49	Transcription
Nuclear pore complex			2.42	Nuclear transport
Proteasome core complex			2.33	Protein degradation
Small ribonucleoprotein			2.18	RNA splicing/degradation. Development
Chromatin/Histones			2.18	Chromatin structure/DNA replication
Proteasome component			1.95	Protein degradation
Organismal growth (negative)			1.95	
Golgi apparatus			1.88	Vesicle /transport
Chaperones			1.77	Protein folding
Tetratricopeptide repeat			1.69	Embryonic development
RNA metabolism/processing			1.68	RNA Splicing
Ubq-dependent proteolysis			1.58	Protein degradation
Nuclear migration			1.40	Mitosis / cytokinesis
Cell division			1.39	
Ubiquitin-ligase			1.38	Protein degradation
Embryonic development			1.32	
Heat shock protein DnaJ			1.30	UPR, protein homeostasis
Axon/ neuron projection			1.26	Development
RNA-recognition motif			1.24	RNA processing
Cell division/cyclins			1.23	
cis-trans isomerase			1.18	Protein folding/ immunity
Signal peptide processing			1.15	Protein processing / maturation
AAA+ ABC transporter			1.08	Detoxifications

Table S4C. Enriched promoter regulatory motifs.				
<i>hcf-1(-) / sir-2.1(O/E) / daf-2(-)</i> – shared genes (693 genes)		<i>daf-2(-)</i> – specific genes (1750 genes)		Known consensus transcription factor binding site
Motif	% of genes with motif	Motif	% of genes with motif	
	48%		70%	Mammalian SP1 p-value<0.001
	45%		66%	Mammalian Fhl p-value<0.001
	16%		13%	
	68%		87%	Mammalian Oct-1 p-value<0.001
	68%		42%	
	54%	Not enriched		(1) Mammalian GATA (<i>C. elegans elt-3,5,6</i>) p-value<0.0001 (2) Mammalian Evi-1 (<i>C. elegans egl-43</i>), p-value<0.0001
	10%	Not enriched		
Not enriched			10%	
DBE: T(G/A)TTTAC ^d	51%	DBE: T(G/A)TTTAC ^d	45%	