Table 1

	Cox Regression			Quantile Analysis					
Group	**Coeff**	p value		**30%**	p value	**50%**	p value	**90%**	p value
Males									
WT vs LID_{10d}	0.39	0.052		**-85.9**	0.04	**-82.6**	0.25	**-54.8**	0.15
WT vs LID_{5m}	0.28	0.14		**-50.9**	0.08	**-23.8**	0.4	**-24.1**	0.71
WT vs LID_{15m}	0.14	0.47		**73.1**	0.007	**15.4**	0.43	**-36.9**	0.21
Females									
WT vs LID_{10d}	-0.33	0.082		**9.2**	0.71	**131.4**	<0.001	**26.5**	0.013
WT vs LID_{5m}	-0.52	0.005		**86.5**	0.009	**136.1**	<0.001	**30**	0.054
WT vs LID_{15m}	-0.37	0.043		**13.4**	0.81	**53.6**	0.29	**37**	<0.001

Supplemental Experimental Procedures

Pathological assessment: A list of pathological lesions was compiled for each mouse that included both neoplastic and non-neoplastic diseases, as previously described (Ikeno et al., 2003; Ikeno et al., 2009). Based on these data, tumor burden, disease burden and severity of each lesion were assessed. Tumor burden was calculated as the sum of the different types of tumors in each mouse. For example, a mouse that had lymphoma and hepatocarcinoma had a tumor burden of 2. Disease burden was similarly calculated as the sum of all histopathological changes in a mouse. The percentage of tumor-bearing mice and overall incidence of disease were calculated for each experimental group. All pathological analyses were accomplished using a double blind procedure by two independent pathologists.

Grading of lesions: The severity of neoplastic lesions and glomerulonephritis was determined using grading systems previously described (Ikeno et al., 2003; Ikeno et al., 2009). For neoplastic lesions- Grade 1: primary site only; Grade 2: primary site and intra-organ or one other organ metastasis; Grade 3: metastasis to 2-3 organs; and Grade 4: metastasis to more than 4 organs or Grade 3 with additional pathology, e.g., pleural effusion, ascites, and subcutaneous edema. For glomerulonephritis- Grade 0: no lesions; Grade 1: minimal change in glomeruli; Grade 2: Grade 1 with a few (less than 10) casts in renal tubules; Grade 3: Grade 1 with more than 10 casts in renal tubules; and Grade 4: Grade 3 with interstitial fibrosis.

Balance Beam: Mice were placed on a 24 inch long, 0.5 inch wide rod, 12 inches above the ground. The average time the animals were able to walk along the balance

beam or maintain the grip on the beam was quanitified. Trials ended at 20 seconds. Each animal was given 3 trials.

Eye Blink Reflex: The ability of the mice to respond to touch of the eye with a q-tip was measured by 2 blinded experimenters. Mice were given a score of 2 if they blinked and turned their head prior to physical contact. A score of a 1 was achieved if the animals did not respond until the q-tip touched the eye, while a 0 was given if the animals did not respond at all. Each eye was independently tested.

SUPPLEMENTAL LEGENDS

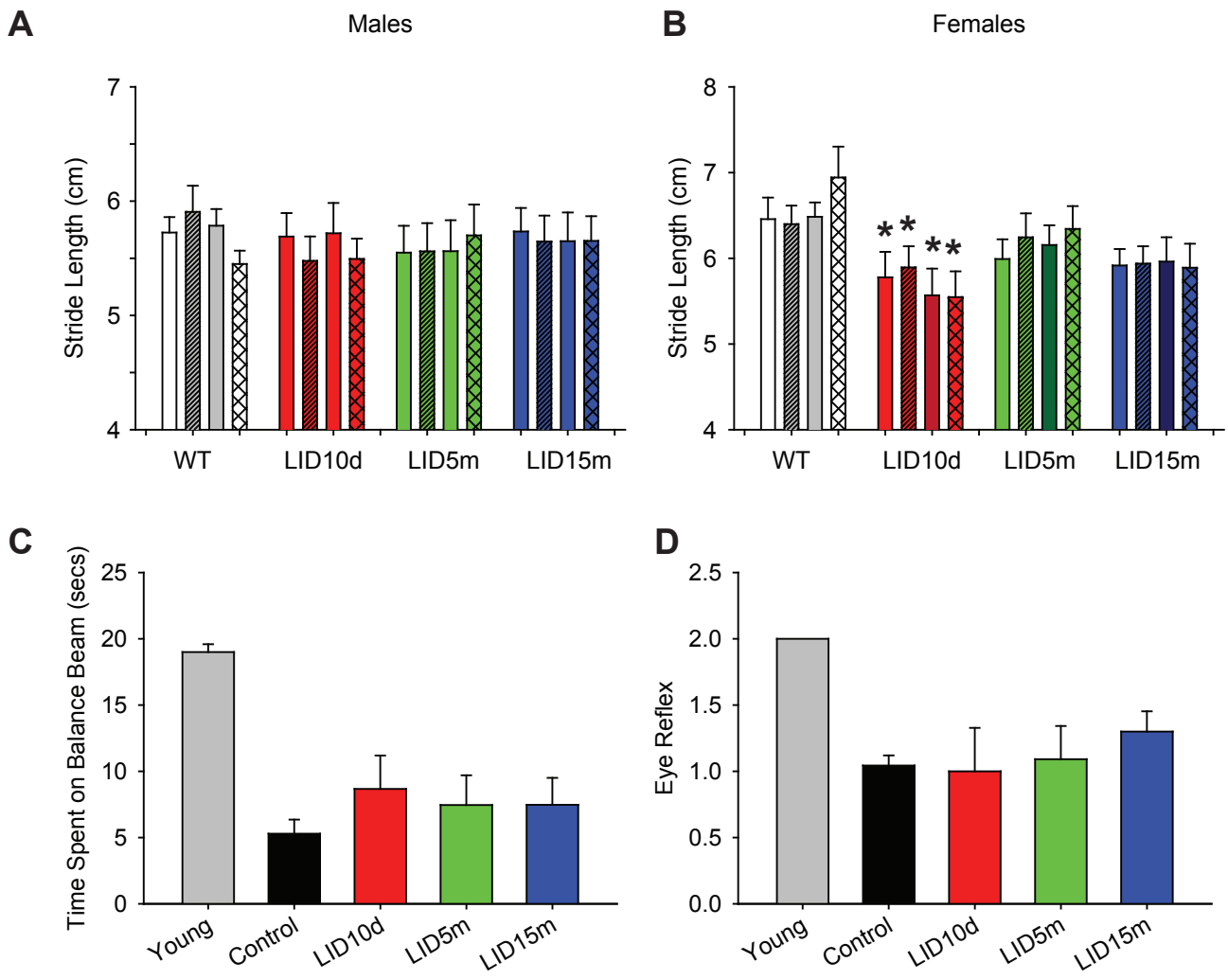
Supplemental Figure 1: IGF-1 deficiency did not improve healthspan. The average stride length (cm) of males (A) and females (B) was assessed at 25-27 months of age. The empty bars represent the front right leg, the dashed represent the hind right leg, the darker bar represents the front left leg, and the hatched represents the hind left leg. The asterisk indicates significant difference compared to the respective control mouse stride length for that leg ($p<0.05$, mean +/- SEM, n=17-51). C) The average time each male mouse was able to maintain balance on a balancing rod. D) The average eye blink reflex in male mice upon touch with a q-tip.

Supplemental Table 1: Description of cross-sectional cohort. Average body and organ weights in the male and female control and IGF-1 deficient mice. All weights are represented in mgs (mean +/- SEM).

Supplemental Table 2: Description of the cross-sectional pathology. The total number of animals analyzed for each lesion type, the total number of animals positive for each lesion, and the percent of animals with each lesion are represented.

Supplemental Table 3: Description of the end-of-life pathology in the lifespan cohort. The total number of animals analyzed for each lesion type, the total number of animals positive for each lesion, and the percent of animals with each lesion are represented.

Supplemental Figure 1



Supplemental Table 1

Male	n	Whole Body	Brain	Hippocampus	Heart	Lung	Spleen	Liver	L. Kidney	R. Kidney	Quadriceps
Young	10	2.57E+04 ± 5.68E+02	422.25 ± 5.30	16.00 ± 0.19	120.50 ± 3.62	199.20 ± 13.20	57.50 ± 1.32	1141.70 ± 24.30	172.30 ± 4.59	170.20 ± 5.34	225.28 ± 8.84
Control	51	2.64E+04 ± 3.39E+02	431.17 ± 1.56	16.56 ± 0.14	164.48 ± 4.13	255.96 ± 22.22	82.37 ± 14.40	1519.64 ± 66.34	219.42 ± 4.51	227.24 ± 4.53	199.39 ± 4.21
LID_{10d}	17	2.36E+04 ± 5.90E+02	416.95 ± 5.34	16.11 ± 0.37	150.47 ± 4.86	236.65 ± 13.42	77.71 ± 9.35	1464.59 ± 67.49	147.06 ± 8.13	161.29 ± 9.23	182.91 ± 7.82
LID_{5m}	15	2.40E+04 ± 5.52E+02	426.53 ± 3.05	16.17 ± 0.23	158.93 ± 4.19	204.67 ± 8.52	104.20 ± 50.56	1506.81 ± 87.71	155.79 ± 4.46	165.68 ± 6.11	195.42 ± 5.67
LID_{15m}	19	2.46E+04 ± 4.95E+02	425.26 ± 2.65	16.34 ± 0.22	150.84 ± 4.80	223.32 ± 7.12	172.26 ± 55.78	1540.53 ± 65.61	168.16 ± 5.66	174.84 ± 7.34	179.53 ± 5.18
Female	**n**	**Whole Body**	**Brain**	**Hippocampus**	**Heart**	**Lung**	**Spleen**	**Liver**	**L. Kidney**	**R. Kidney**	**Quadriceps**
Young	12	2.08E+04 ± 2.14E+02	446.50 ± 2.25	16.91 ± 0.20	110.25 ± 3.45	208.09 ± 13.65	79.42 ± 2.54	834.80 ± 12.73	134.83 ± 3.20	133.83 ± 1.91	
Control	34	2.32E+04 ± 3.74E+02	444.11 ± 1.84	17.09 ± 0.17	146.79 ± 3.81	243.59 ± 9.74	156.82 ± 31.74	1244.53 ± 38.72	199.21 ± 4.02	208.36 ± 5.90	172.05 ± 3.71
LID_{10d}	17	1.87E+04 ± 3.50E+02	408.72 ± 3.36	15.22 ± 0.16	127.18 ± 4.90	216.13 ± 11.44	184.82 ± 67.66	1101.24 ± 38.82	120.35 ± 4.86	130.35 ± 7.80	150.56 ± 5.39
LID_{5m}	18	1.93E+04 ± 3.60E+02	421.05 ± 1.89	16.04 ± 0.13	128.50 ± 4.10	237.11 ± 11.81	79.22 ± 11.98	1247.41 ± 64.44	131.56 ± 4.04	133.61 ± 3.59	160.49 ± 4.67
LID_{15m}	17	1.89E+04 ± 5.85E+02	422.10 ± 4.43	16.23 ± 0.23	143.94 ± 6.65	249.06 ± 23.15	154.38 ± 51.20	1248.94 ± 39.52	147.25 ± 6.32	154.81 ± 6.75	158.70 ± 4.90

Supplemental Table 2

	Males												Females											
		WT			LID_{10}^{d}			LID_{5}^{m}			LID_{15}^{m}			WT			LID_{10}^{d}			LID_{5}^{m}			LID_{15}^{m}	
Neoplastic Lesions	n	#	%	n	#	%	n	#	%	n	#	%	n	#	%	n	#	%	n	#	%	n	#	%
Total	51	49	96.1	17	17	100	15	15	100	19	19	100	34	34	100	17	16	94.1	18	17	94.4	16	15	93.8
Lyphoma	51	49	96.1	17	17	100	15	14	93.3	19	19	100	34	33	97.1	17	16	94.1	18	17	94.4	16	15	93.8
Hepatocarcinoma	51	7	13.7	17	3	17.6	15	3	20.0	19	3	15.8	34	0	0	17	2	11.8	18	3	16.7*	16	0	0
Adenoma, Pituitary													34	10	29.4	17	1	5.9*	18	2	11.1*	16	1	6.3*
Hemangiosarcoma	51	2	3.9	17	0	0	15	0	0	19	0	0	34	2	5.9	17	0	0.0	18	1	5.6	16	0	0
Adenoma, Alveolar	51	4	7.8	17	1	5.9	15	3	20.0	19	3	15.8												
Non-Neoplastic Lesions																								
Glomerular nephritis	51	39	76.5	17	5	29.4	15	8	53.3	19	8	42.1	34	28	82.4	17	2	11.8*	18	10	55.6*	16	14	87.5
Testicular Cyst	51	46	90.2	17	14	82.4	15	14	93.3	19	15	78.9												
Adenoma, Ovarian													34	7	20.6	17	2	11.8	18	1	5.6*	16	1	6.3*
Hemangioma, Ovarian													34	3	8.8	17	1	5.9	18	1	5.6	16	2	12.5
Subcapsular Hyperplasia	51	6	11.8	17	1	5.9	15	0	0	19	0	0	34	29	85.3	17	7	41.2*	18	11	61.1*	16	12	75.0
Lymphocytic Infiltration																								
Salivary	51	33	64.7	17	10	58.8	15	6	40*	19	13	68.4	34	22	64.7	17	12	70.6	18	13	72.2	16	11	62.5
Kidney	51	33	64.7	17	10	58.8	15	10	66.7	19	14	73.7	34	23	67.6	17	10	58.8	18	10	55.6	16	13	81.3
Liver	51	26	51.0	17	8	47.1	15	7	46.7	19	10	52.6	34	18	52.9	17	10	58.8	18	8	44.4	16	5	31.3*
Lung	51	35	68.6	17	14	82.4	15	7	46.7*	19	15	78.9	34	31	91.2	17	16	94.1	18	15	83.3	16	13	81.3*
Spleen	51	42	82.4	17	14	82.4	15	12	80	19	18	94.7	34	31	91.2	17	16	94.1	18	17	94.4	16	13	81.3*
Stomach	51	2	3.9	17	0	0	15	1	6.7	19	0	0	34	1	2.9	17	0	0	18	0	0	16	1	6.3
Pancreas	51	11	21.6	17	6	35.3*	15	5	33.3	19	3	15.8	34	17	50	17	5	29.4*	18	7	38.9	16	8	50
Intestine	51	35	68.6	17	11	64.7	15	8	53.3	19	12	63.2	34	45	44.1	17	8	47.1	18	11	61.1*	16	10	62.5*

Supplemental Table 3

	Male Pathology												Female Pathology											
		WT			LID_{10}^{d}			LID_{5}^{m}			LID_{15}^{m}			WT			LID_{10}^{d}			LID_{5}^{m}			LID_{15}^{m}	
Neoplastic Lesions	n	#	%	n	#	%	n	#	%	n	#	%	n	#	%	n	#	%	n	#	%	n	#	%
Total	113	100	88.5	32	29	90.6	36	31	86.1	34	24	70.6	122	107	87.7	37	33	89.2	38	35	92.1	42	37	88.1
Fatal	113	77	68.1	32	22	68.8	36	26	72.2	34	18	52.9	122	93	76.2	37	25	67.6	38	28	73.7	42	29	69.0
Lymphoma																								
Total	113	93	82.3	32	25	78.1	36	26	72.2	34	16	47.1	122	107	87.7	37	29	78.4	38	29	76.3	42	35	83.3
Fatal	113	67	59.3	32	17	53.1	36	19	52.8	34	16	47.1	122	85	69.7	37	23	62.2	38	26	68.4	42	26	61.9
Hepatocarcinoma																								
Total	113	11	9.7	32	10	31.3	36	8	22.2	34	4	11.8	122	5	4.1	37	5	13.5	38	13	34.2	42	5	11.9
Fatal	113	8	7.1	32	5	15.6	36	8	22.2	34	2	5.9	122	2	1.6	37	3	8.1	38	5	13.2	42	2	4.8
Hemangiosarcoma																								
Total	113	3	2.7	32	3	9.4	36	1	2.8	34	0	0.0	122	0	0.0	37	0	0.0	38	1	2.6	42	1	2.4
Fatal	113	3	2.7	32	2	6.3	36	1	2.8	34	0	0.0	122	0	0.0	37	0	0.0	38	1	2.6	42	0	0.0
Adenoma, Pituitary																								
Total													96	32	33.3	28	2	7.1	27	2	7.4	30	1	3.3
Fatal													96	15	15.6	28	0	0.0	27	0	0.0	30	0	0.0
Non-Neoplastic Lesions																								
Glomerular nephritis																								
Total	113	106	93.8	32	11	34.4	36	23	63.9	34	32	94.1	121	116	95.9	37	21	56.8	38	32	84.2	42	26	61.9
Fatal	113	3	2.7	32	0	0.0	36	0	0.0	34	0	0.0	121	12	9.9	37	0	0.0	38	1	2.6	42		0.0
Thrombus, Heart																								
Total	113	4	3.5	32	2	6.3	36	2	5.6	34	0	0.0	121	9	7.4	37	1	2.7	38	0	0.0	41	1	2.4
Fatal	113	3	2.7	32	2	6.3	36	1	2.8	34	0	0.0	121	4	3.3	37	0	0.0	38	0	0.0	41	0	0.0
Mineralization, Brain																								
Total	112	46	41.1	31	3	9.7	35	9	25.7	34	12	35.3	118	11	9.3	37	4	10.8	35	11	31.4	40	4	10.0
Testicular Cysts																								
Total	113	94	83.2	32	18	56.3	36	18	50.0	34	23	67.6												
Sperm granuloma																								
Total	113	2	1.8	32	1	3.1	36	0	0.0	34	1	2.9												
Adenoma, Ovarian																								
Total													121	2	1.7	37	4	10.8	38	2	5.3	41	3	7.3
Hemangioma, Ovarian																								
Total													121	13	10.7	37	4	10.8	38	4	10.5	41	4	9.8
Subcapsular Hyperplasia																								
Total	113	11	9.7	32	0	0.0	36	0	0.0	34	0	0.0	108	85	78.7	34	13	38.2	36	13	36.1	39	21	53.8
Papillary Hyperplasia, Thyroid																								
Total	34	6	17.6	8	4	50.0	13	4	30.8	9	1	11.1	26	1	3.8	10	0	0.0	10	2	20.0	14	3	21.4
Lymphocytic Infiltration																								
Kidney	113	36	31.9	32	9	28.1	36	7	19.4	34	13	38.2	121	61	50.4	37	14	37.8	38	18	47.4	42	21	50.0
Liver	113	55	48.7	32	15	46.9	36	19	52.8	34	13	38.2	122	69	56.6	37	18	48.6	38	16	42.1	42	21	50.0
Lung	112	47	42.0	31	12	38.7	35	15	42.9	34	13	38.2	118	71	60.2	37	23	62.2	38	21	55.3	41	21	51.2
Urinary	102	3	2.9	30	4	13.3	29	1	3.4	31	3	9.7	83	24	28.9	34	3	8.8	35	5	14.3	31	6	19.4
Stomach	113	0	0.0	32	0	0.0	36	0	0.0	33	0	0.0	110	6	5.5	37	1	2.7	38	1	2.6	42	2	4.8
Intestine	105	21	20.0	32	4	12.5	32	3	9.4	34	3	8.8	109	28	25.7	37	5	13.5	38	4	10.5	43	4	9.3