Common species name	Latin species name	Source	Coriell number (if applicable)	MLS (yrs)	Age	Passage Number	Sup Fig. 1A	SupFig. 1B	Fig. 1	Fig. 2	Sup Fig. 3	Fig. 3A, B	Fig. 3C	Fig. 3F	Fig. 4A, B	Fig. 4C	Fig. S8	Fig. 5A-C
Common Marmoset	*Callithrix jacchus*	In-house (1 line)	-	16.5	3	4-10	X	X	X			X	X	X		X	X	X
Southern Lesser Bushbaby	*Galago moholi*	Coriell	PR00519	16.6	8	16	X	X	X	X			X	X				
Coquerel's Mouse Lemur	*Mizra coquereli*	Coriell	PR01044	17.4	11	12			X	X		X		X		X		
Pygmy Marmoset	*Callithrix pygmaea*	Coriell	PR00839	18.6	5	8-11	X	X			X	X		X		X	X	X
Pygmy Marmoset	*Callithrix pygmaea*	Coriell	PR00644	18.6	6	6					X			X				
Red-bellied Lemur	*Eulemur rubriventer*	Coriell	PR00273	20	7	7-11		X	X	X		X	X	X		X	X	X
Red Tamarin	*Saguinus midas*	Coriell	PR00550	20.5	5	7-15	X	X	X	X		X	X	X		X		
Noisy Douroucouli	*Aotus vociferans*	Coriell	PR00636	22.1	16	7-8		X			X	X	X	X		X	X	X
L'Hoest's Monkey	*Cercopithecus lhoesti*	Coriell	PR01126	24.1	2	11-13	X	X	X	X	X	X	X	X		X	X	X
Red Titi	*Callicebus cupreus*	Coriell	PR00793	26.4	6	8-13	X	X	X		X	X	X	X		X	X	X
Olive Baboon	*Papio anubis*	Coriell	PR00033	27.5	3	5-11	X	X	X	X	X		X	X	X		X	X
Patas Monkey	*Erythrocebus patas*	Coriell	AG06254	28.3	20	9								X				
Squirrel Monkey	*Saimiri sciureus*	Coriell	PR00612	30.2	6	10-11	X	X	X	X	X	X		X		X	X	X
White (Verreaux's) Sifaka	*Propithecus verreauxi*	Coriell	PR00326	30.5	9	5			X			X				X		
Vervet	*Chlorocebus aethiops*	In-house (3 lines)	-	30.8	9 9 9	4-11 3-5 9	X	X	X	X	X	X	X	X	X	X	X	X
Common Woolly Monkey	*Lagothrix lagotricha*	Coriell	AG05356	32	17	15-20	X	X	X		X	X		X		X	X	X
Colobus Monkey	*Colobus guereza*	Coriell	PR00096	35	5	15								X				
Guianan Saki	*Pithecia pithecia*	Coriell	PR00239	36	9	11		X	X			X		X		X		
Ring-tailed Lemur	*Lemur catta*	Coriell	PR00126	37.3	9	14								X				
Hamadryas Baboon	*Papio hamadryas*	In-house (2 lines)	-	37.5	5 6	2-9 7	X	X	X	X	X	X	X	X	X	X	X	X
Cynomolgus	*Macaca fascicularis*	In-house (2 lines)	-	39	6 6	4-6 5-7		X	X		X	X	X	X	X	X		
Rhesus Macaque	*Macaca mulatta*	In-house (3 lines)	-	40	5 4 4	7 12-14 9	X	X	X		X	X			X	X	X	X
Mandrill	*Mandrillus sphinx*	Coriell	PR00399	40	12	6-15					X		X	X	X		X	X
Red-capped Mangabey	*Cercocebus torquatus*	Coriell	PR00485	46	8	12	X	X	X	X	X	X	X	X		X		
Bonobo	*Pan paniscus*	Coriell	PR00236	55	22	6-11	X	X	X	X	X	X		X	X	X	X	X
Bonobo	*Pan paniscus*	Coriell	PR00235	55	28	18-20									X		X	X
Gorilla	*Gorilla gorilla*	Coriell	PR00055	55.4	12	10-18	X	X	X		X	X	X	X		X	X	X
Gorilla	*Gorilla gorilla*	Coriell	PR00279	55.4	23	15-23	X	X	X	X	X	X	X	X	X	X	X	X
White-handed Gibbon	*Hylobatus lar*	Coriell	PR01131	56	5	7-10		X	X	X	X		X	X			X	X
Orangutan	*Pongo pygmaeus*	Coriell	PR01107	59	11	11-19	X	X	X	X	X	X	X	X	X	X	X	X
Chimpanzee	*Pan troglodytes*	Coriell	PR00175	59.4	12	13	X	X	X	X		X	X	X	X	X	X	X
Chimpanzee	*Pan troglodytes*	Coriell	PR00115	59.4	13	12-15			X		X	X	X		X	X		
Human	*Homo sapiens*	Coriell	GM03651	122.5	25	16	X	X	X			X		X	X	X		
Human	*Homo sapiens*	Coriell	GM01948	122.5	27	9					X			X			X	X
Human	*Homo sapiens*	Coriell	GM03652	122.5	24	16			X					X	X			

Supplemental Table 1. List of cell lines used

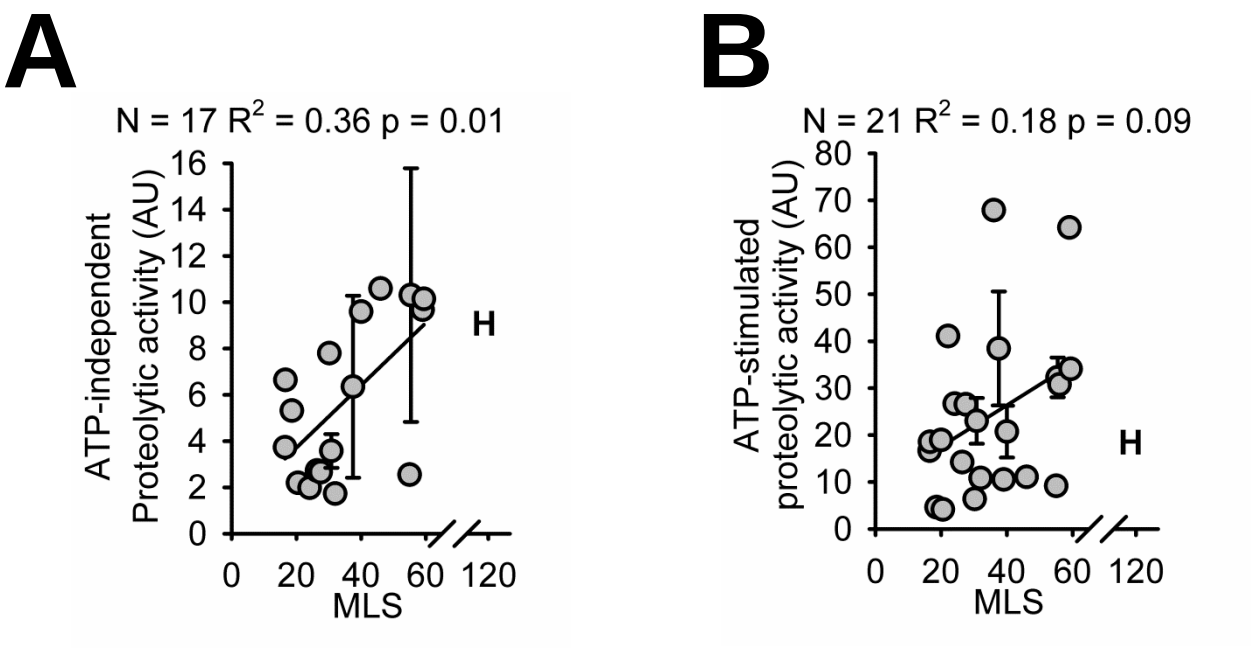
Two-Way ANOVA

	PSMB8			Proteasomal Activity			PSMB5		
	df	F	Sig	df	F	Sig	df	F	Sig
Rapamycin	1,12	80.230	**<0.001**	1,12	7.348	**0.018**	1,12	0.171	**0.686**
Sex	1,12	29.709	**<0.001**	1,12	5.348	**0.039**	1,12	13.349	**0.002**
Rapamycin x Sex	1,12	3.682	0.080	1,12	0.604	0.452	1,12	9.726	0.009
Snell	1,20	9.140	**0.007**	1,20	1.834	**0.191**	1,20	12.530	**0.020**
Sex	1,20	1.659	**0.212**	1,20	1.778	**0.197**	1,20	3.150	**0.091**
Snell x Sex	1,20	0.670	0.423	1,20	2.280	0.147	1,20	4.151	0.055
17-α-Estradiol	1,12	11.291	**0.006**	1,12	2.742	**0.124**	1,12	3.952	**0.070**
Sex	1,12	64.941	**<0.001**	1,12	1.443	**0.253**	1,12	21.076	**0.001**
17-α-Estradiol x Sex	1,12	0.111	0.745	1,12	1.167	0.301	1,12	0.363	0.558
NDGA	1,44	14.214	**<0.001**	1,44	10.408	**0.002**	1,12	0.051	**0.825**
Sex	1,44	17.966	**<0.001**	1,44	16.499	**<0.001**	1,12	1.547	**0.237**
NDGA x Sex	1,44	4.699	0.036	1,44	6.988	0.011	1,12	1.070	0.321

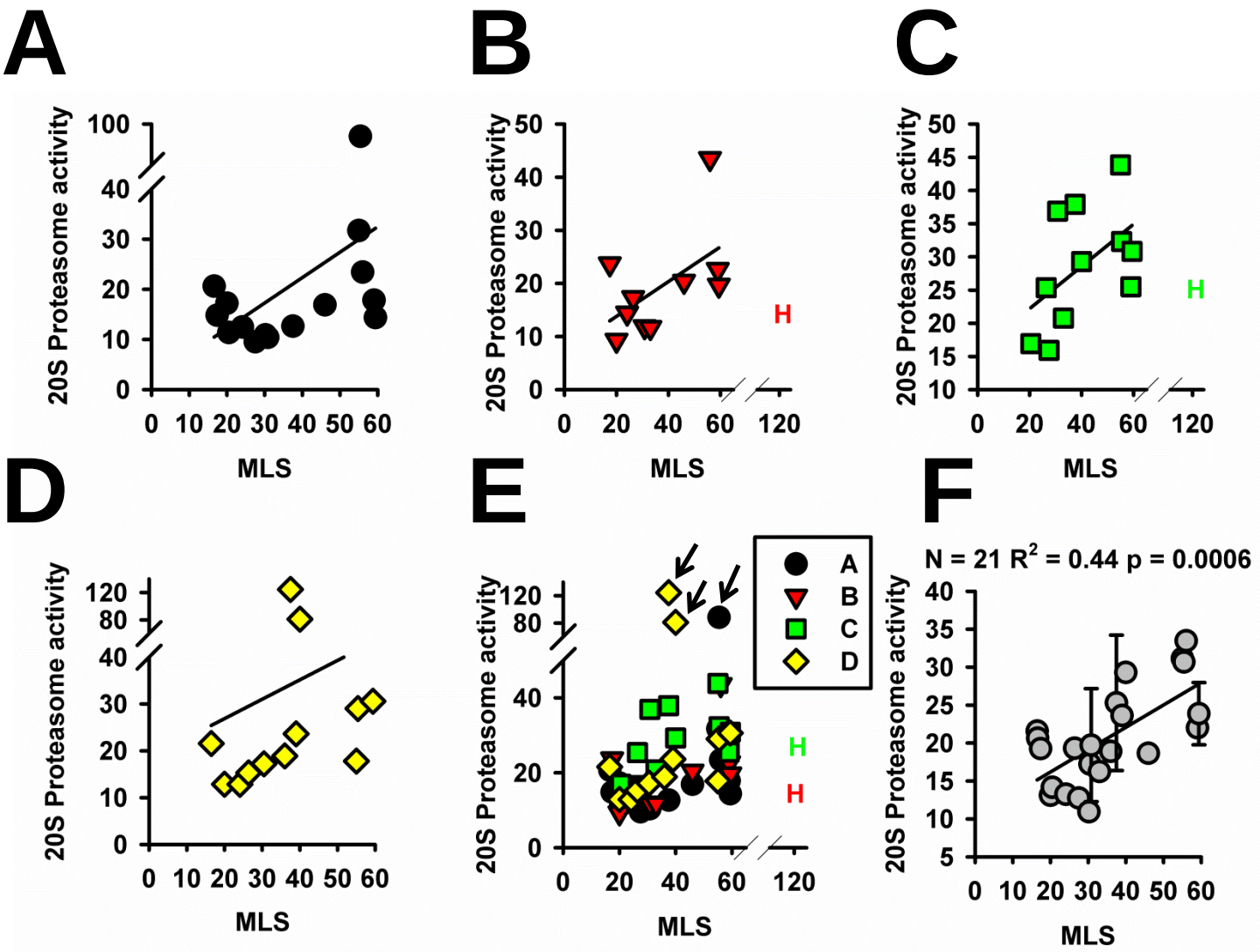
Least Significant Difference Post-Hoc Test

			PSMB8			Proteasomal Activity			PSMB5		
			Mean Diferenc	Std. Error	Sig	Mean Diferenc	Std. Error	Sig	Mean Diference	Std. Error	Sig
Rapamycin	**Male Control**	**Male Drug**	**+67.7**	**27.1**	**0.029**	**+22.4**	**16.1**	**0.189**	**-28.2**	**11.3**	**0.028**
	Male Control	Female Control	+135	27.1	<0.001	+17.5	16.1	0.299	-54.0	11.3	0.299
	Female Control	**Female Drug**	**+141**	**27.1**	**<0.001**	**+40.1**	**16.1**	**0.028**	**+21.6**	**11.1**	**0.08**
	Male Drug	Female Drug	+67.7	27.1	<0.001	+35.2	16.1	0.049	-4.27	11.1	0.712
Snell	**Male Control**	**Male Snell**	**+87.4**	**32.2**	**0.013**	**+51.3**	**25.3**	**0.056**	**+233**	**59.3**	**0.001**
	Male Control	Female Control	+47.9	32.2	0.152	+51.0	25.3	0.058	+11.0	59.3	0.855
	Female Control	**Female Snell**	**+50.1**	**32.2**	**0.135**	**-2.79**	**25.3**	**0.913**	**+63.0**	**59.3**	**0.301**
	Male Snell	Female Snell	+10.7	32.2	0.743	-3.16	25.3	0.902	+159	59.3	0.014
17-α-Estradiol	**Male Control**	**Male Drug**	**+67.7**	**22.6**	**0.023**	**+21.0**	**10.8**	**0.08**	**-26.9**	**14.7**	**0.092**
	Male Control	Female Control	+135	22.6	<0.001	+17.5	10.8	0.133	-54.0	14.7	0.003
	Female Control	**Female Drug**	**+48.3**	**22.6**	**0.054**	**+4.42**	**10.8**	**0.691**	**-14.4**	**14.7**	**0.346**
	Male Drug	Female Drug	+124	22.6	<0.001	-0.93	10.8	0.933	41.5	14.7	0.015
NDGA	**Male Control**	**Male Drug**	**+358**	**141**	**0.014**	**+46.5**	**11.2**	**<0.001**	**+45.7**	**51.3**	**0.390**
	Male Control	Female Control	+92.3	141	0.515	-11.2	11.2	0.321	-7.60	51.3	0.885
	Female Control	**Female Drug**	**+504**	**141**	**0.001**	**+4.61**	**11.2**	**0.682**	**-29.3**	**51.3**	**0.578**
	Male Drug	Female Drug	-239	141	0.096	-53.2	11.2	<0.001	-82.6	51.3	0.133

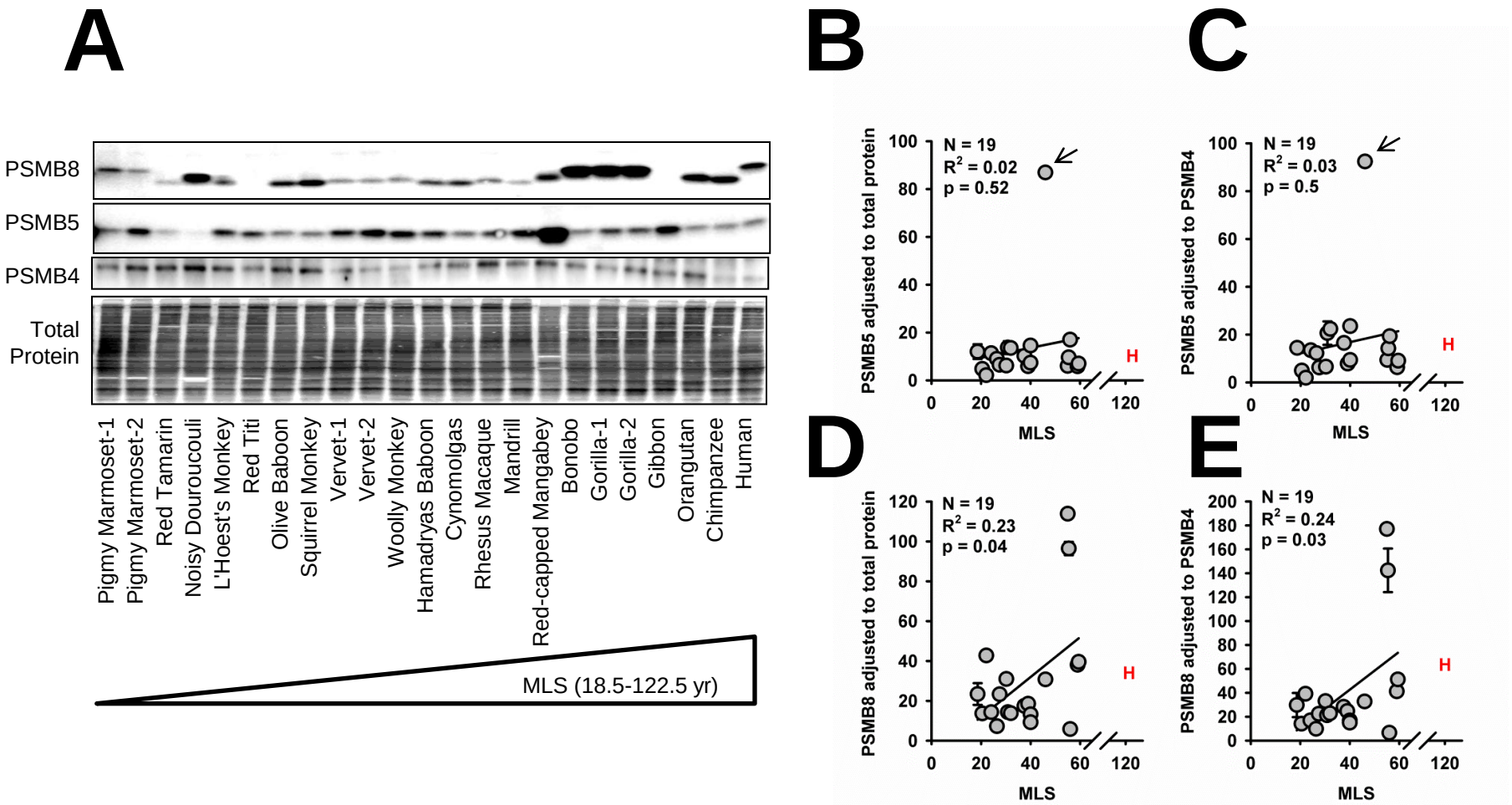
Supplemental Table 2. Two way ANOVA and post-hoc analyses for mouse liver tissue



Supplemental Figure 1. Proteolytic activity in fibroblast lysates increases with lifespan among species of primates. **(A)** Scatterplot of Suc-LLVY-AMC degradation during incubation with cell lysate from different primate species in the absence of ATP. **(B)** Scatterplot of Suc-LLVY-AMC degradation in lysates supplemented with 0.25mM ATP. Error bars if present represent the SEM of two cell lines derived from independent animals. MLS = Maximum Species Lifespan in years. Response from one cell-line of human fibroblasts is shown with an “H”, but is not included in statistical analysis.



Supplemental Figure 2. Fibroblasts from longer lived species of primates have greater 20S proteasome activity **(A-D)** Scatterplots of 4 independent experiments using different independent sets of primate species. Proteasome activity measured in a Native polyacrylamide gel using an in-gel overlay by Suc-LLVY-AMC. **(E)** Combined data from the 4 scatterplots. **(F)** Re-plot of Figure 1B in which three outliers (shown with arrows in panel E) were removed. Removal of these datapoints does not change any of the conclusions drawn from this data. Results for human cell-lines are shown with an "H" but are not included in statistical analysis.



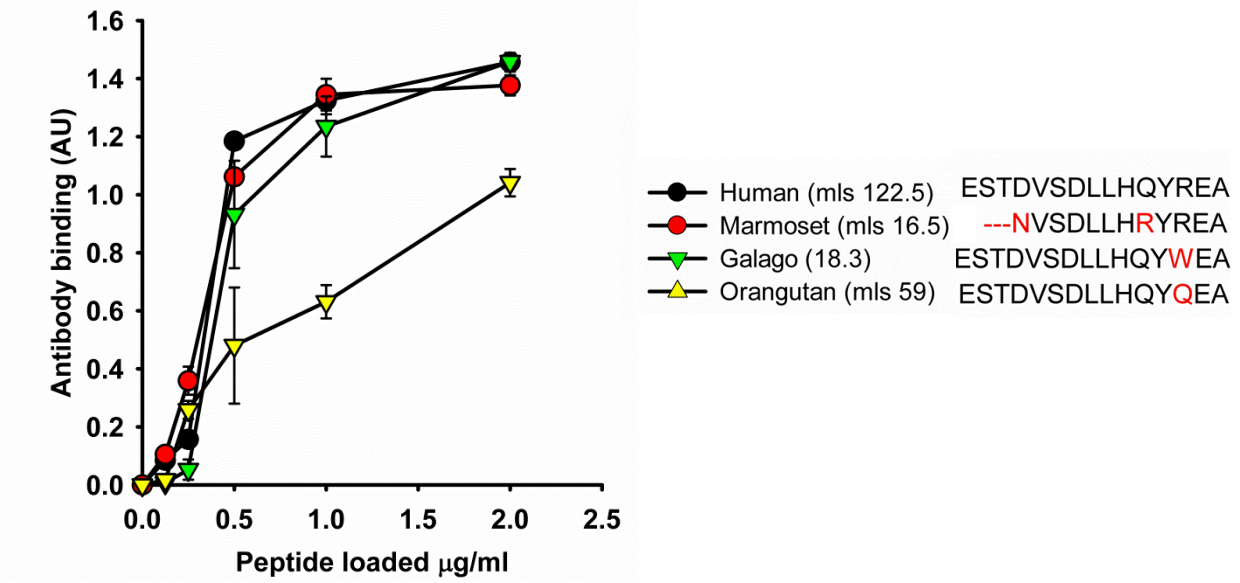
Supplemental Figure 3. Fibroblasts from longer lived species of primates have a significant elevation in PSMB8 levels but no significant lifespan association in levels of PSMB5. (**A**) Representative immunoblot. Samples were run on a SDS polyacrylamide gel, and then developed using antibodies against PSMB5 (standard proteasome specific subunit), PSMB8 (immunoproteasome specific subunit) or PSMB4 as a measure of total proteasome. (**B**) Scatterplot of PSMB5 level adjusted to total protein. (**C**) Scatterplot of PSMB5 level adjusted to PSMB4. (**D**) Scatterplot of PSMB8 level adjusted to total protein. (**E**) Scatterplot of PSMB8 level adjusted to PSMB4. Error bars if present represent the SEM of 2 cell lines derived from independent animals. MLS = Maximum lifespan in years.

The Red-capped Mangabey (indicated with an arrow) was considered an outlier in panels A & B. Removal of this datepoint did not change the conclusions of these panels. With the removal of the Red-capped Mangabey no significant correlation was observed between PSMB5 and lifespan in either panel A (R^2 = 0.01 p = 0.74) or panel B (R^2 = 0.01 p = 0.69).

A

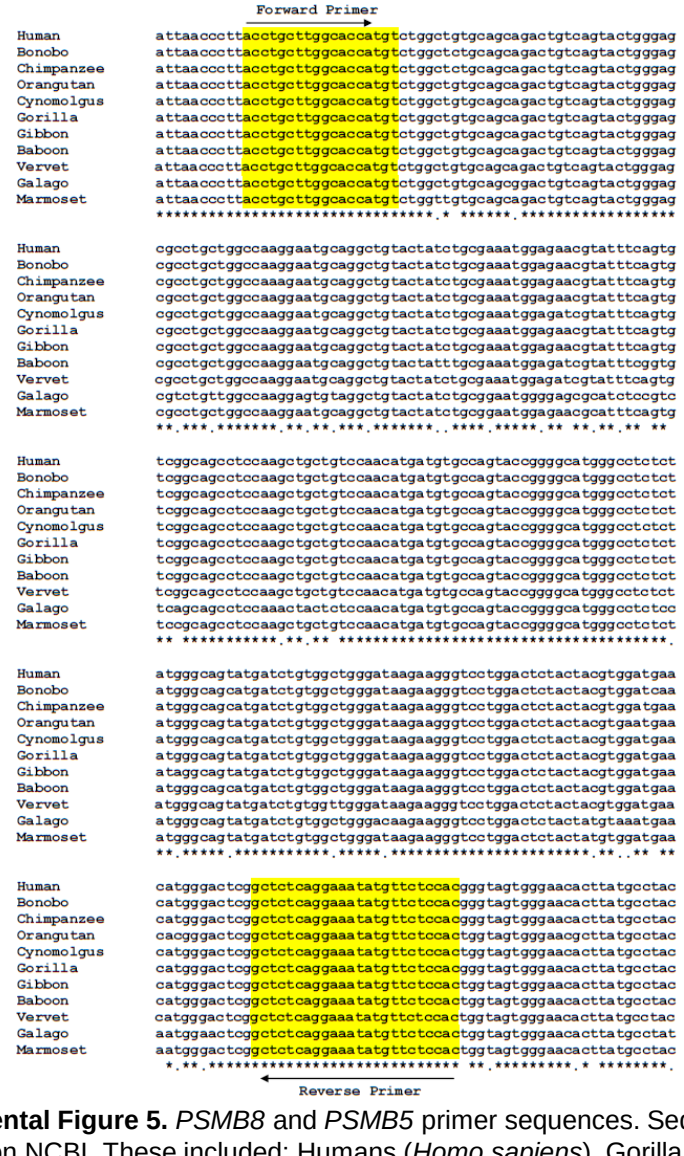
Protein	PSMB5	PSMB8	PSMB4
Antibody name:	ab3330	ab3329	ab166792
Epitope:	**IRVSSDNVADLHEKYS**	**ESTDVSDLLHQYREA**	**QIATVTEKGVE**
Marmoset (mls 16.5)	IRVSSDNVADLHEKYS	- - - NVSDLLHRYREA	QIATVTEKGVE
Galago (mls 18.3)	IRVSSDNVADLHEKYS	ESTDVSDLLHQYWEA	QIATVTEKGVE
Olive baboon (mls 27.5)	IRVSSDNVADLHEKYS	ESTDVSDLLHQYREA	QIATVTEKGVE
Squirrel Monkey (mls30.2)	IRVSSDNVADLHEKYS	ESTDVSDLLHQYREA	QIATVTEKGVE
Cynomolgus (mls 39)	IRVSSDNVADLHEKYS	ESTDVSDLLHQYREA	QIATVTEKGVE
Rhesus Macaque (mls 40)	IRVSSDNVADLHEKYS	ESTDVSDLLHQYREA	QIATVTEKGVE
Gibbon (mls 44.1)	IRVSSDNVADLHEKYS	ESTDVSDLLHQYREA	QIATVTEKGVE
Bonobo (mls 55)	IRVSSDNVADLHEKYS	ESTDVSDLLHQYREA	QIATVTEKGVE
Gorilla (mls 55.4)	IRVSSDNVADLHEKYS	ESTDVSDLLHQYREA	QIATVTEKGVE
Orangutan (mls 59)	IRVSSDNVADLHEKYS	ESTDVSDLLHQYQEA	QIATVTEKGVE
Chimpanzee (mls 59.4)	IRVSSDNVADLHEKYS	ESTDVSDLLHQYREA	QIATVTEKGVE
Human (mls 122.5)	IRVSSDNVADLHEKYS	ESTDVSDLLHQYREA	QIATVTEKGVE

B

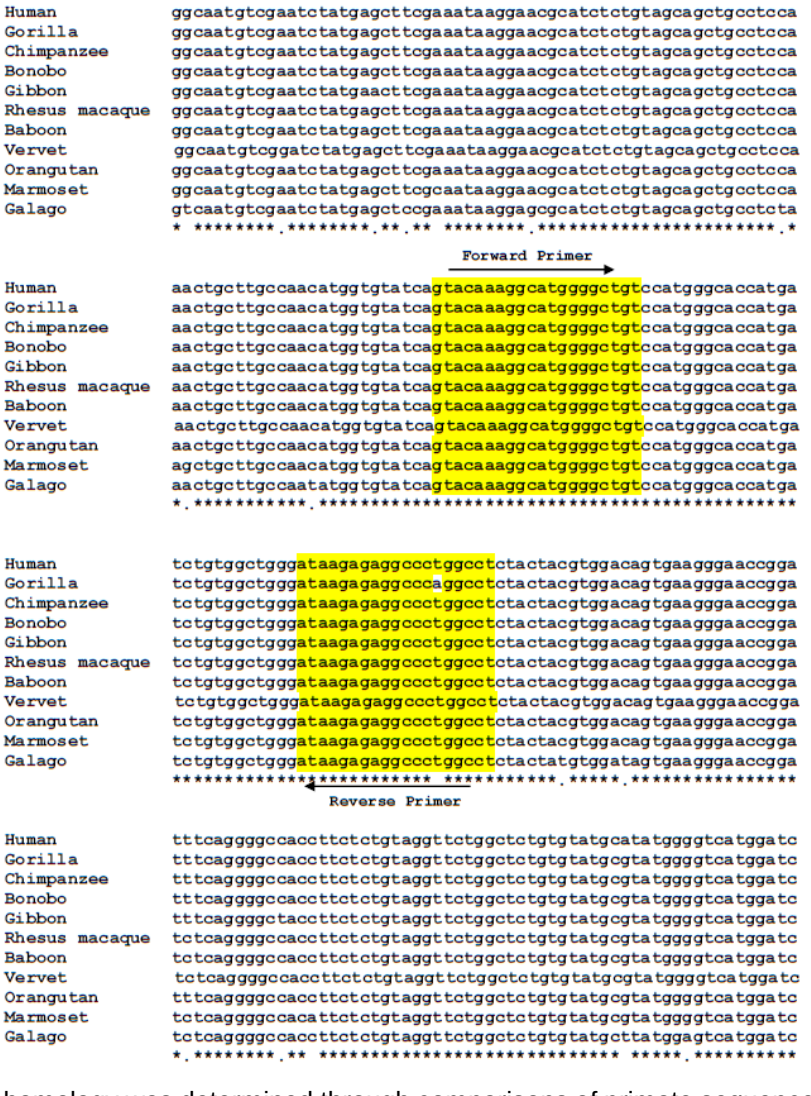


Supplemental Figure 4. (A) Antibody binding epitope based on NCBI sequence data. **(B)** Custom peptide sequences were produced by thermo scientific. Peptides were subjected to a direct ELISA assay and screened by an antibody to PSMB8. Binding was quantified using a TMB substrate

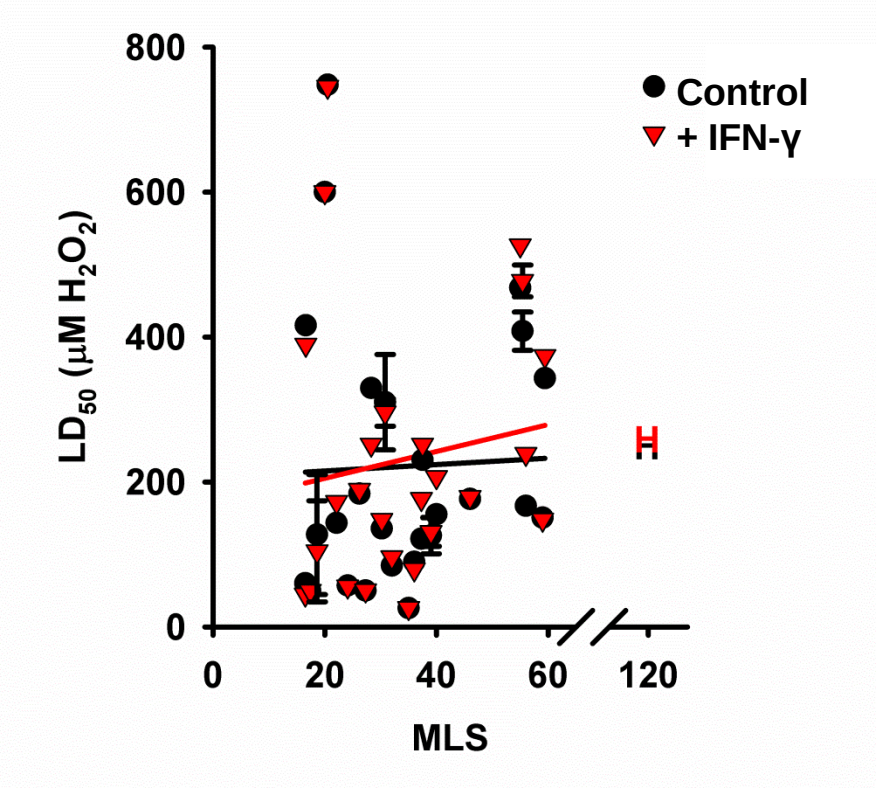
PSMB8 partial mRNA sequence



PSMB5 partial mRNA sequence



Supplemental Figure 5. *PSMB8* and *PSMB5* primer sequences. Sequence homology was determined through comparisons of primate sequences available on NCBI. These included: Humans (*Homo sapiens*), Gorilla (*Gorilla gorilla*), Chimpanzee *(Pan troglodytes*), Bonobo (*Pan paniscus*), Orangutan (*Pongo abelii*), Gibbon (*Hylobatus leucogenys*), Rhesus macaque (*Macaca mulatta*), Cynomolgus (*Macaca fascicularis*), Baboon (*Papio anubis*), Squirrel monkey (*Saimiri boliviensis*), Vervet (*Chlorocebus sabaeus*), Marmoset (*Callithrix jacchus*) and Galago (*Otolemur garnettii*). The set of species for which mRNA data was available was not consistent between genes. The Tarsier (*Tarsius syrichta*) sequence was not included as none of the primate species assayed in this paper were found on that branch of the primate phylogeny. The "*" symbol was used to represent nucleotides that are completely conserved between the species assayed.

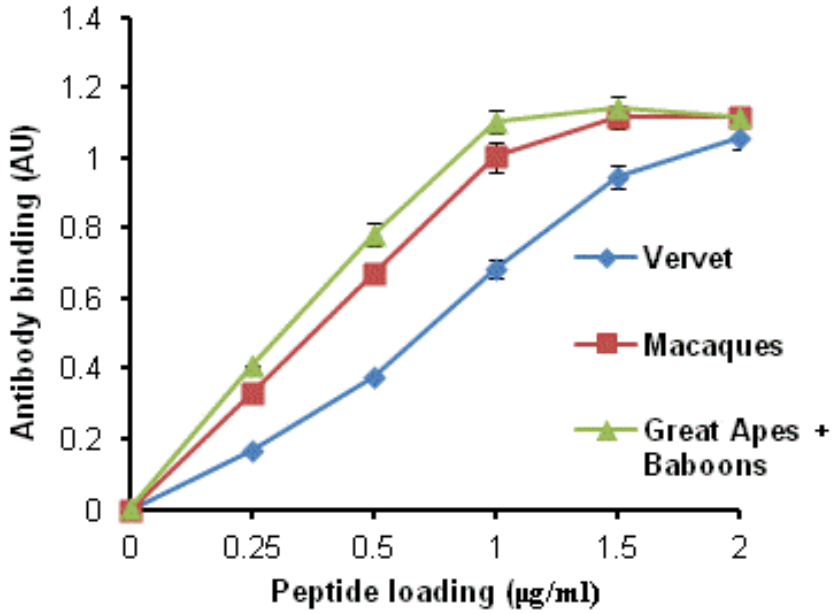


Supplemental Figure 6. Scatterplot of H_2O_2 dose required to reduce cell viability to 50% ± IFN-γ

A

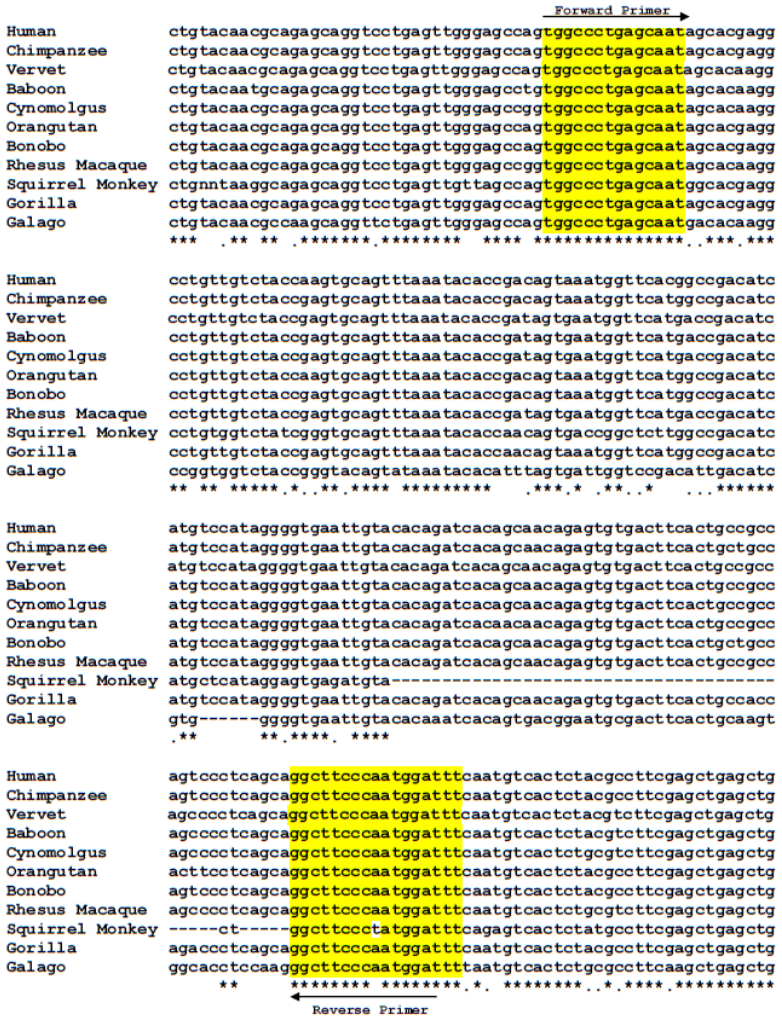
		IFNGR2 antibody (ab175878) epitope
Family	Species	DSSPKDDVWDSVSIISFPEKEQEDVLQTL
Galagonidae	*Galago (mls 18.3)*	NNSPKDDAWDSVFIVSFPEKEHEHVLQTL
Pitheciidae	*Red-bellied Titi (mls 26.4)*	DSSPKDDVWDSVSIISLPEKGQEDVLQT
Cercopithecidae	*Olive Baboon (mls 27.5)*	DSSPKDDVWDSVSIISFPEKEQEDVLQTL
Cercopithecidae	*Vervet (mls 30.8)*	DSSPKDDVWDSVSIISFPEKEQEDVLRTL
Cebidae	*Squirrel Monkey (mls30.2)*	DSSPKDDVWDSVSIILFPEKEQEDVLQT
Cercopithecidae	*Cynomolgus (mls 39)*	DSSPKDDVWDSVSIISFPEKEQDDVLQTL
Cercopithecidae	*Rhesus Macaque (mls 40)*	DSSPKDDVWDSVSIISFPEKEQDDVLQTL
Hominidae	*Bonobo (mls 55)*	DSSPKDDVWDSVSIISFPEKEQEDVLQTL
Hominidae	*Orangutan (mls 59)*	DSSPKDDVWDSVSIISFPEKEQEDVLQTL
Hominidae	*Chimpanzee (mls 59.4)*	DSSPKDDVWDSVSIISFPEKEQEDVLQTL
Hominidae	*Human (mls 122.5)*	DSSPKDDVWDSVSIISFPEKEQEDVLQTL

B

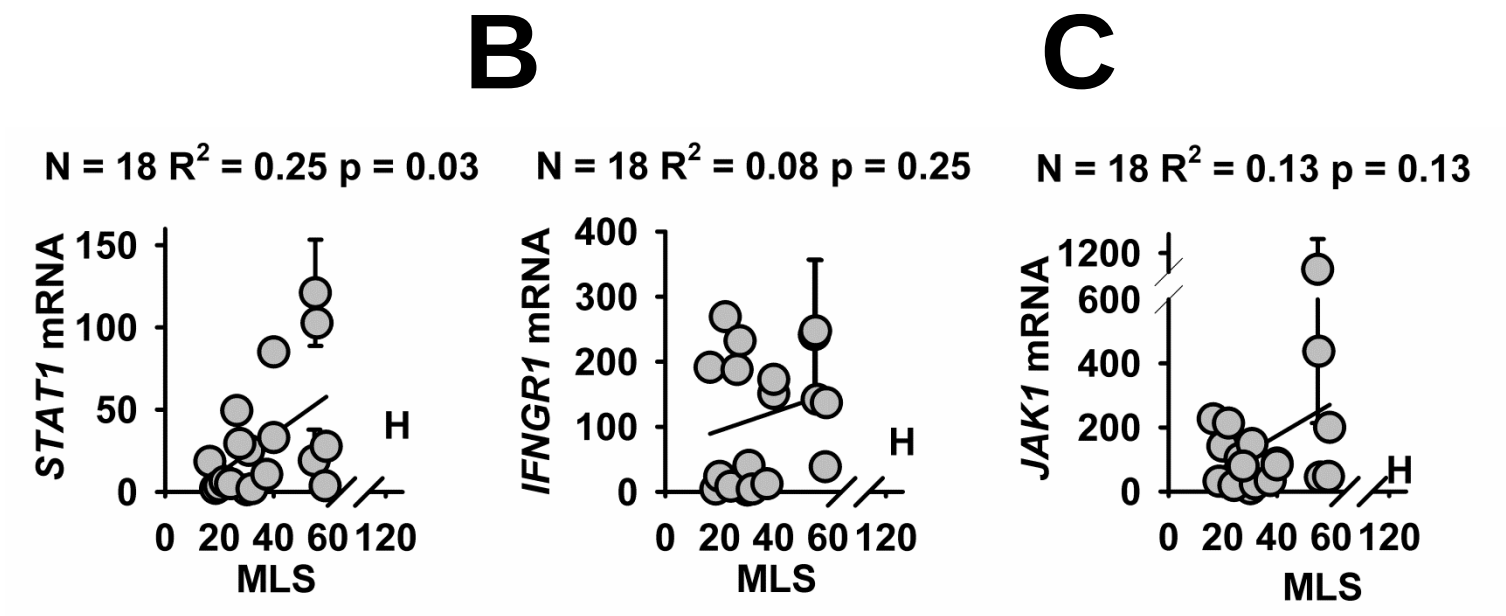


Supplemental Figure 7. (A) Antibody binding epitope based on NCBI sequence data. **(B)** Custom peptide sequences were produced by Thermo Scientific. Antibody binding affinity for New World monkeys and Galagos (not shown) was very different from that of Old World monkeys, Baboons and Great Apes as a result these groups were not used in measurements of IFNGR2. Peptides were subjected to a direct ELISA assay and screened by an antibody to IFNGR2. Binding was quantified using a TMB substrate.

IFNGR2 partial sequence



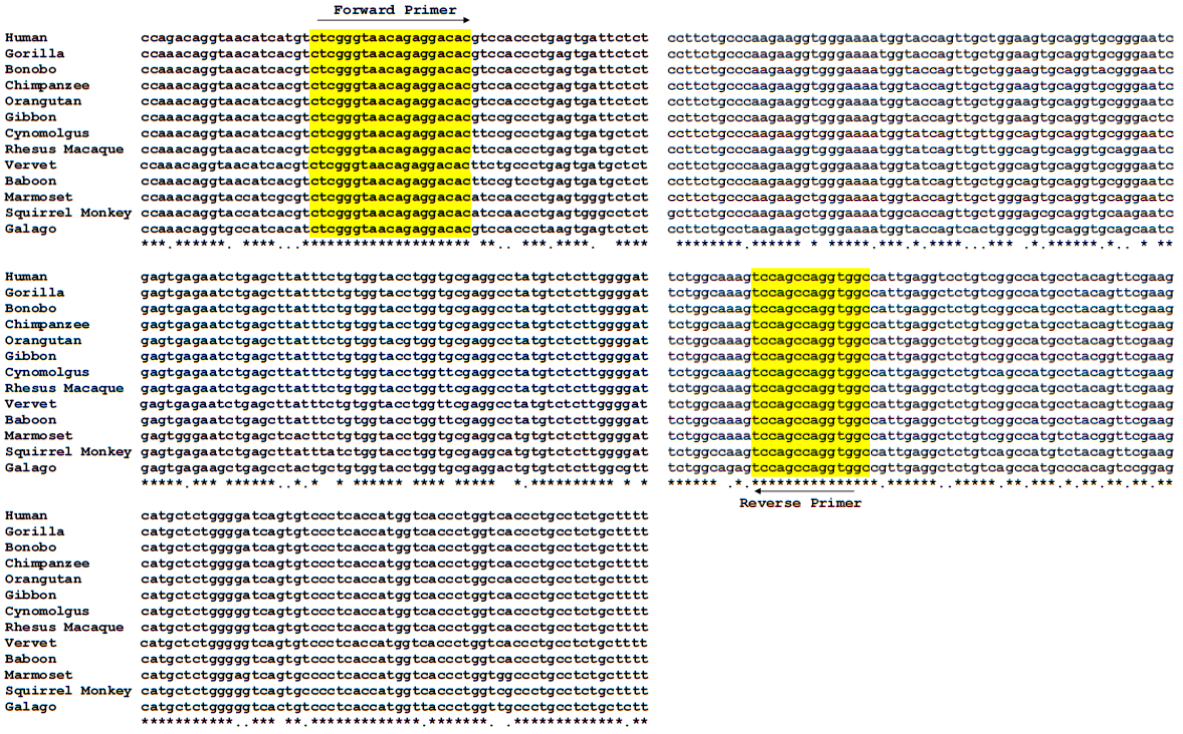
Supplemental Figure 8. *IFNGR2* primer sequence. Sequence homology was determined through comparisons of primate sequences available on NCBI. These included: Humans (*Homo sapiens*), Gorilla (*Gorilla gorilla*), Chimpanzee *(Pan troglodytes*), Bonobo (*Pan paniscus*), Orangutan (*Pongo abelii*), Gibbon (*Hylobatus leucogenys*), Rhesus Macaque (*Macaca mulatta*), Cynomolgus (*Macaca fascicularis*), Baboon (*Papio anubis*), Squirrel Monkey (*Saimiri boliviensis*), Vervet (*Chlorocebus sabaeus*), Marmoset (*Callithrix jacchus*) and Galago (*Otolemur garnettii*). The set of species for which mRNA data was available was not consistent between genes. The Tarsier (*Tarsius syrichta*) sequence was not included as none of the primate species assayed in this paper were found on that branch of the primate phylogeny. The "*" symbol was used to represent nucleotides that are completely conserved between the species assayed.

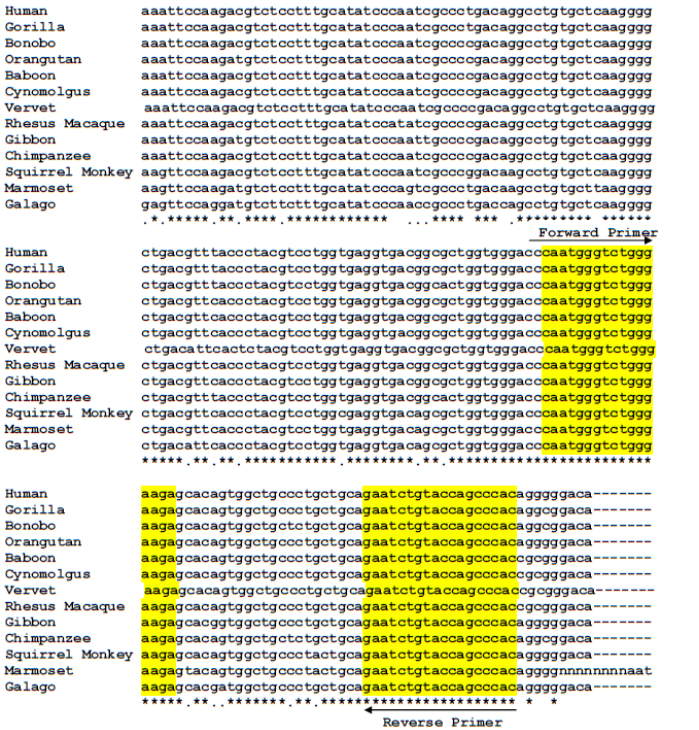


Supplemental Figure 9. Fibroblasts from longer lived species of primates have increased mRNA expression of STAT1 but no significant association to lifespan in mRNA expression for IFNGR1 or JAK1. **(A)** Scatterplot of relative STAT1 mRNA levels. **(B)** Scatterplot of relative IFNGR1 mRNA levels. **(C)** Scatterplot of relative JAK1 mRNA levels. Error bars if present represent the SEM of 2 cell lines derived from independent animals .

TAP1 partial mRNA sequence

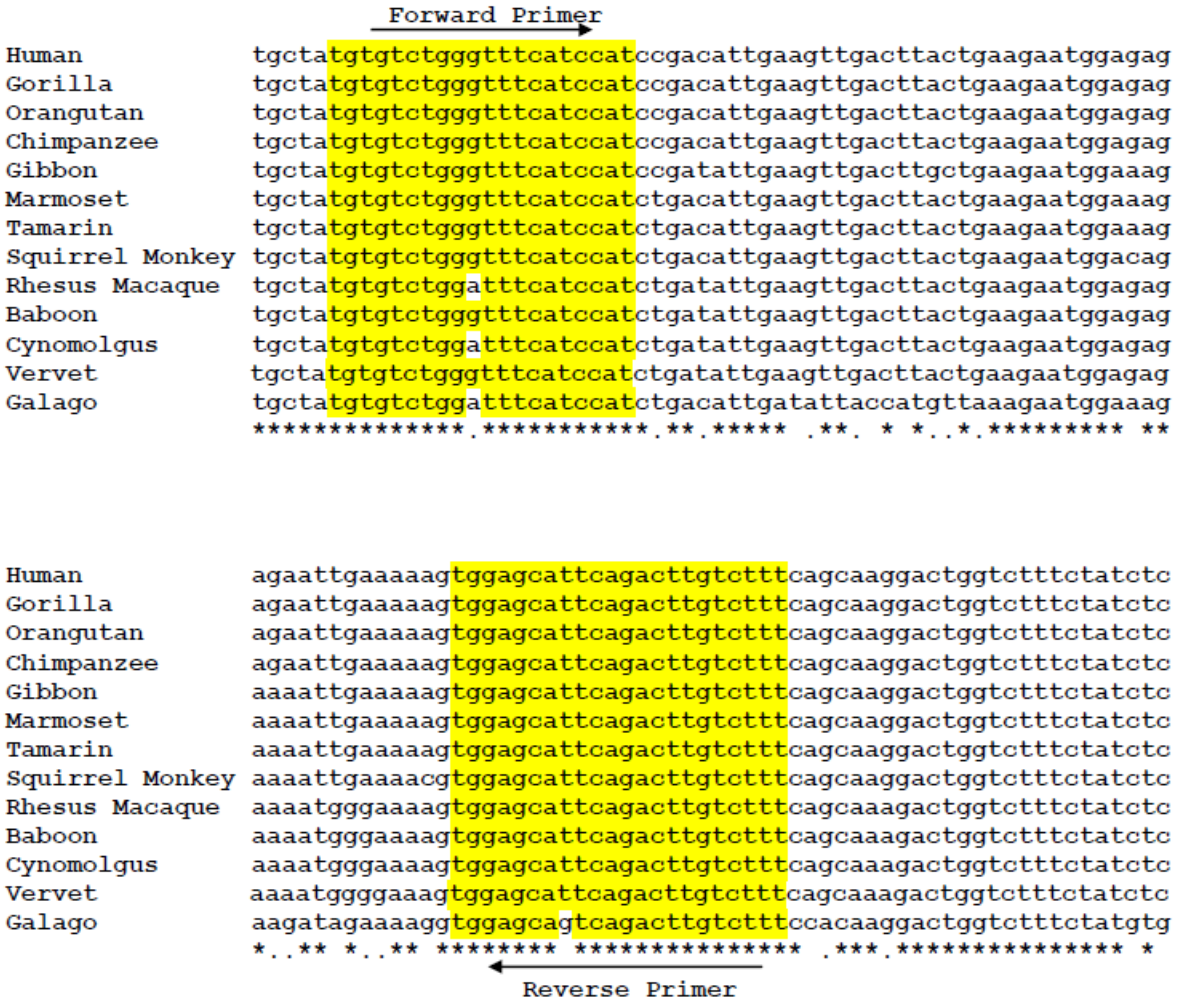
TAP2 partial mRNA sequence



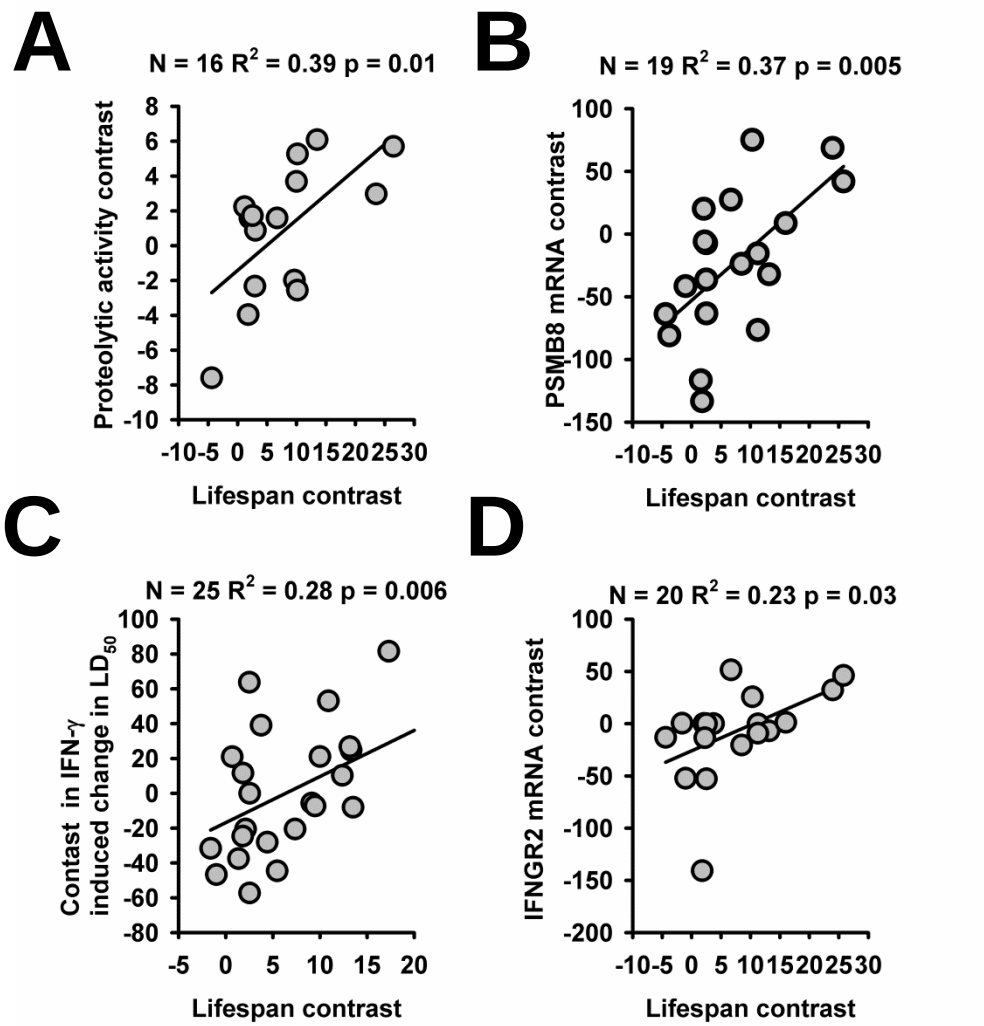


Supplemental Figure 10. *TAP1* and *TAP2* primer sequences. Sequence homology was determined through comparisons of primate sequences available on NCBI. These included: Humans (*Homo sapiens*), Gorilla (*Gorilla gorilla*), Chimpanzee *(Pan trogloytes*), Bonobo (*Pan paniscus*), Orangutan (*Pongo abelii*), Gibbon (*Hylobatus leucogenys*), Rhesus Macaque (*Macaca mulatta*), Cynomolgus (*Macaca fascicularis*), Baboon (*Papio anubis*), Squirrel monkey (*Saimiri boliviensis*), Vervet(*Chlorocebus sabaeus*), Marmoset (*Callithrix jacchus*) and Galago (*Otolemur garnettii*). The set of species for which mRNA data was available was not consistent between genes. The Tarsier (*Tarsius syrichta*) sequence was not included as none of the primate species assayed in this paper were found on that branch of the primate phylogeny. The "*" symbol was used to represent nucleotides that are completely conserved between the species assayed.

β-2 microglobulin partial mRNA sequence

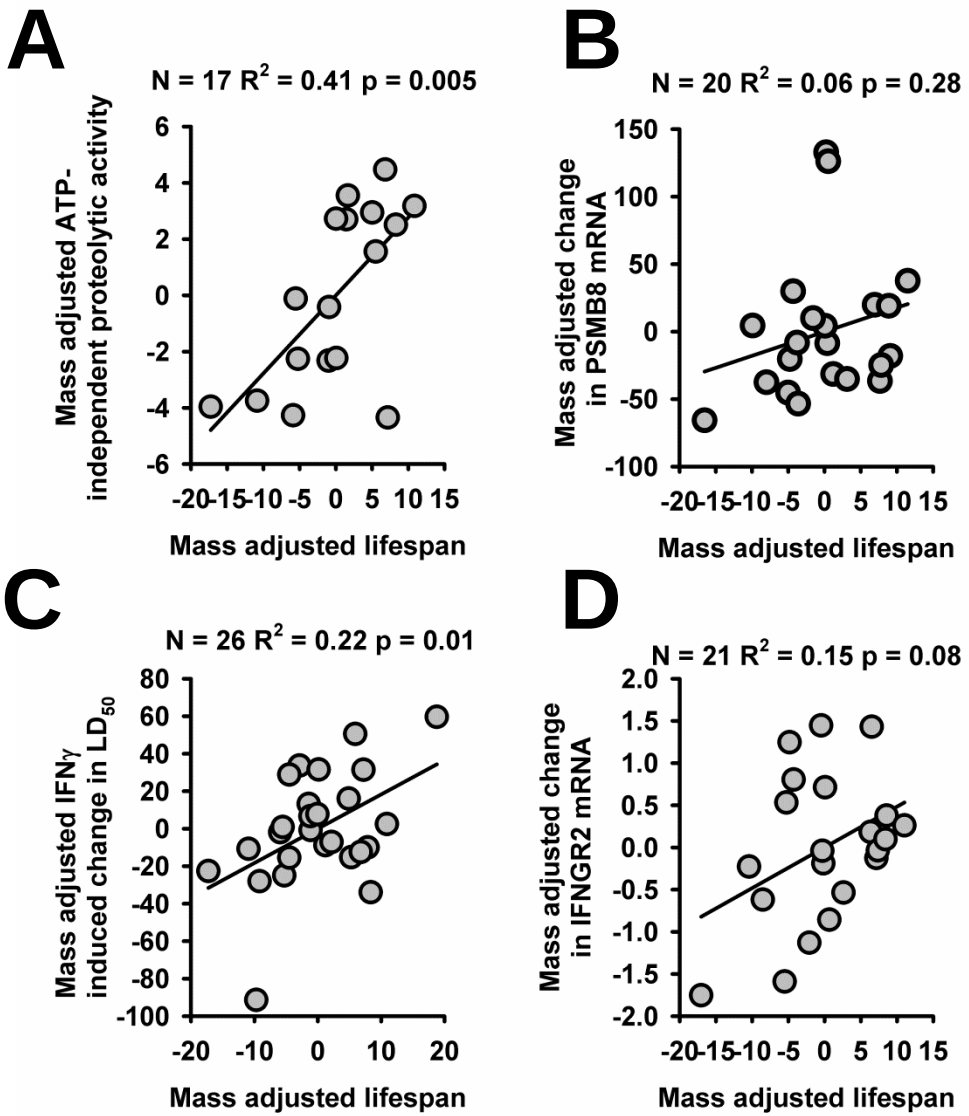


Supplemental Figure 11. *β-2 microglobulin* primer sequences. Sequence homology was determined through comparisons of primate sequences available on NCBI. These included: Humans (*Homo sapiens*), Gorilla (*Gorilla gorilla*), Orangutan (*Pongo abelii*), Chimpanzee *(Pan trogloytes*),, Gibbon (*Nomascus leucogenys*), Marmoset (*Callithrix jacchus*), Tamerin (*Saguinus midas),* Squirrel monkey (*Saimiri boliviensis*), Rhesus macaque (*Macaca mulatta*), Baboon (*Papio anubis*), Cynomolgus (*Macaca fascicularis*), Green monkey (*Chlorocebus sabaeus*), and Galago (*Otolemur garnettii*). The set of species for which mRNA data was available was not consistent between genes. The Tarsier (*Tarsius syrichta*) sequence was not included as none of the primate species assayed in this paper were found on that branch of the primate phylogeny. The "*" symbol was used to represent nucleotides that are completely conserved between the species assayed.

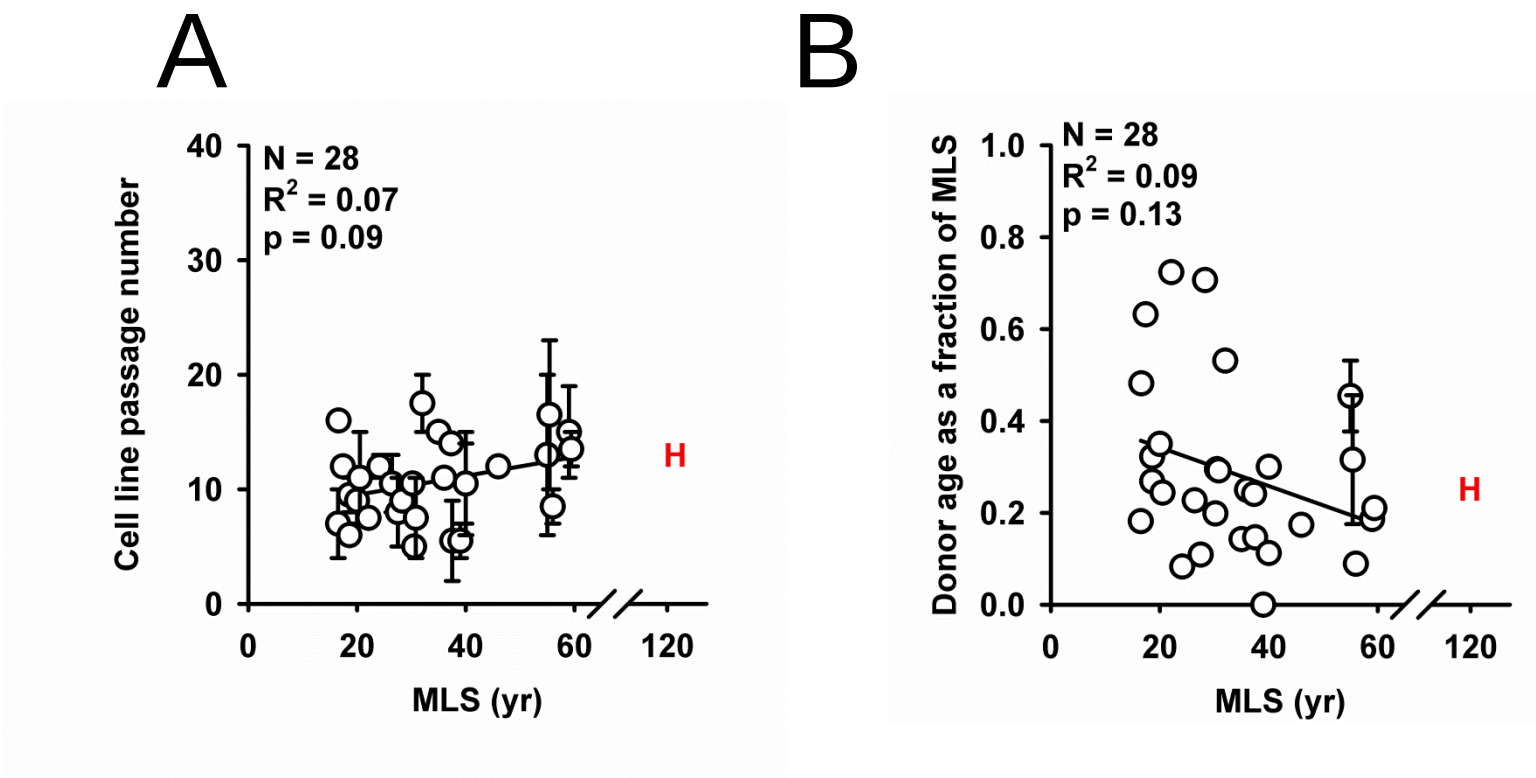


Supplemental Figure 12. Scatterplot showing standardized contrast analysis for **(A)** ATP-independent proteolytic activity. **(B)** *PSMB8* mRNA. **(C)** *INFGR2* mRNA. **(D)** IFN-γ induced change in LD50. Values are calculated as described in *Garland et al., 1994* and are based on the phylogeny in *Pickering et al., 2014* (Note N = N - 1 of original results due to the pairwise comparisons involved in the phylogenetic contrast)

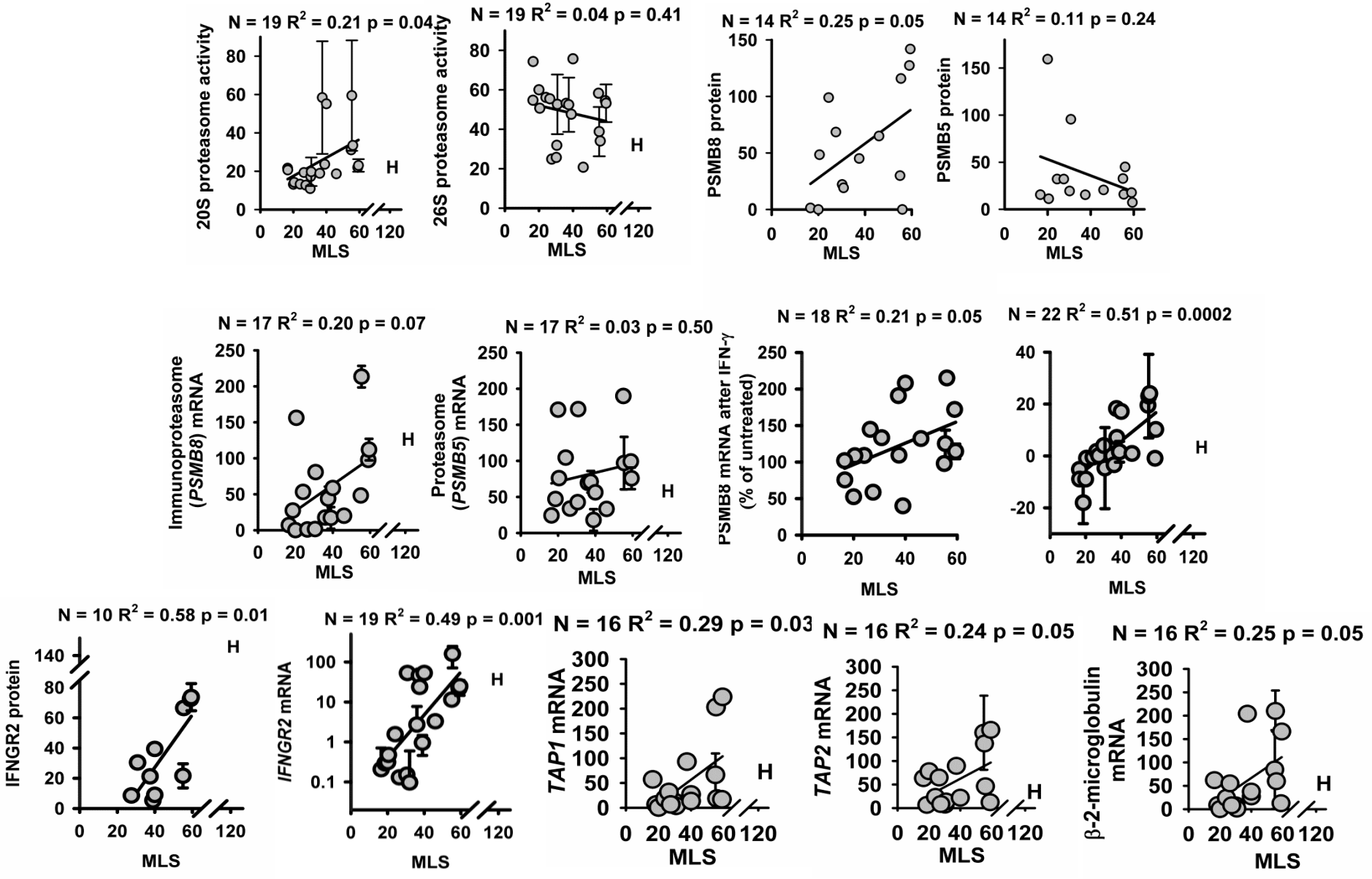
Garland T, Adolph SC. Why Not to Do 2-Species Comparative-Studies - Limitations on Inferring Adaptation. Physiol Zool. 1994 Jul-Aug;**67**(4):797-828.
Pickering, A. M., Lehr, M., Kohler, W. J., Han, M. L. & Miller, R. A. (2014) Fibroblasts From Longer-Lived Species of Primates, Rodents, Bats, Carnivores, and Birds Resist Protein Damage. J Gerontol A Biol Sci Med Sci, doi:10.1093/gerona/glu115.



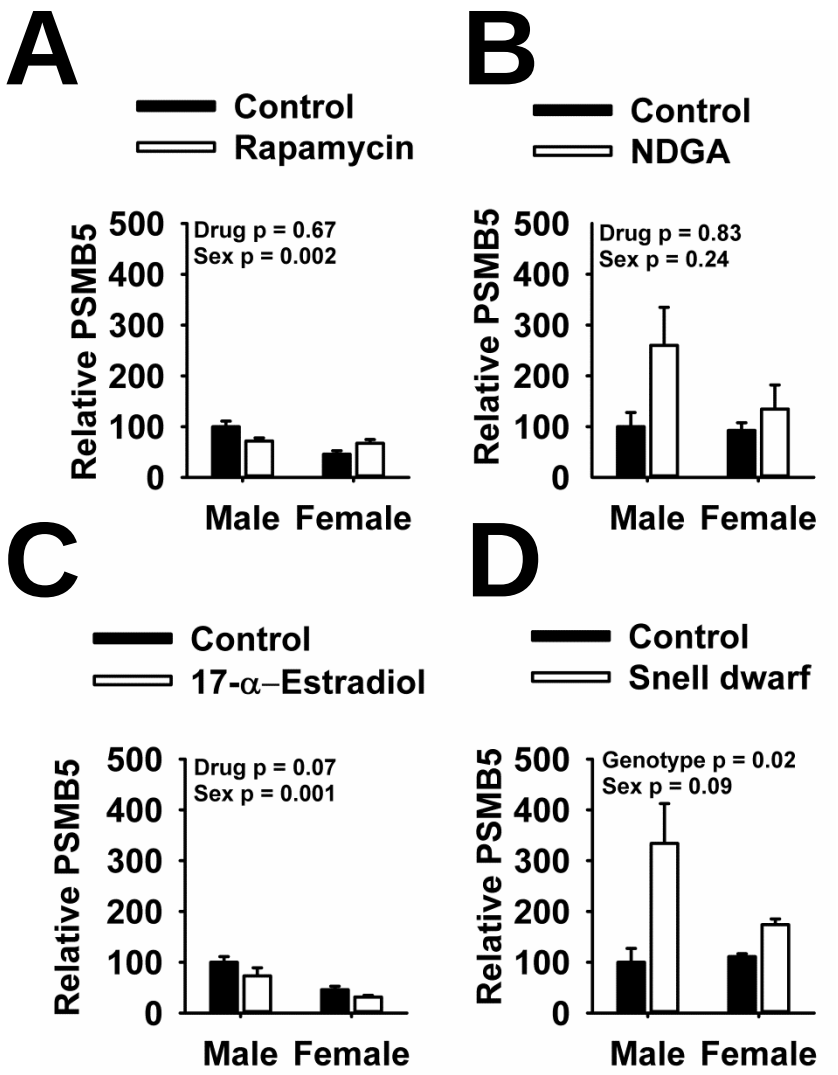
Supplemental Figure 13. Scatterplot of mass-adjusted changes in **(A)** ATP-independent proteolytic activity. **(B)** *PSMB8* mRNA. **(C)** Log_{10} *INFGR2* mRNA. **(D)** IFN-γ induced change in LD50. Values represent the residual from either maximum lifespan, or the variable of interest, plotted against log_{10}(mass) (g).



Supplemental Figure 14. (A) Scatterplot of cell passage number against maximum lifespan. Error bars if present show the highest and lowest passage number used for this cell line. **(B)** Scatterplot of donor animal age against maximum lifespan. (C) Scatterplot of donor animal age (as a fraction of maximum lifespan) against maximum lifespan. Error bars if present show the highest and lowest age of donor animals used. Each data point represents an independent species. Humans are shown with an 'H' but are excluded from analyses.



Supplemental Figure 15. Assessment of cellular endpoints after removal of data from Mouse Lemur, Noisy Douroucouli, Patas Monkey and Woolly Monkey, the four species for which donor age exceeded 50% of species maximum lifespan. The association of MLS with these endpoints is replicated in this truncated set of species, although in one case the association no longer reaches the standard criterion for statistical significance (PSMB8 mRNA, p = 0.07).



Supplemental Figure 16. PSMB5 levels in liver samples of mice subjected to a variety of life-extending interventions. (**A**) Rapamycin. (**B**) NDGA. (**C**) 17-α-Estradiol. (**D**) Snell dwarf. Data are presented as bar graphs of PSMB5 levels adjusted to β-actin. Data are plotted as a percent of control males. Error bars represent SEM where N = 4 (except for Snell dwarfs where N = 6). For rapamycin, NDGA, and 17-α-estradiol, controls were littermates that received mouse chow with no drugs. For the Snell dwarf study, controls were littermates.