## Manuscript Title: Phytochemical compound PB125 attenuates skeletal muscle mitochondrial dysfunction and impaired proteostasis in a preclinical model of musculoskeletal decline

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- Animal model Guinea pig –
- used, if Dunkin Hartley
- applicable Guinea pig

Underlying This study tests the hypothesis that 10 months of PB125 supplementation would attenuate the age/disease related declines in skeletal muscle of Hartley guinea pigs, particularly the declines in mitochondrial respiration and protein synthesis. We were additionally interested in testing the hypothesis that attenuation of the declines in mitochondrial respiration and protein synthesis would yield to maintained mobility in Hartley guinea pigs as their musculoskeletal dysfunction progressed. hypothesis

Definitions of 'n':

The number of guinea pigs. Weekly measurements of weight were used to generate growth curves from all guinea pigs. 01

Refers to averaged technical duplicates acquired from biological sample (permeabilized soleus myofibers). Samples were excluded if CCF was beyond cutoff. Outlier test used to remove any outliers. Refer to methods for details of exclusion. Q2

Refers to averaged technical duplicates acquired from biological sample (permeabilized soleus myofibers). Samples were excluded if CCF was beyond cutoff. Outlier test used to remove any outliers. Refer to methods for details of exclusion. Q3

Q4 Refers to averaged technical duplicates acquired from biological sample (permeabilized soleus myofibers). Samples were excluded if CCF was beyond cutoff. Outlier test used to remove any outliers. Refer to methods for details of exclusion. Q5 Refers to averaged technical duplicates acquired from biological sample (permeabilized soleus myofibers). Samples were excluded if CCF was beyond cutoff. Outlier test used to remove any outliers. Refer to methods for details of exclusion.

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Q6 Q7 Fractionated skeletal muscle tissue of guinea pigs.

Q8 Fractionated skeletal muscle tissue of guinea pigs.

Q9 Fractionated skeletal muscle tissue of guinea pigs.

Q10 Homogenized skeletal muscle tissue of subset of guinea pigs

Q11 Homogenized skeletal muscle tissue of subset of guinea pigs

Q12 The number of guinea pigs that were part of the long term study (excludes guinea pigs that died prematurely,

Experimental Question #	Finding Conclusion	Experimental location/variable						Summary	Statistics (Me	an, SD, n)						Units	Statistical test	Any other variable	in which data are presented	Comments
	The rate of growth was not different between treated and untreated male guinea pigs.	Rate of growth (K)	K values	CON:0.0870 6 PB125:0.08 314	95% CI	CON: PB125:	0.07213 – 0 0.06939 – 0.09784	DFd: 1120 28 animals	(reflects data points used to generate curve) p value 0.7151	3						k	CON vs PB125		Fig 1F	Growth rates (k) were calculated by weekly measurements of mass for each guinea pig over the 10 month period
1. Is growth or size different	The rate of growth was not different between treated and untreated female guinea pigs.	Rate of growth (K)	K values	CON:0.0766 7 PB125: 0.07244	95% CI	CON: PB125:	0.06170 - 0.09263 0.05027 - 0.09687	DFd: 1049 28 animals	(reflects data points used to generate curve) 0.7593	3						k	CON vs PB125		Fig 1G	(reflected by Growth rates (k) were calculated by weekly measurements of mass for each guinea pig over the 10 month period (reflected by DFd)
	Finding Conclusion	Experimental location/variable						Summary	Statistics (Me	an, SD, n)						Units	Statistical test	Any other variable	in which data are	Comments
between treated and					Male CON			Male PB125			Female CON			Female PB125			Three Way ANOVA			
guinea pigs?	Body mass was not different			Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n		Age: <0.0001,			
	between treated and untreated quinea pigs	Body mass	5mo	933	71.9355772	1	2 929.454545	71.375575	1 11 	1 768	62.3409977		11 765.8333	33 75.9591198		12 grams	Sex: <0.0001 Treatment: 0.7693		Fig 1H	
	Relative soleus mass was not different between treated and untreated guinea pigs.	Soleus mass divided by body mass	15mo 5mo 15mo	Mean 0.22714667 0.22258333	<b>SD</b> 0.03191312 0.04945789	n 1 1	2 1205.8 Mean 2 0.22068909 2 0.20233333	93.504367 SD 0.03623283 0.04960843	n n 7 §	Mean 1 0.23381091 0.23033333	98.6894118 SD 0.04446527 0.05332917	n	Mean 11 0.23554 9 0.20	SD 75 0.04152482 31 0.03058122	n	relative mas (muscle mass [mg], 12 body mass [g]) 10	s Age: 0.1148, Sex: 0.4181, Treatment: 0.1611		Fig 1I	
	gastrocnemius mass was not different between treated and untreated	Gastrocnemius mass divided by body mass	5mo 15mo	Mean 1.9676675 1.85941667	<b>SD</b> 0.1261685 0.20458404	<b>n</b> 1	Mean 2 1.99459 2 1.90322222	SD 0.2061759 0.23644808	n 9 1' 3 §	Mean 1 2.01765364 9 1.88288889	SD 0.1972424 0.17785629	n	<b>Mean</b> 11 2.0319 9 1.	<b>SD</b> 85 0.17281013 89 0.19404581	n	relative mas (muscle 12 mass [mg] body mass [g]) 10	s Age: 0.0050, Sex: 0.558, Treatment: 0.5781		Fig 1J	

Experimental Question #	Finding Conclusion	Experimental location/variable	9					Summary Sta	atistics (M	ean, SD, n)				Units	Statistical test	Any other variable	Figure/table in which data are presented	Comment
					Male			Male PB125		Female		Female PB125			Three Way ANOVA		procented	
	There are significant main effects of disease/age and sex on State 3 mitochondrial respiration, but not treatment.	Permeabilized myofibers of soleus	5mo 15mo	<b>Mean</b> 99.5276958 85.8028571 2	SD 18.66274 24.9938572	n 12 14	<b>Mean</b> 97.5147423 97.4923077	<b>SD</b> 23.4106458 24.7245415	n 13 13	Mean         SD           88.5799643         14.0457714           70.4323077         16.9556216	n 14 13	Mean         SD           98.7043107         16.6658579           77.37666667         21.585462	n 14 12	oxygen consumption (pmol O2/(mg*s))	Age: 0.0012, Sex: 0.0057, Treatment: 0.0979		Fig 3A	
2. Are there Disease/Age-, Sex-, and Treatment related effects	There are significant main effects of disease/age, sex, and treatment on ETS capacity (Complex La IV)	Permeabilized myofibers of soleus	5mo 15mo	Mean 107.410796 95.3414286	<b>SD</b> 17.3659599 28.2551403	n 13 14	<b>Mean</b> 107.471711 111.15	<b>SD</b> 23.9735865 22.079589	<b>n</b> 14 13	Mean         SD           95.6786929         12.1086217           80.2938462         20.1534776	n 14 13	Mean         SD           108.909382         16.7000258           85.1191667         20.7205377	n 14 12	oxygen consumption (pmol O2/(mg*s))	Age: 0.0038, Sex: 0.0018, Treatment: 0.0369		Fig 3B	
on skeletal muscle mitochondrial respiration?	significant main effects of disease/age and sex on ETS capacity (Complex II - IV), but not treatment	Permeabilized myofibers of soleus	5mo 15mo	Mean 72.3387346 56.0421429	<b>SD</b> 13.1018151 10.7295983	n 13 14	<b>Mean</b> 71.8934643 61.02	<b>SD</b> 12.2785257 13.0105521	n 14 13	Mean         SD           64.8530143         10.183499           49.1330769         12.814388	n 14 13	Mean         SD           68.6162786         9.4492954           49.035         11.9533864	n 14 12	oxygen consumption (pmol O2/(mg*s))	Age: <0.0001, Sex: 0.0015, Treatment: 0.3686		Fig 3C	
	There is a significant main effect of disease/age on RCR, but not sex or treatment.	Permeabilized myofibers of soleus	5mo 15mo	<b>Mean</b> 13.7375241 2 11.164983 8	<b>SD</b> 2.92464774 5.84144599	n 11 14	<b>Mean</b> 12.4175548 11.0785241	<b>SD</b> 5.91692153 4.47831446	n 12 13	Mean         SD           11.6563386         3.50597489           9.34990257         2.24577659	n 13 13	Mean         SD           14.1583086         4.77056906           11.2413266         4.35138311	n 13 12	Ratio	Age: 0.0117, Sex: 0.5763, Treatment: 0.4027		Fig 3D	
					Male CON			Male PB125		Female CON		Female PB125			Three Way ANOVA			
	There are no effects of disease/age and sex on State 3 fatty acid supported mitochondrial respiration with 0.5 mM ADP present.	Permeabilized myofibers of soleus	5mo 15mo	Mean 42.0946167 41.1203136	<b>SD</b> 5.53852908 7.47993877	n 6 11	Mean 36.3777 39.1209091	<b>SD</b> 10.5266758 8.20109926	n 7 11	Mean         SD           37.3601167         2.43270933           35.255         6.91944493	n 6 12	Mean         SD           39.6061389         5.43781586           41.75         10.6846307	n 9 7	oxygen consumption (pmol O2/(mg*s))	Age: 0.8125, Sex: 0.5343, Treatment: 0.8930		Fig 3E	
3. Are there Disease/Age-, Sex-, and Treatment related effects on fatty acid supported skeletal muscle mitochondrial respiration?	There is a significant effect of treatment on State 3 fatty acid supported mitochondrial respiration with 1.0 mM ADP present, but no effects of either Sex or Treatment.	Permeabilized myofibers of soleus	5mo 15mo	<b>Mean</b> 44.0325636 4 46.9315636 9	<b>SD</b> 8.13458713 9.22131165	n 11 11	Mean 50.6090962 45.7272727	<b>SD</b> 13.2921892 5.37350926	<b>n</b> 13 11	Mean         SD           42.0969409         3.45188836           40.0916667         8.23578537	n 11 12	Mean         SD           45.1631321         6.86170343           47.9957143         13.228866	n 14 7	oxygen consumption (pmol O2/(mg*s))	Age: 0.8789, Sex: 0.1205, Treatment: 0.0349		Fig 3F	
	There was no significant effect of sex, disease/age, or treatment on State 3 fatty acid supported mitochondrial respiration with 6.0 mM ADP present.	Permeabilized myofibers of soleus	5mo 15mo	<b>Mean</b> 62.0050864 58.5307682	SD 7.80694986 12.2325652	n 11 11	<b>Mean</b> 63.8228385 59.38	<b>SD</b> 18.9146688 10.6120177	n 13 11	Mean         SD           53.6398455         5.84251776           50.0083333         13.3945415	n 11 12	Mean         SD           62.0279929         10.281103           58.2357143         16.7850676	n 14 7	oxygen consumption (pmol O2/(mg*s))	Age: 0.1584, Sex: 0.0695, Treatment: 0.0773		Fig 3G	

Experimental Question #	Finding Conclusion	Experimental location/variable						Summary St	atistics (N	lean, SD, n)						Units	Statistical test	Any other variable	Figure/table in which data are presented	Comme
					Male CON			Male PB125			Female CON			Female PB125			Three Way ANOVA			
	There are no effects of			Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n		Age:			
4. Are there	disease/age, treatment, or sex on	Permeabilized myofibers of soleus	5mo	0.42805336	0.08043792	11	0.43372192	0.13929264	12	0.45623588	0.18622498	12	0.38816307	0.10110131	14	ROS Emission (pmol/(mg*s)	0.1234, Sex: 0.1602 ) Treatment:		Fig 3H	
Disease/Age-, Sex-, and Treatment	maximum LEAK.		45	0.40372545	0.13585671	11	0.39790111	0.07993834	9	0.3620104	0.09612577	10	0.39574357	0.17953402	7		0.3179			
related effects on ROS emission in	There are no		1500																	
skeletal muscle mitochondria?	disease/age, treatment, or			Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n		Age:			
	emission during State 3 respiration supported by	Permeabilized myofibers of soleus	5mo	0.21674	0.07113392	6	0.22606338	0.05194098	8	0.23345815	0.08701785	6	0.23281856	0.05402247	9	ROS Emission (pmol/(mg*s)	0.2551, Sex: 0.9241, ) Treatment: 0.9641		Fig 3G	
	subsaturating amounts of ADP.		15mo	0.19293364	0.06461414	11	0.20461111	0.03942281	9	0.2092293	0.04340844	10	0.21227786	0.03719251	7					
					Male CON			Male PB125			Female CON			Female PB125			Three Way ANOVA			
	There are significant effects of Disease/Age, Sex and			Mean	SD	n	Mean	SD	n	Mean	SD	n	Mean	SD	n					
5. Are there Disease/Age-, Sex-, and Treatment	Treatment on ADP Vmax. In addition, PB125 treated 5 mo females have	Permeabilized myofibers of soleus	5mo	50.2081818	6.54644914	11	50.3407692	14.1048741	13	39.3530769	8.53556519	13	52.3653846	10.5011163	13	oxygen consumption (pmol O2/(mg*s))	Age: 0.0495, Sex: 0.0010, Treatment:		Fig 3I	
on ADP Kinetics in skeletal	greater respiration than 5 mo CON.		15mo	54.12	11.8800891	13	61.6061538	11.855594	13	47.3830769	13.3609271	13	46.8591667	9.71323133	12		0.0261, Age x Sex x Treatment: 0.0210			
muscie mitochondria?	There is a			Moon	80		Moon	60		Maan	<b>6</b> D		Moon	50						
	of treatment on ADP Km	Permeabilized myofibers of		0.488775	0.21902066	12	0.83565833	0.57318332	12	0.43314167	0.16610897	12	0.62755455	0.16896954	" 11	concentratio	A		Fig 3J	
	(sensitivity), but no effect of sex or age	soleus	5mo	0.56958571	0.33010164	14	0.79308	0.19993335	10	0.64803077	0.33967186	13	0.58931667	0.24076722	12		Age: 0.4023, Sex: 0.1311, Treatment:			
			15110														0.0069			
	PB125 treatment augments	permeabilized	5mo CON	<b>Mean</b> 44.33	<b>SD</b> 9.337	n 24	oxygen	One-Way Al co	NOVA Dun mparisons	nett's multiple test	p value									
	Vmax	myofibers of soleus	15mo CON	50.75 54.53	12.85 13.04	26 25	(pmol O2/(mg*s))	5mo C	ON vs. 15	mo CON	0.1085								Fig 4A	
			13110 PB123		5mo CON			15mo CON	514 VS. 1511	0 - 6 1 2 3	15mo PB125									
	PB125 treatment			Mean	SD	n	Mean	SD	n	Mean	SD	n	Oxvaen	Two-Way Af	NOVA Dunn	ett's multiple c test	omparisons			
	augments increase in ADP Vmax in males only	permeabilized myofibers of soleus	Male	50.2081818	6.54644914	11	54.12	11.8800891	13	61.6061538	11.855594	13	consumption (pmol O2/(mg*s))	5mo CON vs 15mo CON	0.5692	15mo PB125 5mo CON vs	0.0209		Fig 4B	
			Female	39.3530769	8.53556519	13	47.3830769	13.3609271	13	46.8591667	9.71323133	12		5mo CON vs 15mo CON	0.1067	15mo PB125	0.1479			
	PB125 attenuates the	permeabilized	5mo CON	<b>Mean</b> 93.63	<b>SD</b> 16.94	<b>n</b> 26	oxygen	One-Way Al co	NOVA Dun mparisons	nett's multiple test	p value									
	age-related decline in State	myofibers of soleus	15mo CON	78.4	22.5	27	consumption (pmol	5mo C	ON vs. 15	mo CON	0.0238								Fig 4C	1

	3 respiration.		15mo PB125	87.84	24.9	25	O2/(mg*s))	5mo COI	N vs. 15mo	PB125	0.5358								
	PB125				5mo CON			15mo CON			15mo PB125				WA Dunnett's multiple or	mnaricone			
	attenuates the			Mean	SD	n	Mean	SD	n	Mean	SD	n	000000	Iwo-way Ano	test	Inpansons			
	age-related decline in State 3 respiration in	permeabilized myofibers of soleus	Male	99.5276958	18.66274	12	85.8028571	24.9938572	14	97.4923077	24.7245415	13	consumption (pmol	5mo CON vs 15mo CON	5mo CON Vs 15mo 0.1633 PB125	0.9554		Fig 4D	
	females only	001000	Female	88.5799643	14.0457714	14	70.4323077	16.9556216	13	77.3766667	21.585462	12	O2/(mg*s))	5mo CON vs 15mo CON	15mo 0.0463 PB125	0.2898			
				Mean	SD	n													
	PB125 does not attenuate the disease/age		5mo CON	101.3	15.75	27		One-Way ANC com	OVA Dunne nparisons te	tt's multiple st	p value								
. Does PB125 treatment	related decline in ETS capacity (because there	permeabilized myofibers of soleus	15mo CON	88.1	25.4	27	oxygen consumption (pmol	5mo CC	DN vs. 15mo	CON	0.0605							Fig 4E	
modulate disease/age- related	was not a significant decline in ETS		15mo PB125	98.66	24.83	25	O2/(mg*s))	5mo CO	Nive 15mo	PB125	0.8752								
changes in nitochondrial	canacity in this		101101 2120							5120	0.0102								
respiration? are there any	PB125 does not sex				5mo CON			15mo CON			15mo PB125			Two-Way ANO	VA Dunnett's multiple co	omparisons			1
effects?	speciifcally	nomochilized		Mean	SD	n	Mean	SD	n	Mean	SD	n	oxygen		test 5mo CON vs				1
	age-related decline in ETS	myofibers of soleus	Male	107.410796	17.3659599	13	95.3414286	28.2551403	14	111.308462	22.192122	13	consumption (pmol O2/(ma*s))	5mo CON vs 15mo CON	15mo 0.2314 PB125 5mo CON vs	0.8467		Fig 4F	
	сараску		Female	95.6786929	12.1086217	14	80.2938462	20.1534776	13	85.1191667	20.7205377	12		5mo CON vs 15mo CON	15mo 0.1052 PB125	0.3354			
				Mean	SD	n													1
	PB125 does not attenuate	permeabilized	5mo CON	68.46	12.07	27	oxygen	One-Way ANG com	OVA Dunne parisons te	tt's multiple st	p value								
	related decline in ETS capacity	myofibers of soleus	15mo CON	52.72	12.07	27	(pmol O2/(mg*s))	5mo CC	ON vs. 15mo	CON	<0.0001							Fig 4G	
	(CII- CIV)		15mo PB125	55.27	13.69	25		5mo COI	N vs. 15mo	PB125	0.0006								
					Eme CON			45			45 DD405								
	PB125 does not sex				5110 CON			15mo CON			15mo PB125			Two-Way ANO	VA Dunnett's multiple co	omparisons			
	PB125 does not sex speciifcally attenuate the	nomoobilized		Mean	SD	n	Mean	SD	n	Mean	SD	n	oxygen	Two-Way ANO	VA Dunnett's multiple co test 5mo CON vs	omparisons			
	PB125 does not sex speciifcally attenuate the age-related decline in ETS capacity (CII -	permeabilized myofibers of soleus	Male	<b>Mean</b> 72.3387346	SD 13.1018151	<b>n</b> 13	<b>Mean</b> 56.0421429	SD 10.7295983	<b>n</b> 14	<b>Mean</b> 61.02	SD 13.0105521	<b>n</b> 13	oxygen consumption (pmol O2/(mg*s))	Two-Way ANO 5mo CON vs 15mo CON	VA Dunnett's multiple co test 5mo CON vs 15mo 0.0014 PB125	omparisons 0.0345		Fig 4H	
	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV)	permeabilized myofibers of soleus	Male Female	Mean 72.3387346 64.8530143	<b>SD</b> 13.1018151 10.183499	n 13 14	Mean 56.0421429 49.1330769	SD 10.7295983 12.814388	n 14 13	<b>Mean</b> 61.02 49.035	SD 13.0105521 11.9533864	n 13 12	oxygen consumption (pmol O2/(mg*s))	Two-Way ANO 5mo CON vs 15mo CON vs 15mo CON vs 15mo CON	VA Dunnett's multiple co test 5mo CON vs 15mo 0.0014 PB125 5mo CON vs 15mo 0.0021 PB125	0.0345 0.0025		Fig 4H	
	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV)	permeabilized myofibers of soleus	Male Female	Mean 72.3387346 64.8530143 Mean	SD 13.1018151 10.183499 SD	n 13 14 n	Mean 56.0421429 49.1330769	SD 10.7295983 12.814388	n 14 13	Mean 61.02 49.035	<b>SD</b> 13.0105521 11.9533864	n 13 12	oxygen consumption (pmol O2/(mg*s))	Two-Way ANO 5mo CON vs 15mo CON vs 15mo CON vs 15mo CON	VA Dunnett's multiple co test 5mo CON vs 15mo 0.0014 PB125 5mo CON vs 15mo 0.0021 PB125	omparisons 0.0345 0.0025		Fig 4H	
	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV) PB125 attenuates the	permeabilized myofibers of soleus permeabilized	Male Female 5mo CON	Mean 72.3387346 64.8530143 Mean 12.61	SD SD 13.1018151 10.183499 SD 3.555	n 13 14 n 24	Mean 56.0421429 49.1330769	SD 10.7295983 12.814388 One-Way ANG com	n 14 13 OVA Dunne aparisons te	Mean 61.02 49.035 tt's multiple st	SD 13.0105521 11.9533864 p value	n 13 12	oxygen consumption (pmol O2/(mg*s))	Two-Way ANO 5mo CON vs 15mo CON vs 5mo CON vs 15mo CON	VVA Dunnett's multiple cc test 5mo CON vs 15mo 0.0014 PB125 5mo CON vs 15mo 0.0021 PB125	0.0345 0.0025		Fig 4H	
	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV) PB125 attenuates the disease/age related decline in PCP	permeabilized myofibers of soleus permeabilized myofibers of soleus	Male Female 5mo CON 15mo CON	Mean 72.3387346 64.8530143 Mean 12.61 9.708	SD 13.1018151 10.183499 SD 3.555 3.391 1.000	n 13 14 24 26	Mean 56.0421429 49.1330769 ratio	SD 10.7295983 12.814388 One-Way ANG com 5mo CC	n 14 13 OVA Dunne parisons te DN vs. 15mo	Mean 61.02 49.035 tt's multiple st	SD 13.0105521 11.9533864 p value <0.0001	n 13 12	oxygen consumption (pmol O2/(mg*s))	Two-Way ANO 5mo CON vs 15mo CON 5mo CON vs 15mo CON	VA Dunnett's multiple co test 5mo CON vs 15mo 0.0014 PB125 5mo CON vs 15mo 0.0021 PB125	0.0345 0.0025		Fig 4H Fig 4I	
	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV) PB125 attenuates the disease/age related decline in RCR	permeabilized myofibers of soleus permeabilized myofibers of soleus	Male Female 5mo CON 15mo CON 15mo PB125	Mean 72.3387346 64.8530143 Mean 12.61 9.708 11.16	SD 13.1018151 10.183499 SD 3.555 3.391 4.326	n 13 14 24 26 25	Mean 56.0421429 49.1330769 ratio	SD 10.7295983 12.814388 One-Way ANK com 5mo CO	n 14 13 OVA Dunne parisons te DN vs. 15mo	Mean 61.02 49.035 tt's multiple st • CON PB125	SD 13.0105521 11.9533864 p value <0.0001 0.0006	n 13 12	oxygen consumption (pmol O2/(mg*s))	Two-Way ANO 5mo CON vs 15mo CON vs 5mo CON vs 15mo CON	VA Dunnett's multiple cc test 5mo CON vs 15mo 0.0014 PB125 5mo CON vs 15mo 0.0021 PB125	0.0345 0.0025		Fig 4H Fig 4I	
	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV) PB125 attenuates the disease/age related decline in RCR	permeabilized myofibers of soleus permeabilized myofibers of soleus	Male Female 5mo CON 15mo CON 15mo PB125	Mean 72.3387346 64.8530143 Mean 12.61 9.708 11.16	SING CON SD 13.1018151 10.183499 SD 3.555 3.391 4.326 Smo CON	n 13 14 24 26 25	Mean 56.0421429 49.1330769 ratio	SD 10.7295983 12.814388 One-Way ANK com 5mo CO 5mo CO 15mo CON	n 14 13 DVA Dunne iparisons te DN vs. 15mo N vs. 15mo	Mean 61.02 49.035 tt's multiple st • CON PB125	SD 13.0105521 11.9533864 p value <0.0001 0.0006 15mo PB125	n 13 12	oxygen consumption (pmol O2/(mg*s))	Two-Way ANO           5mo CON vs           15mo CON vs           5mo CON vs           5mo CON vs           15mo CON vs           15mo CON vs           15mo CON vs	VA Dunnett's multiple oc test 5mo CON vs 15mo 0.0014 PB125 5mo CON vs 15mo 0.0021 PB125	0.0345 0.0025		Fig 4H Fig 4I	
	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV) PB125 attenuates the disease/age related decline in RCR	permeabilized myofibers of soleus permeabilized myofibers of soleus	Male Female 5mo CON 15mo PB125	Mean 72.3387346 64.8530143 Mean 12.61 9.708 11.16 Mean	SING CON SD 13.1018151 10.183499 SD 3.555 3.391 4.326 5mo CON SD	n 13 14 24 26 25	Mean 56.0421429 49.1330769 ratio Mean	SD 10.7295983 12.814388 One-Way ANK com 5mo COI 5mo COI 15mo CON SD	n 14 13 DVA Dunne iparisons te DN vs. 15mo N vs. 15mo	Mean 61.02 49.035 tt's multiple st CON PB125 Mean	SD 13.0105521 11.9533864 p value <0.0001 0.0006 15mo PB125 SD	n 13 12	oxygen consumption (pmol O2/(mg*s))	Two-Way ANO           5mo CON vs           15mo CON vs           5mo CON vs           5mo CON vs           15mo CON vs           15mo CON vs           15mo CON vs	VA Dunnett's multiple cc test 5mo CON vs 15mo 0.0014 PB125 5mo CON vs 15mo 0.0021 PB125	omparisons 0.0345 0.0025		Fig 4H Fig 4I	
	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV) PB125 attenuates the disease/age related decline in RCR PB125 attenuates the disease/age related decline in RCR in males only (no age- related decline	permeabilized myofibers of soleus permeabilized myofibers of soleus	Male Female 5mo CON 15mo PB125	Mean           72.3387346           64.8530143           Mean           12.61           9.708           11.16           Mean           13.7375241	SING CON SD 13.1018151 10.183499 SD 3.555 3.391 4.326 5mo CON SD 2.92464774	n 13 14 24 26 25 n 11	Mean 56.0421429 49.1330769 ratio Mean 10.0654575	SD 10.7295983 12.814388 One-Way ANK com 5mo CO 5mo CO 15mo CON SD 4.31627083	n 14 13 DVA Dunne iparisons te DN vs. 15mo N vs. 15mo N vs. 15mo	Mean 61.02 49.035 tt's multiple st CON PB125 Mean 11.0785241	SD 13.0105521 11.9533864 p value <0.0001 0.0006 15mo PB125 SD 4.47831446	n 13 12 n 13	oxygen consumption (prool O2/(mg*s))	Two-Way ANO           5mo CON vs	VVA Dunnett's multiple cc           test         5mo CON vs           15mo         0.0014           PB125         5mo CON vs           15mo         0.0021           PB125         5mo CON vs           15mo         0.0021           PB125         5mo CON vs           15mo         15mo           0.0021         PB125           15mo         15mo           0.356         PB125           5mo CUN vs         15mo	omparisons 0.0345 0.0025 omparisons 0.01516		Fig 4H Fig 4I Fig 4J	
	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV) PB125 attenuates the disease/age related decline in RCR PB125 attenuates the disease/age related decline in RCR in males only (no age- related decline in females)	permeabilized myofibers of soleus permeabilized myofibers of soleus	Male Female 5mo CON 15mo PB125 Male Female	Mean           72.3387346           64.8530143           Mean           12.61           9.708           11.16           Mean           13.7375241           11.6563386	SD           SD           13.1018151           10.183499           SD           3.555           3.391           4.326           5mo CON           SD           2.92464774           3.50597489	n 13 14 24 26 25 7 11	Mean 56.0421429 49.1330769 ratio Mean 10.0654575 9.34990257	SD 10.7295983 12.814388 One-Way ANG com 5mo CO 5mo CO 15mo CON SD 4.31627083 2.24577659	n 14 13 DVA Dunne sparisons te DN vs. 15mo N vs. 15mo N vs. 15mo 13 13	Mean 61.02 49.035 tt's multiple st CON PB125 Mean 11.0785241 11.2413266	SD 13.0105521 11.9533864 p value <0.0001 0.0006 15mo PB125 SD 4.47831446 4.35138311	n 13 12 n 13 13	oxygen consumption (pmol O2/(mg*s)) ratio	Two-Way ANO           5mo CON vs           15mo CON vs           15mo CON vs           5mo CON vs           15mo CON vs           5mo CON vs           15mo CON vs	VA Dunnett's multiple cc test 5mo CON vs 15mo 0.0014 PB125 5mo CON vs 15mo 0.0021 PB125 VA Dunnett's multiple cc test 15mo 0.0356 PB125 5mo CON vs 15mo 0.0358 PB125	0.0345 0.0025 0.0025 0.01516 0.9458		Fig 4H Fig 4I Fig 4J	
Experimental Question #	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV) PB125 attenuates the disease/age related decline in RCR PB125 attenuates the disease/age related decline in RCR in males only (no age- related decline in RCR in males only (no age- related decline in females)	permeabilized myofibers of soleus permeabilized myofibers of soleus permeabilized myofibers of soleus Experimental location/variable	Male Female 5mo CON 15mo PB125 Male Female	Mean           72.3387346           64.8530143           Mean           12.61           9.708           11.16           Mean           13.7375241           11.6563386	SD           SD           13.1018151           10.183499           SD           3.555           3.391           4.326           5mo CON           SD           2.92464774           3.50597489	n 13 14 24 26 25 n 11 13	Mean 56.0421429 49.1330769 ratio Mean 10.0654575 9.34990257	SD 10.7295983 12.814388 One-Way ANK corr 5mo COI 15mo CON SD 4.31627083 2.24577659 Summary Sta	n 14 13 DVA Dunne nparisons te DN vs. 15mo N vs. 15mo 13 13 13	Mean 61.02 49.035 tt's multiple st CON PB125 Mean 11.0785241 11.2413266	SD 13.0105521 11.9533864 p value <0.0001 0.0006 15mo PB125 SD 4.47831446 4.35138311	n 13 12 n 13 12	oxygen consumption (pmol O2/(mg*s)) ratio	Two-Way ANO           Smo CON vs           15mo CON vs           5mo CON vs           15mo CON vs	VVA Dunnett's multiple constraints           5mo CON vs           15mo           0.0014           PB125           5mo CON vs           15mo           0.0021           PB125           15mo           0.0021           PB125           15mo           0.0356           PB125           15mo           0.0356           PB125           15mo           0.0393           PB125           Units	omparisons 0.0345 0.0025 omparisons 0.01516 0.9458 Statistical test	Any other variable	Fig 4H Fig 4I Fig 4J Figure/table in which data are presented	c
Experimental Question #	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV) PB125 attenuates the disease/age related decline in RCR PB125 attenuates the disease/age related decline in RCR in males only (no age- related decline in females) Finding Conclusion	permeabilized myofibers of soleus permeabilized myofibers of soleus permeabilized myofibers of soleus Experimental location/variable	Male Female 5mo CON 15mo PB125 Male Female	Mean           72.3387346           64.8530143           Mean           12.61           9.708           11.16           Mean           13.7375241           11.6563386	SING CON SD 13.1018151 10.183499 SD 3.555 3.391 4.326 5mo CON SD 2.92464774 3.50597489 Male CON	n 13 14 24 26 25 n 11 13	Mean 56.0421429 49.1330769 ratio Mean 10.0654575 9.34990257	SD 10.7295983 12.814388 One-Way ANG com 5mo COI 15mo CON SD 4.31627083 2.24577659 Summary Sta Male BB105	n 14 13 DVA Dunne iparisons te DN vs. 15mo N vs. 15mo N vs. 15mo 13 13 13	Mean 61.02 49.035 tt's multiple st CON PB125 Mean 11.0785241 11.2413266	SD 13.0105521 11.9533864 p value <0.0001 0.0006 15mo PB125 SD 4.47831446 4.35138311 Female	n 13 12 n 13 12	oxygen consumption (pmol O2/(mg*s))	Two-Way ANO Smo CON vs 15mo CO	VA Dunnett's multiple constraints           5mo CON vs           15mo           0.0014           PB125           5mo CON vs           15mo           0.0021           PB125           VA Dunnett's multiple constraints           15mo           0.0021           PB125           0.0356           PB125           5mo CUN vs           15mo           0.0356           PB125           5mo CUN vs           15mo           0.2033           PB125           Units	omparisons 0.0345 0.0025 omparisons 0.01516 0.9458 Statistical test Three Way ANOVA	Any other variable	Fig 4H Fig 4I Fig 4J Figure/table in which data are presented	
Experimental Question #	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV) PB125 attenuates the disease/age related decline in RCR PB125 attenuates the disease/age related decline in RCR in males only (no age- related decline in females) Finding Conclusion	permeabilized myofibers of soleus permeabilized myofibers of soleus permeabilized myofibers of soleus Experimental location/variable	Male Female 5mo CON 15mo PB125 Male Female	Mean 72.3387346 64.8530143 Mean 12.61 9.708 11.16 Mean 13.7375241 11.6563386	SING CON SD 13.1018151 10.183499 SD 3.555 3.391 4.326 5mo CON SD 2.92464774 3.50597489 Male CON	n 13 14 24 26 25 n 11 13	Mean 56.0421429 49.1330769 ratio Mean 10.0654575 9.34990257	SD 10.7295983 12.814388 One-Way ANG com 5mo COI 15mo CON SD 4.31627083 2.24577659 Summary Sta PB125 SD	n 14 13 DVA Dunne iparisons te DN vs. 15mo N vs. 15mo N vs. 15mo 13 13	Mean 61.02 49.035 tt's multiple st CON PB125 Mean 11.0785241 11.2413266 in, SD, n)	SD 13.0105521 11.9533864 p value <0.0001 0.0006 15mo PB125 SD 4.47831446 4.35138311 Female CON	n 13 12 n 13 12	oxygen consumption (pmol O2/(mg*s)) ratio	Two-Way ANO Smo CON vs 15mo CO	VA Dunnett's multiple constraints           5mo CON vs           15mo           0.0014           PB125           5mo CON vs           15mo           0.0021           PB125           VA Dunnett's multiple constraints           15mo           0.0021           PB125           0.0356           PB125           5mo CON vs           15mo           0.0356           PB125           5mo CON vs           15mo           0.0356           PB125           Units	omparisons 0.0345 0.0025 0.0025 0.01516 0.9458 Statistical test Three Way ANOVA	Any other variable	Fig 4H Fig 4I Fig 4J Figure/table in which data are presented	
Experimental Question #	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV) PB125 attenuates the disease/age related decline in RCR PB125 attenuates the disease/age related decline in RCR in males only (no age- related decline in females) Finding Conclusion	permeabilized myofibers of soleus permeabilized myofibers of soleus permeabilized myofibers of soleus Experimental location/variable	Male Female 5mo CON 15mo PB125 Male Female	Mean 72.3387346 64.8530143 Mean 12.61 9.708 11.16 Mean 13.7375241 11.6563386 2.2540528	SING CON SD 13.1018151 10.183499 SD 3.555 3.391 4.326 5mo CON SD 2.92464774 3.50597489 Male CON SD 0.1338218	n 13 14 n 24 26 25 7 11 13	Mean 56.0421429 49.1330769 ratio natio 9.34990257 9.34990257	SD 10.7295983 12.814388 One-Way ANG com 5mo COI 15mo CON SD 4.31627083 2.24577659 Summary Sta Male PB125 SD 0.16137748	n 14 13 OVA Dunne iparisons te N vs. 15mo N vs. 15mo N vs. 15mo 13 13 13	Mean 61.02 49.035 tt's multiple st CON PB125 Mean 11.0785241 11.2413266 an, SD, n)	SD 13.0105521 11.9533864 p value <0.0001 0.0006 15mo PB125 SD 4.47831446 4.35138311 Female CON SD 0.26437344	n 13 12 n 13 12 n 14	oxygen consumption (pmol 02/(mg*s)) ratio	Two-Way ANO Smo CON vs 15mo C	VA Dunnett's multiple co test 5mo CON vs 15mo 0.0014 PB125 5mo CON vs 15mo 0.0021 PB125 0.0021 PB125 0.0026 PB125 0.0356 PB125 5mo CON vs 15mo 0.2093 PB125 Units	omparisons 0.0345 0.0025 0.0025 0.01516 0.9458 Statistical test NOVA ANOVA Age: 0.0015, Sex:	Any other variable	Fig 4H Fig 4I Fig 4J Figure/table in which data are presented	, , ,
Experimental Question #	PB125 does not sex specifically attenuate the age-related decline in ETS capacity (CII - CIV) PB125 attenuates the disease/age related decline in RCR PB125 attenuates the disease/age related decline in RCR in males only (no age- related decline in RCR in males only (no age- related decline in RCR in males only (no age- related decline in RCR in the sonly (no age- related decline in females) Finding Conclusion	permeabilized myofibers of soleus permeabilized myofibers of soleus permeabilized myofibers of soleus Experimental location/variable	Male Female 5mo CON 15mo PB125 Male Female	Mean           72.3387346           64.8530143           Mean           12.61           9.708           11.16           Mean           13.7375241           11.6563386           2.22549538	Shib CON SD 13.1018151 10.183499 SD 3.555 3.391 4.326 5mo CON SD 2.92464774 3.50597489 Male CON SD 0.1338218	n 13 14 24 26 25 7 11 13 13	Mean 56.0421429 49.1330769 ratio Mean 10.0654575 9.34990257 9.34990257	SD 10.7295983 12.814388 One-Way ANG corr 5mo CO 5mo CO 15mo CON SD 4.31627083 2.24577659 Summary Sta PB125 SD 0.16137748	n 14 13 DVA Dunne nparisons te DN vs. 15mo N vs. 15mo n 13 13 tistics (Mea n 13	Mean 61.02 49.035 tt's multiple st CON PB125 Mean 11.0785241 11.2413266 in, SD, n) Mean 2.34915667	SD 13.0105521 11.9533864 p value <0.0001 0.0006 15mo PB125 SD 4.47831446 4.35138311 Female CON SD 0.26437344	n 13 12 n 13 12 n 14	oxygen consumption (pmol O2/(mg*s)) ratio Mean 2.22320641	Two-Way ANO           Simo CON vs           Simo CO	VXA Dunnett's multiple co test 5mo CON vs 15mo 0.0014 PB125 5mo CON vs 15mo 0.0021 PB125 VXA Dunnett's multiple co test 15mo 0.0356 PB125 5mo CON vs 15mo 0.2093 PB125 Units n fractional 13 synthesis rate (%/day)	omparisons 0.0345 0.0025 0.0025 0.0025 0.01516 0.9458 0.9458 Statistical test Three Way ANOVA Age: 0.0015, Sex: 0.5587, Treatment:	Any other variable	Fig 4H Fig 4I Fig 4J Figure/table in which data are presented	 

	Inere is a significant effect of disease/age on mitochondrial protein There is a significant effect of disease/age on cytosolic protein synthesis in the	Mitochondrial subfraction of Soleus muscle Cytosolic subfraction of Soleus muscle	5mo 15mo 5mo	Mean 1.7374618 1.59909881 Mean 2.31875462 2.15263571	SD 0.21034142 0.19148393 SD 0.1373844 0.14790641	n 13 14 n 13 14	Mean 1.72790714 1.69472095 Mean 2.39275643 2.22183778	SD 0.16061741 0.19286796 SD 0.20134459 0.16792303	n 14 12 n 14	Mean 1.7425441 1.57687806 Mean 2.42844222 2.2020925	SD 0.23958803 0.18026636 SD 0.1795843 0.19777053	n 13 12 n 12 12	Mean 1.80200905 1.5874975 Mean 2.43478262 2.25817139	SD 0.30720095 0.30541418 SD 0.35830419 0.12983812	n 14 12 n 14 12	fractional synthesis rate (%/day) fractional synthesis rate (%/day)	Age: 0.0029, Sex: 0.7811, Treatment: 0.3887 Age: <0.0001, Sex: 0.1457, Treatment: 0.2072		Fig 5B Fig 5C	
7. Are there Disease/Age-, Sex and	soleus There is a significant effect of disease/age on Collagen protein synthesis in the soleus	Collagen subfraction of Soleus muscle	15mo 5mo 15mo	Mean 0.91436128 0.6040056	<b>SD</b> 0.23069098 0.31295196	n 13 14	<b>Mean</b> 0.97412077 0.59454028	<b>SD</b> 0.40340964 0.28731824	n 13 12	Mean 0.95704513 0.49936389	<b>SD</b> 0.43079109 0.21940987	n 13 12	<b>Mean</b> 0.81466718 0.6284425	<b>SD</b> 0.20758125 0.33627904	n 13 12	fractional synthesis rate (%/day)	Age: <0.0001, Sex: 0.4539, Treatment: 0.8824		Fig 5D	
Treatment related effects on skeletal muscle protein synthesis?	There is a significant effect of disease/age on myofibrillar protein synthesis in the gastrocnemius	Myofibrillar subfraction of gastrocnemius muscle	5mo 15mo	<b>Mean</b> 1.93359333 1.71260976	<b>SD</b> 0.14684657 0.13716658	n 13 14	<b>Mean</b> 1.99464857 1.73493436	<b>SD</b> 0.15391676 0.15787186	n 14 12	<b>Mean</b> 1.96200154 1.70658614	<b>SD</b> 0.13141966 0.18465984	n 13 12	Mean 1.99989103 1.6994478	<b>SD</b> 0.3017671 0.07726639	n 13 12	fractional synthesis rate (%/day)	Age: <0.0001, Sex: 0.9541, Treatment: 0.4042		Fig 5E	
	significant effect of disease/age on mitochondrial protein synthesis in the	Mitochondrial subfraction of gastrocnemius muscle	5mo 15mo	<b>Mean</b> 1.88033974 1.69435933	<b>SD</b> 0.13536286 0.17251916	n 13 14	<b>Mean</b> 1.89296846 1.6289415	<b>SD</b> 0.18749823 0.12684399	n 13 12	Mean 1.83008461 1.68996803	<b>SD</b> 0.14552234 0.16671628	n 13 12	<b>Mean</b> 1.89414026 1.66856568	<b>SD</b> 0.31656624 0.06898468	n 13 12	fractional synthesis rate (%/day)	Age: <0.0001, Sex: 0.9226, Treatment: 0.9433		Fig 5F	
	There is a significant effect of disease/age on cytosolic protein synthesis in the gastrocnemius	Cytosolic subfraction of gastrocnemius muscle	5mo 15mo	<b>Mean</b> 2.00498769 1.81458095	<b>SD</b> 0.13776247 0.11138432	n 13 14	<b>Mean</b> 2.08004821 1.82554111	<b>SD</b> 0.14146105 0.19333809	n 13 12	Mean 2.14378051 1.80076306	<b>SD</b> 0.22920456 0.16847819	n 13 12	<b>Mean</b> 2.15360048 1.8164975	<b>SD</b> 0.29833302 0.07900233	n 14 12	fractional synthesis rate (%/day)	Age: <0.0001, Sex: 0.1948, Treatment: 0.4439		Fig 5G	
	There is a significant effect of disease/age on collagen protein synthesis in the gastrocnemius	Collagen subfraction of gastrocnemius muscle	5mo 15mo	<b>Mean</b> 1.46383154 1.14150524	<b>SD</b> 0.22666781 0.2450633	n 13 14	<b>Mean</b> 1.52458881 1.06753111	<b>SD</b> 0.41531949 0.32596463	n 14 12	<b>Mean</b> 1.52812897 1.29843417	<b>SD</b> 0.23259949 0.17711874	n 13 12	<b>Mean</b> 1.56839128 1.11631778	<b>SD</b> 0.41492193 0.35655402	n 13 12	fractional synthesis rate (%/day)	Age: <0.0001, Sex: 0.2064, Treatment: 0.5310		Fig 5H	
Experimental Question #	Finding Conclusion	Experimental location/variable	2					Summary Sta	atistics (M	ean, SD, n)						Units	Statistical test	Any other variable	Figure/table in which data are presented	Commer
	PB125 treatment attenuates the age related decline in FSR in the myofibrillar fraction of the soleus	Myofibrillar subfraction of Soleus muscle	5mo CON 15mo CON 15mo PB125	<b>Mean</b> 2.262 2.107 2.195	<b>SD</b> 0.1673 0.1691 0.1554	n 26 26 24	fractional synthesis rate (%/day)	One-Way AN cor 5mo Cl 5mo CO	IOVA Dunr mparisons f ON vs. 15m	nett's multiple lest no CON o PB125	<b>p value</b> 0.0021 0.2566								Fig 6A	
	PB125 treatment attenuates the age related decline in FSR in the myofibrillar fraction of the soleus in females only	Myofibrillar subfraction of Soleus muscle	Male Female	<b>Mean</b> 2.22549538 2.29895667	5mo CON SD 0.1338218 0.19364181	n 13 13	<b>Mean</b> 2.09324976 2.12306806	15mo CON <b>SD</b> 0.18108292 0.16032488	n 14 12	<b>Mean</b> 2.20301389 2.18618639	15mo PB125 SD 0.18551335 0.12621223	n 12 12	fractional synthesis rate (%/day)	Two-Way ANC 5mo CON vs 15mo CON vs 5mo CON vs 15mo CON	0 <b>VA Dunnett</b> tes 0.0769	<b>'s multiple co</b> <b>st</b> 15mo PB125 15mo PB125 PB125	omparisons 0.9201 0.1661		Fig 6B	
	PB125 treatment attenuates the age related decline in FSR in the mitochondrial fraction of the soleus	Myofibrillar subfraction of Soleus muscle	5mo CON 15mo CON 15mo PB125	Mean 1.74 1.589 1.641	SD 0.2209 0.183 0.2557	n 26 26 24	fractional synthesis rate (%/day)	One-Way AN cor 5mo Cl 5mo CC	IOVA Dunr mparisons † ON vs. 15m	iett's multiple iest no CON o PB125	<b>p value</b> 0.0299 0.2051								Fig 6C	

8. Does PB125 treatment modulate disease/age- related	PB125 treatment attenuates the age related decline in FSR in the mitochondrial fraction of the	Mitochondrial subfraction of Soleus muscle	Male Female	<b>Mean</b> 1.7374618 1.7425441	5mo CON SD 0.21034142 0.23958803	n 13 13	<b>Mean</b> 1.59909881 1.57687806	15mo CON <b>SD</b> 0.19148393 0.18026636	<b>n</b> 14 12	<b>Mean</b> 1.69472095 1.5874975	15mo PB125 SD 5 0.19286796 0.30541418	n 12 12	fractional synthesis rate (%/day)	Two-Way ANG 5mo CON vs 15mo CON vs 5mo CON vs 15mo CON	DVA Dunnett's n test 5m 0.1948 15r 15r 0.1221 PB	multiple co no CON vs mo mo 125	omparisons 0.8481 0.1546		Fig 6D
and the sole of th	PB125 treatment does not attenuate the age related decline in FSR in the cytosolic fraction of the soleus when pooling male and female guinea bios	Cytosolic subfraction of Soleus muscle	5mo CON 15mo CON 15mo PB125	Mean 2.371 2.158 2.24	<b>SD</b> 0.1654 0.1479 0.148	n 25 25 24	fractional synthesis rate (%/day)	One-Way AN cor 5mo CO 5mo CO	IOVA Dunn nparisons t ON vs. 15m N vs. 15m	ett's multiple est no CON 9 PB125	p value <0.0001 0.0075								Fig 6E
	PB125 treatment attenuates the age related decline in FSR in the cytosolic fraction of the soleus in males only	Cytosolic subfraction of Soleus muscle	Male Female	<b>Mean</b> 2.31875462 2.42844222	5mo CON SD 0.1373844 0.1795843	<b>n</b> 13 12	<b>Mean</b> 2.15263571 2.16412727	15mo CON SD 0.14790641 0.15491472	n 14 11	<b>Mean</b> 2.22183778 2.25817139	15mo PB125 SD 3 0.16792303 9 0.12983812	<b>n</b> 12 12	fractional synthesis rate (%/day)	Two-Way ANG 5mo CON vs 15mo CON 5mo CON vs 15mo CON	DVA Dunnett's n test 5m 0.0123 15r 15r 0.0002 PB	multiple co no CON vs mo no 125	omparisons 0.2065 0.0158		Fig 6F
	PB125 treatment does not attenuate the age related decline in FSR in the collagen fraction of the soleus	Collagen subfraction of Soleus muscle	5mo CON 15mo CON 15mo PB125	<b>Mean</b> 0.9357 0.5557 0.6115	<b>SD</b> 0.3393 0.2738 0.3064	n 26 26 24	fractional synthesis rate (%/day)	One-Way AN cor 5mo Cl 5mo CC	IOVA Dunn mparisons t ON vs. 15m N vs. 15mc	ett's multiple est io CON 9 PB125	<b>p value</b> <0.0001 0.0008								Fig 6G
	PB125 treatment does not attenuate the age related decline in ESR				5mo CON			15mo CON			15mo PB125			Two-Way ANG	OVA Dunnett's n	multiple co	omparisons		
Functionatel	in the collagen fraction of the soleus in either males or females	Collagen subfraction of Soleus muscle	Male Female	Mean 0.91436128 0.95704513	SD 0.23069098 0.43079109	n 13 13	Mean 0.6040056 0.49936389	SD 0.31295196 0.21940987	n 14 12	Mean 0.59454028 0.6284425	SD 3 0.28731824 0.33627904	n 12 12	fractional synthesis rate (%/day)	5mo CON vs 15mo CON 5mo CON vs 15mo CON	test 15m 0.0225 PB סוות 15r 0.001 PB	mo 125 10 CON VS mo 125	0.0238 0.0199	A other	Fig 6H
Experimental Question #	in the collagen fraction of the soleus in either males or females Finding Conclusion	Collagen subfraction of Soleus muscle Experimental location/variable	Male Female	Mean 0.91436128 0.95704513	SD 0.23069098 0.43079109	n 13 13	Mean 0.6040056 0.49936389	SD 0.31295196 0.21940987 Summary Sta	n 14 12 atistics (Me	Mean 0.59454028 0.6284425 ean, SD, n)	SD 3 0.28731824 0.33627904	n 12 12	fractional synthesis rate (%/day)	5mo CON vs 15mo CON 5mo CON vs 15mo CON	test 115r 0.0225 PB 910 115r 0.001 PB	0 CON VS mo 125 0 CON VS mo 125 Units	0.0238 0.0199 Statistical test	Any other variable	Fig 6H Figure/table in which data are presented
Experimental Question #	in the collagen fraction of the soleus in either males or females Finding Conclusion PB125 treatment does not attenuate the age related decline in FSR in the myofibrillar fraction of the	Collagen subfraction of Soleus muscle Experimental location/variable Myofibrillar subfraction of gastrocnemius muscle	Male Female 5mo CON 15mo CON 15mo PB125	Mean 0.91436128 0.95704513 Mean 1.948 1.71 1.717	SD           0.23069098           0.43079109           0.1373           0.1575           0.1229	n 13 13 n 26 26 24	Mean 0.6040056 0.49936389 fractional synthesis rate (%/day)	SD 0.31295196 0.21940987 Summary Sta One-Way AN cor 5mo Cl 5mo Cl	n 14 12 atistics (Me IOVA Dunn mparisons t ON vs. 15m	Mean 0.59454028 0.6284425 ean, SD, n) ett's multiple est to CON 0 PB125	SD 3 0.28731824 0.33627904 p value <0.0001	n 12 12	fractional synthesis rate (%/day)	5mo CON vs 15mo CON 5mo CON vs 15mo CON	test 15r 0.0225 PB 910 15r 0.001 PB	0 COIN VS mo 125 0 COIN VS mo 125 Units	0.0238 0.0199 Statistical test	Any other variable	Fig 6H Figure/table in which data are presented Fig 6I
Experimental Question #	Finding Fraction of the soleus in either males or females Finding Conclusion PB125 treatment does not attenuate the age related decline in FSR in the myofibrillar fraction of the PB125 treatment does not attenuate the age related decline in FSR in the myofibrillar fraction of the gastrocnemius in either male or females	Collagen subfraction of Soleus muscle Experimental location/variable Myofibrillar gastrocnemius muscle Myofibbrillar subfraction of gastrocnemius muscle	Male Female 5mo CON 15mo CON 15mo PB125 Male Female	Mean 0.91436128 0.95704513 Mean 1.948 1.71 1.717 Mean 1.93359333 1.96200154	SD 0.23069098 0.43079109 SD 0.1373 0.1575 0.1229 5mo CON SD 0.14684657 0.13141966	n 13 13 13 26 26 24 24 n 13	Mean 0.6040056 0.49936389 fractional synthesis rate (%/day) Mean 1.71260976 1.70658614	SD 0.31295196 0.21940987 Summary Sta One-Way AN cor 5mo CO 5mo CO 5mo CO 15mo CON SD 0.137166588 0.18465984	n 14 12 Attistics (Me IOVA Dunn mparisons t ON vs. 15m IN vs. 15m IN vs. 15m IN vs. 15m	Mean 0.59454028 0.6284425 ean, SD, n) ett's multiple est o CON 0 PB125 Mean 1.73493436 1.6994478	SD 3 0.28731824 0.33627904 p value <0.0001 15m0 PB125 SD 0.15787186 0.07726639	n 12 12 12 12 12	fractional synthesis rate (%/day) fractional synthesis rate (%/day)	5mo CON vs 15mo CON vs	test 157 0.0225 PB 0.0215 PB 0.001 PB 0.001 PB 0.0003 157 5m 0.0003 157 5m 0.0001 PB	multiple cc to CON vs mo 125 Units units	0.0238 0.0199 Statistical test omparisons 0.0017 <0.0001	Any other variable	Fig 6H Figure/table in which data are presented Fig 6I Fig 6J
Experimental Question #	Finding models in either males or females Finding Conclusion PB125 treatment does not attenuate the age related decline in FSR in the myofibrillar fraction of the PB125 treatment does not attenuate the age related decline in FSR in the myofibrillar fraction of the gastrocnemius in either male or females PB125 treatment attenuates the age related decline in FSR in the myofibrillar fraction of the gastrocnemius in either male or females PB125 treatment attenuates the age related decline in FSR in the mitochondrial fraction of the	Collagen subfraction of Soleus muscle Experimental location/variable Myofibrillar subfraction of gastrocnemius muscle Myofibrillar subfraction of gastrocnemius muscle	Male Female	Mean 0.91436128 0.95704513 Mean 1.948 1.71 1.717 Mean 1.93359333 1.96200154 Mean 1.855 1.692 1.649	SD 0.23069098 0.43079109 SD 0.1373 0.1575 0.1229 5mo CON SD 0.14684657 0.13141966 SD 0.1401 0.1665 0.1019	n 13 13 13 26 26 24 13 13 13 13 26 26 26 24	Mean 0.6040056 0.49936389 fractional synthesis rate (%/day) Mean 1.71260976 1.70658614 fractional synthesis rate (%/day)	SD 0.31295196 0.21940987 Summary Sta One-Way AN Cor 5mo CO 15mo CON 0.13716658 0.18465984 One-Way AN Cor 5mo CO	n 14 12 IOVA Dunn mparisons t ON vs. 15m N vs. 15m 14 12 IOVA Dunn mparisons t ON vs. 15m	Mean 0.59454028 0.6284425 ean, SD, n) ett's multiple est 0 CON 0 PB125 Mean 1.73493436 1.6994478 ett's multiple est 0 CON 0 PB125	SD 3 0.28731824 0.33627904	n 12 12 12 12 12	fractional synthesis rate (%/day) fractional synthesis rate (%/day)	5mo CON vs 15mo CON vs	test 157 0.0225 PB 911 157 0.001 PB 0.001 PB 0.0003 157 5mm 157 0.0001 PB	multiple cc to CON vs mo 125 Units units	0.0238 0.0199 Statistical test 0.0017 <0.0001	Any other variable	Fig 6H Figure/table in which data are presented Fig 6I Fig 6J Fig 6K

Comments

9. Does PB125 treatment modulate disease/age- related changes in protein synthesis in the gastrocnemius ? Are there any sex specific effects?	attenuates the age related decline in FSR in the mitochondrial fraction of the solaus is not FD 120 treatment does not attenuate the age related decline in FSR in the cytosolic fraction of the soleus when pooling male and female guinea pigs	Mitochondrial subfraction of gastrocnemius muscle	Male Female 5mo CON 15mo CON 15mo PB125	Mean 1.88033974 1.83008461 Mean 2.074 1.808 1.821	<b>SD</b> 0.13536286 0.14552234 <b>SD</b> 0.1983 0.1378 0.1445	n 13 13 13 26 26 26 24	Mean 1.69435933 1.68996803 fractional synthesis rate (%/day)	SD 0.17251916 0.16671628 One-Way AN cor 5mo Cl 5mo CO	n 14 12 IOVA Dunn mparisons ON vs. 15m N vs. 15m	Mean 1.6289415 1.66856568 nett's multiple test mo CON o PB125	SD 0.12684399 0.06898468 p value <0.0001	n 12 12	fractional synthesis rate (%/day)	Two-Way A 5mo CON vs 15mo CON 5mo CON vs 15mo CON	NOVA Dunne t 0.002 <sup>-</sup> 0.0294	ett's multiple c test 5mo CON vs 15mo CON vs 15mo 4 PB125	comparisons		Fig 6L Fig 6M
	PB125 treatment attenuates the age related decline in FSR in the cytosolic fraction of the soleus in males only	Cytosolic subfraction of gastrocnemius muscle	Male Female	<b>Mean</b> 2.00498769 2.14378051	5mo CON SD 0.13776247 0.22920456	n 13 13	<b>Mean</b> 1.81458095 1.80076306	15mo CON SD 0.11138432 0.16847819	n 14 12	<b>Mean</b> 1.82554111 1.8164975	15mo PB125 SD 0.19333809 0.07900233	<b>n</b> 12 12	fractional synthesis rate (%/day)	Two-Way A 5mo CON vs 15mo CON vs 5mo CON vs 15mo CON	NOVA Dunne t 0.0058 <0.0001	ett's multiple of test 5mo CON vs 15mo 8 PB125 15mo PB125	comparisons . 0.0131 <0.0001		Fig 6N
	PB125 treatment does not attenuate the age related decline in FSR in the collagen fraction of the soleus	Collagen subfraction of gastroonemius muscle	5mo CON 15mo CON 15mo PB125	<b>Mean</b> 1.496 1.214 1.092	<b>SD</b> 0.2274 0.2267 0.335	n 26 26 24	fractional synthesis rate (%/day)	One-Way AN cor 5mo Cl 5mo CO	IOVA Dunn mparisons ON vs. 15r DN vs. 15m	nett's multiple test no CON o PB125	<b>p value</b> 0.0005 <0.0001								Fig 6O
	PB125 treatment does not attenuate the age related decline in FSR in the collagen fraction of the soleus in either males or females	Collagen subfraction of gastrocnemius muscle	Male Female	<b>Mean</b> 1.46383154 1.52812897	5mo CON SD 0.226666781 0.23259949	n 13 13	<b>Mean</b> 1.14150524 1.29843417	15mo CON SD 0.2450633 0.17711874	n 14 12	<b>Mean</b> 1.06753111 1.11631778	15mo PB125 SD 0.32596463 0.35655402	n 12 12	fractional synthesis rate (%/day)	Two-Way A 5mo CON vs 15mo CON vs 5mo CON vs 15mo CON	NOVA Dunne t 0.0047 0.0636	ett's multiple o test 15mo 7 PB125 5mo CON vs 15mo 6 PB125	comparisons 0.0008 0.0005		Fig 6P
Experimental Question #	Finding Conclusion	Experimental location/variable						Summary Sta	atistics (M	ean, SD, n)						Units	Statistical test	Any other variable	Figure/table in which data are presented
	i nere are significant effects of			Moon	Male CON	n	Moon	Male PB125		Moon	Female CON		Moan	Female PB125	n		Three Way ANOVA		·
10. Are there Disease/Age-, Sex-, and Treatment related effects	Disease/Age and Treatment, but not Sex, on Nrf2 content in the gastrocnemius. There is a significant interaction between	Homogenized gastrocnemius	5mo	0.99999992 1.66123992	0.23115772	12	1.25295275 1.05320842	0.31956989	12	1.12621233 1.64818992	0.22878589	12	1.32893917 1.07813308	0.31560442	12	Arbitrary units	Age: 0.0250, Sex: 0.5069, Treatment: 0.0270, Age x Trt: <0.0001		Fig 7A
on Nrf2 or HO-1 content in the gastrocnemius	Disease/Age		15mo	Mean	60		Martin	60		Maran	60			65					
?	between Disease/Age and Treatment on HO-1 protein content in the	Homogenized gastrocnemius	5mo	Mean 1	0.24490753	9	wean	0.64069604	<b>n</b> 9	меап 1.25892978	0.39100794	<b>n</b> 9	меал 1.65851622	<b>50</b> 0.91520416	<b>n</b> 9	Arbitrary units	Age: 0.1800, Sex: 0.9351, Treatment: 0.989, Age x		Fig 7B
	gastrocnemius, but no main effect of any		45	2.330179	1.10079732	9	1.13138967	0.69051276	9	2.15458922	1.28148039	9	1.00671233	0.60616972	9		TR: <0.0001		
	gastrocnemius, but no main effect of any factor.		15mo	2.330179	1.10079732 Male CON	9	1.13138967	0.69051276 Male PB125	9	2.15458922	1.28148039 Female CON	9	1.00671233	0.60616972 Female PB125	9		Three Way ANOVA		

11. Are there Disease/Age-, Sex-, and Treatment related effects on carbonyl	Disease/Age, Treatment, or Sex, on carbonyl content in the soleus. There was a significant Sex x Age interaction	Homogenized soleus	5mo 15mo	1 1.20697333	0.25154744 0.08339618	6	1.092113 1.211697	0.1105629 0.13721804	6	1.12699967 1.1378355	0.09041707 0.16632006	6	1.16333067 0 1.00069025 0	).10674212 ).05576008	6	Arbitrary units	Age: 0.3032, Sex: 0.6274, Treatment: 0.9812, Age x Sex: 0.0069	Fig 7C
gastrocnemius ?	There are no effects of Disease/Age, Treatment, or Sex, on carbonyl content in the gastrocnemius.	Homogenized gastrocnemius	5mo 15mo	Mean 1.2 2.81992767	SD 0.32426597 1.08704093	n 5 6	Mean 1.74343667 2.4613865	SD 1.28779756 0.94397067	n 6	Mean 1.16942083 1.9843642	<b>SD</b> 0.42427076 0.86731134	<b>n</b> 6 5	<b>Mean</b> 2.93925883 1 2.07796683 0	<b>SD</b> 1.81713991 ).99866852	<b>n</b> 6	Arbitrary units	Age: 0.0814, Sex: 0.9667, Treatment: 0.1179	Fig 7D
12. Does PB125 treatment slow the progression of disability in either male or	PB125 does not slow the loss of mobility in male guinea pigs	Voluntary movement in an enclosed area.		Survival c PB:	:urve CON Males: 1 125 Males: 12	4				Chi square 0.058	86		Median Surv 0.4	vival Ratio (A/B) 95% Cl 4127 – 3.354	1.176	Cessation of voluntary movement	Gehan- Breslow- Wilcoxon test CON vs PB125 P value 0.8083	Fig 7E
female guinea pigs? (as defined by a cessation	PB125 does not slow the loss of mobility in female guinea pigs	Voluntary movement in an enclosed area.		Survival cu PB1	urve CON Females: 25 Females: 12	12				Chi square 0.058	00		Median Surv 0.2	vival Ratio (A/B) 95% Cl 2175 – 1.501	0.5714	Cessation of voluntary movement	Gehan- Breslow- Wilcoxon test CON vs PB125 P value 0.4463	Fig 7F