Le Statine Modulano L'attività Telomerasica E La Lunghezza Telomerica Nell'invecchiamento

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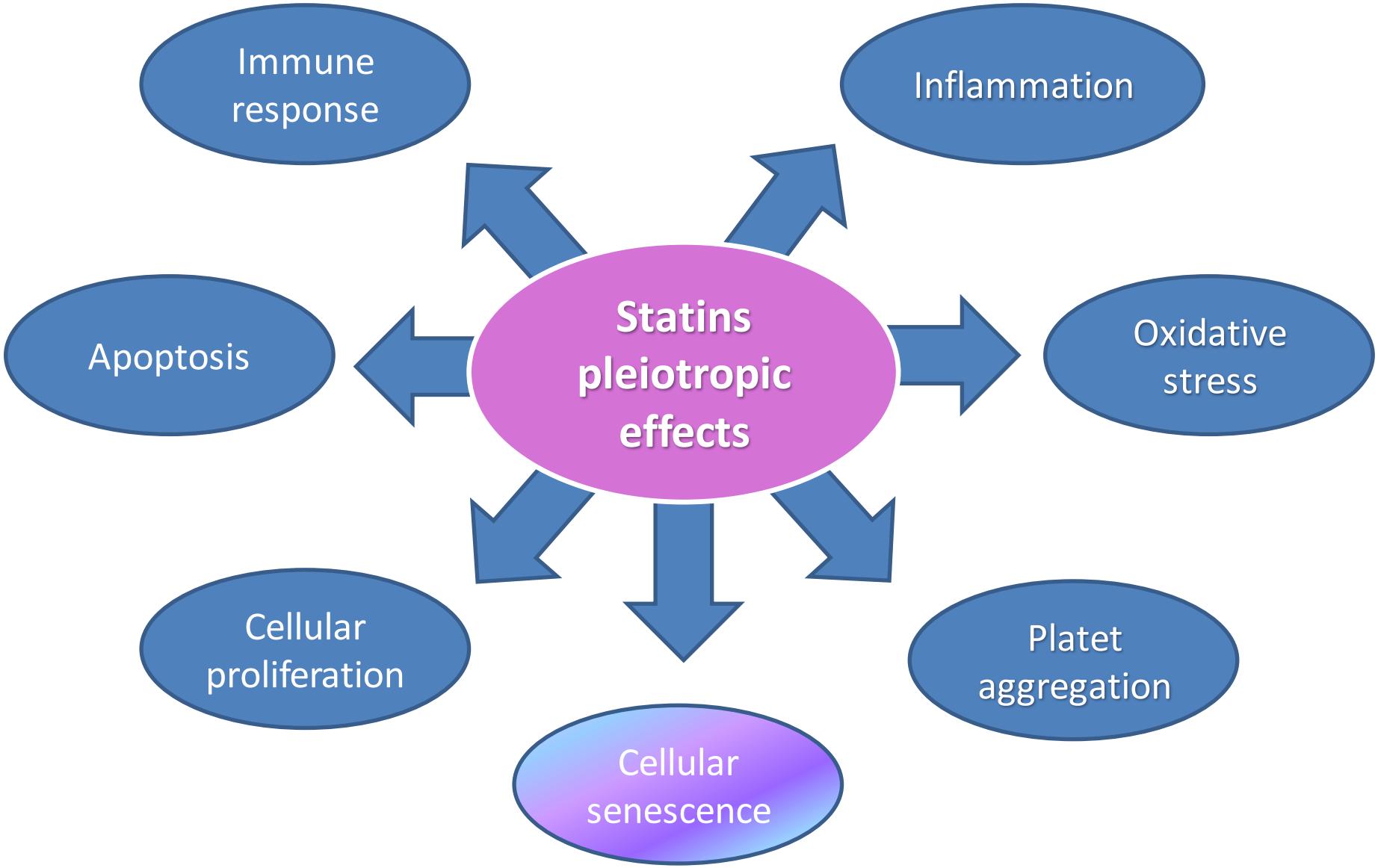
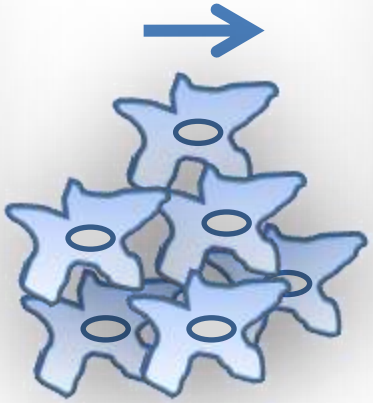


JK Liao 2009; J Davignon 2004; AJ Nordamn 2012

Cellular senescence and aging

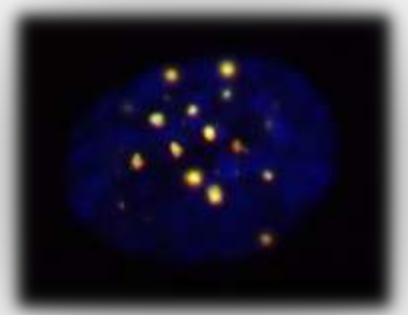
Cellular senescence



Ageing

Telomere shortening

Oncogenes



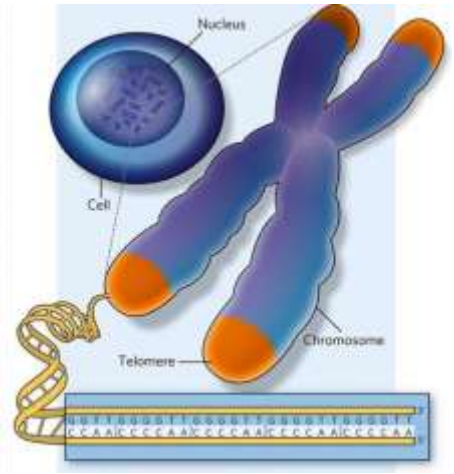
Dna damage response

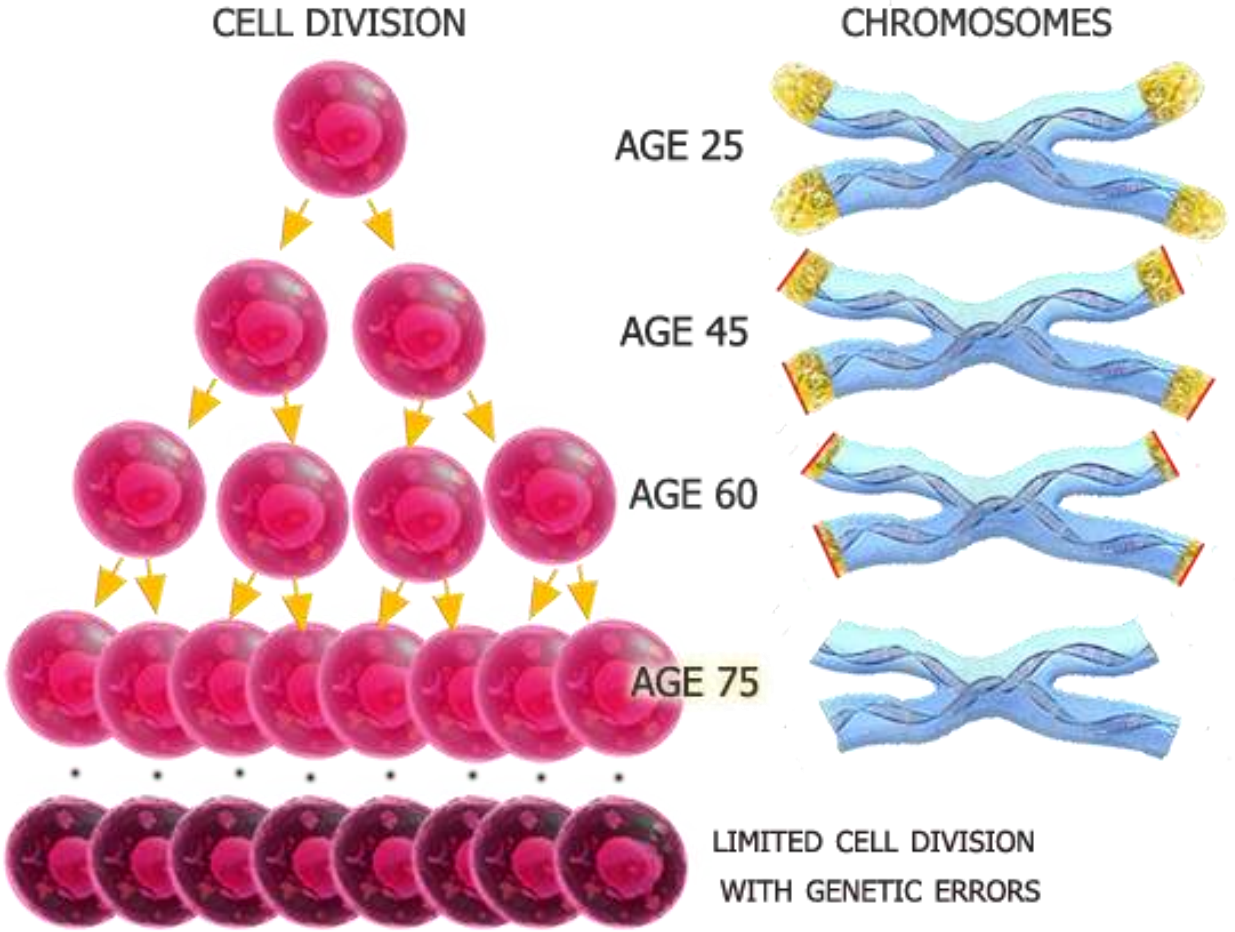
Oxidative damage

Ionizing radiation

Telomere uncapping

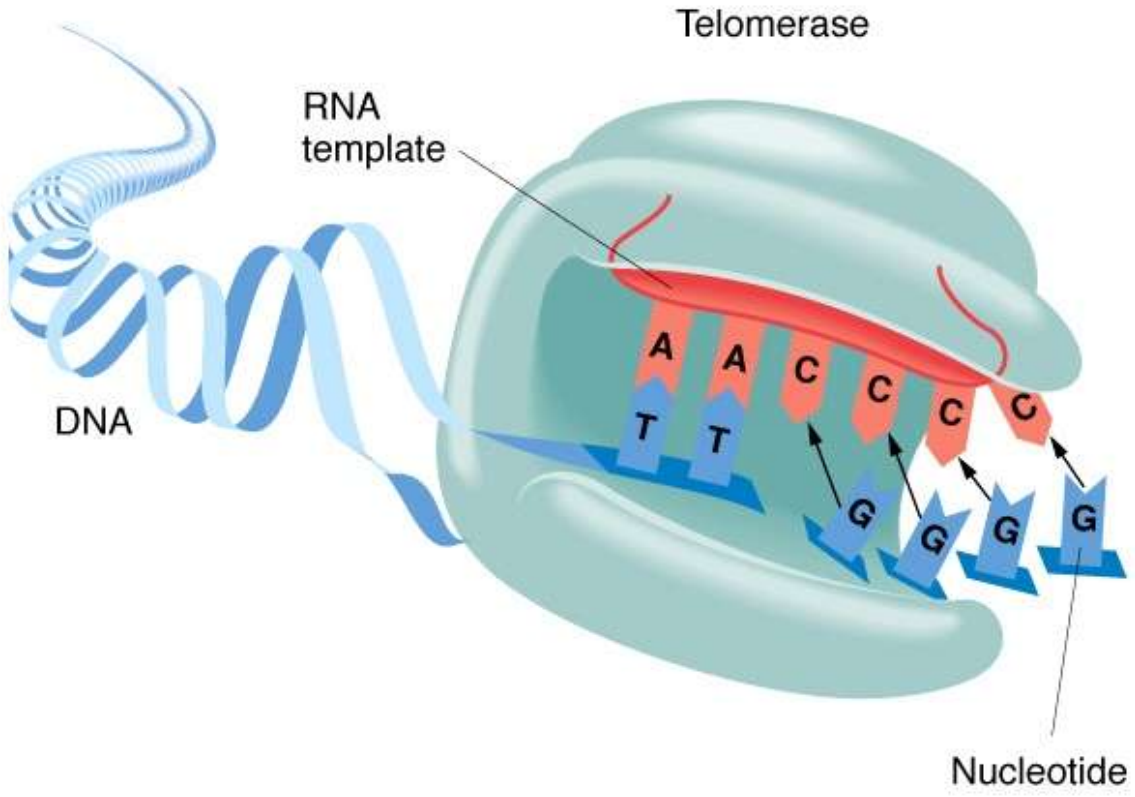
Telomere shortening: replicative senescence



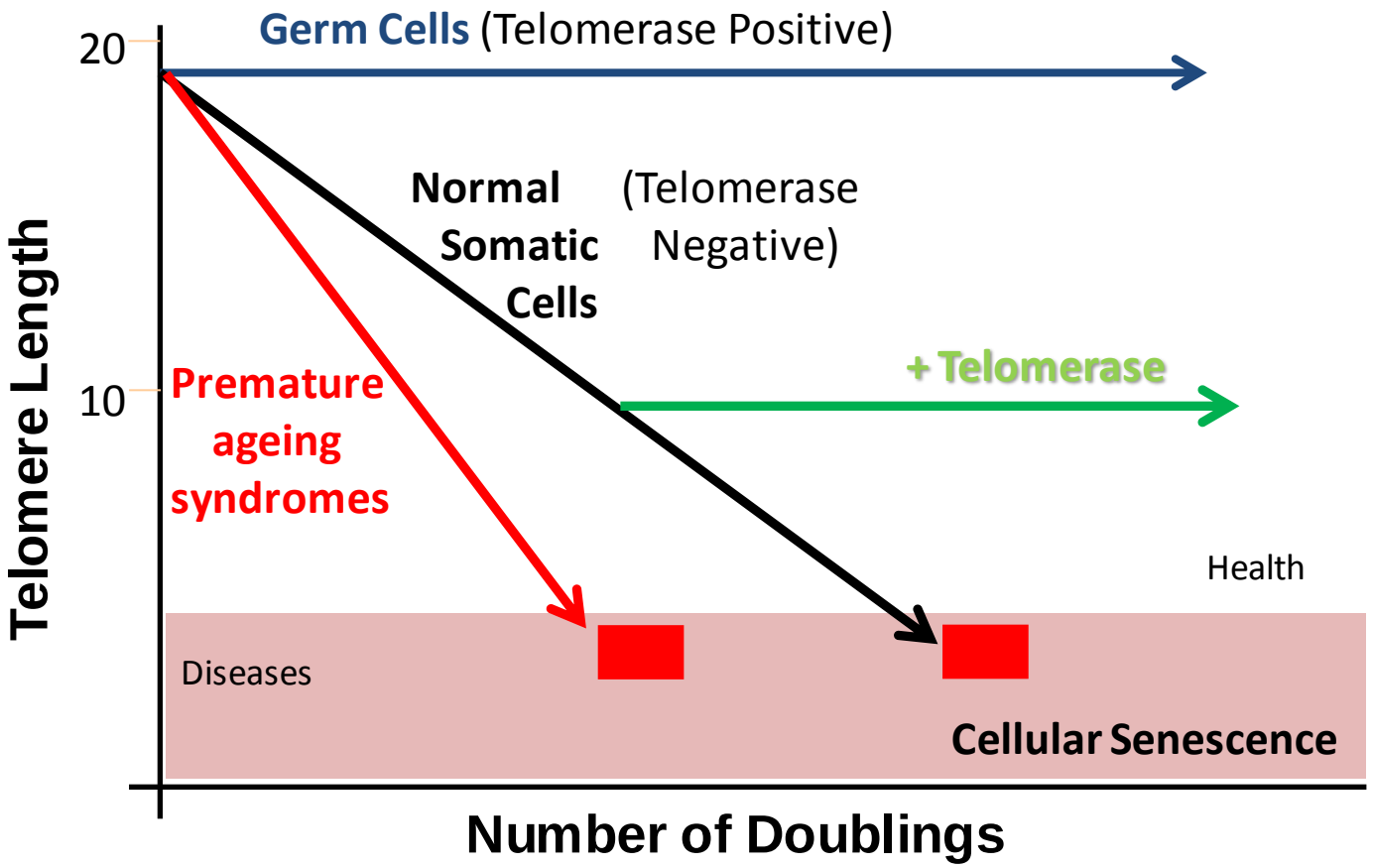


Harley CB, Vaziri H, Counter CM, Allsopp RC. (1992). *Exp. Gerontol* Armanios M. 2009, Annu Rev Genomic Hum Genet

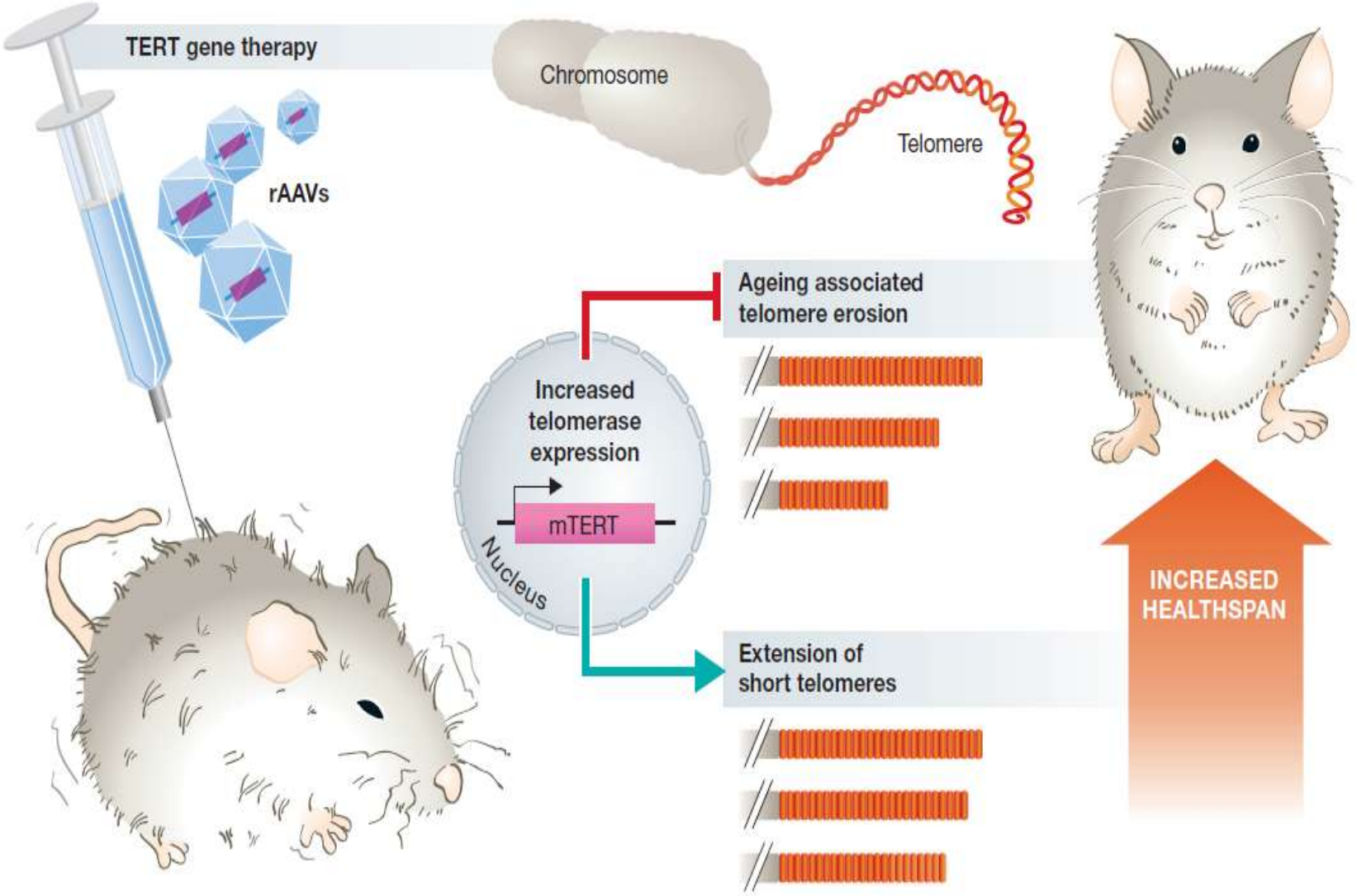
TELOMERASE



Telomere, TELOMERASE and age-related diseases



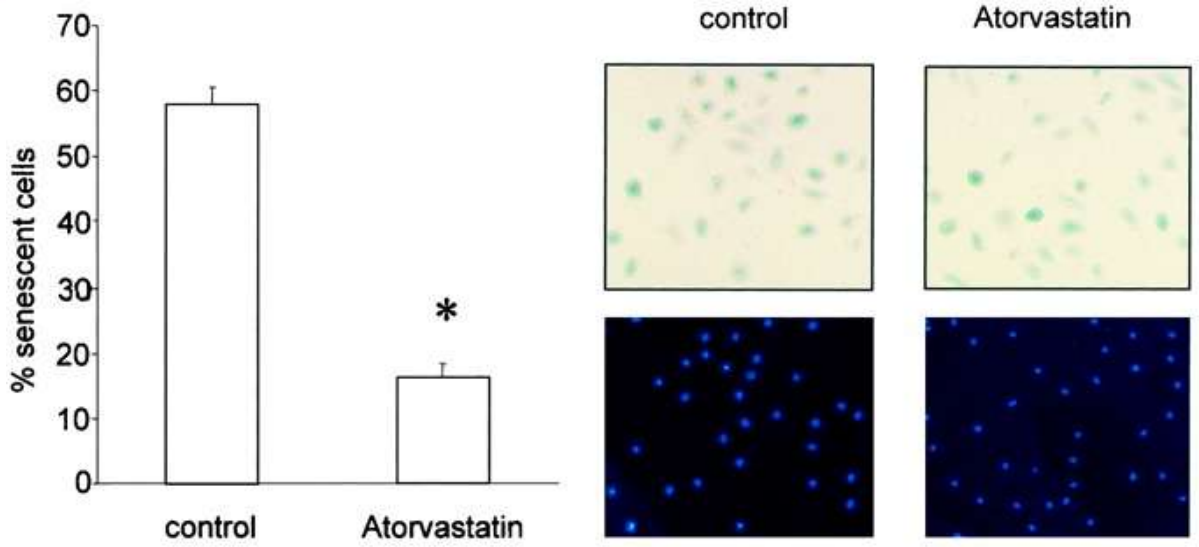
Telomerase and Healthspan

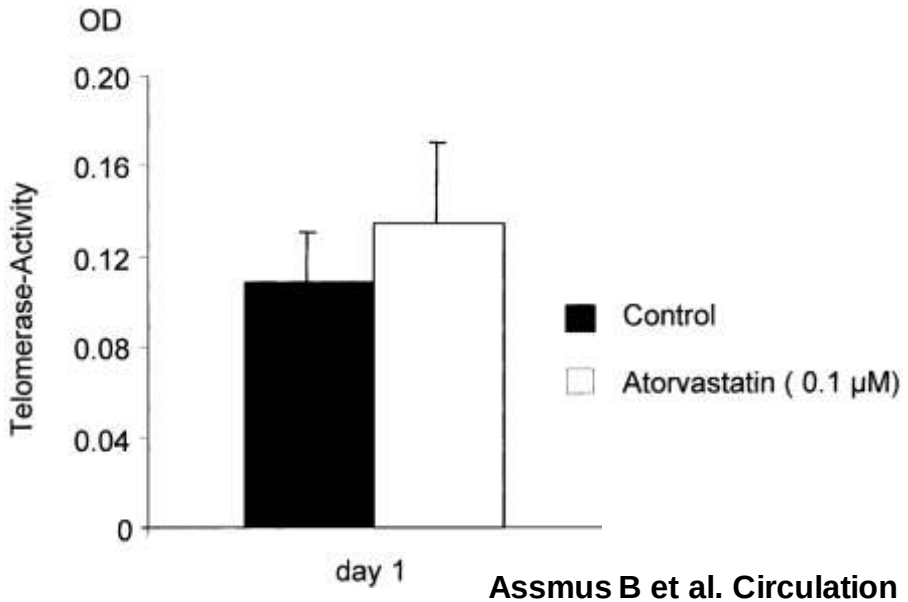


V Boccardi et al. Embo Journal Molecular Medicine, 2012

Circulation Research
Journal of the American Heart Association

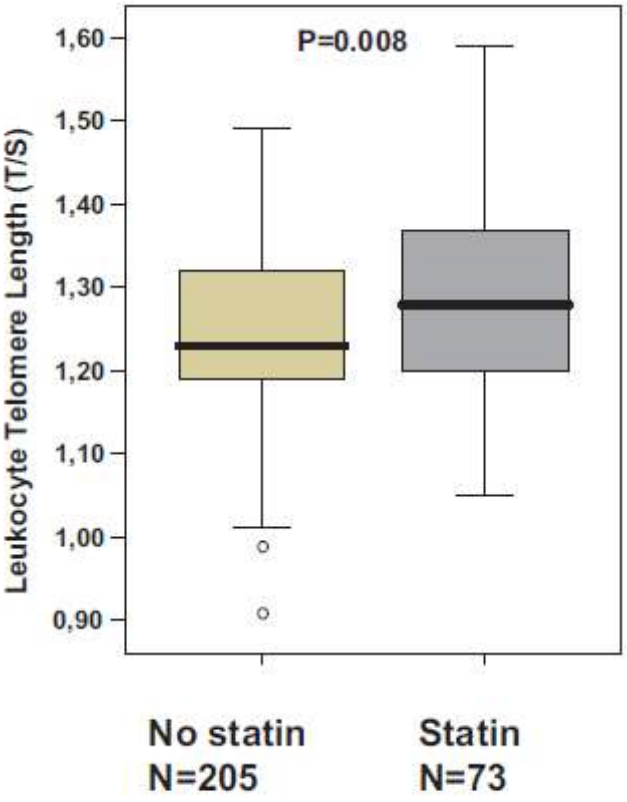
Statins and Telomeres Biology

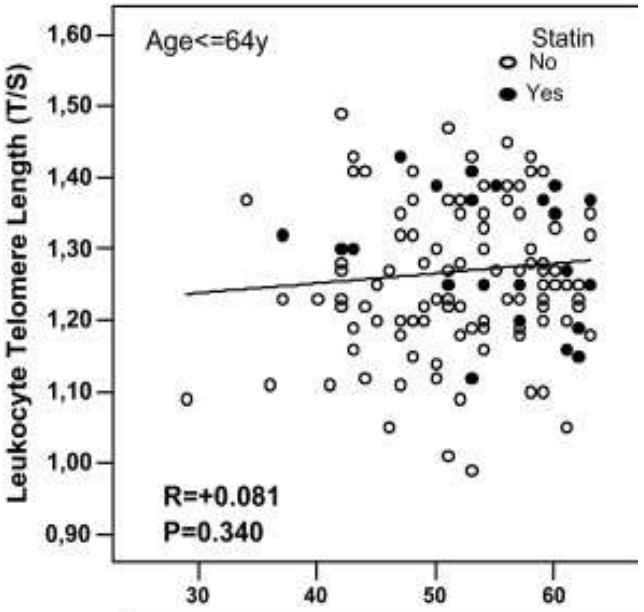


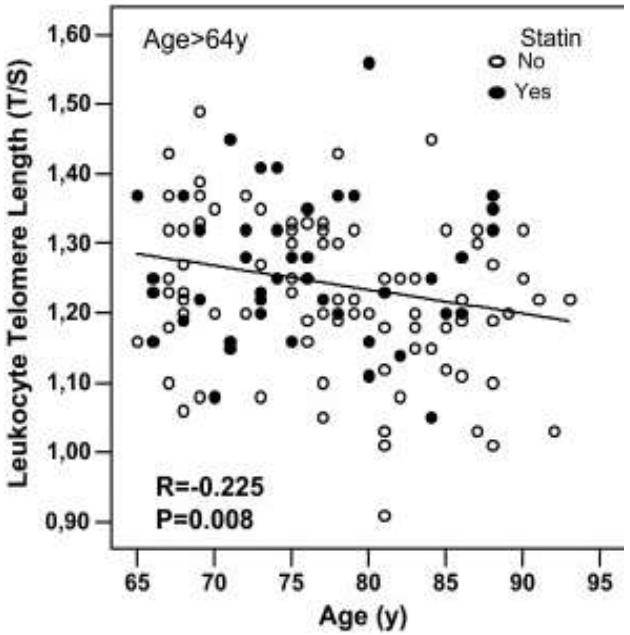


Assmus B et al. Circulation Research 2003;92:1049-1055

Statins and Telomeres Biology

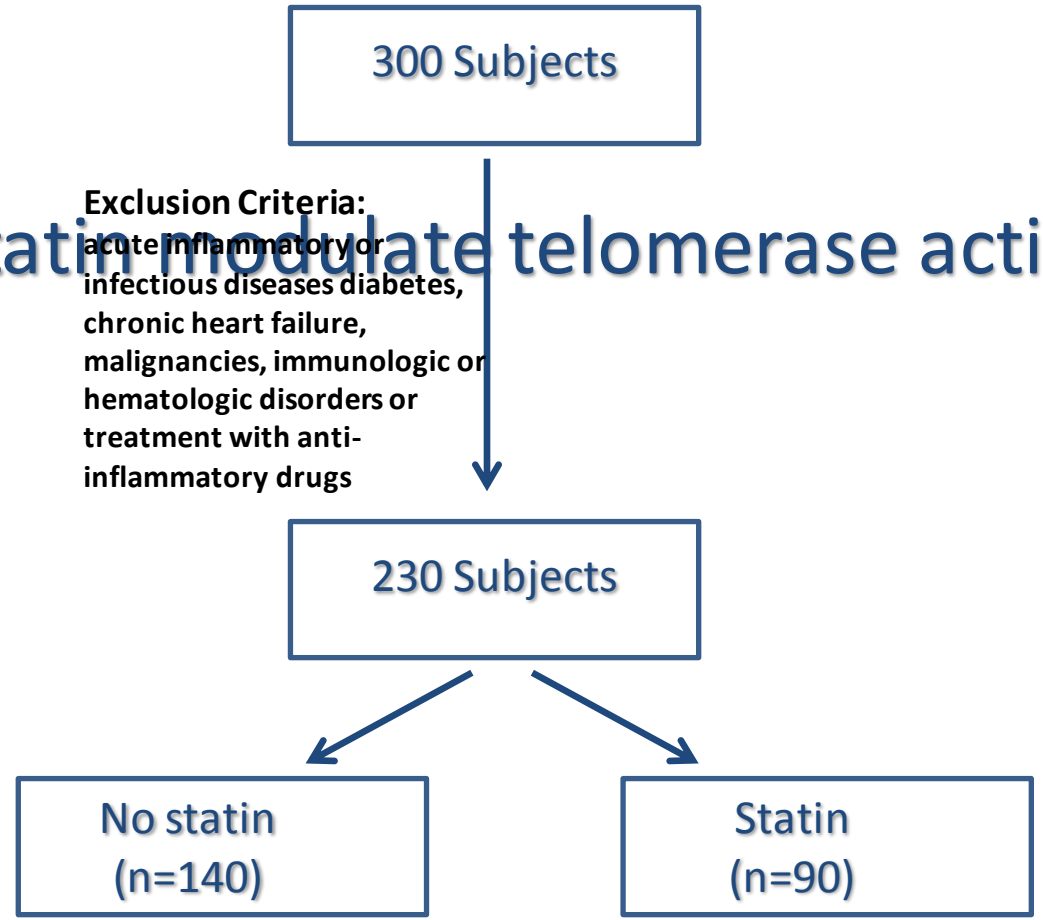






Saliques et al Atherosclerosis, 2011

Does statin modulate telomerase activity?

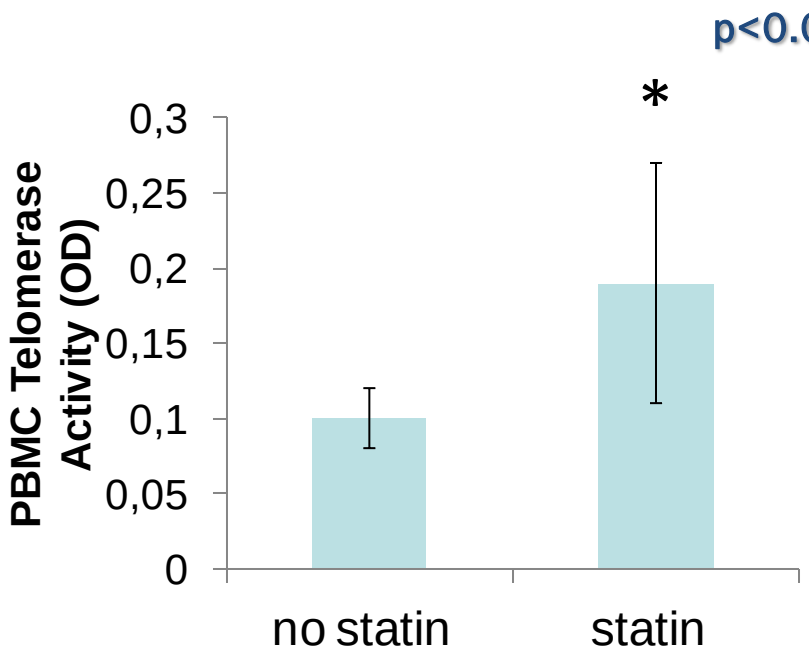


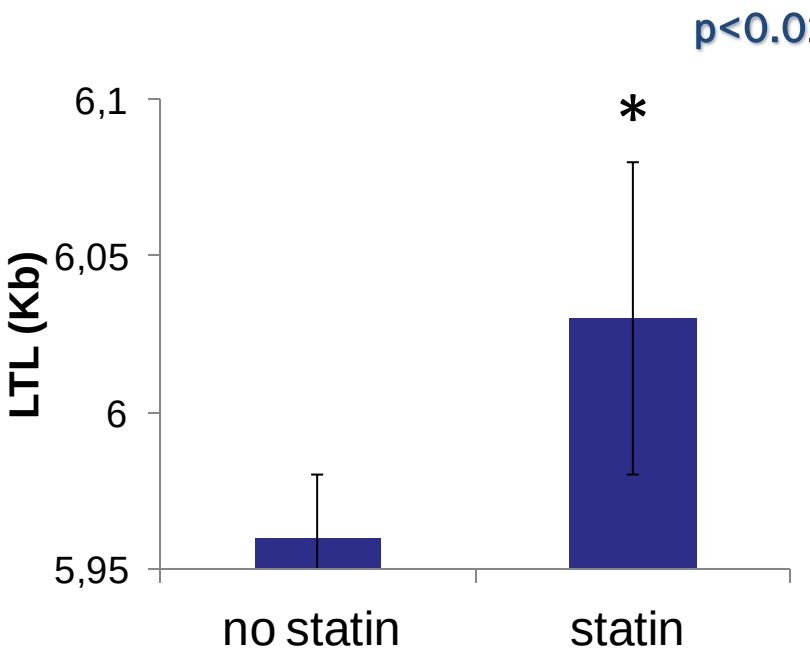
- Telomerase activity (PCR-Elisa)
- Telomeres length (Real time PCR)

Clinical characteristics of study population

	All (n=230)	No statin (n=140)	p	Statin (n=90)
Age (years)	64 ± 14	65 ± 13	0.557	62 ± 14
Gender (M/F)	125/105	80/60*		45/45
Smoker (n)	55	25	0.257	30
BMI (kg/m^2)	27 ± 3	28 ± 4	0.075	26 ± 2
Glucose (mmol/L)	5.50 ± 2.06	6.06 ± 2.44	0.068	5.11 ± 0.83
TC (mmol/L)	4.96 ± 1.24	5.30 ± 1.32	0.001	4.60 ± 1.19
LDL C (mmol/L)	2.92 ± 0.96	3.23 ± 0.96	0.001	2.61 ± 0.96
HDL C (mmol/L)	1.37 ± 0.41	1.37 ± 0.49	0.969	1.37 ± 0.31
Triglycerides (mmol/L)	1.20 ± 0.36	1.21 ± 0.34	0.853	1.19 ± 0.38
CRP (mg/l)	0.41 ± 0.63	0.56 ± 0.81	0.156	0.23 ± 0.20
WBC (10^3/µl)	6.8 ± 1.3	7.1 ± 1.3	0.162	6.4 ± 1.2

PBMC telomerase activity and LTL according to statin group





LTL and telomerase activity significantly correlate (r= 0.564 p=0.015)

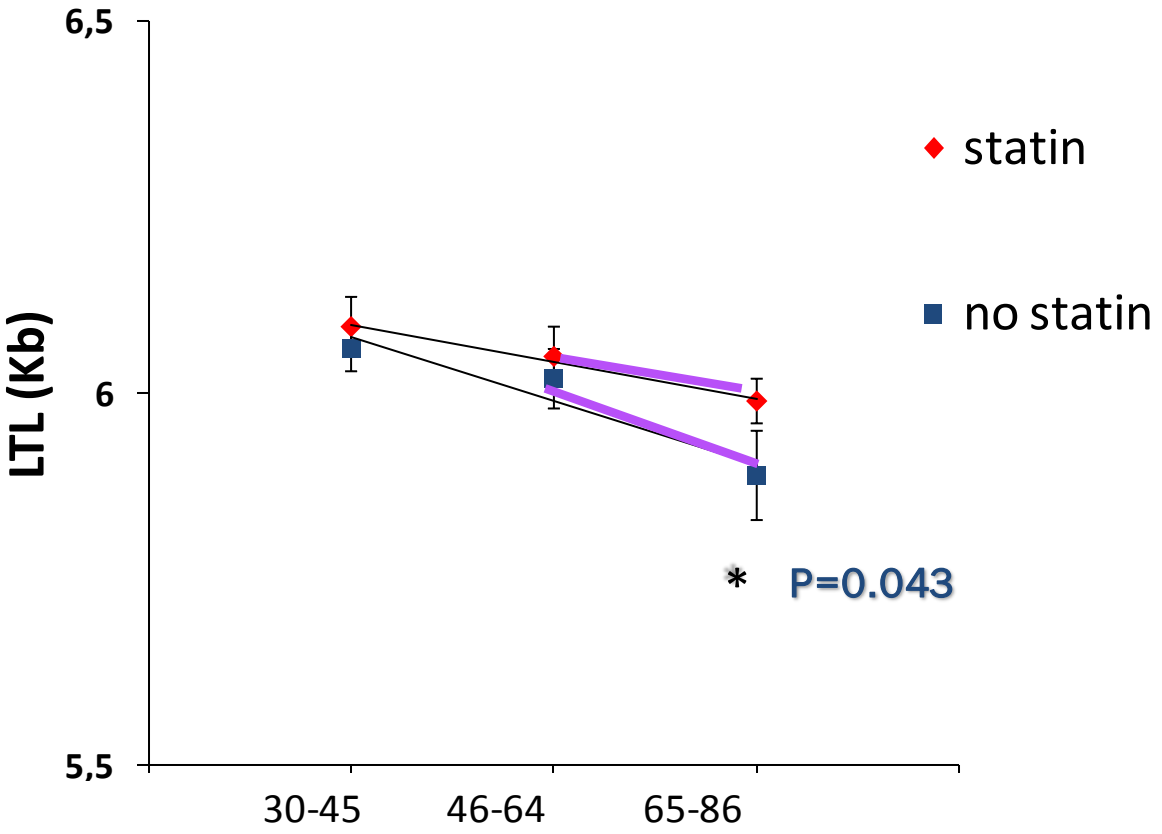
Linear regression analyses with telomerase activity as dependent variable

Model	β	*p*	R^2
Age	0.623	0.019	
Gender	0.328	0. 112	
Smoking habit	- 0.132	0.505	
BMI	0.335	0.125	
LDL-C	-0.213	0.266	
Glucose	0.252	0.227	
DBP	-0.415	0.072	
Inflammation	-0.150	0.443	
Statin	0.549	0.019	
			0.902

Linear regression analyses with LTL as dependent variable

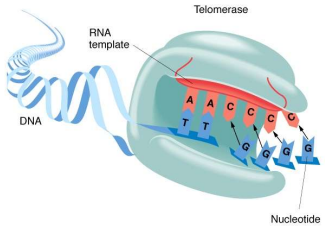
Model 1	β	*p*	R^2
Age	-0.608	<0.001	
Gender	-0 .404	<0.001	
Smoking habit	-0.394	0.073	
Statin	0.685	0.005	
			0.506
Model 2			
Age	-0.575	0.001	
Gender	-0.396	0.001	
Smoking habit	-0.186	0.111	
Statin	0.059	0.687	
Telomerase	0.383	0.045	
			0.600

Rate of telomere shortening along with aging



In no statin group the mean telomere length decreases by 58 base pairs per year, twice as much as telomere erosion rate in statin group (33 base pairs per year).

Conclusions

- ✓Statin treatment is associated with higher telomerase activity and longer LTL
- ✓LTL variability is explained by the modulatory statin effect on telomerase activity
- ✓Statin therapy is associated with lower telomeres shortening along with aging

STATIN