IS PESSIMISM ACTUALLY SHORTENING YOUR LIFE?

GENETICS PERSPECTIVE

Studium Generale, Spring 2018

Maria Vassileva, School of Science

WHY DO WE AGE?

What happens when we age?

Why some people age faster than others?

Let me tell you a story…

So our story starts with:

THE CELL THEORY

In 1838

Schleiden, Schwann and Virchow announced:

All living things are made of cells!

All cells come from other cells!

Cells are the basic unit of life!

And then…

THE HAYFLICK LIMIT

In 1961

Hayflick announced:

Most cells divide only 50 times and then STOP!

WHY?

But before we get there, lest ask:

CELL RENEWAL

How is all that related to aging?

Our body cells renew all the time!

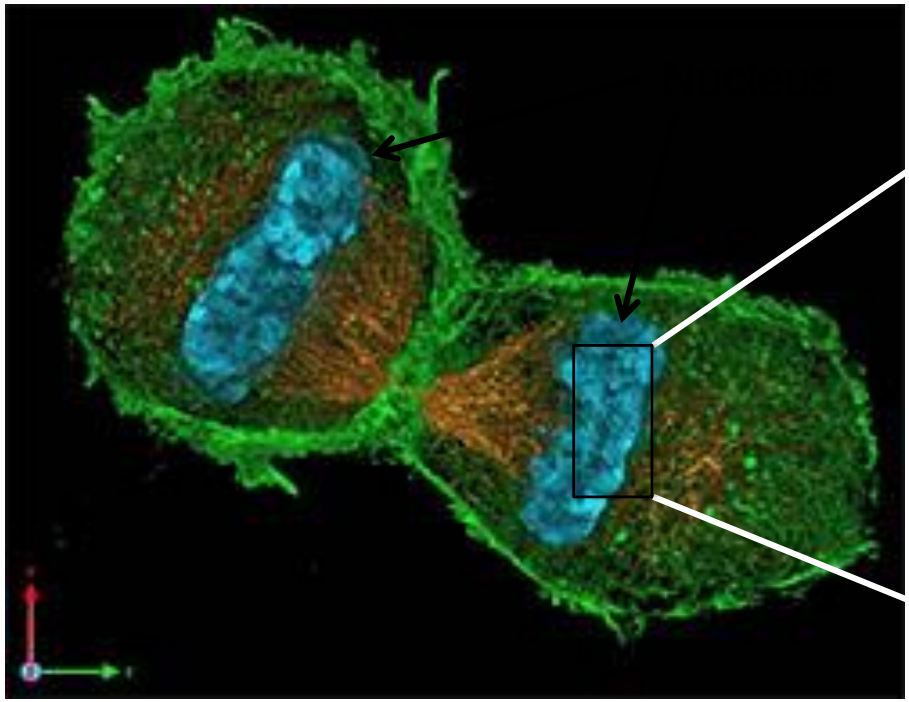
- Wound healing
- Hair fall and regrow
- Blood donation
- Diarrhea recovery

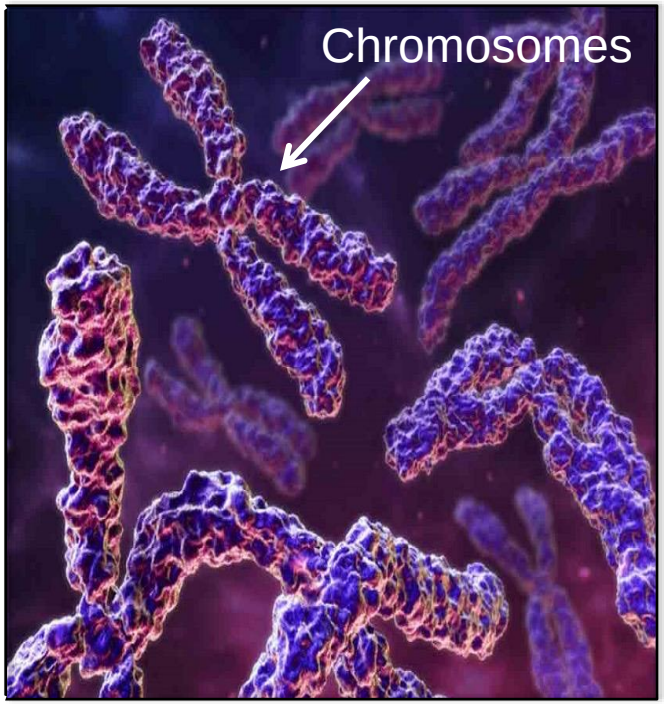
cell type	turnover time
small intestine epithelium	2-4 days
stomach	2-9 days
blood Neutrophils	1-5 days
white blood cells Eosinophils	2-5 days
gastrointestinal colon crypt cells	3-4 days
cervix	6 days
lungs alveoli	8 days
tongue taste buds (rat)	10 days
platelets	10 days
bone osteoclasts	2 weeks
intestine Paneth cells	20 days
skin epidermis cells	10-30 days
pancreas beta cells (rat)	20-50 days
blood B cells (mouse)	4-7 weeks
trachea	1-2 months
hematopoietic stem cells	2 months
sperm (male gametes)	2 months
bone osteoblasts	3 months
red blood cells	4 months
liver hepatocyte cells	0.5-1 year
fat cells	8 years
cardiomyocytes	0.5-10% per year
central nervous system	life time
skeleton	10% per year
lens cells	life time
oocytes (female gametes)	life time

http://book.bionumbers.org/how-quickly-do-different-cells-in-the-body-replace-themselves/ 2018/05/16

What happens when cells divide?

CELL DIVISION AND DNA



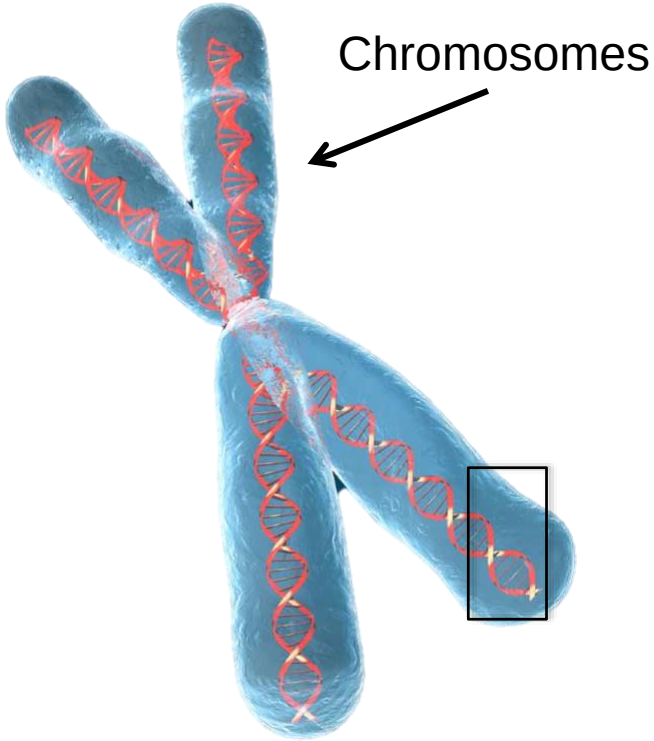


https://en.wikipedia.org/wiki/Super-resolution_microscopy 2018/05/16

https://madreshoy.com/%C2%BFque-son-las-alteraciones-cromosomicas/ 201/05/16

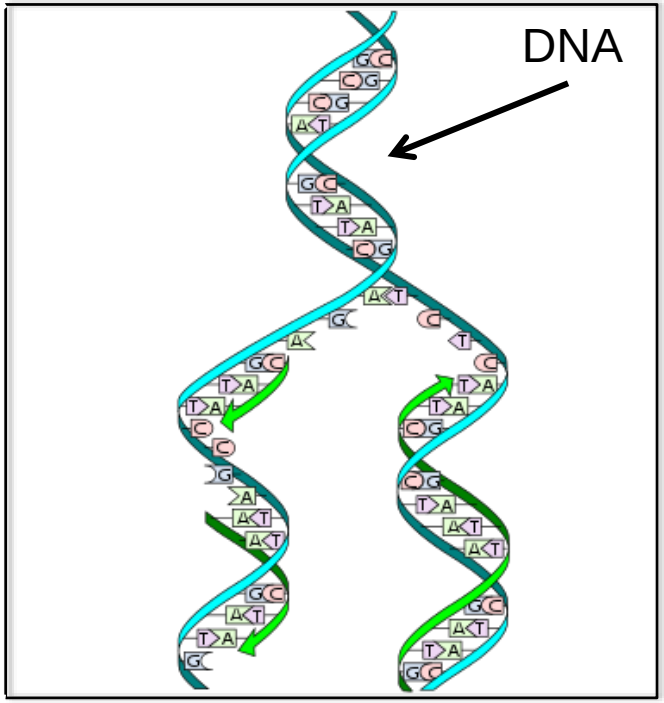
What happens when cells divide?

CELL DIVISION AND DNA



http://www.biologydiscussion.com/chromosomes/fine-or-ultrastructure-of-chromosome-biology/533 2018/05/16

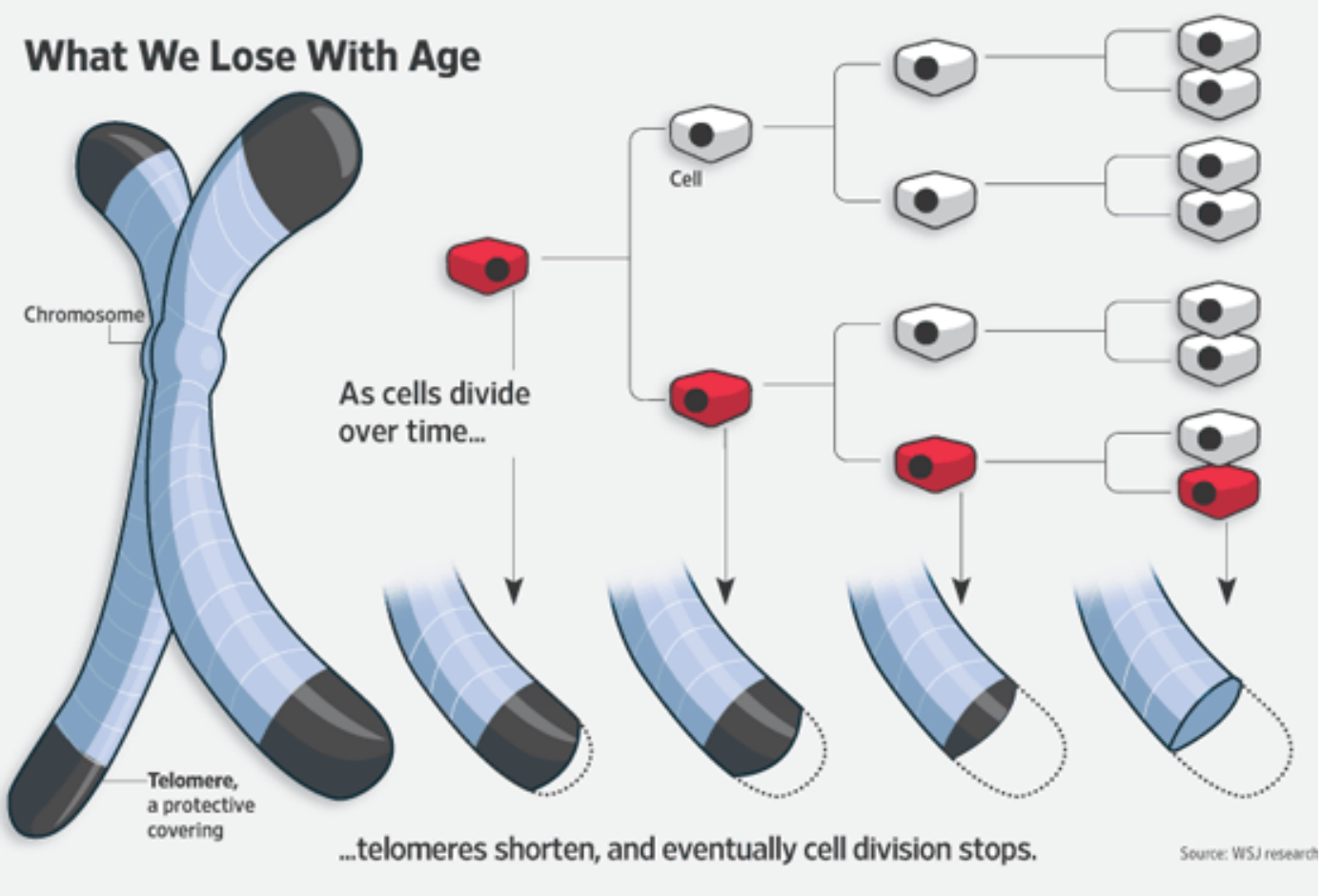
https://ja.wikipedia.org/wiki/DNA%E8%A4%87%E8%A3%BD 2018/05/16



wikipedia

What happens when cells divide?

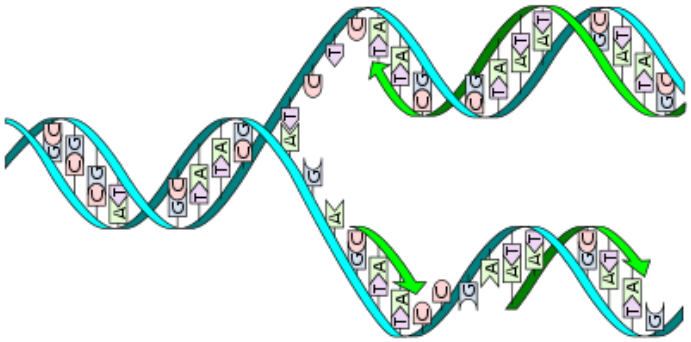
TELOMERES



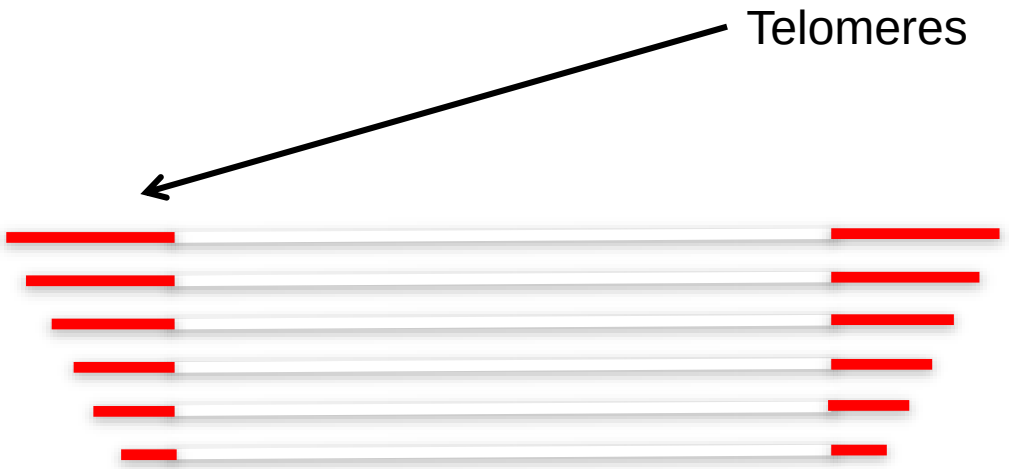
https://www.tasciences.com/what-is-a-telomere/ 2018/05/16

WHY?

END-REPLICATION PROBLEM



wikipedia



https://ja.wikipedia.org/wiki/DNA%E8%A4%87%E8%A3%BD 2018/05/16

Here we come to…

TELOMERASE

https://www.nobelprize.org/nobel_prizes/medicine/laureates/2009/blackburn-facts.html 2018/05/16

Elizabeth Blackburn

The Nobel Prize in Physiology or Medicine 2009

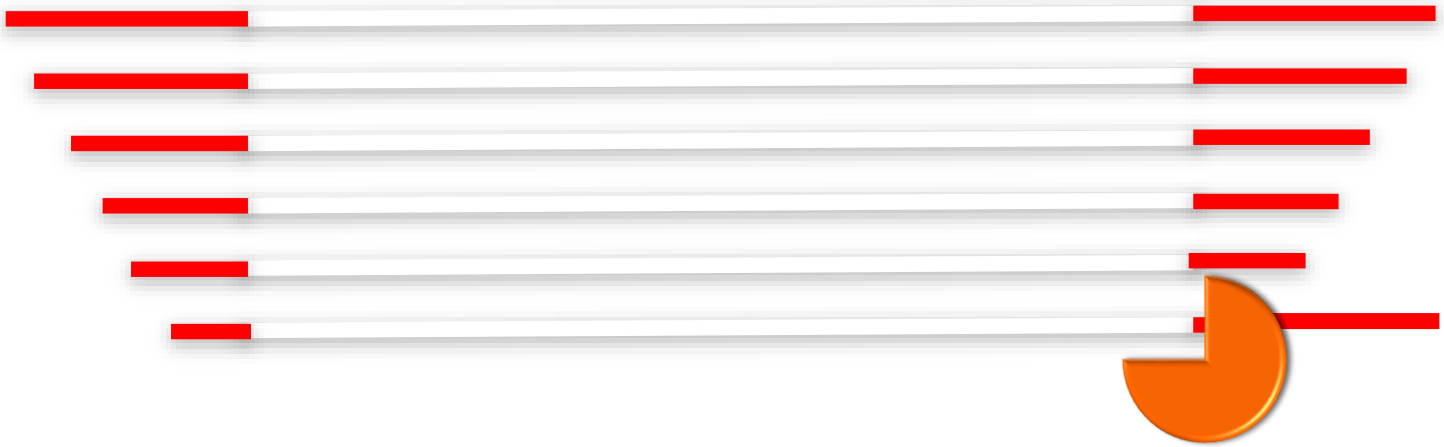
Elizabeth H. Blackburn, Carol W. Greider, Jack W. Szostak

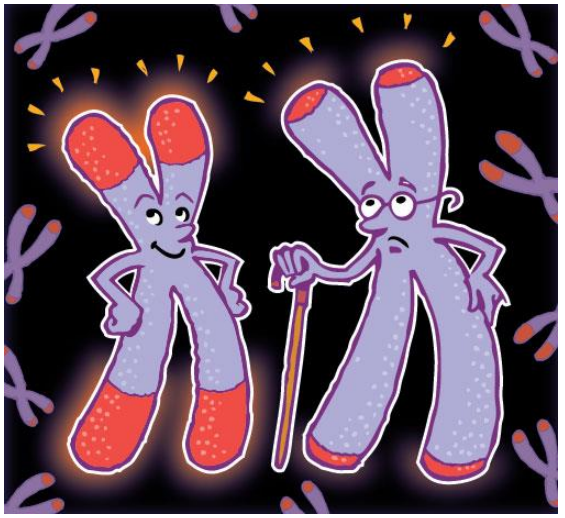
For the discovery of how chromosomes are protected by telomeres and the enzyme telomerase

WHAT IS THAT?

What does telomerase do?

TELOMERASE





http://longevityreporter.org/blog/2015/11/13/repairing-the-clock-another-new-enzyme-found-to-lengthen-telomeres 2018/05/16

A good news and a bad news:

TELOMERASE

It`s active only in stem cells and actively dividing cells (white blood cells)

Most cells don`t have a telomerase

So…what does this all leave us with?

Cell renewal depends on cell division

Cell division depends on telomerase activity

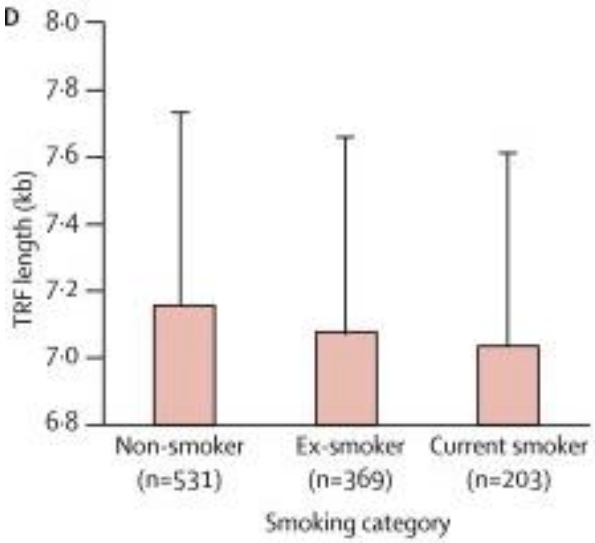
Reduced telomerase activity – less cell renewal

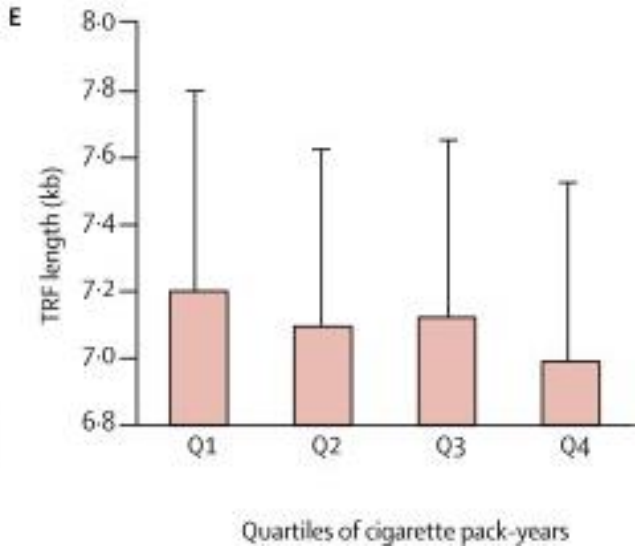
Less renewal in white blood cells – weaker immunity

Weaker immunity – diseases and quick aging

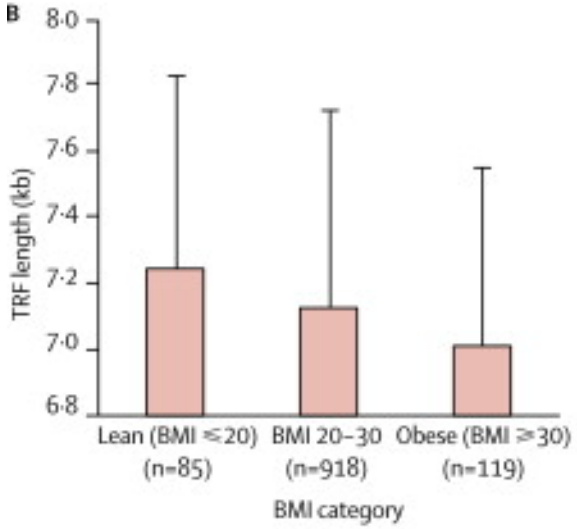
For example, smoking and obesity:

smoking





obesity



https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(05)66630-5/fulltext?code=lancet-site 2018/05/16

TELOMERASE AND BAD HEALTH

And then…telomerase and stress

TELOMERASE AND STRESS

Accelerated telomere shortening in response to life stress

Elissa S. Epel*†, Elizabeth H. Blackburn‡, Jue Lin‡, Firdaus S. Dhabhar§, Nancy E. Adler*, Jason D. Morrow¶, and Richard M. Cawthon‖

*Department of Psychiatry, University of California, 3333 California Street, Suite 465, San Francisco, CA 94143; ‡Department of Biochemistry and Biophysics, University of California, San Francisco, CA 94143; §Department of Oral Biology, College of Dentistry, and Department of Molecular Virology, Immunology, and Medical Genetics, College of Medicine, Ohio State University, Columbus, OH 43210; ¶Department of Medicine and Pharmacology, Vanderbilt University School of Medicine, Nashville, TN 37232; and ‖Department of Human Genetics, University of Utah, 15 North 2030 E Street, Room 2100, Salt Lake City, UT 84112

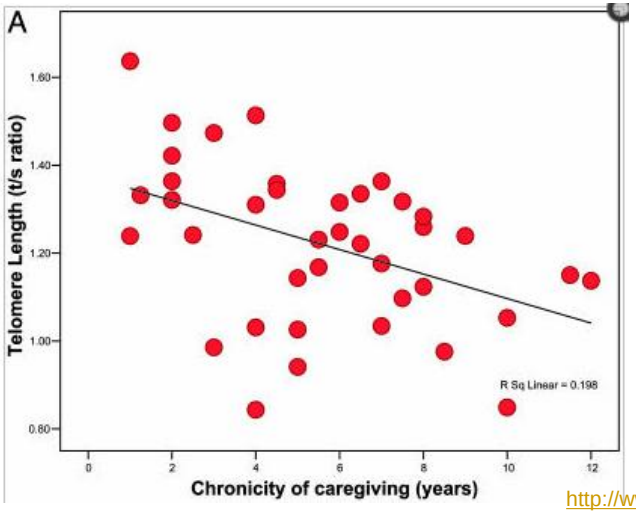
Contributed by Elizabeth H. Blackburn, September 28, 2004

Mothers of healthy and of chronically ill children

Who has shorter telomeres?

Accelerated telomere shortening in response to life stress

http://www.pnas.org/content/101/49/17312 2018/05/16

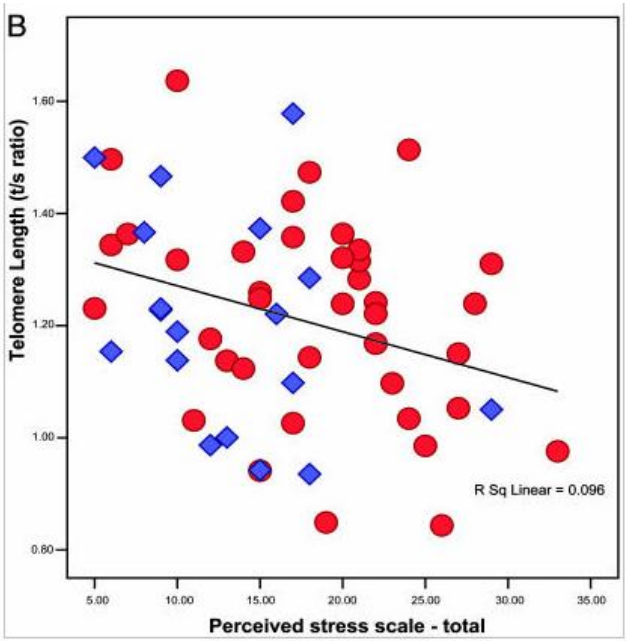


The longer the duration of child illness (objective measure)

the shorter the telomeres, the lower telomerase activity.

BUT

http://www.pnas.org/content/101/49/17312 2018/05/16



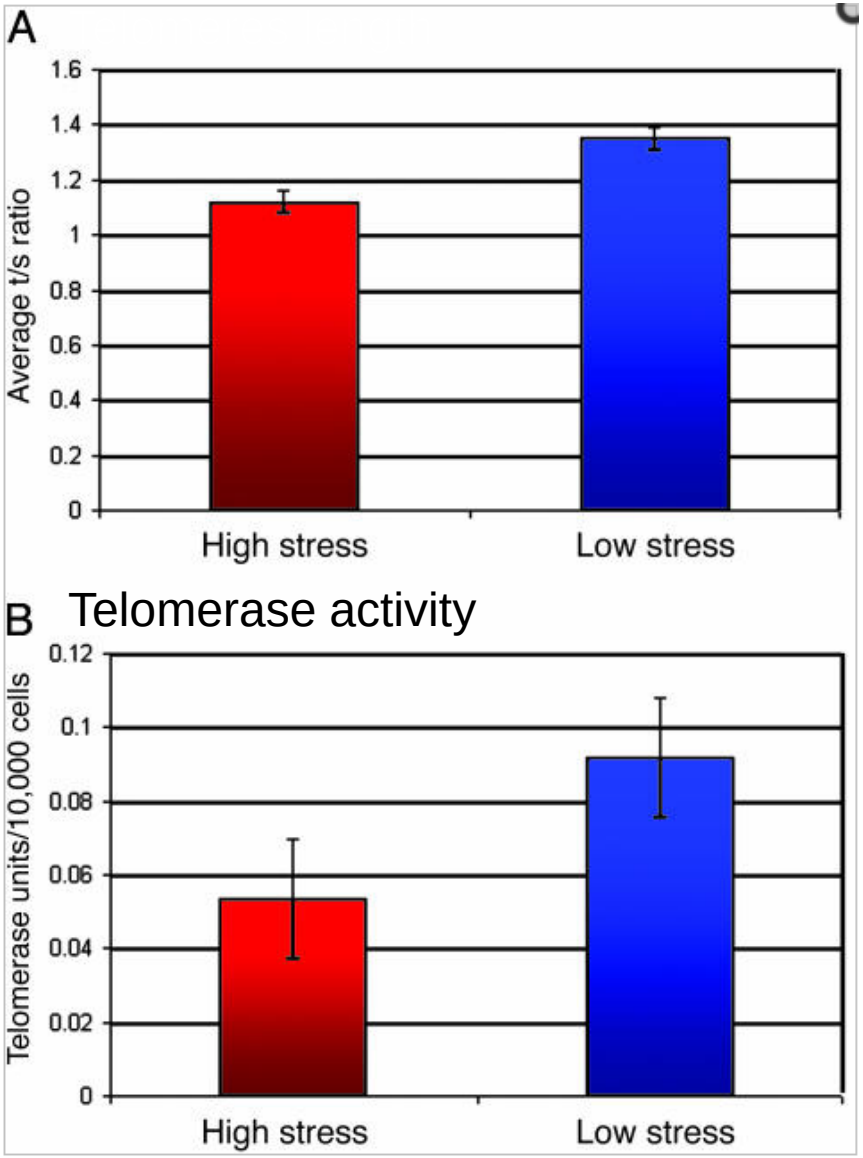
Telomere length was related to perceived stress (subjective measure)

in both groups (controls included)!

Red dots – caregiver of a chronically ill child
Blue squares – caregiver of a healthy child (control group)

Accelerated telomere shortening in response to life stress

http://www.pnas.org/content/101/49/17312 2018/05/16



Comparison of two extreme groups:

Lowest perceived level of stress (control)
And highest perceived level of stress

Approximately 9–17 years worth of accelerated aging!

Accelerated telomere shortening in response to life stress

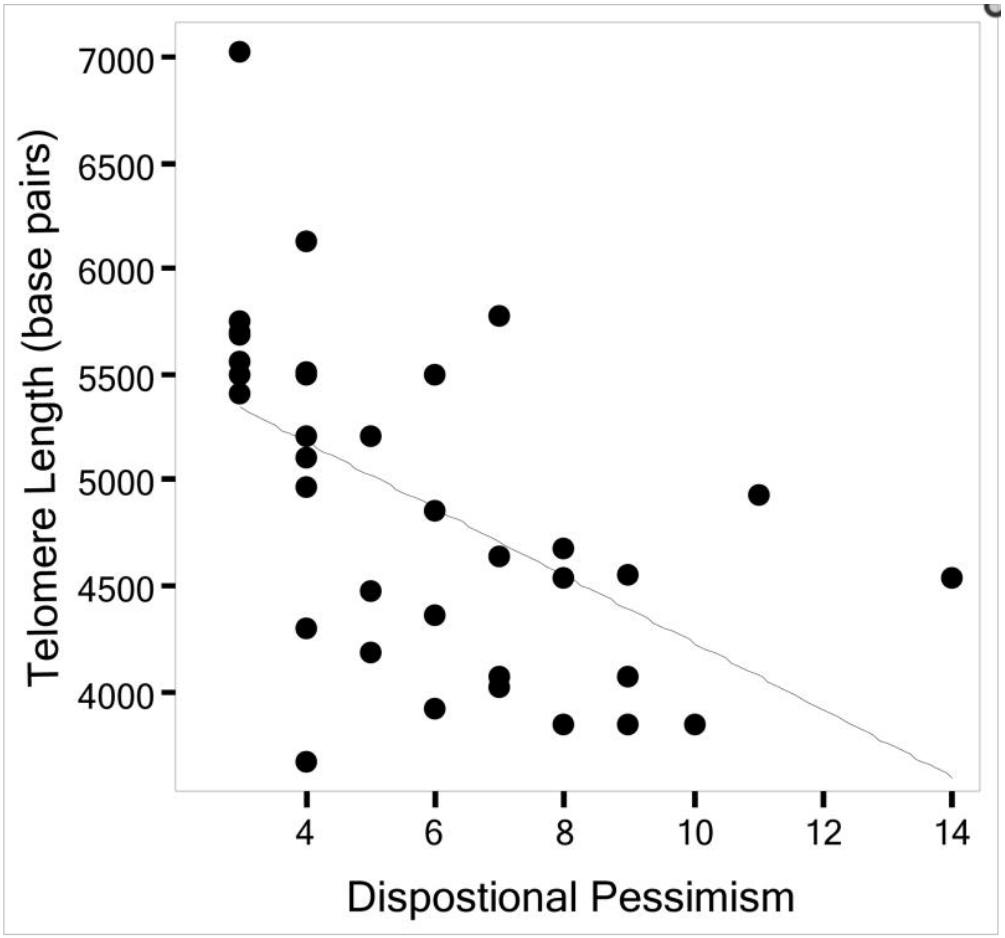
Conclusion

"Prolonged and major stress
predicts worsening of aging (telomerase length)."

But not only that!

PESSIMISM CORRELATES WITH LEUKOCYTE TELOMERE SHORTNESS AND ELEVATED INTERLEUKIN-6 IN POST-MENOPAUSAL WOMEN

A. O'Donovan,[1,2] J. Lin,[3] F.S. Dhabhar,[4] O. Wolkowitz,[1] J.M. Tillie,[4] E. Blackburn,[3] and E. Epel[1,*]



More pessimistic the person
Shorter the telomeres!

https://www.ncbi.nlm.nih.gov/pubmed/19111922 2018/05/16

nature International weekly journal of science

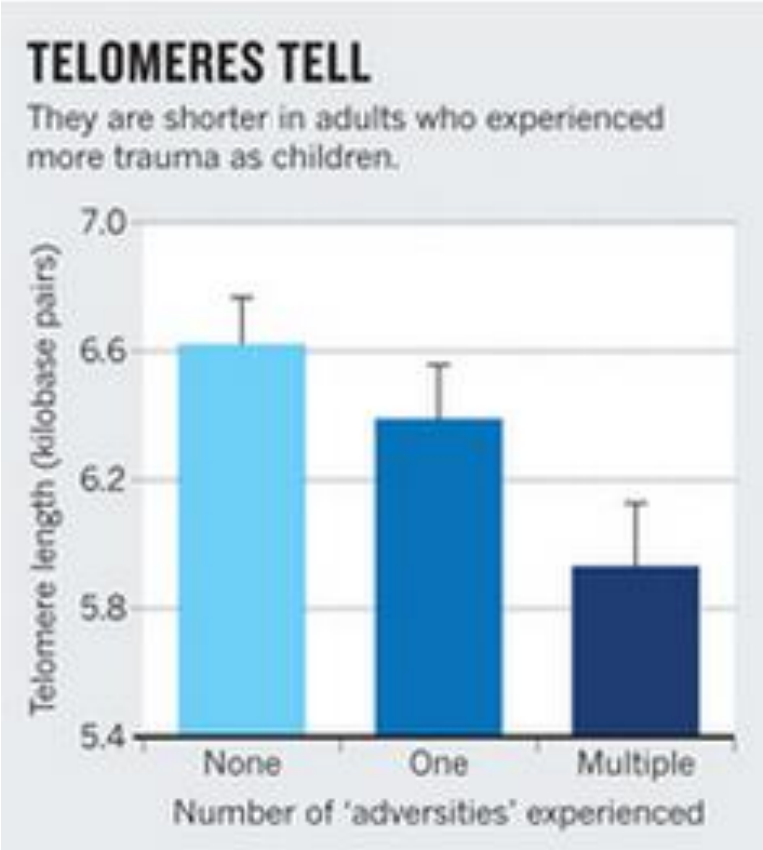
Home | News & Comment | Research | Careers & Jobs | Current Issue | Archive | Audio

Archive > Volume 490 > Issue 7419 > Comment > Article

NATURE | COMMENT

Telomeres and adversity: Too toxic to ignore

Elizabeth H. Blackburn & Elissa S. Epel



https://www.nature.com/articles/490169a 2018/05/16

Even with levels of severe stress experienced by their mothers during pregnancy.

How to explain this?

Organismal stress and telomeric aging: An unexpected connection

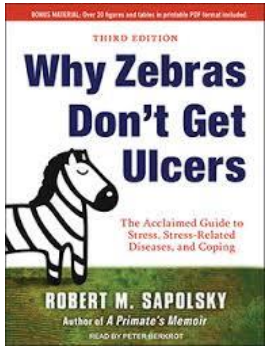
Robert M. Sapolsky*
Departments of Biological Sciences and Neurology and Neurological Sciences, Stanford University, Gilbert Lab MC 5020,

https://www.goodreads.com/author/show/187.Robert_M_Sapolsky 2018/05/16

Chronic stress

Personality – modulated perception

Chronic activation of stress response
Hormonal response (cortisol, adrenalin)



https://www.amazon.co.uk/Why-Zebras-Dont-Get-Ulcers/dp/1452611416 2018/05/16

Shortened telomeres (of white blood cells)

Disease and accelerated aging

Why psychological stress affects physiological processes?

Key connection – hypothalamus!

https://iheartguts.com/blogs/meet-the-guts/14652321-hypothalamus-this-gland-s-in-demand 2018/05/16

You thought you are in control of your body, your behavior and your life?
Big mistake! This guy is!

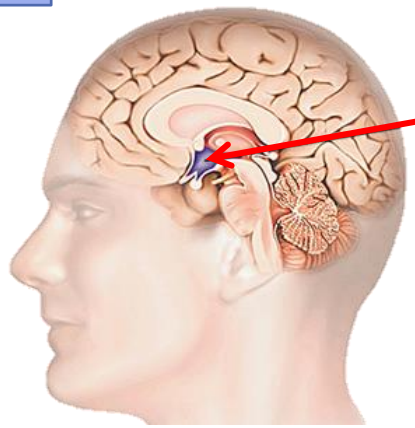
HYPOTHALAMUS AND STRESS

What does hypothalamus do?

Autonomous nervous system (internal organs)

Homeostasis control (temperature, glucose, water, food intake)

Endocrine system (hormones)



Hypothalamus

(the size of a bean)

Part of the limbic system

(Control of emotions)

https://healthjade.com/what-does-the-hypothalamus-do/ 2018/05/16

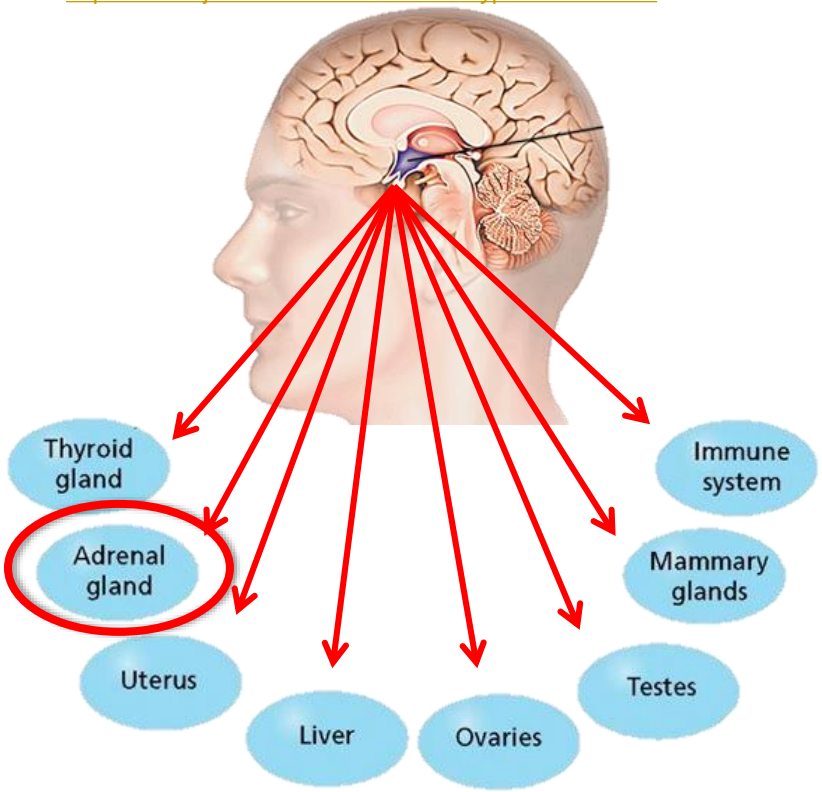
Connections with cerebral cortex (effect from/ on consciousness)

THE CHIEF - HYPOTHALAMUS

What is the endocrine system?

Regulates growth and basic behaviors: fight/flight, feeding, mating, AND social bonding

https://healthjade.com/what-does-the-hypothalamus-do/ 2018/05/16



Glucocorticoids (cortisol)

Adrenalin (epinephrine)

Stress hormones

THE ENDOCRINE SYSTEM

All of this is pretty pessimistic…

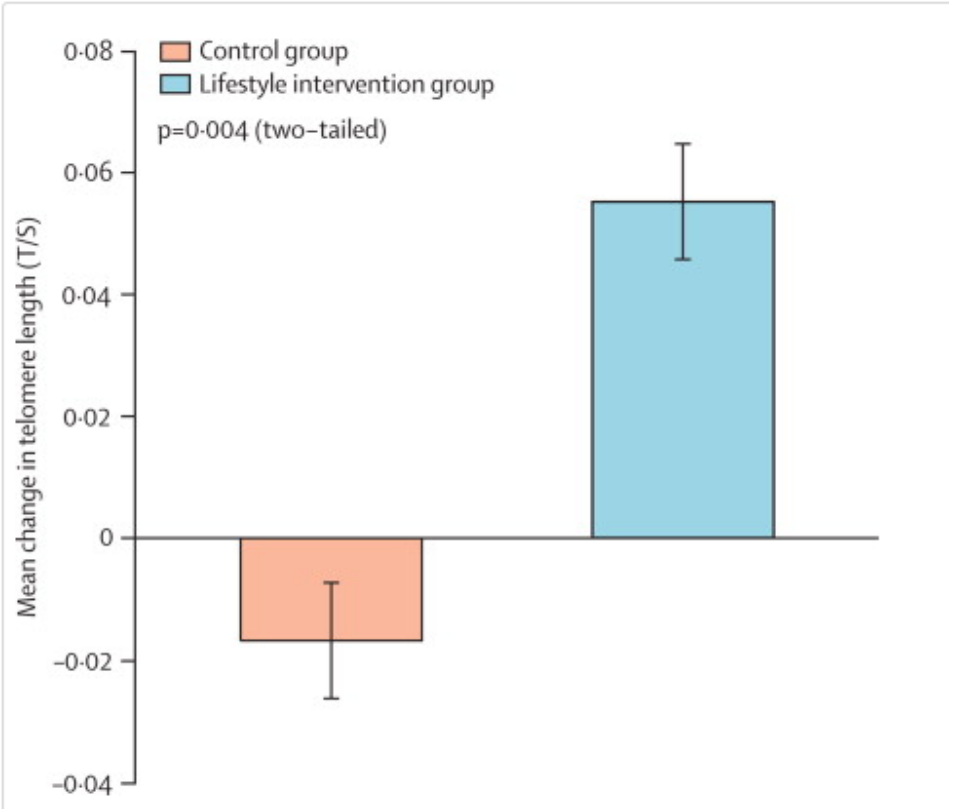
BUT, IF STRESS SHORTENS TELOMERES, CAN DE-STRESS REDUCE THIS EFFECT?

THE LANCET Oncology

Volume 14, Issue 11, October 2013, Pages 1112–1120

Articles

Effect of comprehensive lifestyle changes on telomerase activity and telomere length in men with biopsy-proven low-risk prostate cancer: 5-year follow-up of a descriptive pilot study



Positive lifestyle changes:

- Diet
- Physical activity
- Stress management

https://www.thelancet.com/journals/lanonc/article/PIIS1470-2045(13)70366-8/fulltext 2018/05/16

Can meditation slow rate of cellular aging? Cognitive stress, mindfulness, and telomeres

Elissa Epel, PhD.[1,*], Jennifer Daubenmier, Ph.D.[1], Judith T. Moskowitz, Ph.D.[2], Susan Folkman, PhD.[2], and Elizabeth Blackburn, PhD.[3]

MEDITATION
Mindfulness

Clear focus on the present, curiosity and acceptance

Reduced stress perception

Increased telomerase activity

http://longevityreporter.org/blog/2015/11/13/repairing-the-clock-another-new-enzyme-found-to-lengthen-telomeres 2018/05/16

To sum up...

https://thekindnessfactory.wordpress.com/2012/08/16/lets-go/ 2018/05/16

It looks like
It`s all in our hands!

Just be happy and keep on moving!

THANK YOU!