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THE LONG VIEW

Investing in the Age Longevity with Jim Mellon

WIN £10,000 CASH!*



Pick best performing exhibiting stock over next year

Winner to be announced next year

Details available on competition entry form

*Terms and conditions apply

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JUVENESCENCE

INVESTING IN THE AGE OF LONGEVITY

Investment

MARKET
OVERVIEW

S U M M A R Y

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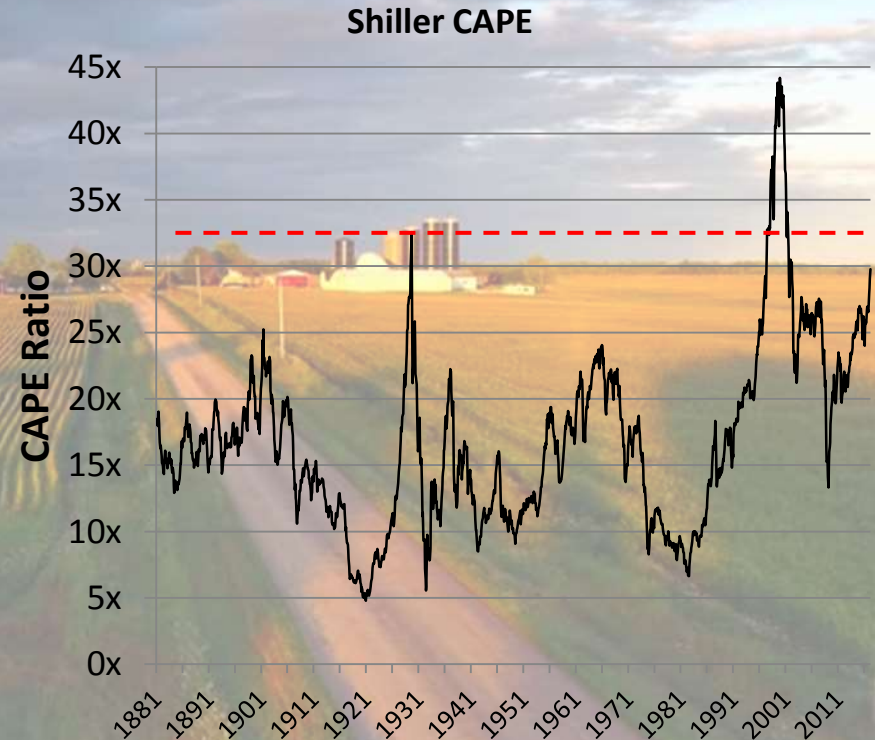
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U.S. & Trump

- Trump a Keynesian Laffer curve man
- Substantial borrowing for infrastructure
- Higher interest rates coming
- Offshore USD repatriation amnesty a possibility
- Markets priced to perfection

Cyclically Adjusted PE Ratio

- Excluding dot com exuberance
CAPE is approaching all time high
- Ten-year forward average returns
fall monotonically as CAPE at entry
increase
- BEWARE of the “this time is
different” pundits – fundamental
valuation ALWAYS matters



Characteristics of US Stock Market	1976	1996	2016
Number of listed companies	4,796	7,322	3,671
Market cap USD billions (2016)	\$2,975	\$12,322	\$25,303
GDP billions (2016)	\$6,325	\$11,769	\$18,565
Market cap as % GDP	47.0%	104.7%	136.3%
Individual direct ownership	50.0%	27.2%	21.5%
Number of ETFs (US domestic)	0	2	658
NYSE annual share volume	5,360	104,636	316,495
Equity options traded (contracts in millions)	32	199	3,626

Characteristics of US Stock Market (USD b)	1976	1996	2016
Mutual funds	\$40	\$1,725	\$3,725
Index funds	<\$1	\$85	\$1,990
Hedge funds – long/short equity	<\$1	\$130	\$850
Venture capital	\$4	\$48	\$333
Buyout	<\$1	\$80	\$827



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SIDESHOW

STATE FAIR FREAKZ PRESENTS

The

**BIG CIRCUS
SIDE SHOW**

THE STRANGEST SHOW ON EARTH!!!



MAIN ENTRANCE



BREXIT

The Brexit Side Show

- Brexit likely to become a side show due to major imbalances within the EU:
 - Unsustainable debt levels in periphery
 - Highly vulnerable banking system
 - Germany export dependent – TARGET 2
 - Election cycle – France & Germany

UK's EU Budget Contributions

- UK's payments to the EU budget since 1973 approx. £500b
- UK's rebates reduces this figure to £380b which is still nearly £9b p.a.

What could £380b buy you?



9 x HS2 projects



26 Crossrails



4,750 Cristiano Ronaldos



3.3 years of 2016 NHS budget



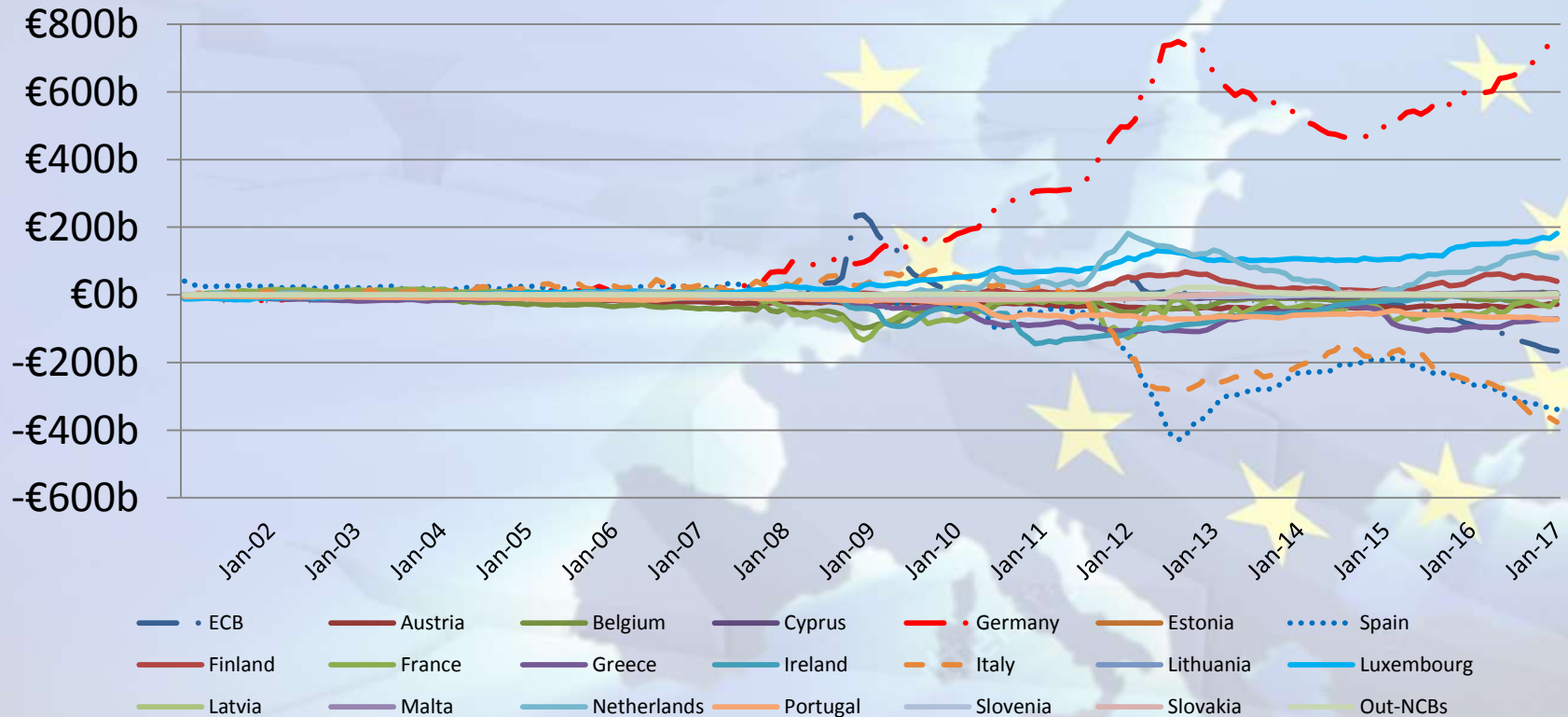
17 x Aircraft Carriers



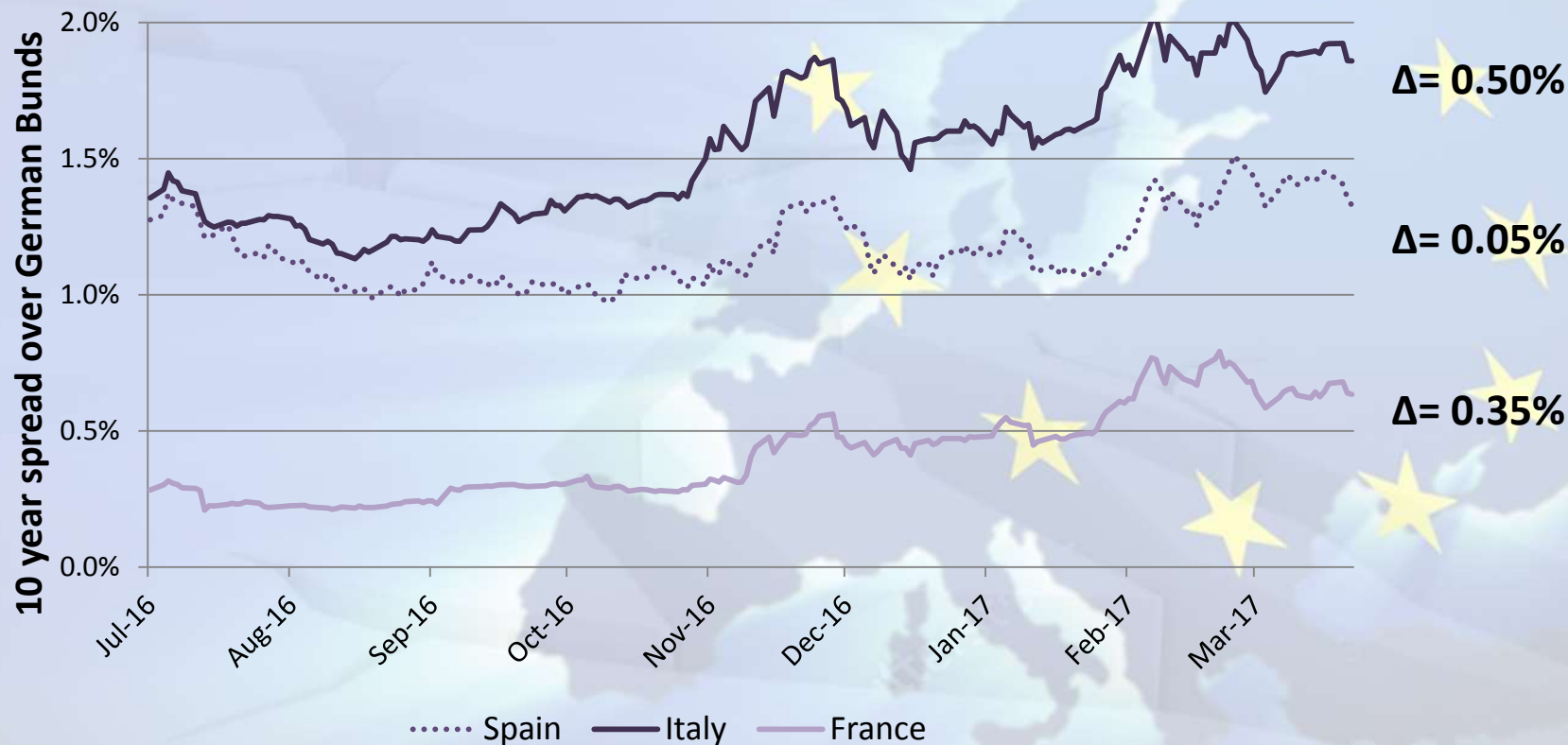
Europe

- Europe continues to move from crisis to crisis
- Elections loom in Germany and France
- Populism makes further integration unlikely
- Fully expect EU to lose further member **in the next 3 years**

Target2 Balances



Euro Area 10 Year Spread Over Bunds



Emerging Markets

- Strong USD a negative for EMs
- China significant non-performing loans
- Significant debt problems elsewhere
- Still commodity dependent



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Macro Summary

- Central bank derived capital misallocation
- China slowdown
- Imbalances within the EU remain
- Strong USD
- Equity and bond markets priced to perfection

THE NEXT BIG THING



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Internet of things

Human redundancy

Depreciating yen

Prime London real estate

Uranium bull market

Biotech bull market

Gold bull market

Unsustainable Chinese growth

Renewable energy boom

Robotics

3D printing

Fracking

Battery technology

Eurozone crisis

Global Financial Crisis

Artificial intelligence

BREXIT

Age of automation



The illustration shows two men. The man on the left is smiling and holding a Gillette razor. The man on the right is shaving his face with a straight razor, looking uncomfortable. Below the illustration is a black banner with the text 'Gillette Safety Razor' in white. Underneath the banner is a white box containing text about the razor's benefits and price.

Gillette Safety Razor

This picture is self-explaining. It tells the story! The man who to-day shaves with a Gillette shaves with comfort and with safety. Other men take chances or are slaves to the "barber habit." Which kind of man are you?

A single trial will convince the most incredulous. It is not what we say alone, but what others say who use a Gillette Safety Razor, that will have with you the greatest weight. Ask the man who uses a Gillette and hear what he says.

\$5.00 Complete — An Ideal Christmas Gift

The Razor is triple silver-plated; has 12 thin, flexible, highly tempered, and keen double-edged blades. These blades are sharpened and ground by a secret process and require no honing or stropping. New Blades \$1.00 per dozen. Each Blade will give from Twenty to Forty Smooth and Delightful Shaves



"I don't have a vision of the future. I have a vision of now."

King Gillette - Founder Gillette Safety Razor Company

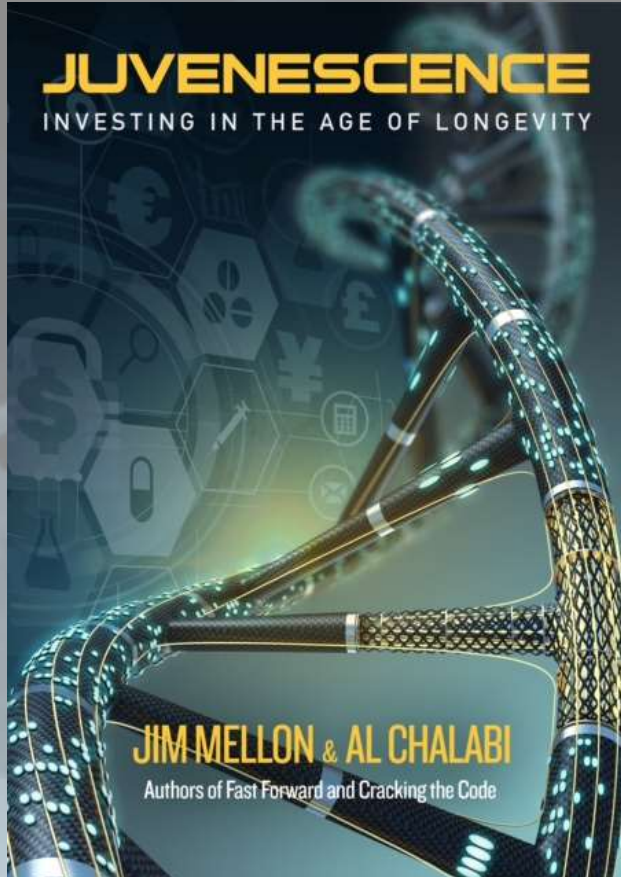
INVESTING IN THE AGE OF LONGEVITY





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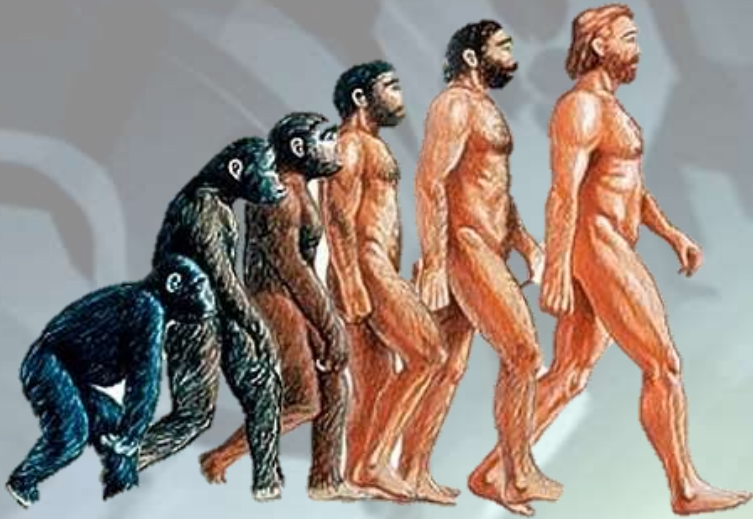


- What is Ageing?
- Is Ageing Pre-Programmed?
- Bridge to Longevity
- Actuarial Escape Velocity

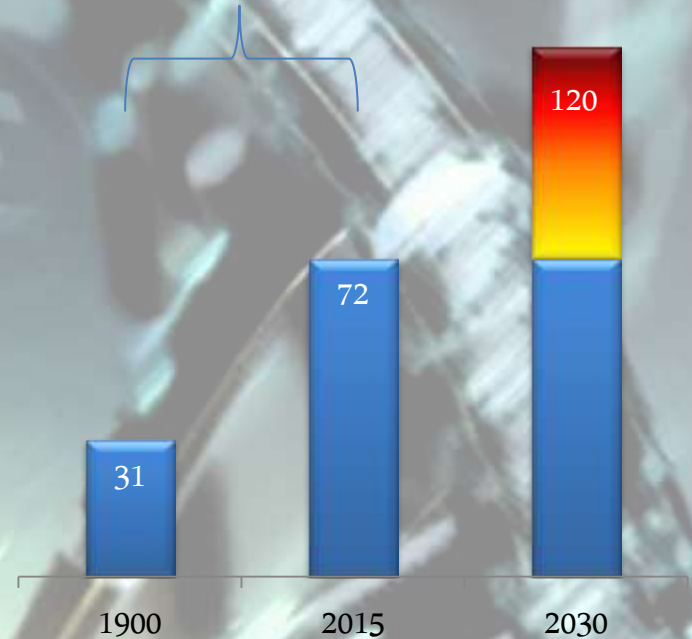


WORLDWIDE LIFE EXPECTANCY

Four million years produced an 11-year
increase from 20 to 31



115 years produced
a 41 year increase



WHAT IS AGEING?

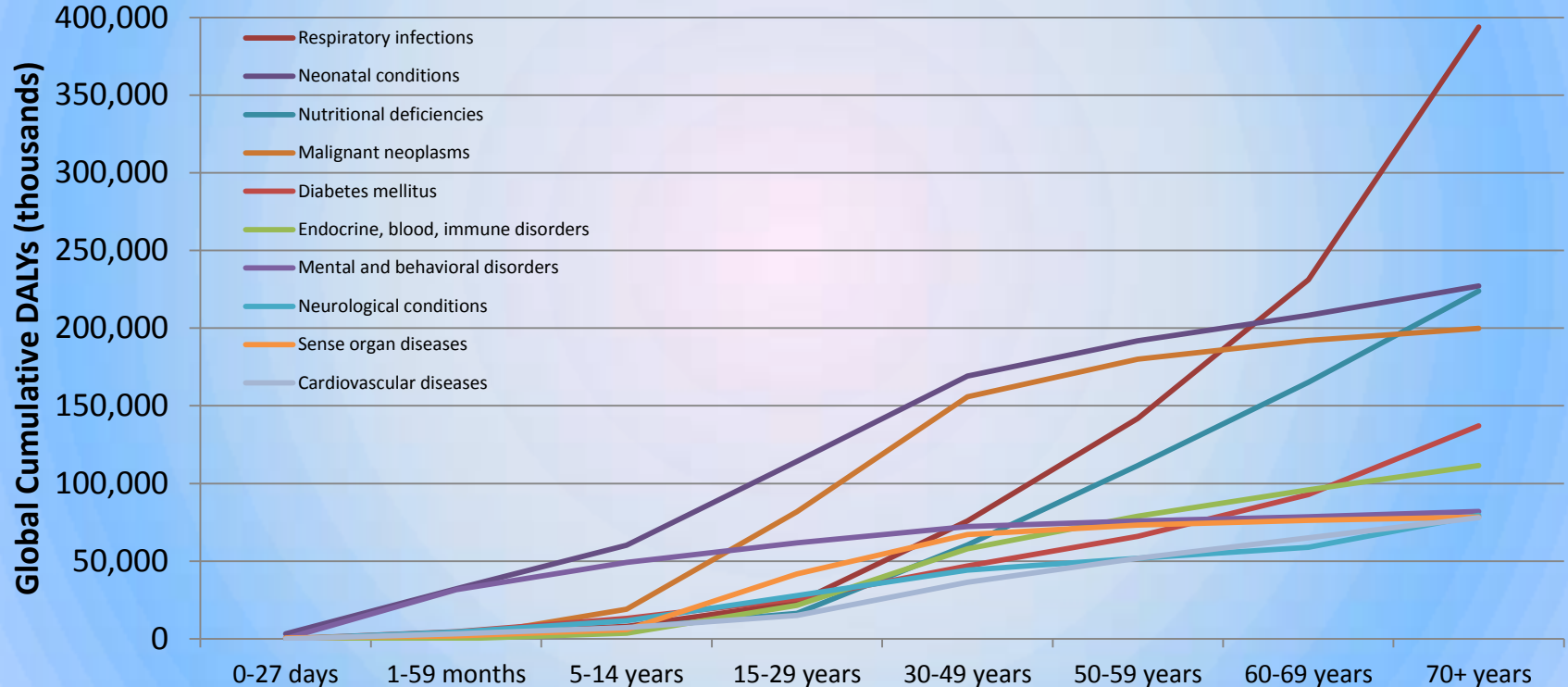


When wear and tear out runs repair.

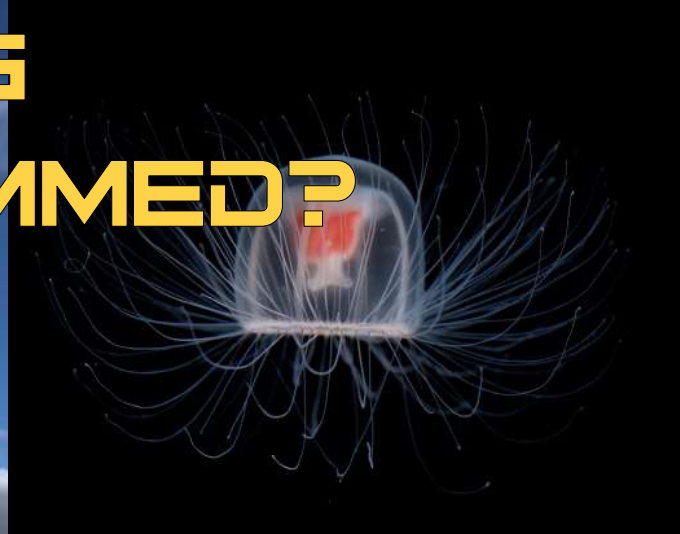


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CORRELATION BETWEEN AGEING & DISEASE



IS AGEING PRE-PROGRAMMED?



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MODELS OF AGEING



Yeast - *Saccharomyces cerevisiae*



Mouse - *Mus musculus*



Earth worm - *Caenorhabditis elegans*

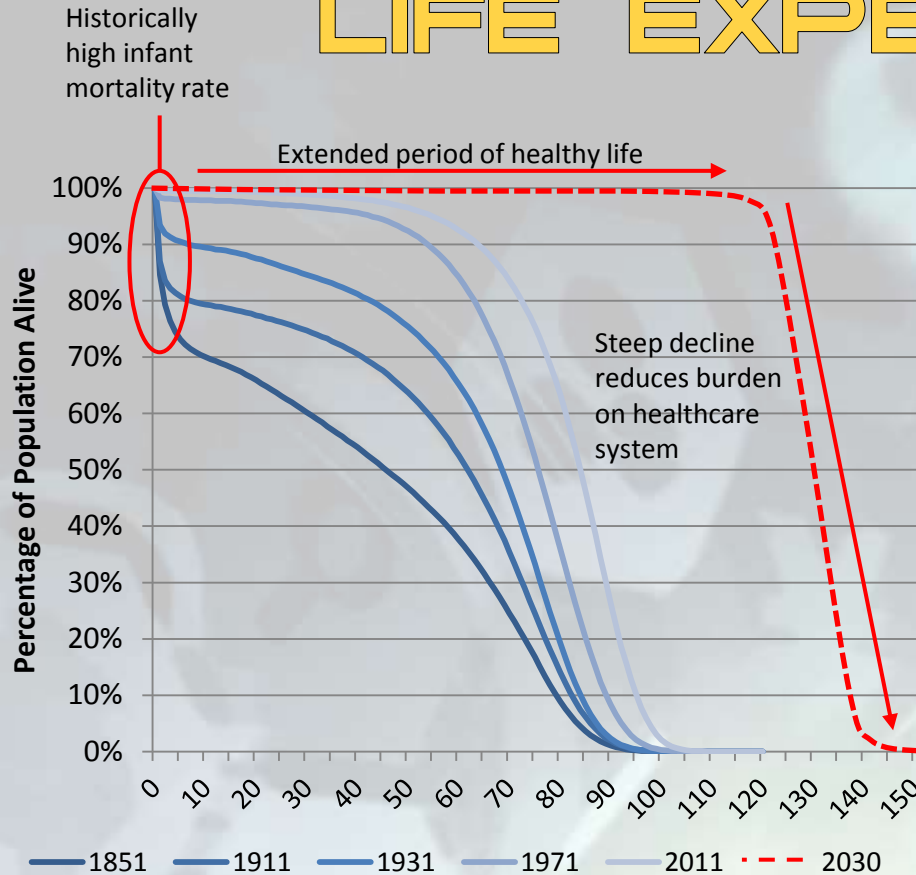


Fruit fly - *Drosophila melanogaster*



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LIFE EXPECTANCY



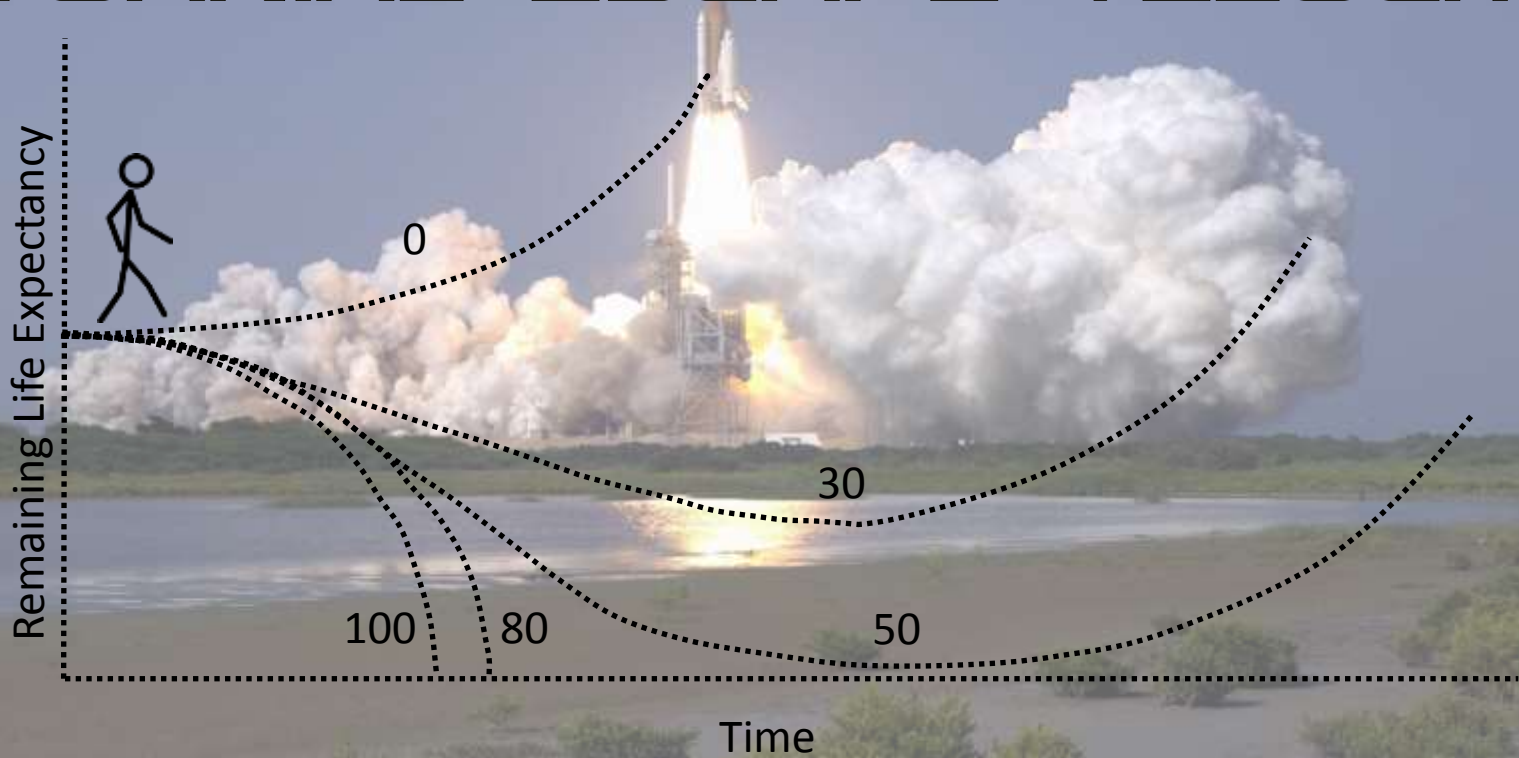
	1900	% of deaths	2015	% of deaths
Influenza and pneumonia	12%	Heart disease	23%	
Tuberculosis	11%	Cancer	23%	
Diarrheal disease	8%	COPD	6%	
Heart disease	8%	Accidents	5%	
Stroke	6%	Stroke	5%	
Kidney disease	5%	Alzheimer's disease	4%	
Accidents	4%	Diabetes mellitus	3%	
Cancer	4%	Influenza and pneumonia	2%	
Senility	3%	Kidney disease	2%	
Diphtheria	2%	Suicide	2%	







ACTUARIAL ESCAPE VELOCITY



At present, more than one year of research is required for each additional year of expected life. Longevity escape velocity occurs when this ratio reverses, so that life expectancy increases faster than one year per one year of research, as long as that rate of advance is sustainable.

BRIDGE TO ACTUARIAL ESCAPE VELOCITY

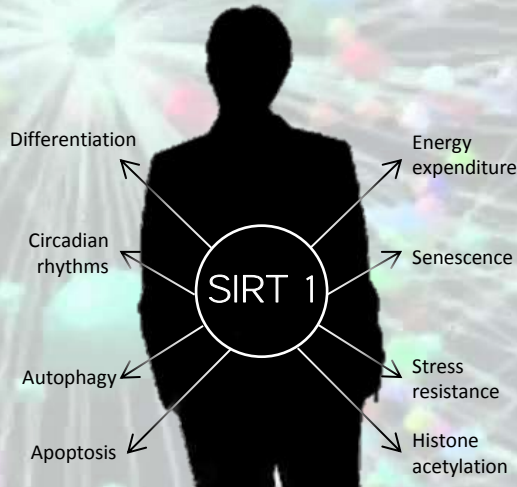
Usual Suspects:

- Stop smoking
- Stay active
- Lose excess fat
- Eat a balanced diet
- Get enough sleep
- Exercise your brain

Experimental Options:

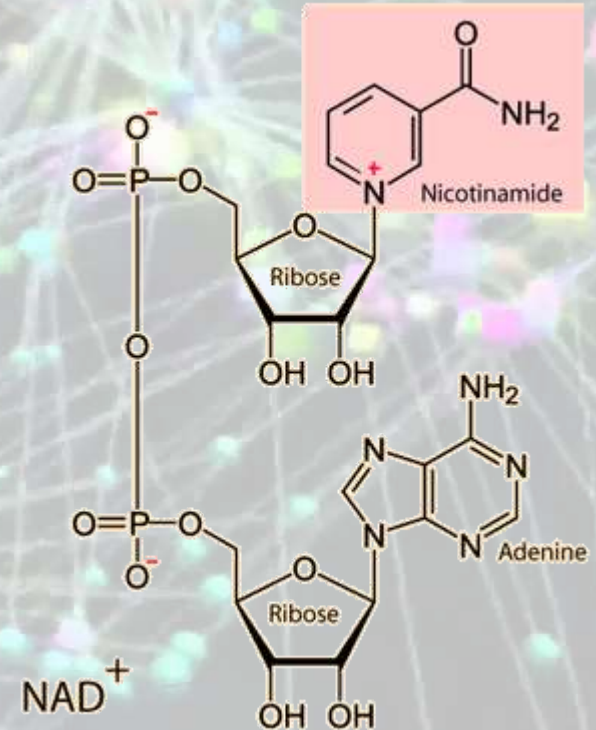
- Metformin
- Resveratrol/pterostilbine
- Nicotinamide (NR/NMN)
- Rapamycin/rapalogs
- Bromocriptine
- Organ replacement
- Gene therapy
- Bio-printing – tissue and organ

DRUGS/TARGETS & PATHWAYS OF AGEING



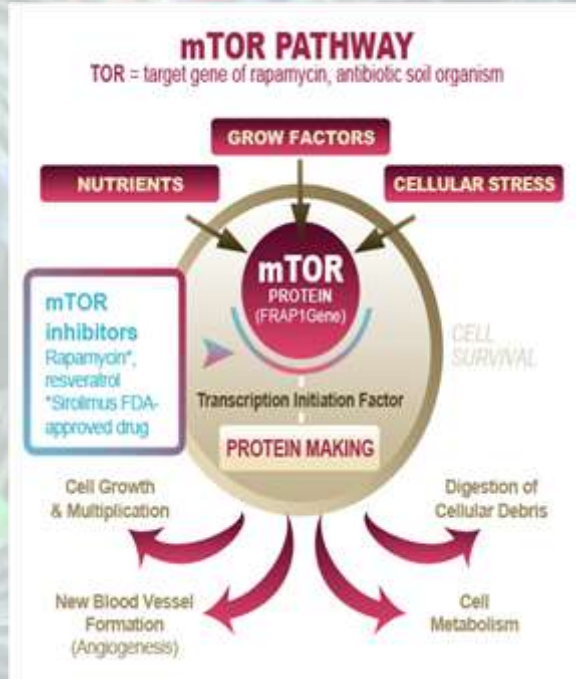
Sirtuins

- Sirtuins are a family of proteins
- Intimate connection between sirtuins and NAD^+ (Nicotinamide adenine dinucleotide)
- NAD^+ availability decreases over age
- Mechanistically regulate energy and metabolism
- NAD^+ & sirtuins crucial in ageing/longevity control



DRUGS/TARGETS & PATHWAYS OF AGEING

Rapamycin

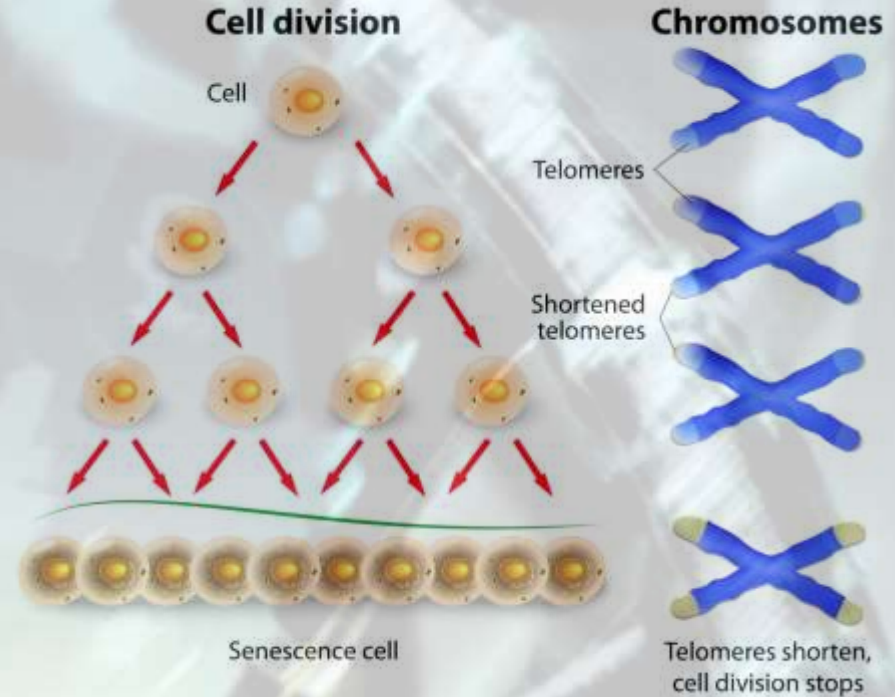


Metformin



CELLULAR SENESCENCE

- Phenomenon by which normal cells cease to divide
- Not solely caused by ageing – more generally due to DNA damage in response to endogenous and exogenous environment
- Leonard Hayflick observed replicative senescence whereby fibroblasts reach a maximum of 50 divisions then become senescent – the Hayflick Limit
- Senescent cells don't die, remain metabolically active and often promote inflammation





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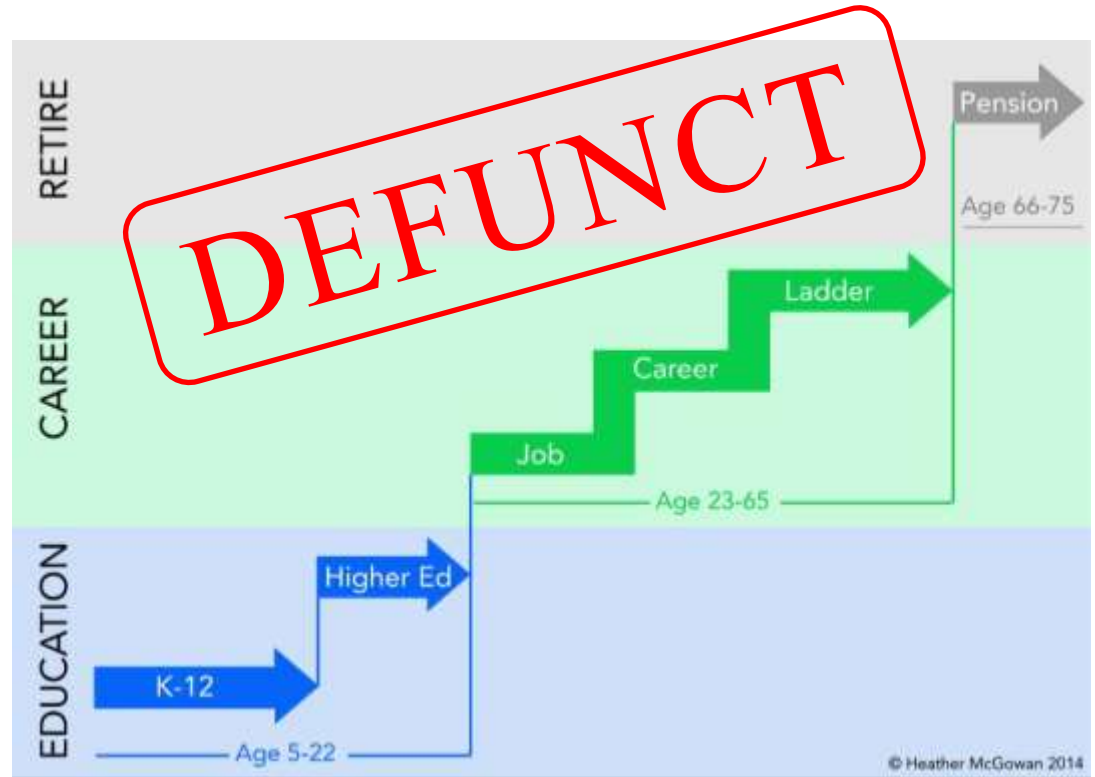
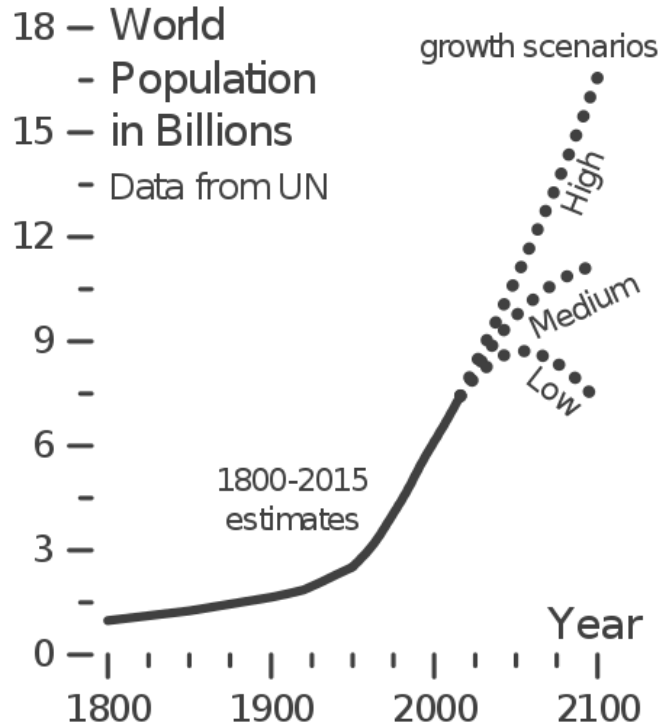
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IMPLICATIONS OF INCREASING LONGEVITY

- Conventional education model broken
- Work longer and have multiple careers
- When to have children?
- Where does it stop 100, 200 ... 500 years old?
- War, famine and plagues become determinants of life span



IMPLICATIONS OF INCREASING LONGEVITY



KEY OPINION LEADERS

- **Professor David Sinclair**
 - Department of Genetics Harvard Medical School
- **Aubrey de Grey**
 - Chief Scientific Officer, SENS Research Foundation
- **Dr Walter Bortz**
 - Professor of Medicine, Stanford University School of Medicine
- **Cynthia Kenyon**
 - Vice President Ageing Research, Calico
- **Dr Nir Barzilai**
 - Founding Director, Institute for Aging Research
- **Dr Alex Zhavoronkov**
 - Chief Executive Officer, Insilico Medicine
- **Nathanial David**
 - President, Unity Biotechnology
- **Professor Linda Partridge**
 - Max Planck Institute for Biology of Ageing
- **Laura Deming**
 - Partner, The Longevity Fund
- **Elizabeth Parish**
 - Chief Executive Officer – Bioviva
- **Patrick Cox**
 - Maudlin Economics
- **John Mauldin**
 - Founder, Maudlin Economics
- **Dr Peter Attia**
 - The Eating Academy
- **Professor Alastair Buchan**
 - Dean of Medical School, Oxford University
- **Dr Matthew Freeman**
 - Head, Sir William Dunn School of Pathology, Oxford U



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LONGEVITY COMPANIES

- | | | |
|-------------------------|--------------------------------|--------------------------------|
| 1. Alkahest | 13. Gero | 25. Organovo Holdings, Inc. |
| 2. BioTime | 14. Grail | 26. Proteostasis Therapeutics |
| 3. Bioviva Science | 15. Human Longevity Inc | 27. Regeneron |
| 4. Bluebird Bio | 16. Hydra Life Sciences | 28. Samumed |
| 5. Calico | 17. Insilico Medicine, Inc | 29. Sangamo BioSciences, Inc |
| 6. Chronos Therapeutics | 18. Intellia Therapeutics, Inc | 30. SENS |
| 7. CohBar | 19. KITE Pharma | 31. The Methuselah Foundation. |
| 8. Dignity | 20. L-Nutra | 32. Service Corporation |
| 9. Editas Medicine, Inc | 21. Metrobiotech | 33. Sibelius Natural Products |
| 10. Elysium Health Inc | 22. Navitor Pharmaceuticals | 34. SIWA Therapeutics |
| 11. Freenome | 23. Oisin Biotechnologies | 35. Unity Biotech |
| 12. Genescent | 24. Omnity | |

READING LIST

1. NEJM
2. BMA Journal
3. New Scientist
4. Scientific American
5. National Geographic
6. Wired
7. Master Investor Magazine
8. How Stuff Works
9. BioWorld
10. Nature
11. Science

Macro Ideas

- Gold
- Silver
- Nikkei 225 – Jap. equity ind.
- KOPSI – Korean equity ind.
- Malaysian Ringgit (vs. USD)
- Mexican Peso (vs. USD)
- Short French bonds
- Short Italian bonds

Long Ideas

Long	US Market Cap	Dividend Yield	P/E Ratio	EV / EBITDA
Amarin Corp PLC	868	0.00%	-	-
Amgen Inc	122,281	2.77%	15.57	8.78
Aurora Labs Ltd	103	0.00%	-	-
Avation PLC	163	1.13%	7.13	9.87
Bristol-Myers Squibb Co	92,425	2.78%	20.16	18.08
Condor Gold PLC	52	0.00%	-	-
Editas Medicine Inc	792	0.00%	-	-
Gilead Sciences Inc	88,528	3.07%	6.40	4.70
Reinsurance Group of America I	8,138	1.29%	12.07	-
Salvarx Group PLC	13	0.00%	-	-
Sony Corp	40,967	0.56%	-	8.72
Synergy Pharmaceuticals Inc	1,007	0.00%	-	-
Wal-Mart Stores Inc	214,954	2.92%	16.15	7.52
Zenith Minerals Ltd	18	0.00%	-	-

Short Ideas

Short	US Market Cap	Dividend Yield	P/E Ratio	EV / EBITDA
Alphabet Inc	572,898	0.00%	29.88	15.39
Amazon.com Inc	405,164	0.00%	172.47	28.62
Deutsche Bank AG	26,223	1.22%	-	-
Facebook Inc	405,407	0.00%	43.01	20.51

Summary

- Macro picture is confused but Japan is best bet for gains
- The fall of American titan stocks cannot be too far away
- Longevity will be a money fountain
- It will also transform the trajectory of lives, and leads to questions about automation ,education etc.



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WHAT'S THE DIFFERENCE BETWEEN LIVING TO 83 VS 110?

27 MASTER

INVESTOR SHOWS!

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Senolytics

p16INK4a

SA-β-gal