Healthy aging and the role of nutrition

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Do not try to live forever, you will not succeed

George Bernard Shaw (1856–1950)
A metaphor for a promise or tradeoff that at first seems appealing, but with time becomes a bad bargain.
Life expectancy low in mid 19th century

Decrease in child/infant mortality

Rapid evolution of medical science and technology in mid 20th century

Increase in life expectancy from 30-40 years to 60-70 years

Dramatic increase in age-related chronic and debilitating diseases

Cancer
Heart disease
Alzheimer
Dementia
Parkinson
Diabetes
Stroke

Rise of anti-aging industry
Multibillion dollar industry
The anti aging industry

Thrives on the promise that the fountain of youth is within our grasp

The promise of longer life has always fascinated mankind

The anti aging industry is referred to as ‘the second oldest profession’
According to Transparency Market Research, the global anti-aging industry will be worth nearly $200 billion by 2019.

It is anticipated to grow at a rate of 7.5% between 2016 and 2021.
When will you start using anti-aging products?

Source: Bank of America Merrill Lynch Global Research
AGING ......

In 1951, Sir Peter Medawar delivered a lecture at University College, London, entitled ‘An Unsolved Problem in Biology’. The Unsolved problem was aging

Aging is No Longer an Unsolved Problem in Biology, 2006, NYAS
ROBIN HOLLIDAY
Australian Academy of Science, Canberra, Australia
Nine tentative hallmarks that represent common denominators of aging in different organisms, with special emphasis on mammalian aging.

Lopez-Otin, C. et al 2013, Cell, 1194-1217
Basic questions ......

Why do we age?

How do we age?
Nothing in Biology Makes Sense Except in the Light of Evolution
essay by the evolutionary biologist Theodosius Dobzhansky 1973

From an evolutionary perspective:
If we live longer than we are required to live naturally, ageing will set in....

Fulfillment of the Darvinian purpose of life
Why do living organisms age?

It is apparent that the best strategy for animal survival is to develop to an adult, but not to invest resources in maintaining the body, or soma, indefinitely...

Animals must survive to reproduce, but it is counterproductive to invest in the maintenance of the body, or soma, after reproduction.
The human body is made up of dividing cells, and also, non-dividing cells that have to last a lifetime.

There are many components of the body that have finite lifespan, lens and retina, collagen and elastin become cross linked, structure of bone joints, changes in skin. All these features are the result of million of years of evolution.

Thus the anatomical design of the body is not compatible with indefinite survival.
### Three types of lifespan

<table>
<thead>
<tr>
<th></th>
<th>Maximum LS</th>
<th>Average LS</th>
<th>Essential LS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruitflies</td>
<td>80 days</td>
<td>30-40 days</td>
<td>7-10 days</td>
</tr>
<tr>
<td>Rats/mice</td>
<td>36 months</td>
<td>20-24 months</td>
<td>10-12 months</td>
</tr>
<tr>
<td>Humans</td>
<td>122 years</td>
<td>75-80 years</td>
<td>40-45 years</td>
</tr>
</tbody>
</table>
Basic questions ……

Why do we age?

How do we age?

• What happens during ageing?
• What is the molecular cause of ageing?
• How to intervene……
The good news.....

There are no genes whose “function” is to cause ageing or to kill the organism.

But genes surely affect the length and quality of life – these genes are called virtual gerontogenes.
There are more than 300 theories (hypotheses !) of aging.

The lack of a unified theory of aging underlines the multifaceted, diverse and complex nature of aging !!
Main theories of aging

Accumulated mutation theory
Antagonistic pleiotropy theory
Disposable soma theory
Protein error theory of aging
Role of telomerase in aging
The mitochondrial theory of aging
The free radical theory of aging
The free radical theory of aging

“Aging results from the deleterious effects of free radicals produced in the course of cellular metabolism”
Denham Harman, 1956

“Aging is the sum of the free radical damage associated with suboptimal living conditions plus that produced by inborn aging process”
Denham Harman, 2002

“Aging is a growing expression with time of free radical damage by both endogenous and exogenous sources, incompletely repaired by processes dependent on ATP”
Denham Harman, 2006
Electron transport chain
Reactive Oxygen Species

- **Oxygen centered radicals:**
  - Superoxide anion (\(\cdot O_2^-\))
  - Hydroxyl radical (\(HO^-\))
  - Hydroperoxyl radical (\(HOO^-\))
  - Peroxyl radical (\(ROO^-\))

- **Oxygen centered non-radicals:**
  - Hydrogen peroxide (\(H_2O_2\))
  - Singlet oxygen (\(^1O_2\))
**Defense systems in vivo against oxidative damage**

Under normal physiological conditions about 1-5% of the oxygen consumed by mitochondria is converted to ROS (superoxide anions, \( \text{H}_2\text{O}_2 \) and hydroxyl radicals).

Cells have evolved a variety of enzymatic and non-enzymatic systems capable of converting ROS into less toxic or non toxic species.

<table>
<thead>
<tr>
<th>Enzyme</th>
<th>Reaction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Catalase</td>
<td>Decomposition of ( \text{H}_2\text{O}_2 )</td>
</tr>
<tr>
<td>Glutathione peroxidase</td>
<td>Decomposition of ( \text{H}_2\text{O}_2 )</td>
</tr>
<tr>
<td>Peroxidase</td>
<td>Decomposition of ( \text{H}_2\text{O}_2 ) and lipid peroxides</td>
</tr>
<tr>
<td>Glutathione –S-Transferase</td>
<td>Decomposition of lipid peroxides</td>
</tr>
<tr>
<td>Superoxide dismutase</td>
<td>Decomposition of superoxide</td>
</tr>
<tr>
<td>Caretonoids, vitamin A</td>
<td>Quenching of singlet oxygen</td>
</tr>
</tbody>
</table>

**Hydrophilic antioxidants:** Vitamin C, uric acid, bilirubin

**Lipophilic:** Vitamin E, ubiquinol, flavonoids
My research group has been studying the biochemical markers of oxidative stress in blood, as a function of age, in healthy humans and rats.

Wistar rats have an average life span of 24 months. We have studied markers of oxidative stress in rats at different stages of their life span. We have also studied the effect of black tea supplementation on blood redox status as a function of animal age.

Studies were carried out on subjects ranging in ages 20 – 80 years. Difficult to maintain uniform conditions due to factors: nutritional, lifestyle, social background, etc.
The final frontier……
Quest for a potential anti-aging therapy

Since time immemorial man has been fascinated by possible interventions which might delay the aging process
The elusive elixir of life

- According to the Rigveda (ancient Indian text, > 1000 BC), amrita is a drink that bestows immortality.

- In text of Ayurveda (ancient Indian text), there has been a mention of rasayana, a combination of many herbs and minerals, designed to rejuvenate the body, mind, and self at the deepest possible level.

- In ancient Chinese texts a key ingredient in the elixir of life is said to be a mushroom, the Lingzhi, also known as the Mushroom of Immortality.

- According to some Yogic traditions, Amrita can be released from the pituitary gland during deep meditation.

- The idea of ingesting liquid metals for longevity is present in alchemic traditions from China to Mesopotamia to Europe. These include gold, mercury and arsenic.
### Documented oldest living individuals

<table>
<thead>
<tr>
<th>Rank</th>
<th>Name</th>
<th>Sex</th>
<th>Birth date</th>
<th>Death date</th>
<th>Age</th>
<th>Place of death or residence</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Jeanne Calment</td>
<td>F</td>
<td>21 February 1875</td>
<td>4 August 1997</td>
<td>122 years, 164 days</td>
<td>France</td>
</tr>
<tr>
<td>2</td>
<td>Sarah Knauss</td>
<td>F</td>
<td>24 September 1880</td>
<td>30 December 1999</td>
<td>119 years, 97 days</td>
<td>United States</td>
</tr>
<tr>
<td>3</td>
<td>Lucy Hannah</td>
<td>F</td>
<td>16 July 1875</td>
<td>21 March 1993</td>
<td>117 years, 248 days</td>
<td>United States</td>
</tr>
<tr>
<td>4</td>
<td>Marie-Louise Meilleur</td>
<td>F</td>
<td>29 August 1880</td>
<td>16 April 1998</td>
<td>117 years, 230 days</td>
<td>Canada</td>
</tr>
<tr>
<td>5</td>
<td>Violet Brown</td>
<td>F</td>
<td>10 March 1900</td>
<td>Living</td>
<td>117 years, 189 days</td>
<td>Jamaica</td>
</tr>
<tr>
<td>6</td>
<td>Emma Morano</td>
<td>F</td>
<td>29 November 1899</td>
<td>15 April 2017</td>
<td>117 years, 137 days</td>
<td>Italy</td>
</tr>
<tr>
<td>7</td>
<td>Nabi Tajima</td>
<td>F</td>
<td>4 August 1900</td>
<td>Living</td>
<td>117 years, 42 days</td>
<td>Japan</td>
</tr>
<tr>
<td>8</td>
<td>Misao Okawa</td>
<td>F</td>
<td>5 March 1898</td>
<td>1 April 2015</td>
<td>117 years, 27 days</td>
<td>Japan</td>
</tr>
<tr>
<td>9</td>
<td>María Capovilla</td>
<td>F</td>
<td>14 September 1889</td>
<td>27 August 2006</td>
<td>116 years, 347 days</td>
<td>Ecuador</td>
</tr>
<tr>
<td>10</td>
<td>Susannah Mushatt Jones</td>
<td>F</td>
<td>6 July 1899</td>
<td>12 May 2016</td>
<td>116 years, 311 days</td>
<td>United States</td>
</tr>
</tbody>
</table>
Proposed interventions to delay onset of Aging

• Caloric restriction (CR)
• Hormonal therapies
• Antioxidant supplementation
• Autophagy induction
• Senolytic drugs
• Telomerase activation
• Epigenetic regulation
Caloric restriction

Calorie restriction (CR) also sometimes referred to as dietary restriction (DR), involves restricting intake of a nutritious diet by 20–60% from ad libitum levels.

Caloric restriction is the most effective and reproducible dietary intervention known to regulate aging and increase the healthy lifespan in various model organisms, ranging from the unicellular yeast to worms, flies, rodents, and primates.

Abundant experimental evidence indicates that the CR effect on stimulating health impinges several metabolic and stress-resistance pathways. The precise mechanistic aspects of CR are yet to be settled.

CR application in humans is not yet proved.
In 1935, McCay et al. first provided evidence that reducing caloric intake by 40% may extend the mean and median lifespan of rats by 50%. They reported that the lifespan of white rats was increased when growth was retarded by limiting the calories.
Free Radical Theory and caloric restriction

Although McCay believed that CR worked by retarding growth, later studies subsequent to Harman’s free radical theory of aging, presumed that CR works by reducing oxidative stress.
Energetic Stress

PI3K
Akt
Tsc2
Tsc1
Rheb
mTOR
AMPK
NAD+
Sirtuin

Stress Resistance
Metabolism
Ribosome Biogenesis
Translation
Stress Response
Autophagy
↓Apoptosis
Glucose/Lipid Metabolism
Mitochondrial Biogenesis

Caloric Restriction

Reduced insulin/TGF1 Signaling

Glucagon/Catecholamine

Epac1
RapGT
P
PL
CamK II
CamKK β
ATP
cAM P

Longevity
The CR Paradox

• Evidence is available that life-long CR could produce similar beneficial effects in humans as observed in rodents. However, implementation of this intervention would be highly problematic.

• The potential negative side effects include hypotension, loss of libido, menstrual irregularities, infertility, bone thinning and osteoporosis, cold sensitivity, loss of strength and stamina, slower wound healing, and psychological conditions such as depression, emotional deadening, and irritability.

• Some short term studies have shown that the physiological and psychological effects of caloric restriction that occur in animals may impact the human life very differently.
The concept of Caloric Restriction Mimetic (CRM)

Compounds that mimic CR by targeting metabolic and stress response Pathways affected by CR, without actually restricting caloric intake

An important criteria for CRM, at least over a short duration, is that it should not reduce food intake

Review

Calorie restriction mimetics: Can you have your cake and eat it, too?

Donald K. Ingram\textsuperscript{a,}, George S. Roth\textsuperscript{b}
Manipulation of health span and function by dietary caloric restriction mimetics

George S. Roth¹ and Donald K. Ingram²

Energy restriction and potential energy restriction mimetics

Sibylle Nikolai*, Kathrin Pallauf, Patricia Huebbe and Gerald Rimbach
Institute of Human Nutrition and Food Science, University of Kiel, Kiel, Germany

Energetic interventions for healthspan and resiliency with aging

Derek M. Huffman a,b,*, Marissa J. Schafer c, Nathan K. LeBrasseur c
Caloric Restriction Mimetics

**Glycolytic Inhibitors:** 2-deoxy-d-glucose, Glucosamine, Iodoacetate, 3-Bomopyruvate, Mannoheptulose

**Insulin Signaling:** Metformin

**Growth Hormone/IGF1:** Pegvisomemt

**Sirtuin activators:** Resveratrol, Sirtuin activating compounds (STACs), Nicotinamide, Oxaloacetate

**mTOR inhibitors:** Rapamycin

**Polyamines**

**Spermidine**
Inhibitors of glucose processing and absorption

Blocking energy availability and absorption at the gut level and blocking energy utilization at the cellular level is most promising strategy for developing CR.

The proposed compounds are:

• 2-Deoxy-D-glucose
• Glucosamine
• Mannoheptulose
• Acarbose
Inhibitors of somatotropic (growth hormone/IGF-1) axis

- Diminished somatotropic activity is associated with a retarded rate of aging, delayed onset of age-related diseases, and frailty associated with extended longevity.

- Genetic manipulation of GH and IGF-1 signalling has been proved to be an impressive strategy for developing CR.

Proposed inhibitor of GH and IGF-1 signalling: Pegvisomert (a GH receptor antagonist) also known as somavert is available commercially.
Activators of AMPK
(AMP activated protein kinase)

- AMP-activated protein kinase (AMPK) is a serine/threonine protein kinase complex that acts as central regulator of energy homeostasis.

- It gets activated upon an increase in the AMP-to-ATP ratio, which reflects the energy status of the cell.

- Upon activation, AMPK turns on catabolic pathways to restore ATP levels both in a short time frame, by promoting glycolysis and fatty acid oxidation, and in a long time frame, by increasing mitochondrial content and the use of mitochondrial substrates as an energy source.
• It has been speculated that AMPK might mediate the beneficial effects of CR.
• Thus, activators of AMPK may have potential as novel therapeutics for regulation of life span and a mediating the beneficial effects of CR.

• Metformin (N,N-dimethylbiguanide), a biguanide, that is widely used to treat type 2 diabetes mellitus.

• AMPK activation by metformin is not a result of direct activation; instead, metformin inhibits complex I of the mitochondrial respiratory chain, leading to an increased AMP:ATP ratio. However some actions of metformin are also independent of AMPK activation.
Inhibitors of mTOR

- Mammalian target of rapamycin, a 289-kDa serine-threonine kinase that belongs to the phosphoinositide 3-kinase (PI3K)-related kinase family which is highly conserved among eukaryotes.

- In the presence of nutrients, mTOR turns off stress resistance and autophagy and activates translation which accelerates the process of aging.

- CR deactivates the TOR pathway, thus slowing aging and delaying diseases of aging.

- Rapamycin, a potent immunosuppressant drug, is a main antagonist of mTOR signaling.
Metformin is a first-line medication for the treatment of type 2 diabetes. It decreases hyperglycemia primarily by suppressing hepatic gluconeogenesis.

The molecular mechanism of metformin is incompletely understood:

- Inhibition of the mitochondrial respiratory chain (complex I),
- Activation of AMP-activated protein kinase (AMPK),
- Inhibition of glucagon-induced elevation of cyclic adenosine monophosphate (cAMP) with reduced activation of protein kinase A.

The history of metformin can be drawn directly from the use in medieval Europe of Galega officina. The active compound from the extract of G. officinalis was found to be guanidine possessing hypoglycemic activity.
TAME project
Targeting Aging with Metformin

Researchers hope to find drugs that extend a person’s healthy years.

Ageing pushed as treatable condition

“What we’re trying to do is increase health span, not look for eternal life.”

Nir Barzilai
Albert Einstein College of medicine, New York
Metformin as a Tool to Target Aging

Nir Barzilai,1,* Jill P. Crandall,1 Stephen B. Kritchevsky,2 and Mark A. Espeland2
1Institute for Aging Research, Albert Einstein College of Medicine, Bronx, NY 10461, USA
2Wake Forest Older Americans Independence Center and the Sticht Center on Aging, Wake Forest School of Medicine, Winston-Salem, NC 27157, USA
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http://dx.doi.org/10.1016/j.cmet.2016.05.011

1060 Cell Metabolism 23, June 14, 2016 © 2016 Published by Elsevier Inc.

REVIEW ARTICLE
Repurposing metformin: an old drug with new tricks in its binding pockets
Rosalina Pryor* and Filipe Cabrelro*1
1Institute of Structural and Molecular Biology, University College London, Gower Street, London WC1E 6BT, U.K.

Cell Cycle
ISSN: 1538-4101 (Print) 1551-4005 (Online) Journal homepage: http://www.tandfonline.com/loi/kccy20

Metformin: Do we finally have an anti-aging drug?
Vladimir N. Anisimov

To cite this article: Vladimir N. Anisimov (2013) Metformin: Do we finally have an anti-aging drug?, Cell Cycle, 12:22, 3483-3488, DOI: 10.4161/cc.26928
Metformin Alleviates Altered Erythrocyte Redox Status During Aging in Rats

Geetika Garg, Sandeep Singh, Abhishek Kumar Singh, and Syed Ibrahim Rizvi

Antiaging Effect of Metformin on Brain in Naturally Aged and Accelerated Senescence Model of Rat

Geetika Garg, Sandeep Singh, Abhishek Kumar Singh, and Syed Ibrahim Rizvi
Functions of ascorbic acid in humans and other mammals

- **Antioxidant**

- **Cofactor in several important enzymatic reactions:**
  Synthesis of catecholamines, carnitine, cholesterol, amino acids
  And certain peptide hormones

- Hydroxylation of proline and lysine residues in collagen, allowing proper
  Intracellular Folding of procollagen for export and deposition as mature collagen

- Assisting other prolyl and lysyl hydroxylases in the hydroxylation of hypoxia
  Inducible factor 1α (H1F - 1α)

In all its functions, ascorbate serves as a one-electron donor,
 generating the ascorbate free radical (AFR)
PLASMA MEMBRANE REDOX SYSTEM

Eukaryotic cells display a plasma membrane redox system (PMRS) that transfers electrons from intracellular substrates to extra cellular electron acceptors.

**Proposed functions:**

- maintenance of redox state of sulfhydryl residues in membrane proteins
- neutralization of oxidative stressors outside the cells
- stimulation of cell growth
- recycling of α tocopherol
- reduction of lipid hydroperoxides
- maintenance of the extra cellular concentration of ascorbic acid
Ascorbate recycling between plasma and erythrocytes

- **PMRS AFR reductase**
- **L-ascorbic acid (AA)**
- **Ascorbate free radical (AFR)**
- **Dehydro ascorbic acid (DHA)**
- **Diketogulonic acid**

**Only man, monkeys, guinea pigs, some birds cannot synthesize AA.**

**Significantly aging is much faster in humans compared to animals which synthesize AA.**

**GSSG**

**GSH**

**DHA**

**Glut**

**RBC**

**Plasma**

**NADPH**

**AA**
A significant positive correlation between the activity of PMRS of erythrocytes and human age.

The role of PMRS in the survival of rho cells have been studied.

Elevated activity of PMRS reported in diabetic nephropathy.
The Essential Nutrient Theory (ENT) of John Ely

The nutritional deficiency of ascorbic acid is perhaps the cause of most visible signs of aging.

All connective tissue throughout the body exhibits both loss of flexibility and elasticity.

Aging is characterized by cross linking and loss of solubility of collagen and elastin.

AGING IS SCURVY

\[ R = \frac{\text{Life Expentancy (LE)}}{\text{Age of first estrus (AFE)}} \]

Humans have \( R \approx 8 \), mammals which can synthesize ascorbic acid have high \( R \) (horse > 20)

Antioxidant-Rich Beverages

How do the popular beverages compare in antioxidant activity?

Antioxidant compounds are found in vegetables, fruits and many natural beverages like tea. Balanced diets are naturally-rich in antioxidants. Enjoy the variety, flavours and health potential in every serving!

2 cups black tea = 1 glass red wine = 7 glasses orange juice = 20 glasses apple juice

Electron transport chain

Food → Carbohydrates → Lipids → Protein

Krebs Cycle (Citric Acid Cycle)

Electron transport chain diagram:
- Complex I: FeS + NADH → FAD + Q
- Complex III: Q → Cytc → Cytc1 → Cytc2 → Cytaa3
- Complex IV: Cytaa3 → CuA → Cyta, O2 + 4H+ → H2O

Intermembrane space
Inner mitochondrial membrane
Matrix
Anti-oxidant effect of black tea supplementation in rats

1.75 g tea + 100 ml
Kept at 90° C. Left for 15 min centrifuged

Infusion given to rats for 5 weeks (1ml/100 g body weight)
Single dose

Black tea infusion

Antioxidant potential of plasma
Lipid peroxidation
Protein oxidation
Intracellular GSH
Membrane –SH groups
Plasma membrane redox system
Antioxidant enzymes

Measurement of different parameters of oxidative stress

Blood obtained from rats

Infusion given to rats

Anti-oxidant effect of black tea supplementation in rats

Black tea
Effect of black tea supplementation on parameters of oxidative stress in rats

- FRAP (plasma) measurements:
  - Young (5 months)
  - Aged (18 months)

- PMRS activity measurements:
  - Young (5 months)
  - Aged (18 months)
Effect of black tea supplementation on parameters of oxidative stress in rats

- Reduced glutathione
- Malondialdehyde content

Young (5 months) vs Aged (18 months)

- Control BTS
- Control BTS
Effect of black tea supplementation on parameters of oxidative stress in rats
THE FRENCH PARADOX

The French exhibit an astonishing 42% lower incidence of heart disease while consuming one of the highest fat diets and smoking habits.

Resveratrol, in wine is thought to account large part for the so-called “French Paradox".
Polyphenols constitute one of the most ubiquitously distributed group of secondary metabolites found widely in fruits, vegetables, wine, tea, extra virgin olive oil, chocolate and other cocoa products.

More than 6000 polyphenols have been found which show a great diversity.
Anti aging interventions ..... 

Tocopherol (vitamin E)

The vitamin E or a-tocopherol is a powerful lipophilic chainbreaking antioxidant that acts as an inhibitor of lipid peroxidation

Carnosine

Carnosine (b-alanyl-L-histidine) a naturally occurring dipeptide is found in many tissues, particularly in skeletal tissues. It is often termed as an anti-aging peptide and there is evidence which suggests that the tissue level of carnosine declines with age

Lipoic acid (LA)

Is a naturally occurring compound that is synthesized by both plants and animals, including humans, and can be obtained from spinach, tomatoes and rice bran. The potential therapeutic use of LA is gaining increased scientific and medical interest as an anti-aging supplement
**Anti aging interventions .....**

**Cysteine : Amino acid having a free –SH group**

Food sources of cysteine include poultry, yogurt, egg yolks, red peppers, garlic, onions, broccoli, and wheat germ
Curcumin from curcuma longa

- Antioxidant
- Anti-inflammatory
- Anti-cancer
- Anti-atherosclerosis
- Anti-osteoarthritis
- Anti-rheumatoid arthritis
- Anti-microbial
- Neuro-protection
- Wound healing
**Aging intervention …..**

**Hormesis**: It has been suggested by Suresh Rattan that if cells and organisms are exposed to brief periods of stress so that their stress response – induced gene expression is upregulated and the related pathways of maintenance and repair are stimulated, one should observe anti-aging and longevity promoting effects. Intermittent fasting has been reported to have beneficial effects. The importance of fasting in different religions?
Exercise as a paradigm for hormesis

- Biochemically, exercise is damaging.

- But, biologically, it is generally good - **HORMETICALLY**
Fisetin as a caloric restriction mimetic protects rat brain against aging induced oxidative stress, apoptosis and neurodegeneration

Sandeep Singh¹, Abhishek Kumar Singh¹, Geetika Garg, Syed Ibrahim Rizwi*  
Department of Biochemistry, University of Allahabad, Allahabad 211002, India
Fisetin as a CRM protects the brain against age-dependent oxidative stress, apoptosis and neurodegeneration via activation of autophagy in rats
Fisetin as a CRM protects the brain against age-dependent oxidative stress, apoptosis and neurodegeneration via activation of autophagy in rats.
**Fisetin** as a CRM protects the brain against age-dependent oxidative stress, apoptosis and neurodegeneration via activation of autophagy in rats.
**Fisetin** as a CRM protects the brain against age-dependent oxidative stress, apoptosis and neurodegeneration via activation of autophagy in...
Redox imbalance in a model of rat mimicking Hutchinson-Gilford progeria syndrome

Manoj Kumar Chaudhary, Sandeep Singh, Syed Ibrahim Rizvi

Department of Biochemistry, University of Allahabad, Allahabad 211002, India
The human lifespan is the longest amongst other animals of comparable mass.

Evolutionary forces have extended human lifespan. Thus interventions which show promise on short-lived organisms may not work on humans.
Can human life be extended?

Prof Leonard Hayflick:  No

Prof Aubrey de Grey:  Yes

SENS
Strategies for Engineered Negligible Senescence

Although the prospect of extending human lifespan seems inconceivable, all efforts aimed to extend human life span will continue to fascinate mankind!!
This presentation is dedicated to the real son of India

Captain Kapil Kundu, who died fighting at the border

his words

Life must be big, not long
May you live until 120

in HEBREW: עד מאה ושערים שנה

THANK YOU
Nothing in Biology Makes Sense
Except in the Light of Evolution

THEODOROS DUBHANSKY

The human lifespan is the longest amongst other animals of comparable mass

Evolutionary forces have extended human lifespan. Thus interventions which show promise on short-lived organisms may not work on humans.
May you live until 120",

(in Hebrew: "ועד מאה ועשרים שנה")