Kyle Brewer
ETTA Biotechnology
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kyle@ettabiotechnology.com

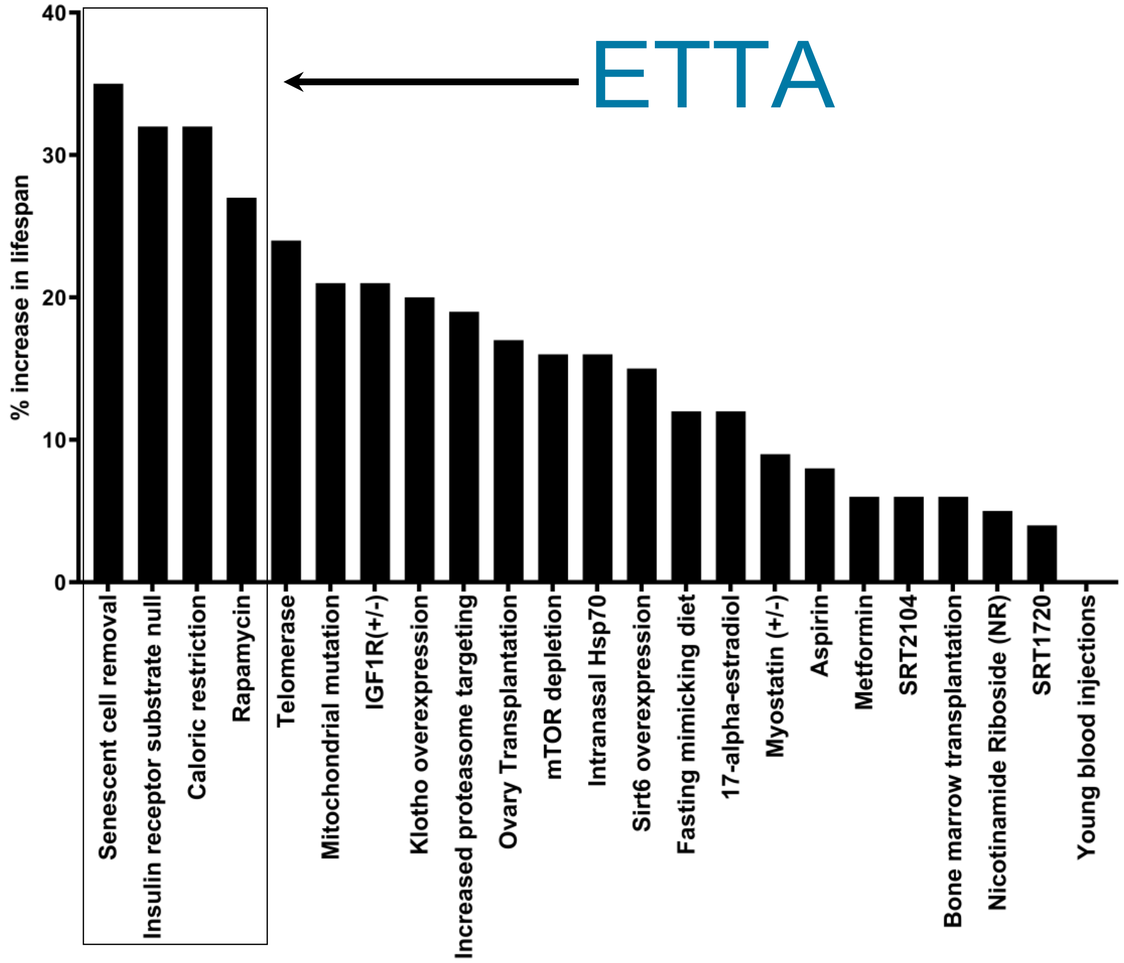
Founder: Kyle Brewer

- Designed and developed >100 preclinical mRNA and DNA therapies.
- Second scientist at Rejuvenation Technologies, a Stanford mRNA startup.
- Postdoc at Stanford in the Wyss-Coray lab (young blood factors for brain rejuvenation).
- 2 patents filed for oral and topical fisetin nanoparticles.

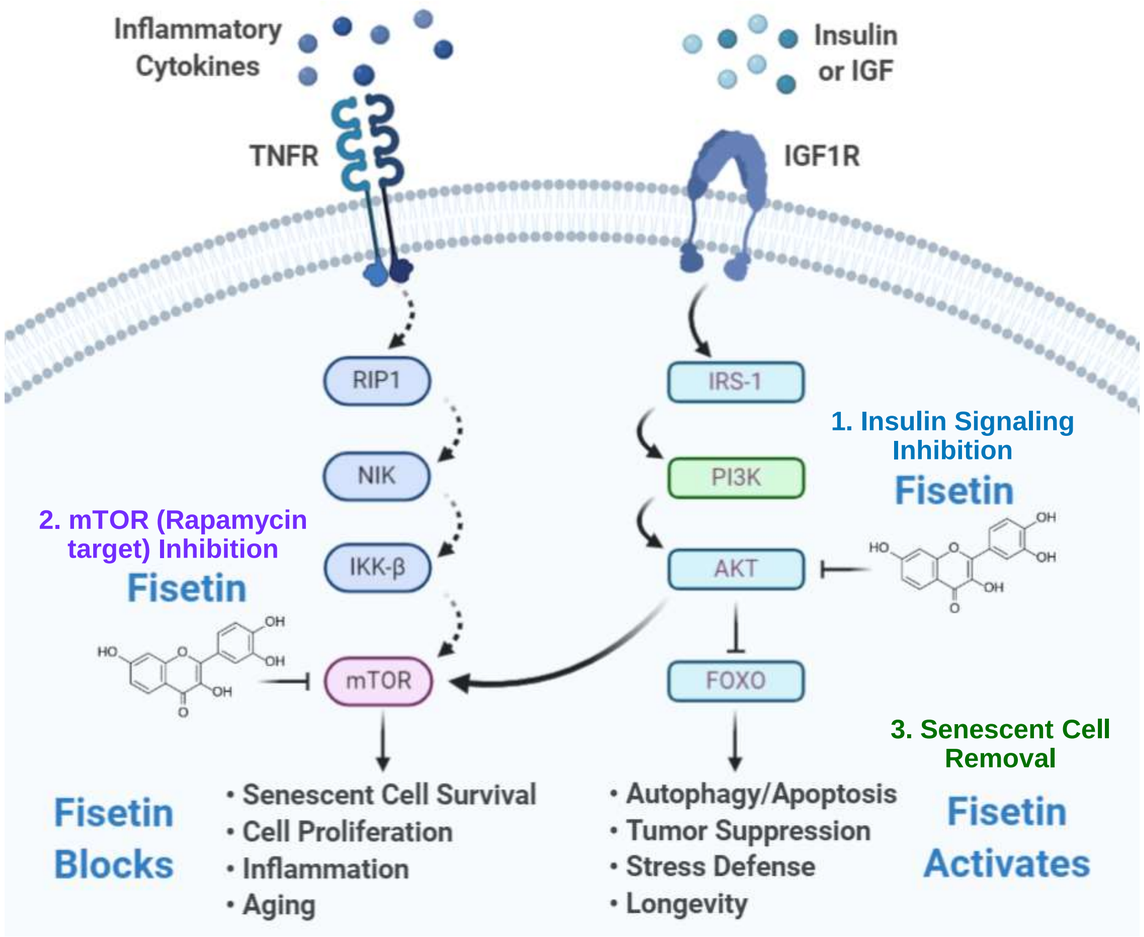
ETTA Biotechnology Highlights

- **Potential to extend healthy lifespan by 30 years.**
- **Emerging evidence to treat over 60 diseases and conditions.**
- **Estimated to be a $367 trillion market by London economists.**
- **90%+ efficacy in initial tests and case studies.**

ETTA‘s Goal Is to Make the Most Powerful Aging Interventions



Fisetin as a Therapeutic for Aging



Kyle Brewer - ETTA Biotechnology
Matthew J Yousefzadeh et al, 2018 EBioMedicine
Vaqar Mustafa Adhami et al, 2012 Biochem Pharmacol

Emerging Evidence for Benefits of Fisetin In:

Crohn's Disease and Colitis (Inflammatory Bowel Disease), Poor Digestion
Psoriasis, Dermatitis, Scarring
Alzheimer's, Parkinson's, Huntington's, Multiple Sclerosis, Dementia, Neurodegeneration, Poor Sleep, Headaches
Heart Disease, Atherosclerosis, Stroke, Hypertension, Heart Failure, Cardiomyopathy, Vascular Disease, Calcification
Chronic Obstructive Pulmonary Disease (COPD), Pulmonary Fibrosis, Tobacco/Vaping (Smokers Lung)
Fatty Liver Disease, Liver Cirrhosis, Kidney Disease, Renal Failure
Cancer (Colon, Lung, Brain, Skin, Gastric, Kidney, Liver, Pancreas, Lymphoma, Melanoma)
Osteoporosis. Osteoarthritis, Sarcopenia, Frailty
Progeria, Cockayne Syndrome, Werner Syndrome
Macular Degeneration, Cataracts, Glaucoma
Organ Transplantation Failure
Prostate Hypertrophy
Diabetes, Obesity
Hay Fever, Asthma
Inflammation, Lupus
COVID-19, Influenza, Infections, Wound Healing
Lifespan, Healthspan, Fertility

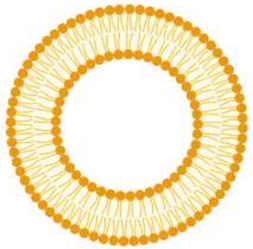
***However, fisetin has poor solubility (0.01 mg/mL) and short half-life (5 minutes)**

Harish C. Pal et al., 2016 Adv Exp Med Biol
Muhammad Imran et al., 2020 Food Sci Nutr
Grzegorz Grynkiewicz and Oleg M. Demchuk, 2019 Front Chem
Naghma Khan et al., 2013 Antioxid Redox Signal

ETTA's Nanoparticle Platform

1. Nanoparticle

Metal Core

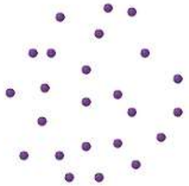


Lipid Encapsulating

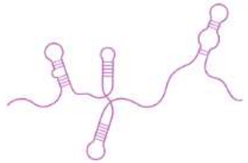
Mesoporous

And More
Iron Oxide
Copper
Gold
Platinum
Titanium Dioxide
Silica
Polymer
Hydrogels
Micelles
Coatings
Thermal Release

2. Cargo



Small Molecules



RNA

Peptides

Proteins
DNA
Antibodies
Aptamers
Lipids

3. Targeting Molecule

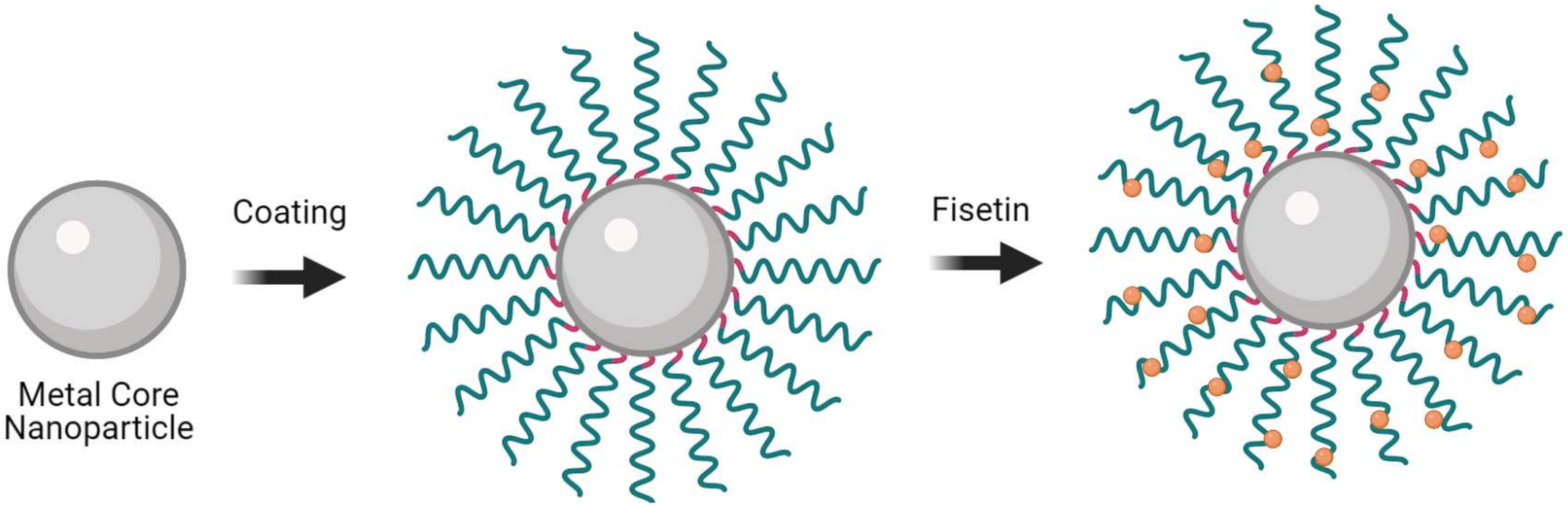
Antibodies

Cytokines

Chemical Ligands

Aptamers
Peptides
Lipids

Proprietary Topical Fisetin Nanoparticles



IP Filed

Case Study of Scar Prevention

Day 0

Day 60

- Patient presented with fingernail and chunk of flesh missing.
- Attending physician noted injury would definitely leave a scar.

Case Study of Psoriasis

Day 0

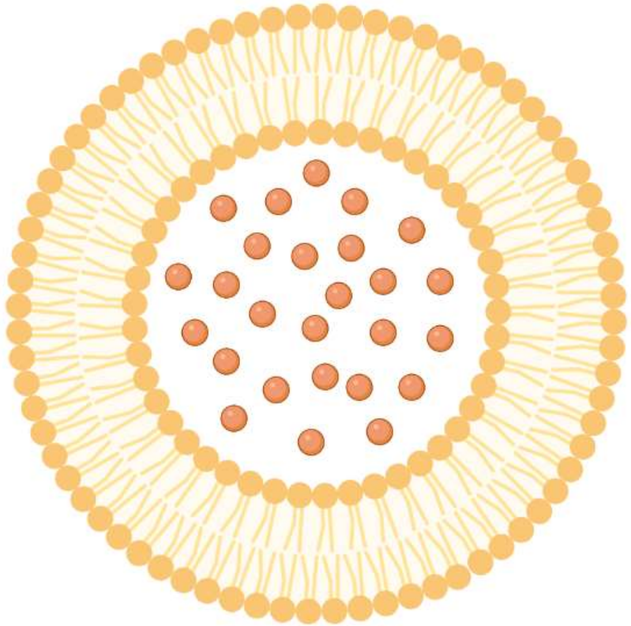
Day 7

Day 0

Day 7

- Completed: Irritation test of 25 healthy volunteers - no irritation and reports of improved skin appearance.
- More information: Reduced acne and wrinkles in collaboration with a cosmeceutical distributor.

Proprietary Oral Fisetin Nanoparticles



ET-001 Fisetin
Lipid Nanoparticle

3 People Dosed During Preliminary Safety Study:
No Negative Side Effects Observed or Reported at Highest Dose

Unexpected Early Results:
1. Improved Digestion
2. Chronic Joint Pain Permanently Relieved
3. Blood Sugar Level Lowered to Normal Level (7.3 mmol/L to 5.1 mmol/L)
4. Slight Weight Loss (0-2 kg - All Normal Weight Volunteers)
5. Brain Clarity
6. Faster Wound Healing (2x faster)
7. Reduced Headaches
8. Improved Sleep Quality

IP Filed

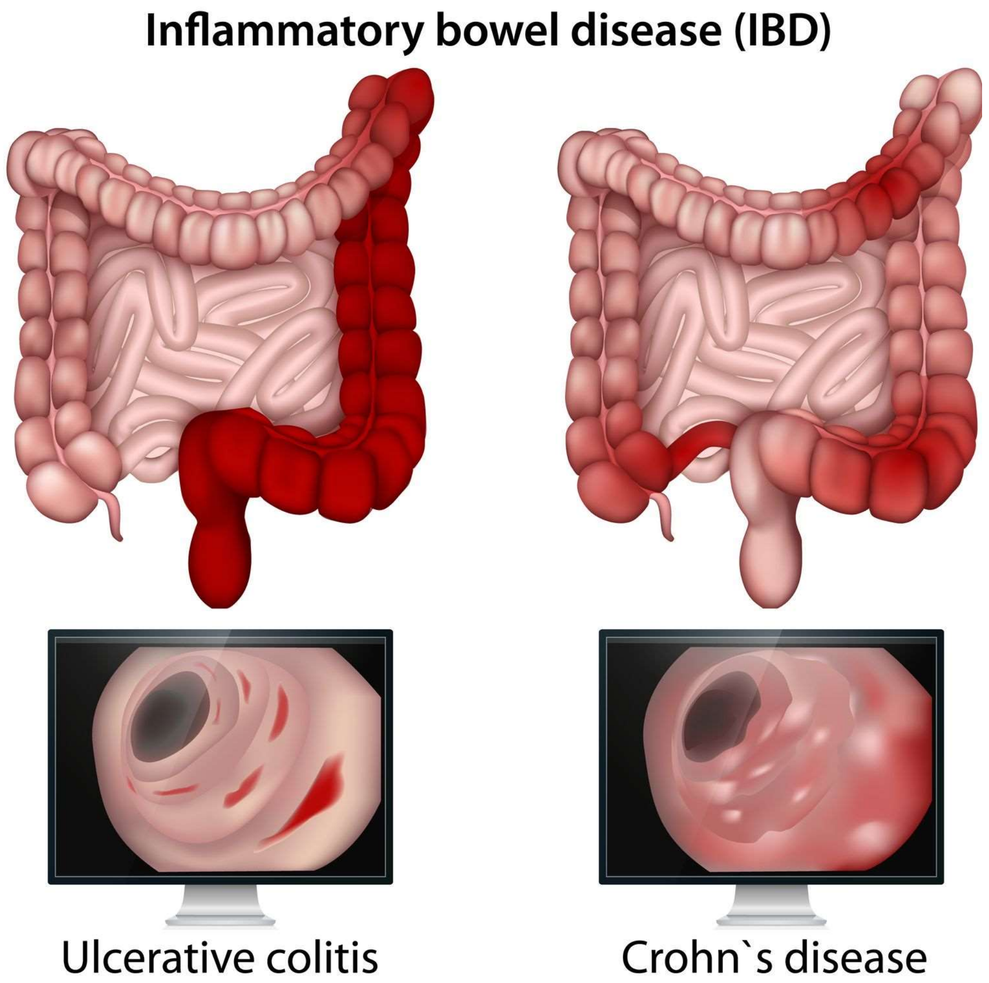
Inflammatory Bowel Disease (IBD)

IBD - $20 Billion per Year Market

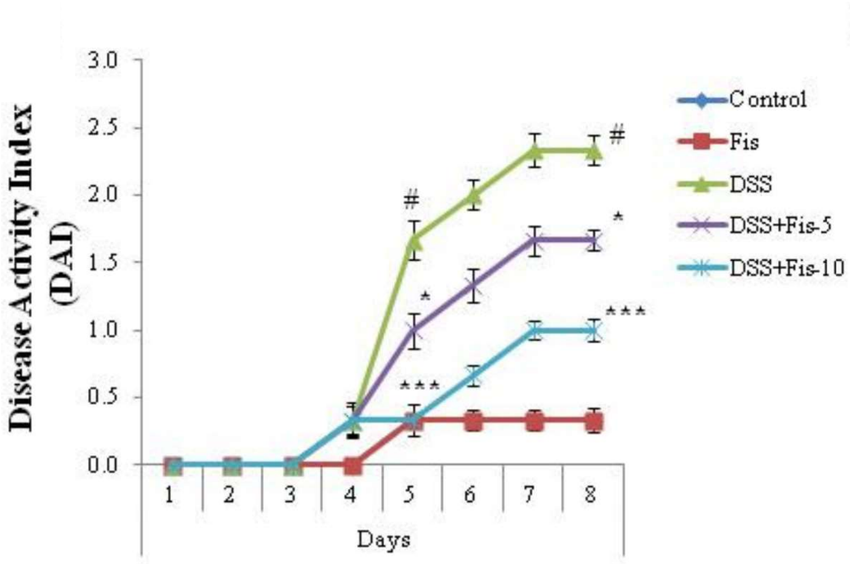
1,600,000 Million Patients in the US

Features Inflammation and Scarring

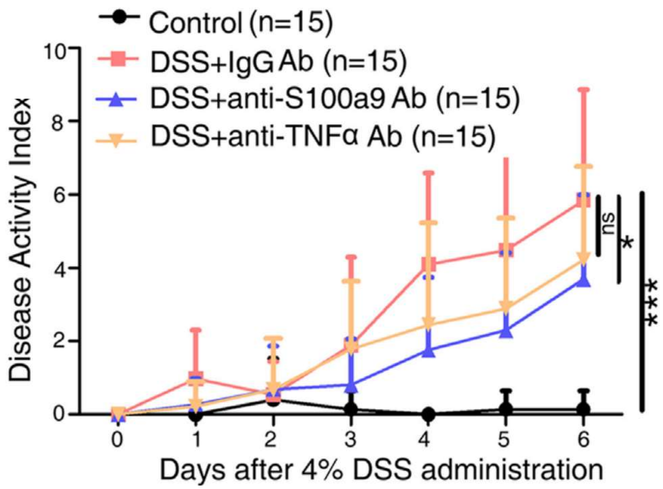
Available treatments are expensive, non-oral (biologics), hit-or-miss, or ineffective



Fisetin Outperforms Standard of Care Treatment in the Gold Standard Colitis Mouse Model of IBD



Disease Index After Fisetin



Disease Index After Standard of Care Treatment (anti-TNFα - Humira)

Goal: Iterate with fisetin nanoparticles, nanoparticle combinations, and fisetin derivatives.

***Note: Humira is the 2nd most profitable drug of all time. Pricing is $84,000 per year per patient.**

Bidya Dhar Sahu et al., 2015 JNB
Xuemei Zhang et al., 2017 Front Immunol

Economists: Increasing Life Expectancy Is Worth $367 Trillion

ANALYSIS
https://doi.org/10.1038/s43587-021-00080-0
nature aging

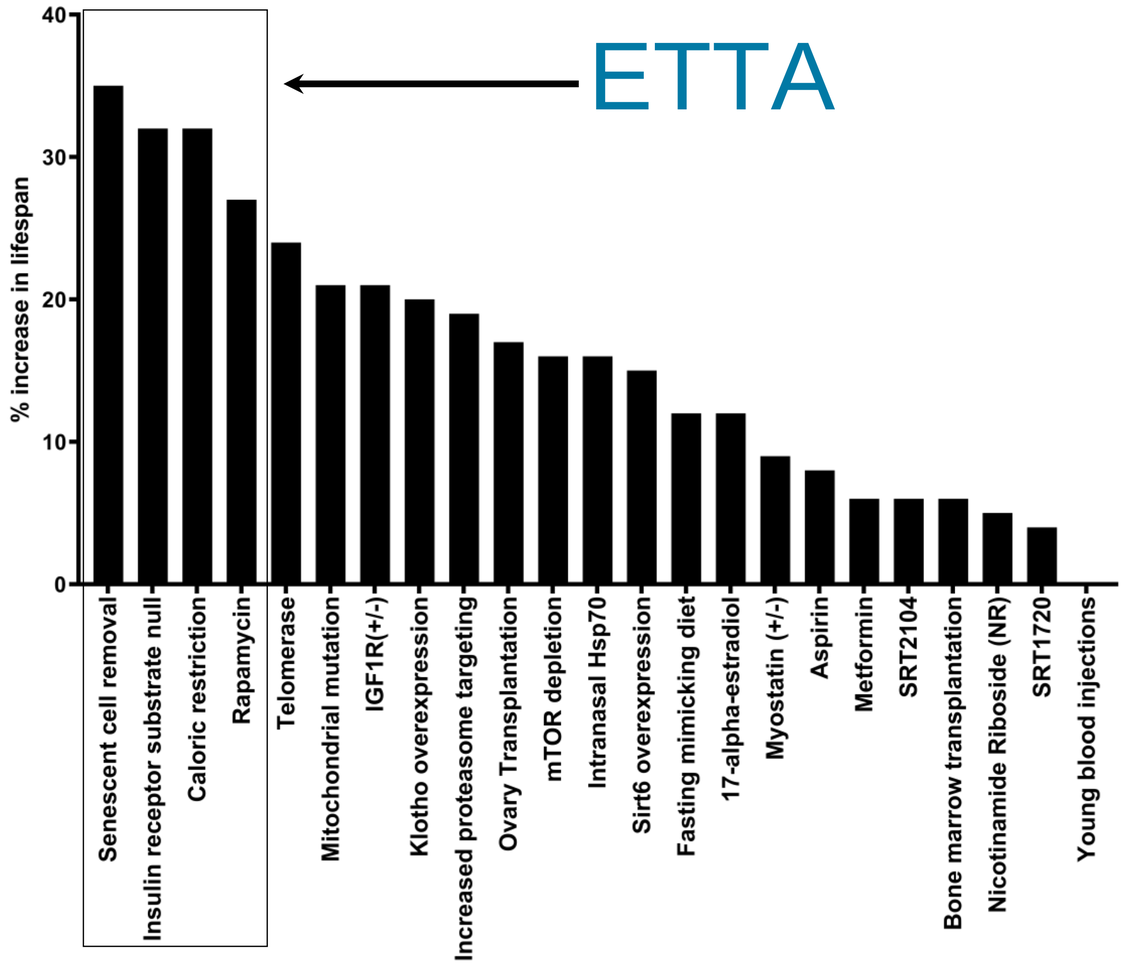
OPEN

The economic value of targeting aging

Andrew J. Scott[1]✉, Martin Ellison[2] and David A. Sinclair[3]

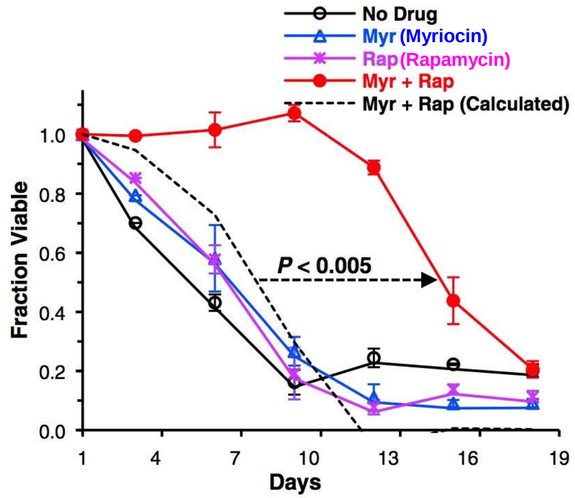
Developments in life expectancy and the growing emphasis on biological and 'healthy' aging raise a number of important questions for health scientists and economists alike. Is it preferable to make lives healthier by compressing morbidity, or longer by extending life? What are the gains from targeting aging itself compared to efforts to eradicate specific diseases? Here we analyze existing data to evaluate the economic value of increases in life expectancy, improvements in health and treatments that target aging. We show that a compression of morbidity that improves health is more valuable than further increases in life expectancy, and that targeting aging offers potentially larger economic gains than eradicating individual diseases. We show that a slowdown in aging that increases life expectancy by 1 year is worth US$38 trillion, and by 10 years, US$367 trillion. Ultimately, the more progress that is made in improving how we age, the greater the value of further improvements.

ETTA‘s Goal Is to Make the Most Powerful Aging Interventions

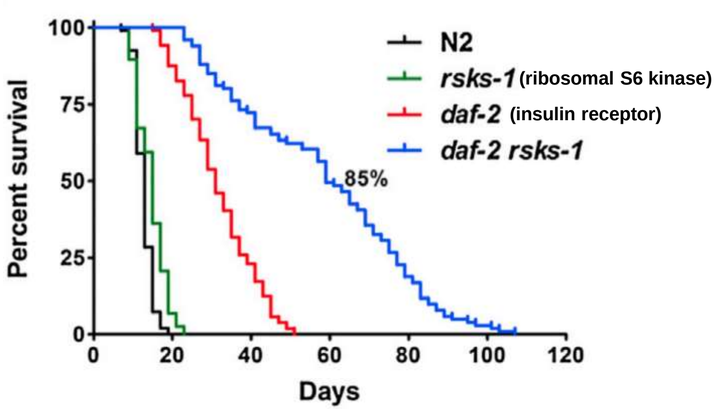


Combinations are the Future of Aging Interventions

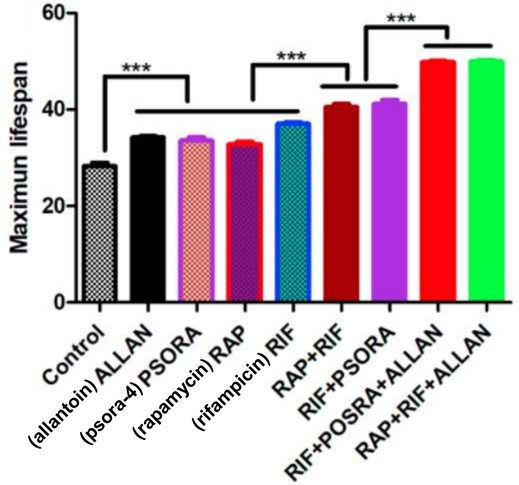
Yeast



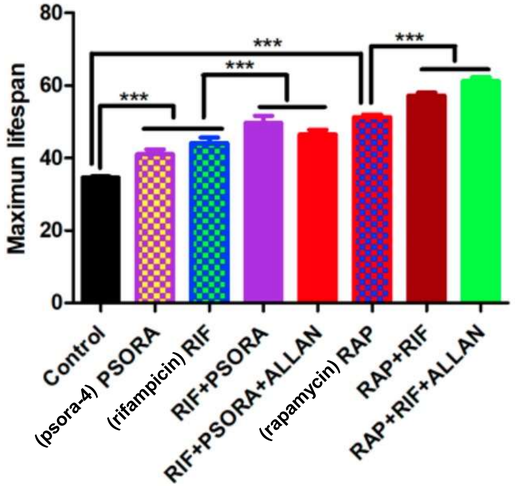
Worms



Worms



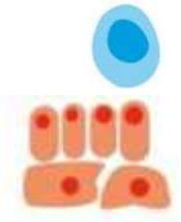
Flies



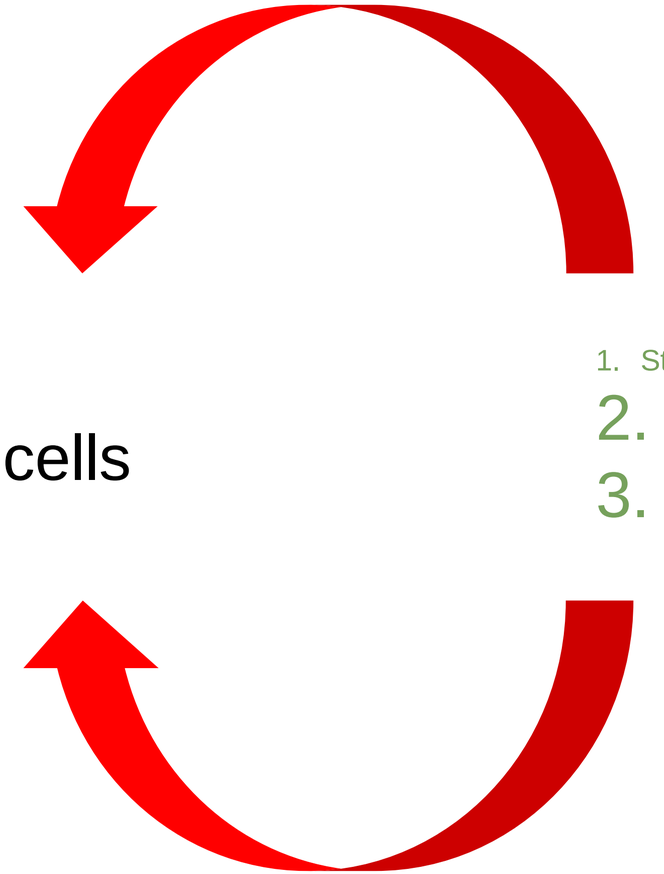
Xinhe Huang et al., 2013 Aging Cell
Di Chen et al., 2013 Cell Reports
Tesfahun Adamsu et al., 2018 Developmental Cell

Minimal Model of Aging and Rejuvenation

Rejuvenated

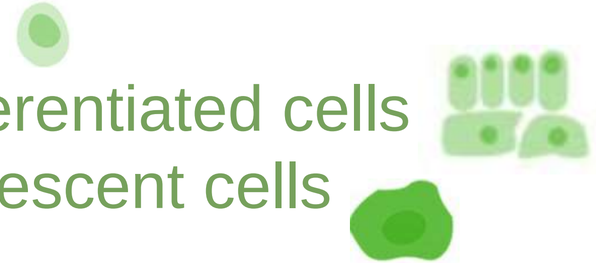


1. Stem cells
2. Differentiated cells



Old

1. Stem cells
2. Differentiated cells
3. Senescent cells



Xinhe Huang et al., 2013 Aging Cell
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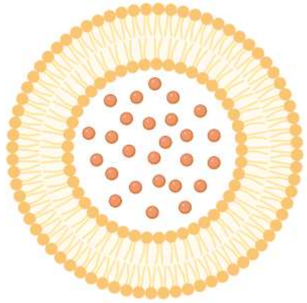
ETTA’s Nanoparticles

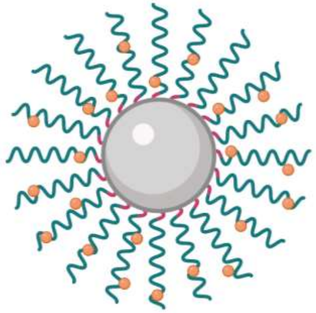


ET-001

Oral Fisetin Nanoparticle

Remove the Senescent Cells
(+35% Lifespan)

IP Filed

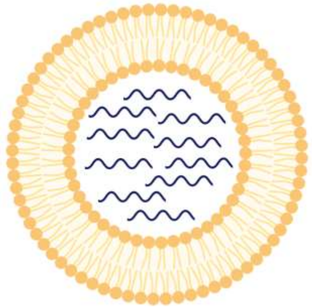


ET-002

Topical Fisetin Nanoparticle

Treat Skin Conditions and Aging

IP Filed

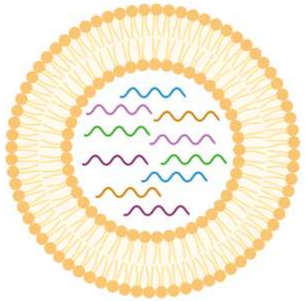


ET-003

Gene X Nanoparticle

Provide Exceptional Longevity
(+40% Lifespan)

Upcoming



ET-004

mRNA Reprogramming Nanoparticle

Restore the Stem Cells
(+15% Lifespan?)

Planned

Team

Kyle Brewer, PhD

15 years experience with nanoparticles, including for drug delivery, mRNA delivery, DNA delivery, tissue targeting, and aging

Lulu Lorien, MSFA

5 years experience in cosmeceutical and nanotechnology industries

Biao Zhang, PhD

30 years experience as a serial entrepreneur in nanotechnology with multiple successful exits

- Reflectivity, Inc acquired by Texas Instruments in 2008
- True Material acquired by Affymetrix in 2011

Matt Yousefzadeh, PhD

Assistant Professor - U. of Minnesota
Discovered Fisetin is a Senotherapeutic and Extends Lifespan

Jean Chamcheu, PhD

Assistant Professor - U. of Louisiana Monroe
Dermatology of Fisetin Topicals

Khalid El Sayed, PhD

Professor - U. of Louisiana Monroe
Pharmacology of Fisetin

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