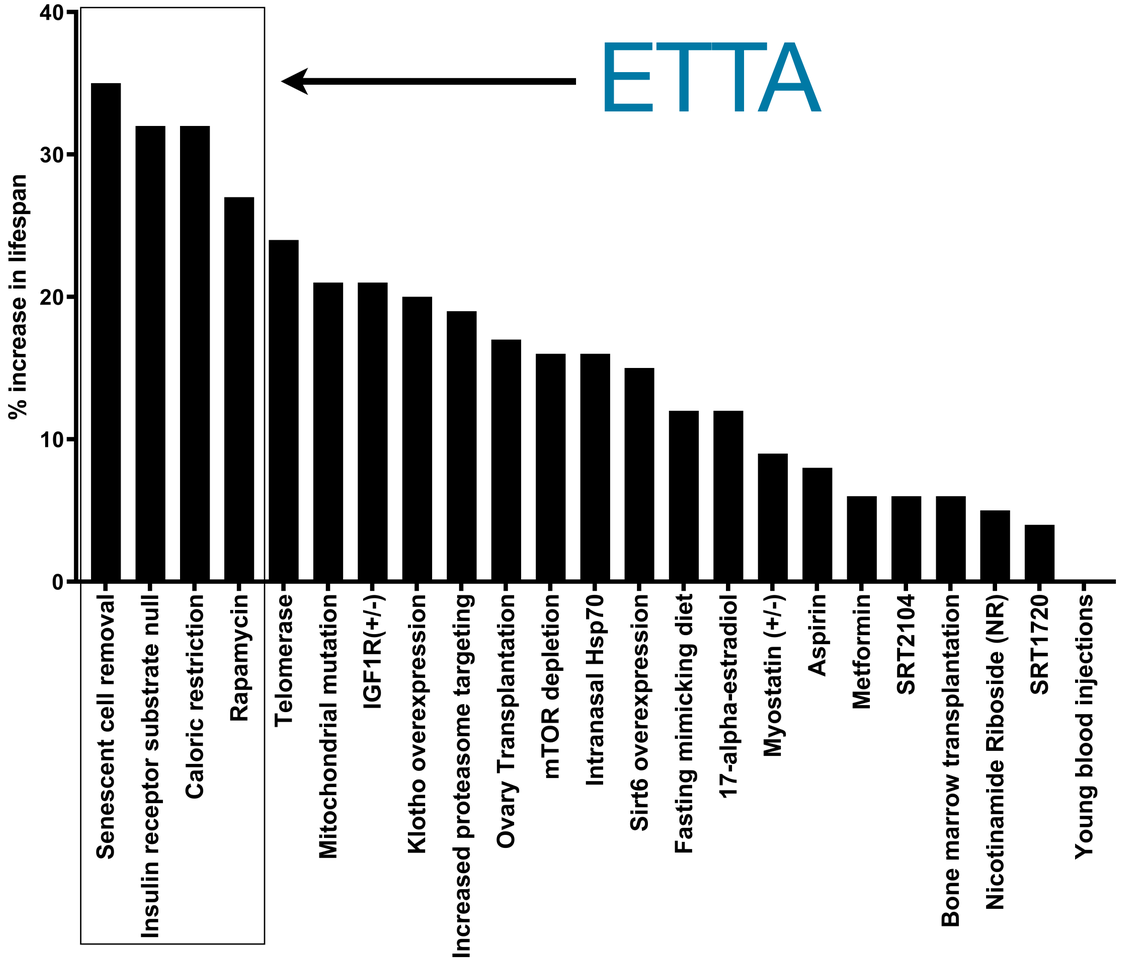
ETTA Biotechnology

Evidence-based Treatments Targeting Aging

ETTA Makes the Most Powerful Aging Interventions



- **1 year**
- **40+ people dosed**
- **90%+ efficacy in tests and case studies**

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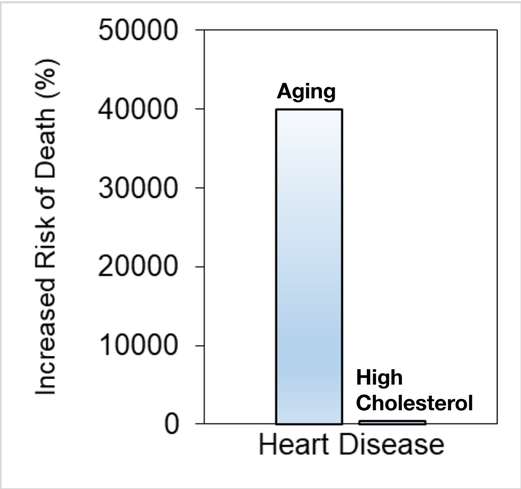
100×

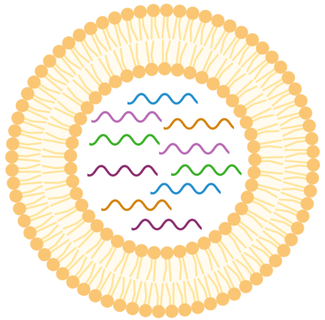
Larger effect size over traditional approaches by targeting aging.



200+ Cell Types

Nanoparticle Platform

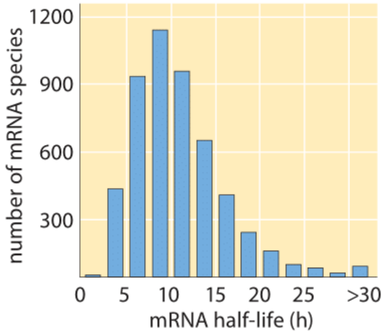
Developing the ability to target all cells, not just a few.



1 Day to 10 Year

Gene Therapy Platform

The versatility of mRNA without the transience.



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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 ETTA Biotechnology (oral and topical fisetin nanoparticles).

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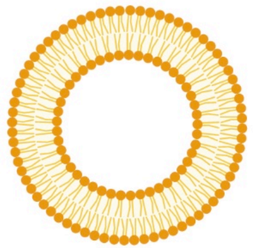
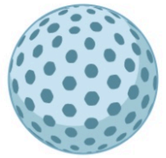
ETTA's Nanoparticle Platform

1. Nanoparticle

Metal Core



Lipid Encapsulating

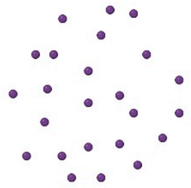


Mesoporous

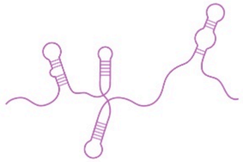
And More

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

2. Cargo



Small Molecules



RNA

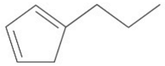
Peptides

Proteins
DNA
Antibodies
Aptamers
Lipids

3. Targeting Molecule

Antibodies

Cytokines



Chemical Ligands

Aptamers
Peptides
Lipids

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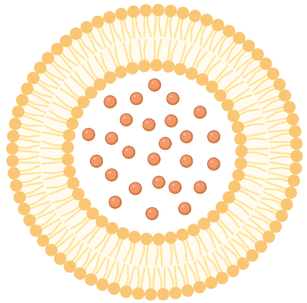
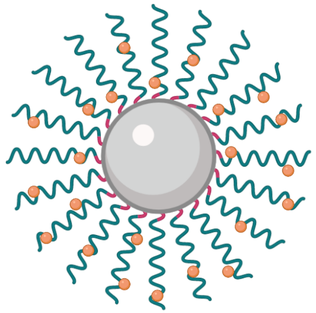
Our Nanoparticles



Oral Fisetin Nanoparticle

ET-001

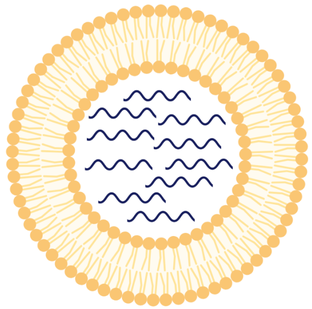
IP Filed



Topical Fisetin Nanoparticle

ET-002

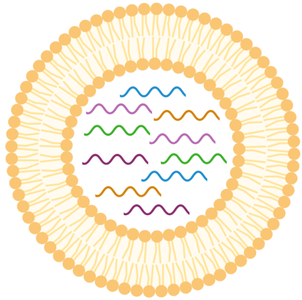
IP Filed



Gene X Nanoparticle

ET-003

Designed



mRNA Reprogramming Nanoparticle

ET-004

Planned

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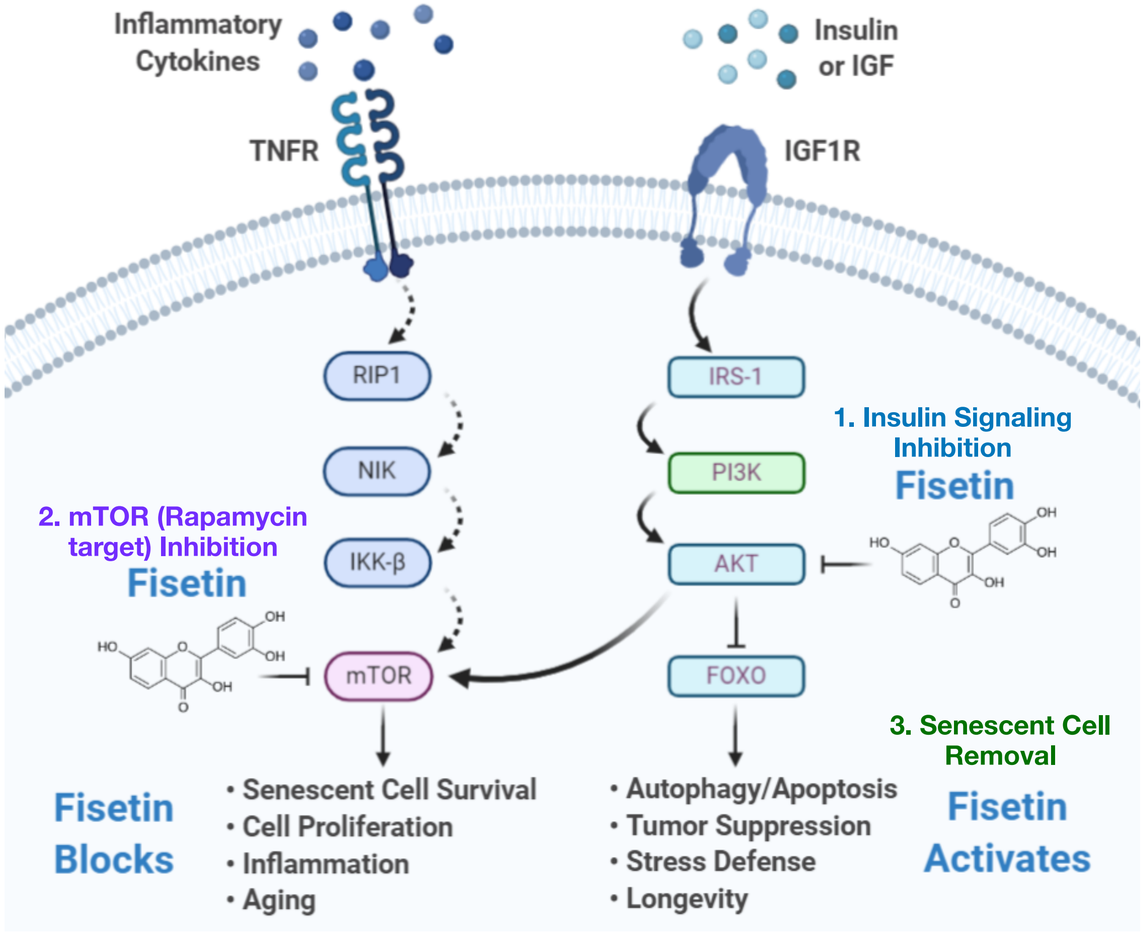
Fisetin as a Therapeutic for Aging



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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, 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

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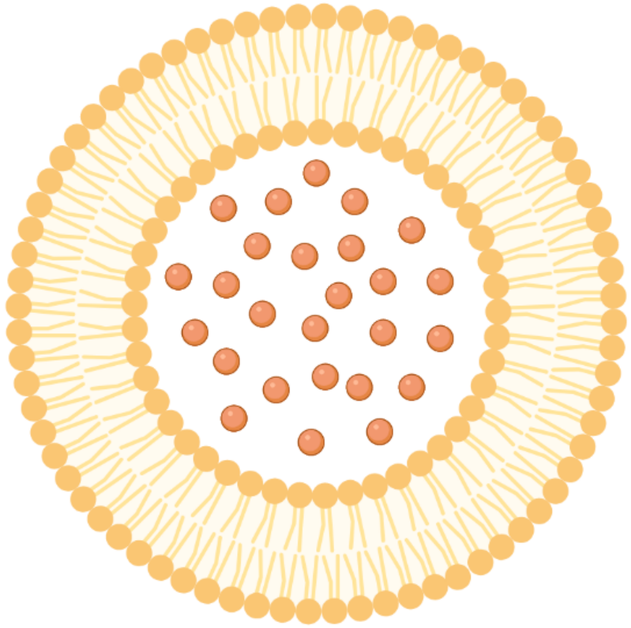
Harish C. Pal et al., 2016 Adv Exp Med Biol
Muhammad Imran et al., 2020 Food Sci Nutr

ET-001: Our Proprietary Oral Fisetin Nanoparticles for Aging



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

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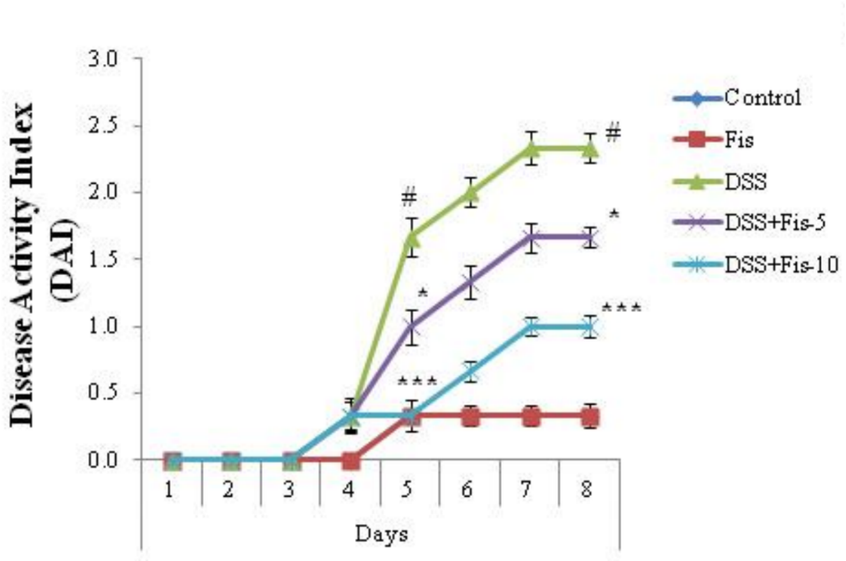
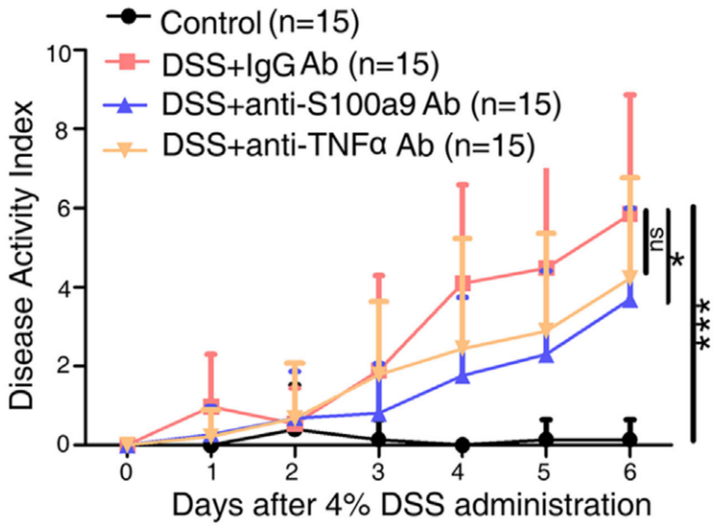
Fisetin: Inflammatory Bowel Disease (IBD) as Initial Indication

IBD - $20 Billion per Year Market
1,600,000 Million Patients in the US



Disease Index After Fisetin



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

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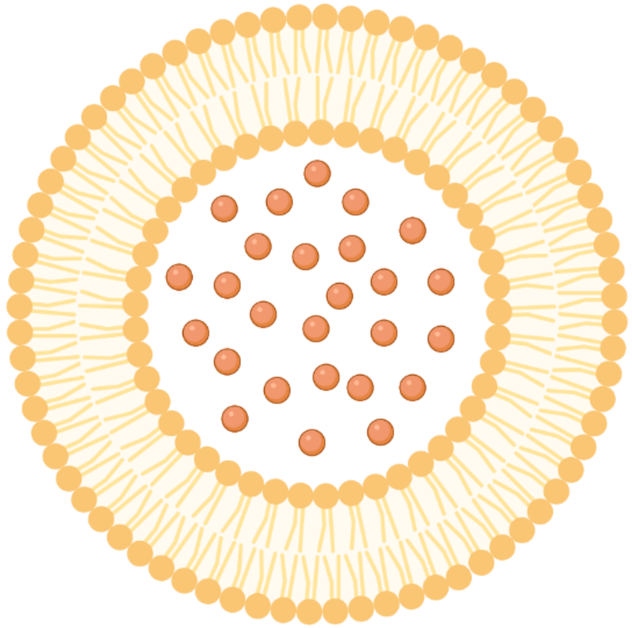
Bidya Dhar Sahu et al., 2015 J Nutr Biochem
Xuemei Zhang et al., 2017 Front Immunol

Market Estimate for ET-001



ET-001 Fisetin
Lipid Nanoparticle

Cost of production

$5 per dose (60 doses taken per year)

US, Europe, and China

1.25 billion people x $12000 profit per year = $15 trillion profit per year

Market Capitalization

$300 Trillion

Note: Humira costs $84,000 per year

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Economists: Increasing Life Expectancy Is Worth $367 Trillion

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

nature aging

Check for updates

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.

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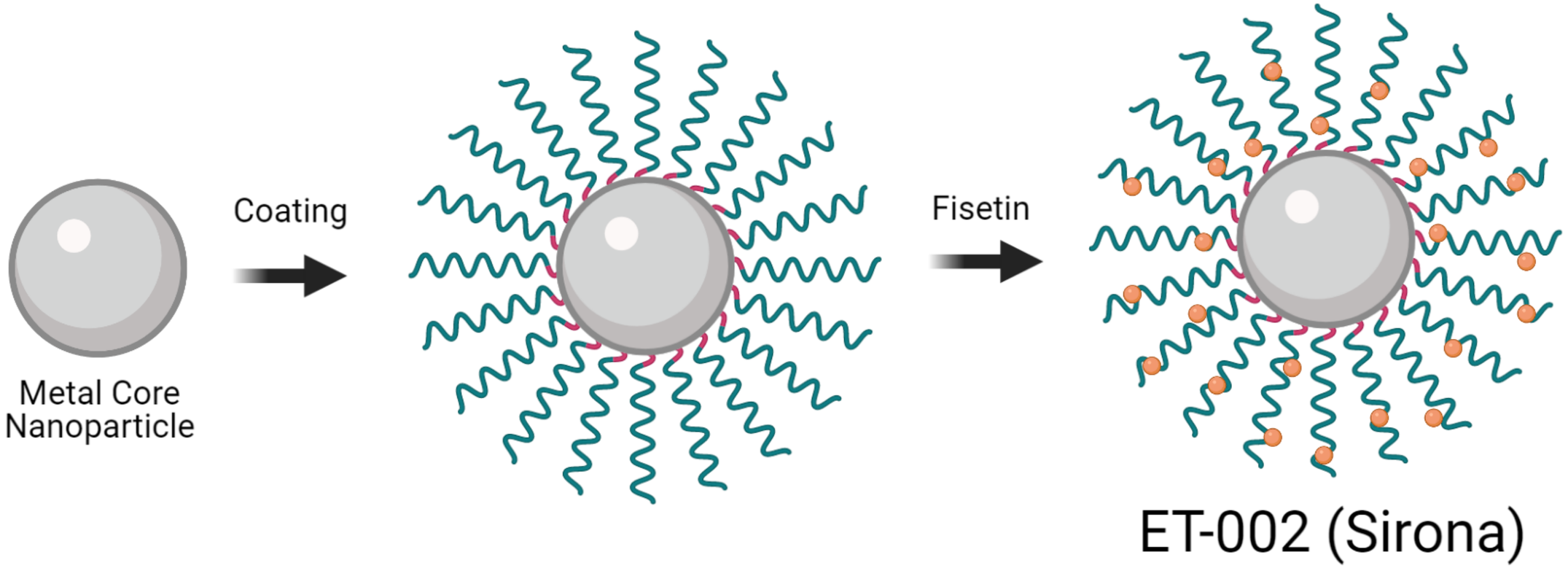
ET-002 (Sirona): Our Proprietary Topical Skin Nanoparticles



IP Filed

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Case Study of Scar Prevention Using ET-002

Day 0

Day 60

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

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Case Study of Psoriasis Using ET-002

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 large cosmeceutical distributor.

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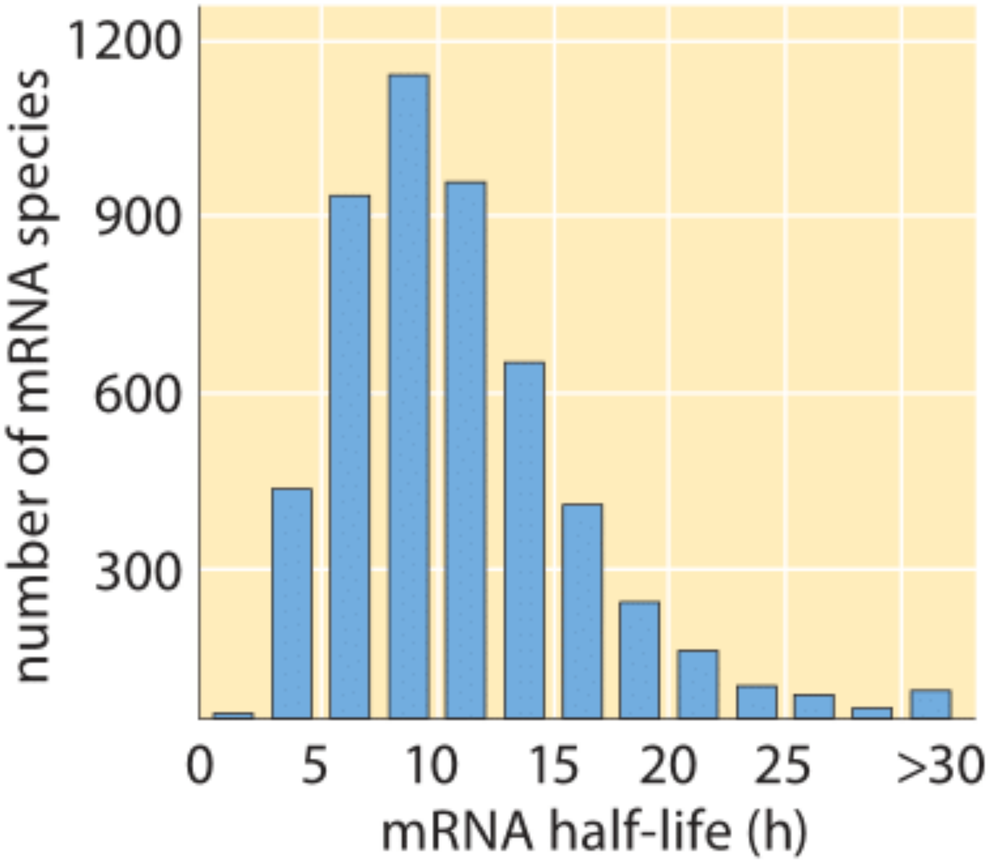
Short mRNA Half-Life Is Often a Major Drawback



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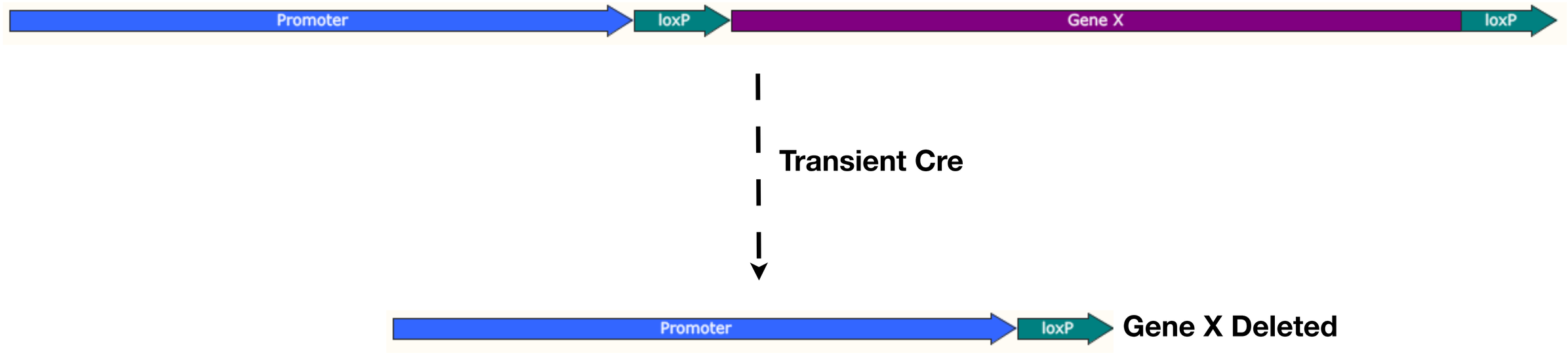
adapted from Jonathan A Bernstein et al, 2002 PNAS

Our Tunable, Reversible, Controllable Gene Therapy Platform



Expression of delivered DNA gene can be turned down or off by transient introduction of Cre protein.

- Overcomes the transient nature of mRNA for gene delivery as long as wanted or needed.
- Gene dose can be turned down for personalized medicine with lower doses of transient Cre

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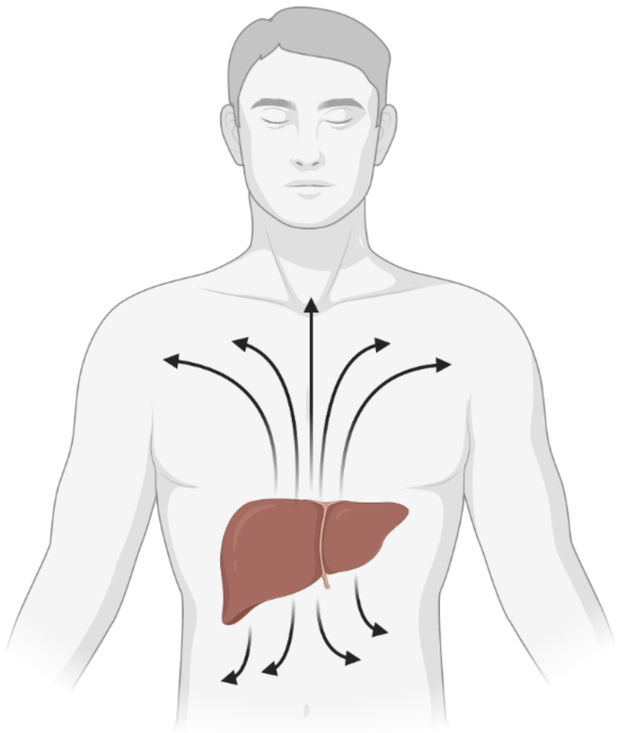
Gene X Nanoparticle: Treatment for High Cholesterol and Lifespan



Gene X

High Cholesterol - $22.6 Billion per Year Market
94,000,000 Million Patients in the US

Gene X increased lifespan by 40% in transgenic mice, **and Gene X protein delivery reduces cholesterol** in mice.

In humans, higher Gene X level is associated with **lower LDL, higher HDL, lower body weight, lower blood pressure.**

Gene X is delivered to the liver with nanoparticles, where it is secreted to the rest of the body.

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Gene X Analog Clinical Trial

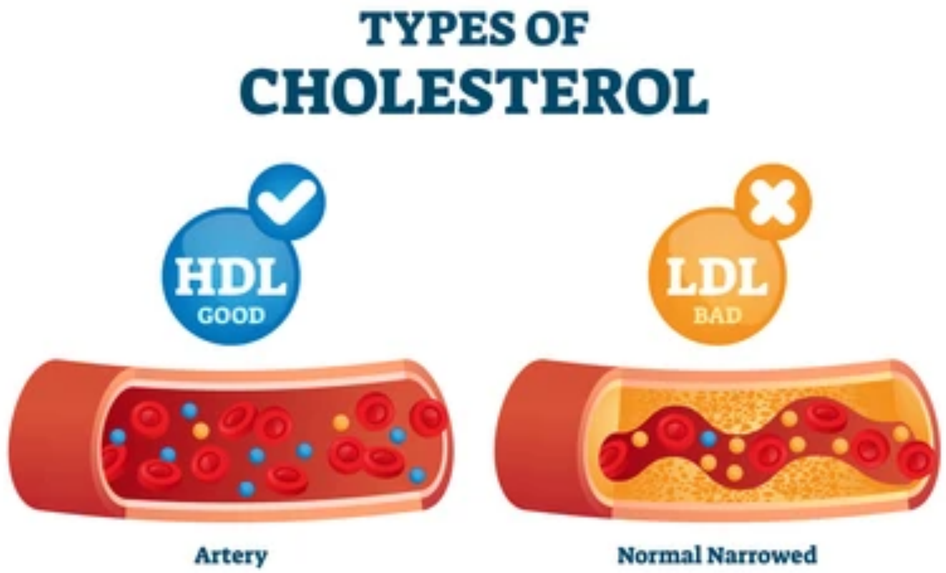
In 1 to 3 weeks:

Total Cholesterol ↓17%

Triglycerides ↓36%

HDL ↑17%

LDL ↓25%



These results indicate mRNA/DNA delivery of Gene X will also work well in human trials.

mRNA Is Still in the Medieval Period

November 15, 2021 11:17 AM EST *Updated 03:52 PM* | R&D, Cell/Gene Tx

AstraZeneca, Moderna start to raise the curtain on a new mRNA heart drug — but efficacy will have to wait

Amber Tong
Senior Editor

Can injecting messenger RNA directly into the heart of patients who've experienced heart failure help repair the organ? More than three years after AstraZeneca and Moderna launched a first-of-its-kind Phase II trial to test the idea, the pair has now shown the procedure is at least safe.

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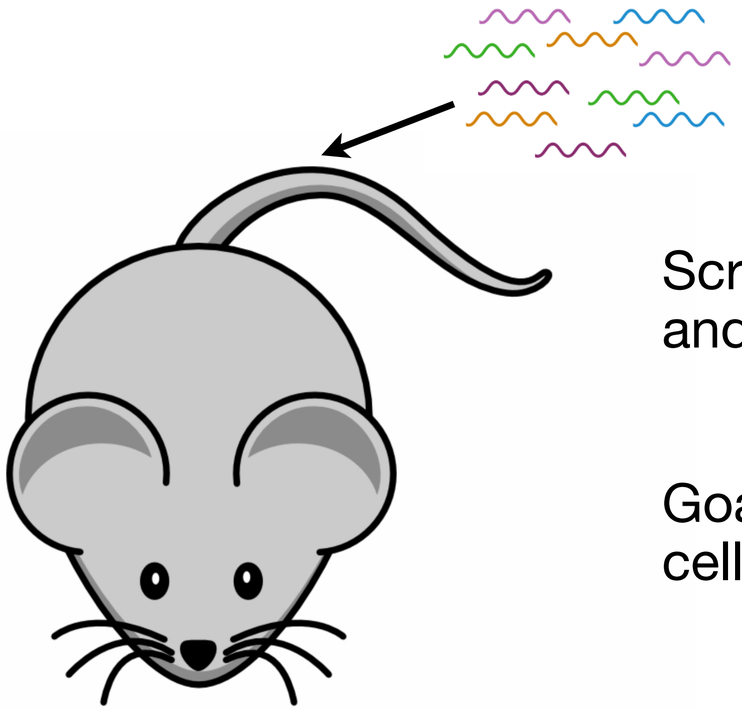
Targeted Nanoparticles: mRNA/DNA Delivery Platform



Screen 10^{14}-10^{16} targeting molecules *in vivo* to determine cell and tissue specificity.

Goal: 200+ potential patents for targeted nanoparticles to every cell and tissue type.

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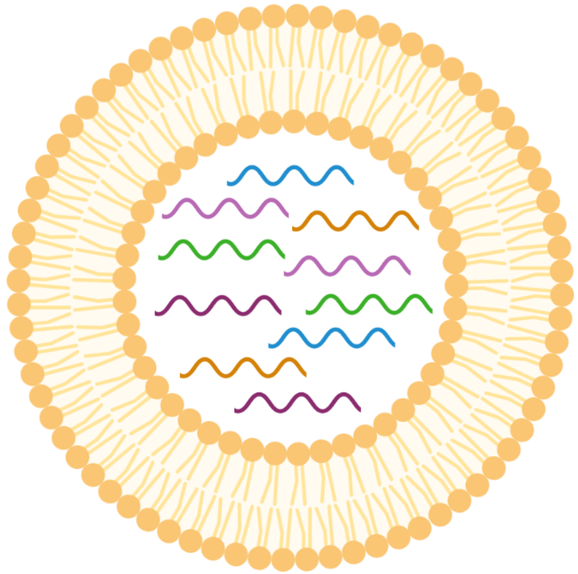
Tapash Jay Sarkar et al, 2020 Nat Commun

mRNA Reprogramming Nanoparticle



Creating iPSCs to restore youthful cells compliments other therapies because it will make a stem cell niche to rejuvenate tissues.

Will deliver to specific cells and tissues with our targeting tech.

Improved Reprogramming

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Tapash Jay Sarkar et al, 2020 Nat Commun

Revenue Model

1. Internally develop FDA approved therapies using our nanoparticle platform

2. Externally license targeted nanoparticles to mRNA and DNA delivery companies.

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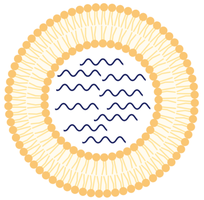
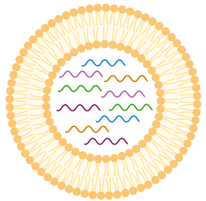
Immediate and Long-Term Strategy

1. Deliver most effective current treatments targeting aging because aging causes >90% of deaths from disease in the US (100x larger risk factor than typical drug targets).



2. Develop nanoparticle platform to target specific cells and tissues with mRNA and DNA for licensing and therapies.



3. Determine complementarity of our stand-alone therapies using machine learning (ML) models of aging for an unmatchable suite of treatments.

ETTA Biotechnology

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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