Dr. Alexander Asanov

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Total Internal Reflection Fluorescence

i-rejuvenate substances and methods provide the opportunity to add 20+ years to your healthy and happy life

Primum Non Nocere - Rejuvenate safely - First, Do No Harm



i-Rejuvenate

Raw draft of the project UNDER Construction

Inspirational

- Set an altruistic Goal larger than yourself
- Make a plan
- Cultivate a pattern to pursue the Goal
- ~4 weeks after watch that the entire Universe works for your Goal. Have fun



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1. INTRODUCTION

Rejuvenation is a topic as old as mankind. For centuries people were in quest for the fountain of youth and everlasting life. The literature on rejuvenation and longevity is enormous and rapidly growing. The recent progress was fantastic. In 2022-2024, several experts at the Longevity Summits, Dublin, claimed that If you manage to be alive in 2032-2034, you will have an opportunity to live 150-200 years or more [wwww.longevitysummitdublin.com]. There is no doubt that our children will have the opportunity of living 150-200 years or more. The drug Rapamycin, known for its potential to extend lifespan in mice, is being studied in dogs through the Dog Aging Project's "Test of Rapamycin in Aging Dogs" (TRIAD) clinical trial, with the goal of potentially extending healthy lifespan in dogs and gaining insights into human longevity. Rapamycin prolongs life in yeast, worms and flies, and it prevents age-related conditions in rodents, nonhuman primates and humans. Rapamycin and its analog, everolimus, are FDA approved for human use and have been used safely for decades. The purpose of this brochure and *i*-rejuvenate webpage is to share our findings and thoughts. We are excited about rejuvenation opportunities and hope that you will be too. Your feedback and comments will be greatly appreciated.

Primum Non Nocere – **First, Do No Harm** - **Hippocratic Oath.** We base our *i*-rejuvenate efforts on the core principle of the Hippocratic Oath – *First, Do No Harm*. There are numerous biohackers and misconceptions - underwater rocks you want to avoid. On the other hand, there are paradise islands you want to dwell on, and there are other ships sailing in the rejuvenation ocean. Certainly, longevity programs of Calico, Harvard University, NIH, and other big and small laboratories will result in revolutionary new findings and practical methods of rejuvenation. There is already a substantial body of well-verified, reliable, and harmless methods and cures. It is time to use them for your benefit to add minimum 20-40 years to an active and happy life.

Unfortunately, in the area of rejuvenation there are also plenty of harmful methods, toxic substances, and bad actors to avoid. They include biohackers who commit honest errors> Sometimes their errors are fatal. Additionally, there are knowingly toxic products and adverse methods that are driven to the market by for-profit purposes. For example, during last decade a group of celebrities died from the experimental stem cell therapy. Their ads sounded innocently: "We take your cells, cultivate them in vitro, and inject them back into your body." It may sound simple and attractive, if simplified down to one phrase. But life is a complex phenomenon. Each live cell is as complex as the Universe, while human body is like a Universe of Universes. We love simplifications. But in the case of the human body over-simplifications may be

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fatal. We should remember the principle of "Irreducible complexity", a term coined by Michael Behe, which refers to a biological system composed of several interacting parts, where the removal of any one part causes the system to cease functioning. The purpose of this webpage is to share with you our findings and thoughts. We would appreciate your comments and your thoughts. Please email to alex.asanov@tirf-labs.com.

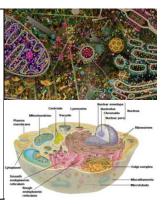
<u>Exciting Recent News</u>: Clinical trial of a drug to **regrow new tooth** is underway in Japan. It is only the beginning: https://medicalxpress.com/news/2024-12-japanese-drug-regrow-teeth.html#google_vignette

2. MULTIPLE DIMENSIONS OF HUMAN BEING

As a scientist, I am striving to understand the mechanism of aging and rejuvenation. When I look under the microscope at a live cell, I experience a religious feeling of appreciation to the supreme intelligence, which is behind life.



Fig. 1. Human body is encoded by ~25,000 genes that produce ~2 million unique proteins to build ~10 trillion of our own cells. We share our body with ~20 trillion bacterial cells and ~100 trillion bacteriophages - viruses that control bacteria. Each mammalian cell is as complex as the Universe. Images at right show simplified ideas about molecular machinery of live cells. Amazing design, isn't it? The most amazing part is that this machinery functions properly and we are healthy most of the time!





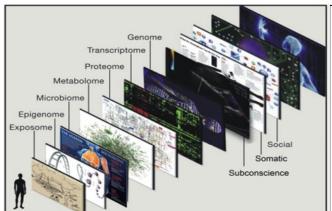


Fig. 2. There are multiple dimensions of human body, numerous systems, subsystems, organs, tissues, cells, organelles, extracellular matrix, and molecules that are related to each other, interact and depend on each other. To simplify studies, scientists created distinct disciplines, such as genomics, proteomics, microbiomics, that systematically accumulate knowledge about, genes, proteins, microbes. Mother Nature does not care about the boundaries between disciplines. All of them closely interact and depend on each other. Certain areas, such as genomics, are in advanced state, in comparison with proteomics. Genes encode, but proteins actually rule our body. DNA are more stable than proteins. For this reason genomics received abundant funding over the last decades, while proteomics and other "dimensions" still await the stage of explosive growth. Several areas are still in the stage of their infancy. One of them is the dimension of "subconscience." The effects of placebo and nocebo occur in the dimension of subconscience. However, the mechanisms are still not clear. Over decades pharma blocked funding of studies in this field.

Albert Einstein, four of my gurus, physicists, noble prize winners Dr. Semenov, Kapitza, Sakharov and Ginzburg believed in intelligent creation of life. The trial and error approach of natural evolution, in principle, cannot result in such a fantastically complex machine, which functions properly most of the time and is capable of reproducing itself. Besides, living creatures are capable of healing wounds and even regenerate lost body limbs and organs. At cellular and molecular levels it means rejuvenation — reversing back "the clicking time of aging" not just slowing down. Aging, longevity, rejuvenation are extremely complex multidimensional processes that scientists only recently began to study in depth.

3. MECHANISMS OF AGEING AND REJUVENATION

DNA methylation, telomere shortening, blood vessels blocking, mitochondria decline

To initiate the discussion, to make it interesting and practical to you, I would like to share with you my practical findings about the longevity drugs, substances, food additives, and lifestyle. I have analyzed the literature and other sources on the effects of different substances on longevity from the standpoint: "Do no harm." My mother was a medical doctor and she taught me about this ancient principle. She was an extraordinary ophthalmologist, always at high demand and busy schedule at her clinic. I was raised between home and hospitals, absorbing many good medical principles from her and her Page 2 of 15 TIRF-Labs.com/insights | Ivermectin, Vit C, DMSO provide an opportunity to add 20+++ years to your healthy and happy life

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colleagues. **"Do no harm"** is in my DNA and epigenetics from my mother. When I am ranking rejuvenation/longevity substances I base my assessments on the principle "**Do no harm"**. In the first place, they should not be toxic or harmful.

Below is my list. Later, I will add details, references to the literature, figures, video, and summary of your comments. Please send your comments and editions to alex.asanov@TIRF-Labs.com. Note: Every human being is unique and uniquely responds to medications, substances, and other stimuli. In the perfect world all medical interventions should be personalized. The literature on the effects of senolytic/rejuvenation drugs such as Dasatinib, Quercetin, Fisetin and Navitoclax, Yamanaka factors, Doxycycline, only recently was published. In particular the data on Yamanaka factors await further studies. Several independent studies demonstrated that Doxycycline in small doses is capable of reprogramming cellular aging; short-term course – 3 week of doxy 2-day/w; long-term rejuvenation - 10-months of doxy 2 d/week.

Longevity substance number 1- Vitamin C - ascorbic acid. Vitamin C is a highly potent antioxidant. It has been shown to protect against various forms of cancer, and to extend lifespan in laboratory animals. Vitamin C appears to be a uniquely non-toxic compound. It is difficult if not impossible to obtain toxic concentration in blood by mouth. Moreover, very high concentrations in blood that were obtained by intravenous (IV) infusion of Vitamin C have been shown to be non-toxic to healthy cells and tissues, while selectively destroy cancer cells. High IV doses of Vitamin C might be a sensible alternative to toxic and expensive anti-cancer chemotherapies. Its low cost, off-patent and off-label status are behind the fact that official medicine, which is controlled by big pharma, does not approve it for anti-cancer and other tratments.

Vitamin C has many benefits for human health, including: 1) Anti-oxidation effect —it protects cells from damages caused by free radicals that are produced in food metabolism and may contribute to the development of cancer, heart disease, and arthritis. 2) Vitamin C is necessary for the growth, development, and repair of all body tissues, including bones, cartilage, blood vessels, and muscle. 3) Ascorbic acid supports the proper functioning of the immune system. 4) Ascorbic acid helps the body absorb iron from plant-based foods. 5) Studies suggest that high vitamin C intake protects intellectual capabilities and memory; while low levels of vitamin C correlate with impaired thinking and memory. 6) Vitamin C promotes healthy gums, reduces allergy-related responses and the effects of sun exposure.

The body doesn't store Vitamin C. It's important to get it from your diet regularly. It helps the body make collagen, which is important for wound healing, healthy skin, cartilage, tendons, ligaments, and blood vessels. You can get ascorbic acid from fruits and vegetables, and it's also available in pill form. Linus Pauling, winner of two Nobel Prizes, studied Vitamin C and discovered numerous therapeutic benefits of this natural compound. Literature references are available here: www.lpi.oregonstate.edu. Ascorbic acid is one of a few compounds that are so non-toxic that it is impossible to consume poisonous amounts by mouth. High-dose intravenously administered vitamin C is widely used in cancer patients by complementary and alternative medicine practitioners [www.pmc.ncbi.nlm.nih.gov/articles/PMC7996511].

This section requires additional subsections on different applications and literature references.

Longevity substance number 2 - Melatonin - is the most documented anti-aging therapy. The literature on Melatonin is vast and rapidly growing. Similar to Vitamin C, Melatonin is a highly potent antioxidant, which protects us against neurological aging. There are data showing that Melatonin protects against every known age-related disease. It has been shown to extend lifespan in laboratory animals. Melatonin also regulates night sleep and other circadian rhythms. Although there has been no evidence of toxicity in any of the published studies on Melatonin, my personal experience showed some discomfort. If I took 3 mg before bed, it resulted in good night sleep, while taking 10 mg gave me a minor headache in the morning. In Europe Melatonin is a prescription drug. In the U.S. you can buy it as a food additive.

This section requires additional subsections on different applications and literature references.

Longevity substance number 3 - Acetyl-L-carnitine. There is an explosion of publications about acetyl-l-carnitine for life extension. This is a modified amino acid compound, which enters the bloodstream and penetrates cell membranes more effectively than regular l-carnitine. Acetyl-l-carnitine is beneficial to heart muscle cells, immune system, and probably enhances energy production in every cell of the body. The multi-faceted benefits of acetyl-l-carnitine in brain cells makes it the single most important supplement we can take to maintain and improve overall neurological health. Acetyl-l-carnitine has been shown to improve neurological function even after we stop taking it, which suggests that acetyl-l-carnitine may re-program neuronal and neurotransmitter functions to enable the brain to function in a more youthful, energetic state.

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Healthy individuals are recommended to take at least two 50-day cycles (2 capsules each day) of acetyl-l-carnitine supplementation every year. If you can afford to take acetyl-l-carnitine more often, this should produce greater benefits.

This section requires additional subsections on different applications and literature references.

Longevity substance number 4 - Deprenyl, also known as Eldepryl. Deprenyl is a potent inhibitor of MAO-B, the type of MAO protein that damages brain cells during normal aging. Taking Deprenyl results in dramatic life extension effects in animals. However, it appears that Deprenyl alone will not do as well in humans. In laboratory rats, the elevation of monoamine oxidase (MAO) plays a greater role in the aging process than in humans. Some patients take Deprenyl to help prevent Parkinson's disease and the symptoms of aging that are very similar to those suffered by Parkinson's patients. There is substaintial body of evidence, which suggests that Deprenyl protects many types of brain cells from premature aging and death. There is also evidence that Deprenyl boosts cellular production of SOD and catalase, the natural antioxidant enzymes that are depleted in aging. Typical protocol suggests 2-5 Deprenyl tablets (5 mg) a week for those in their 40s. The older you are, the more deprenyl you should take, but it is advisable not to take more than one 5-mg tablet (or capsule) of Deprenyl a day unless you have the early symptoms of Parkinson's or Alzheimer's disease. In this case, you should take 10 mg of Deprenyl a day under the supervision of a physician.

This section requires additional subsections on different applications and literature references.

Longevity substance number 5 - Metformin. Metformin is an FDA approved first-line drug for the treatment of type 2 diabetes. Recently, FDA approved Metformin for extended studies on human subjects for its effect on lifespan extension. Metformin has been known for its beneficial effects on glucose metabolism. Evidence from animal models and in vitro studies suggest that in addition to its effects on glucose metabolism, Metformin may influence metabolic and cellular processes associated with the development of age-related conditions, such as inflammation, oxidative damage, diminished autophagy, cell apoptosis. As such, Metformin is of particular interest in clinical translational research in aging since it may influence fundamental aging factors that underlie multiple age-related conditions. The investigators proposed a study to examine the effect of Metformin on the biology of aging in humans, namely, whether treatment with Metformin will restore the gene expression profile of older adults with impaired glucose tolerance (IGT) to that of young healthy subjects. Metformin is a prescription drug.

This section requires additional subsections on different applications and literature references.

Longevity substance number 6 - Phosphatidylserine (PS) is sold as a drug in Europe at outrageously high prices, despite this being a phospholipid, which is easy and inexpensive to produce. In the U.S. Phosphatidylserine is available as a dietary supplement. There is extensive evidence about the anti-aging benefits of Phosphatidylserine. Phosphatidylserine may produce a cumulative effect that could enable people to reduce their dosage of the drug after attaining the desired cognitive enhancing benefits.

This section requires additional subsections on different applications and literature references.

Longevity substance number 7 - Centrophenoxine. Longevity studies have documented anti-aging properties for the combination of DMAE and p-chlorophenoxyacetate. These two ingredients make up Centrophenoxine - a potent life-extension drug sold under several names, including Lucidril. Centrophenoxine has been shown to extend the lifespan of laboratory mice. It reduces a type of cellular debris called lipofuscin (aging pigment) in the neurons that populate our brain and central nervous system. The excessive accumulation of lipofuscin with advancing age has been linked to age-related neurologic diseases. Centrophenoxine speeds up information processing in the brain and enhances brain cell uptake of glucose. Brain cells use glucose to produce the energy they need to perform their neurological functions and to maintain cell viability. Some people cannot tolerate even one tablet a day of centrophenoxine, while others can take 1-4 tablets a day and experience dramatic cognitive and energy enhancing effects. Centrophenoxine is available from sources in Europe at affordable prices.

This section requires additional subsections on different applications and literature references.

Longevity substance number 7 - GH3 and K.H.3. GH3 and K.H.3 are popular longevity compounds. Their active agent is procaine, an anti-aging drug discovered in the 1950s by Romanian physician Ana Asian. Both GH3 and K.H.3

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suppress monoamine oxidase (MAO) levels. Elevated MAO destroys the essential neurotransmitters dopamine and norepinephrine. GH3 or KH3 also suppress elevated serum cortisol levels, which has been linked to several of the degenerative diseases of aging. GH3 and K.H.3 can be taken every day including the days you take Deprenyl, which is a selective MAO inhibitor. An appropriate dose of these drugs is one to two GH3 or KH3 tablets daily. Some doctors believe you should take a five day break from these drugs once a month to avoid too much monoamine oxidase suppression. However, the literature does not support the need for taking such a break.

This section requires additional subsections on different applications and literature references.

Longevity substance number 8 - Piracetam. It is the most frequently used offshore drug to boost short-term memory and overall cognitive function. There are more than 800 published studies documenting that Piracetam promotes youthful neurologic function, including enhanced cellular protein synthesis, interhemispheric and intercellular communication. Stroke victims might avoid paralysis, if given piracetam after entering the hospital. Even in patients who suffered stroke-induced brain cell injury years ago, there is evidence that piracetam may help to improve the functioning of these damaged cells. Piracetam is available in Europe.

This section requires additional subsections on different applications and literature references.

Longevity substance number 9 - Human Growth Hormone. Growth hormone deficiency is a major reason for the decline in immune function and protein synthesis with aging in both muscle and neurologic tissues. Injections of synthetic human growth hormone have been used by geriatric physicians to rejuvenate aging men by increasing their muscle mass, strength, flexibility, and coordination. Recent studies suggest that growth hormone may be an effective treatment for Alzheimer's disease and Parkinson's patients. Unfortunately, human growth hormone is artificially overpriced. The current cost of synthetic human growth hormone ranges from \$12,000-225,000 annually, while its cost is \$200-300/year. FDA restricts its sale in the United States. Producing synthetic growth hormones is as inexpensive as to synthesize insulin. Without FDA interference, most aging Americans could easily afford injections of growth hormone in an attempt to slow aging. The need to inject growth hormone also limits the availability of this highly potent life extension drug.

This section requires additional subsections on different applications and literature references.

Longevity substance number 10 - Rapamycin. The drug Rapamycin, known for its potential to extend lifespan in mice, is being studied in dogs through the Dog Aging Project's "Test of Rapamycin in Aging Dogs" (TRIAD) clinical trial, with the goal of potentially extending healthy lifespan in dogs and gaining insights into human longevity. Rapamycin also prolongs life in yeast, worms and flies, and it prevents age-related conditions in rodents, nonhuman primates and humans. Rapamycin and its analog, everolimus, are FDA approved for human use and have been used safely for decades.

This section requires additional subsections on different applications and literature references.

Longevity method number 11 - Intermittent fasting. 11A. No cow milk diet – Dr. Jane Plant Dr. Jane Plant, UK – Non-dairy diet – cured breast cancer; China, Japan – no dairy diet. Milk free diet. 11. Low calories longevity - or calorie-restriction diet (without malnutrition) has been shown to work in a variety of species, including yeast, fish, rodents, and dogs to decelerate the biological aging process, resulting in longer maintenance of youthful health and an increase in both median and maximum life-span. The life-extending effect of calorie restriction however is not shown to be universal. This effect appears to be related to reduced oxidative stress. It is an interesting topic to discuss.

This section requires additional subsections on different applications and literature references.

Longevity method number 12 - Aromatherapy Fountain of Youth and Volcano of Joy.

This section requires additional subsections on different applications and literature references.

Longevity method number 13 - Dr Petrik

This section requires additional subsections on different applications and literature references.

Longevity methods number 14 – tDCS and other Effects of Electric Field, electromagnetic and electrochemical polarization. Lyapko applicator, Volcano Zapper, tDCS, LifeWave.com. The effect of electric field and electrochemical

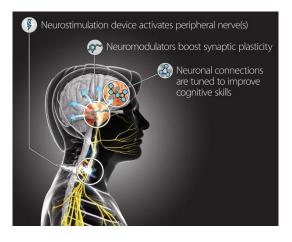
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polarization is already enormous and rapidly growing area. **tDCS** - US military successfully employs transcranial direct current stimulation (tDCS) is a non-invasive brain stimulation technique that uses weak electrical currents to modulate brain activity. tDCS device does not inject any substances into human body, but stimulates brain to enhance memory and intelligence skills of military staff. Study paves way for personnel such as drone operators to have electrical pulses sent into their brains to improve effectiveness in high pressure situations [www.theguardian.com/science/2016/nov/07/us-military-successfully-tests-electrical-brain-stimulation-to-enhance-staff-skills].In 2017 DARPA funded studies of electrical brain stimulation to speed learning [www.defense.gov/News/News-Stories/Article/Article/1164793/darpa-funds-brain-stimulation-research-to-speed-learning]. DARPA studies demonstrated the effect of tDCS even in dogs and monkey, excluding the placebo effect. The



literature on tDCS and similar effects is enormous. There are numerous other biologically active methods that employ electric and electromagnetic field, electrochemical effects, photonic devices based on lasers and LEDs. Some of them are used golden standards of scientific studies and double blinded clinical trials to prove reproducibility of the results. On the other hand, there are many products at the market that have no scientific studies and clinical trials to support their effectiveness. Related methods: reflexotherapy, acupuncture, electroic pulse stimulators, Lyapko applicator with galvanic pairs. This section requires additional insights, description of rejuvenation applications and references literature.

Longevity methods/substances number 15 – Microbiome, probiotic, prebiotic, fibers, fecal implants, This section requires additional subsections on different applications and literature references.

Longevity method number 16 Doxycycline – reprogramming short-term – 3 week of doxy 2-day/w; long-term rejuvenation 10-months of doxy 2 d/week

This section requires additional subsections on different applications and literature references.

Longevity method number 17 - Rapamycin? NAD+; Hydrogen;

Longevity methods number 18 - Plasmapheresis, hemosorbtion, Dr. Igor Yuriy Sarkisov, visit www.gemos.ru This section requires additional subsections on different applications and literature references.

Longevity substance number 19 -Ivermectin - Nobel-Prize-winning Miracle Drug

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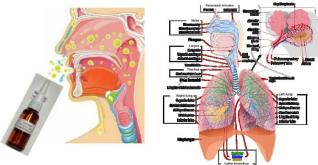
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Ivermectin offers a global solution against all known RNA viruses, certain DNA viruses, and many other diseases, including tuberculosis, certain cancers, inflammation, and more... "First, Do No Harm" (Latin – "Primum Non Nocere") – is one of the basic principles of Hippocrates. Ivermectin, DMSO, and Vitamin C - are 3 of a few compounds that meet the requirement Do

No Harm, unlike most other substances, including OTC drugs like aspirin. Biomedical experts concur that Ivermectin is a genuine miracle developed by Mother Nature. Soil bacteria designed Ivermectin during millions of years to combat a broad range of viruses and bacteria. It was revealed in 1970-s and found to be uniquely non-toxic. In 2015, the Nobel Prize honored the Ivermectin discovery. During 40+ years it was deployed against an array of tropical diseases caused by parasites. Numerous other successful medical applications (off-label use) of Ivermectin were found. The main problem is that Ivermectin is too cheap; big pharma and other actors cannot make money on Ivermectin. It is common that a compound approved for one disease turns to be active for others, because Nature gradually modified the same receptors for performing different biological functions. E.g. Viagra was originally discovered as a cardio drug for pediatric patients found for ED disorder. Viagra is still prescribed to young girls with cardiac disorders, causing public confusion: which one is OFF-LABEL use?



For prophylactics of Corona, flu and other RNA viruses apply one spray, which is ~1.5 mg of Ivermectin, into your mouth. Do not swallow; inhale the vapor into your lung; exhale through your nose to populate you sinus cavities with Ivermectin solution vapor. This breath works for 3-4 hours as prophylactics against any RNA virus, including COVID-19 and flu. For treatment of Corona and flu symptoms apply 10 sprays (~15 mg) into your mouth and swallow after 1-2 minutes.

Pandemic hysteria, panic, and corruption turned flu-like Corona pandemic into a crisis of the global healthcare system. The corruption crisis, rather than mild pathogen, made it difficult to repurpose inexpensive FDA-approved drugs to treat COVID.

Indeed, the ~231 million North India state Uttar Pradesh has achieved one of the GREATEST PUBLIC HEALTH SUCCESSES IN HISTORY - eradicated COVID-19 with Ivermectin: https://pierrekorymedicalmusings.com/p/the-miracle-not-heard-around-the. This success was and is kept as a global secret. Dr. Ben Carson, Johns Hopkins University, treated himself with Ivermectin and stated that "...we now effectively know that the anti-parasite drug Ivermectin has a significant effect on reducing COVID mortality." However, clinical trials require ~\$50 Million, which only a recently patented drug could engage in hopes of selling a priced remedy to millions. Off-patent, inexpensive drugs like Ivermectin for off-label use does not promise large profits. It is the real problem. Nevertheless, Ivermectin also stopped pandemics in Brazil and Africa: https://doi.org/10.1101/2021.03.26.21254377. The State of Nebraska was the first U.S. state, which approved Ivermectin for COVID-19 prophylactics and treatment.

Ivermectin is uniquely non-toxic. In 2023, Donfo-Azafack informed [Journal of Medical Case Reports (2023) 17:141 https://doi.org/10.1186/s13256-023-03891-4] that an amount of Ivermectin which ~100X exceeded the standard dose taken with the evident suicide purpose was not toxic. Her suicide attempt failed, because Ivermectin is uniquely safe, even at exceptionally high doses. Ivermectin has successfully passed through numerous clinical trials for prophylaxis and treatment of COVID [https://clinicaltrials.gov]. In 2020 a review on antiviral use of Ivermectin was published: "...Efficacy of Ivermectin in the Prophylaxis and Treatment of COVID-19." Kory P, Am J Ther. 2021.

Additionally, Ivermectin overcomes all RNA viral infections, including all variants of Corona and flu viruses. Besides, it is efficient against many DNA viruses, several types of cancer, tuberculosis, inflammations, and other diseases. Ivermectin studies describe it as a real wonder drug [www.ncbi.nlm.nih.gov/pmc/articles/ PMC3043740]. New Microbes New Infect, 2021 Aug 3;43:100924. Ivermectin: a multifaceted drug of Nobel prize-honored distinction with indicated efficacy against a new global scourge, COVID-19. A Santin et al]. On the other hand, a multitude of novel and expensive anti-COVID therapeutic agents failed to pass clinical trials. The lack of sufficient anti-viral properties was shown for all new and expensive pharmaceutical agents, including mRNA jabs – dangerous biological weapons. New agents turned out to be ineffective in reducing the mortality of COVID-19 and extremely dangerous with their short-term and long-term adverse side effects. According to the SOLIDARITY trial, the results eliminated any treatment role for Remdesivir, Lopinavir, Ritonavir, Interferon, mRNA jabs, and Tocilizumab. In contrast to failed therapeutics, the FLCCC discovered that Ivermectin has highly potent anti-viral, and anti-inflammatory properties against COVID-19, many other RNA and DNA viruses, tuberculosis, certain cancers, and other diseases. *This section requires additional subsections on different applications and literature references*.

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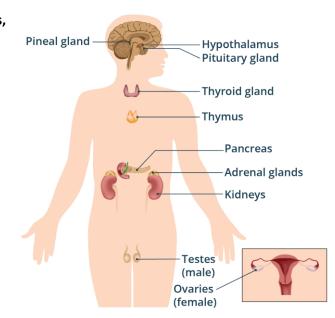
Longevity substance number 20 - Dimethyl Sulfoxide (DMSO). DMSO is one more miracle compound of natural origin. DMSO is obtained from wood and has been shown to be a panacea from numerous health problems. More than 40,000 research articles have been published on the greatest range of healing effects ever recorded for a single compound. Its comprehensive healing properties are unique, all working in synergistic harmony. However, the general public remains unaware of these discoveries, partly as a result of efforts from certain quarters to suppress the dissemination of that information, similar to that for Ivermectin. Having been treasured as a secret for many years by a small number of specialists and alternative practitioners, DMSO is currently enjoying a remarkable comeback.

Handbooks on DMSO include THE DMSO HANDBOOK, A New Paradigm in Healthcare by Dr. H. A. Fischer and Dr. S. Dafydd, available here: https://books.google.com/books/about/The DMSO Handbook.html?id=t7nijwEACAAJ ISBN-13 978-3981525557, First English edition, December 17, 2015 Daniel Peter-Verlag Publisher for new consciousness. This book is a comprehensive reference work on DMSO intended as a practical, application-oriented reference book for patients who treat themselves, as well as for medical doctors and alternative health practitioners. Medical and pharmaceutical studies have shown that DMSO has the greatest range of healing effects for a single substance. Over the last 60 years, more than_FORTY THOUSAND RESEARCH ARTICLES on this substance have been published. "The DMSO Handbook" makes this information available in an engaging manner, revealing all about this universal medicine and its applications. Dr. Fischer, a health practitioner with a background in pharmaceutical research, has been studying DMSO for many years and uses it privately and professionally in his practice. One more handbook by Archie H. Scott, iUniverse, LLC, Bloomington, 2015.02.01 can be downloaded free of charge here: https://www.eden-shop.eu/wp-content/uploads/2020/06/Scott-Archie-DMSO-Handbook.pdf. The table of contents below demonstrates the broad spectrum of DMSO applications. The Concentrations Chart provides practical recommendations for DMSO uses. This section requires additional subsections on different applications and literature references.

Anti- Longevity Substance NUMBER ONE - Ethanol - Alcohol. There is no safe dose of ethanol. Numerous studies demonstrated that even "small" doses of ethanol consumed with wine or beer result in systematic changes in cell membranes, increase of extracellular calcium, pathological changes in ECM (extracellular matrix) and damages to cellular organelles, including mitochondria. Short-term abstinence from alcoholic beverages results in decrease of ethanol concentration in blood and other bodily fluids. However, elevated levels of extracellular calcium, cell membrane composition, and many other alcohol-dependent biomarkers stay high during 6-8 weeks after the last dose of ethanol was consumed. If you apply for a job at the FBI or CIA, your blood analysis will reveal your alcohol consumption or abstinence during the last 6-8 weeks. 2% of ethanol metabolites into a phospholipid-AZX, which affects ionic sensitivity of membranes in the entire body. While major ethanol metabolites such as acetone, aldehydes, and acetates are removed in 4-8 hours, it takes 6-8 weeks to metabolite out ethanol-related lipid phospholipid-AZX. There are numerous other biomarkers of alcoholism in blood and urine.

Anti- Longevity Substances number 2 - toxic food additives, dyes, preservatives, conservatives, taste enhancers, MSG, etc. RFK Jr. claims that $^{\sim}10,000$ food additives approved by FDA for use in the USA, but forbidden in Europe.

Placebo and Nocebo effects exhibit gigantic potential for rejuvenation. In clinical trials 65% of tested respond to placebo pill of neurological drugs similar to that for real substance. The average for all drugs, including aspirin, is 15%. What is the problem with these 65% and 15%? Without any substances their bodies respond to their faith that they are taking the real drug the same way as for those with the real drug circulating in their blood? In fact, even much better – no toxic substances are needed for their response. Why 65 and 15% and not 100%-100%? The answer is in FAITH. Not everyone believes that your faith, your thoughts can stimulate your endocrine system better than a toxic pharmaceutical substance. Pineal, pituitary and other glands in your brain can be stimulated via



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psychic directives, meditation, self-hypnosis, sub-conscious and mindful sentiments to produce equal or better response in the entire body. It means that placebo responder produces in his/her body natural compounds that are as efficient as real drugs, but have no toxic side effects. Placebo effect awaits careful attention and fundamental studies. The factor of faith is an imperative constituent of the effect. If you do not trust, a sugar pill will not work. It appears that many marginal technologies exploit the placebo effect.

Nocebo is an even more powerful effect than placebo. It is an effect of a sugar pill or harmless treatment which is administered to a patient and the patient is told that the pill is associated with undesirable or harmful side effects. Up to 80% of patients experience nocebo effects. Students of medical schools often experience "What we study - is what we are sick with". Unlike placebo, the nocebo effect involves fears – more powerful biological reactions. Subconscious fears and negative expectations produce the effect similar to toxic drug or harmful treatment. *This section requires additional subsections on different applications and literature references*.

Other topic to discuss:

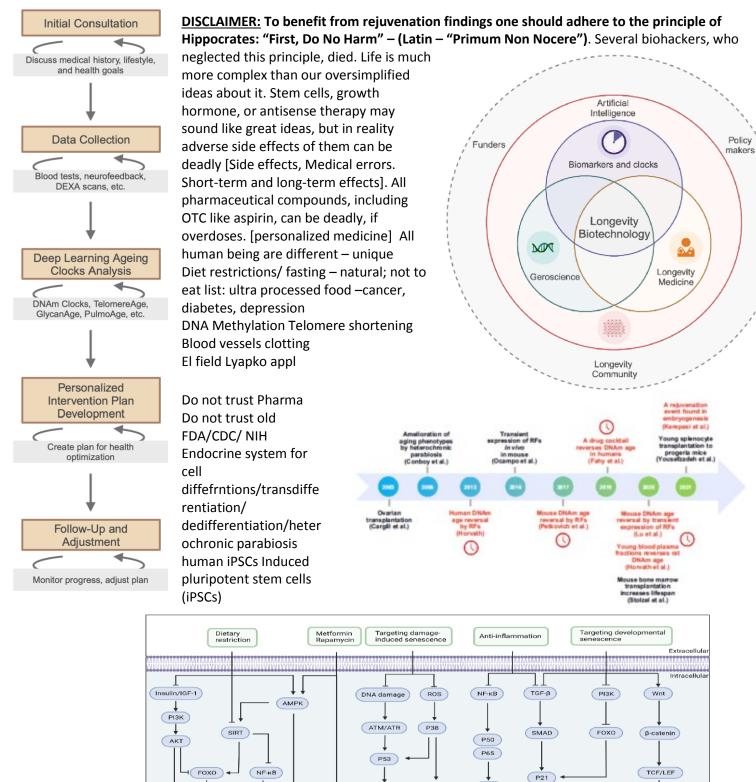
- Meditation, Reiki practice, Chinese medicine (1) Acupuncture, (2) Herbal prescriptions, (3) Massage or tuina, (4) Diet/Nutrition/Lifestyle and (5) gentle exercises, called Qi Gong (цигун).
- Personalized medicine
- Ageing biomarkers panel
- Blue longevity zones
- Chemistry of Happiness
- Longevity and rejuvenation workshop
- Over-diagnosing /under-diagnosing
- Over treatment/under treatment
- Medical errors ?3rd or ?1st cause of death in the USA: official -3rd, in practice 1st
- Pharma corruption 30% useless, toxic drugs, \$15B/year industry of hoax
- Senolytic drugs Quercetin, Doxycycline, Yamanaka factors
- Doxycycline reprogram short-term 3 week of doxy 2-day/w; long-term rejuvenation 10-months of doxy 2 d/week
- Electric-field effects no toxic chemicals
- Herb remedies
- Perform the best diagnosing of yourself: listen to the responses of your body 24/7/365.
- Unique response unique treatment
- Fast and slow responses: 0-3 days, 0-4 weeks, 1 month 10 years. Look at you family history, your genes.
- Nice pics for illustration micro pic cell under microscope: ECM structure
- Self-hypnosis
- Young blood transfusion
- Blood vessels cleaning
- At Longevity Summit Dublin 2022 several internationally renowned speakers claimed: If you manage to survive till 2035, you will have the opportunity to live 150-200 years in good health and happiness. The progress in the area of longevity explodes with rejuvenation studies. Scientists are capable not only of slowing down aging, but reversing the process back.
- https://newatlas.com/medical/tooth-regrowing-human-trial/

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P21

Autophagy
Stress resistance

Mitochondrial function

CDKs

Cell cycle arrest

TNF-a

IL-1

IL-6

Inflammation reduction

P27

Cell cycle regulation

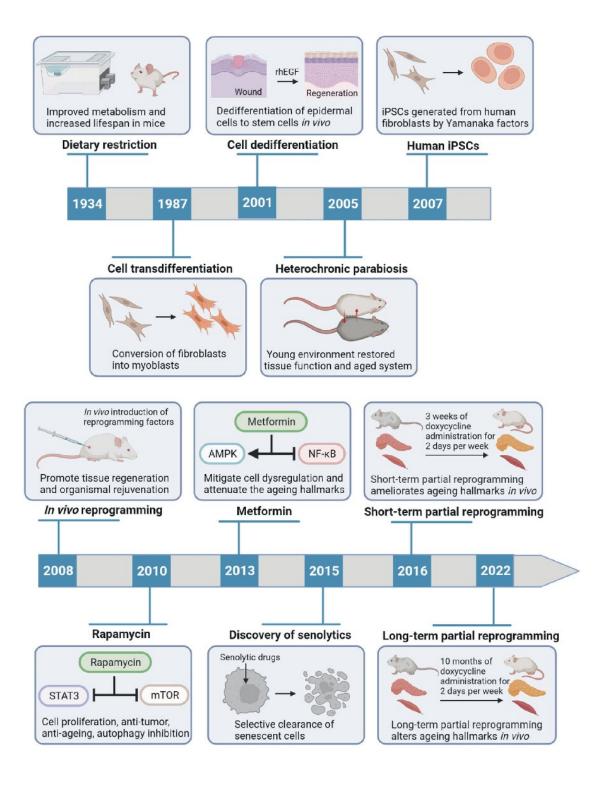
P15

CDKs

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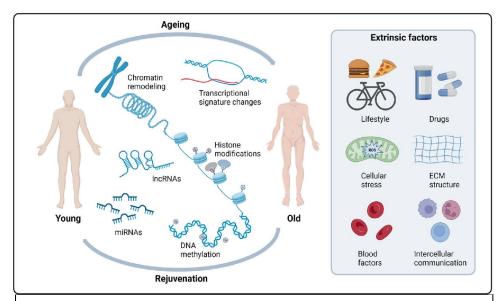
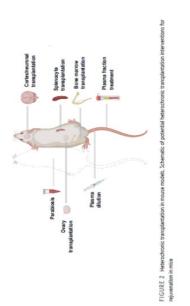
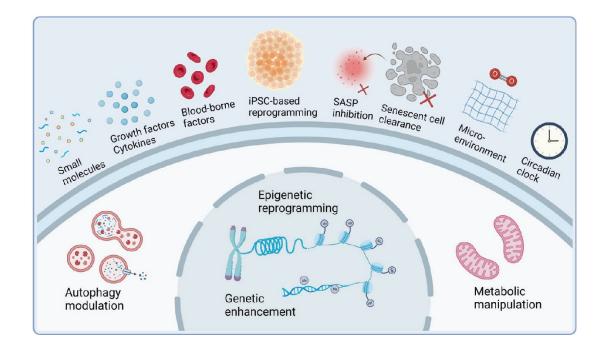


Fig. 2 The epigenetic states of ageing and rejuvenation. Ageing and rejuvenation can be affected by intrinsic epigenetic alterations and genetic instability, like DNA methylation and chromatin remodeling. Moreover, many extrinsic factors, like microenvironmental

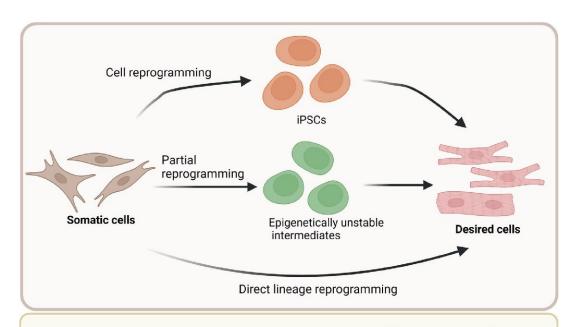




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iPSCs

- · With pluripotent states
- · Similar to ESCs
- · With epigenome rejuvenation
- Personalized medicine
- Modeling of diseases
- Potential in cell transplatantion, gene editing, drug screening

Partial reprogramming

- · Intermediate states without pluripotency
- Short-term induction of OSKM
- With epigenome rejuvenation
- No cell identity changes
- Suitable for in vitro manipulations
- In vivo amelioration of ageassociated hallmarks

Lineage reprogramming

- · No intermediate pluripotent states
- · Conducted by lineage-specific
- transcription factors
- · Transition between different epigenetic states
- More efficient and fast
- Suitable for in vivo tissue repair
- · Avoiding risks for tumorigenesis

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Table 1. List of senolytic drugs and their potential use in age-related diseases.

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Target	Molecules	Age-related diseases treated	In vivo activity	Clinical trials	Effects observed
BCL-2 proteins	Navitoclax, Venetoclax	Myelofibrosis, Idiopathic pulmonary fibrosis			
Tyrosine kinase/BCL-2 family	Dasatinib/Quercetin	chronic kidney disease, Alzheimer's disease, aging, bone resorption			Reduction of senescent cells and SASP factors
Antioxidant	Fisetin	Sepsis, osteoarthritis, cartilage degeneration, femoroacetabular ImpIngement			
HSP90 inhibitors	17-DMAG/IPI504	Pulmonary fibrosis, age- related macular degeneration			
P53 pathway	UBX0101/FOXO4- DRI peptide	Osteoarthritis, pulmonary fibrosis			No effect observed
NA+/K+ ATPase	Cardiotonic steroids	Lung fibrosis			
Galactosidase prodrugs	GMD/SSK1	Lung fibrosis, cancer			

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LITERATURE CITED *Literature requires additional references to original studies.*

1. Ji S, et al, Signal Transduction and Targeted Therapy (2023) 8:116; https://doi.org/10.1038/s41392-023-01343-5
Abstract: The ageing process is a systemic decline from cellular dysfunction to organ degeneration, with more predisposition to deteriorated disorders. Rejuvenation refers to giving aged cells or organisms more youthful characteristics through various techniques, such as cellular reprogramming and epigenetic regulation. The great leaps in cellular rejuvenation prove that ageing is not a one-way street, and many rejuvenative interventions have emerged to delay and even reverse the ageing process. Defining the mechanism by which roadblocks and signaling inputs influence complex ageing programs is essential for understanding and developing rejuvenative strategies. Here, we discuss the intrinsic and extrinsic factors that counteract cell rejuvenation, and the targeted cells and core mechanisms involved in this process. Then, we critically summarize the latest advances in state-of-art strategies of cellular rejuvenation. Various rejuvenation methods also provide insights for treating specific ageing-related diseases, including cellular reprogramming, the removal of senescence cells (SCs) and suppression of senescence-associated secretory phenotype (SASP),

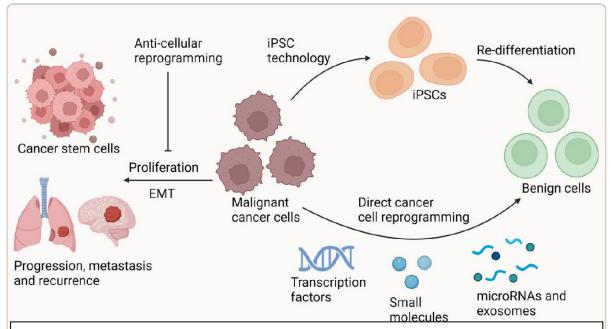


Fig. 6 The mechanisms for cellular reprogramming in cancer. Cancer cell reprogramming treatment aims to convert the malignancy to benignity or provide a therapeutic target to inhibit the formation of CSCs. Yamanaka factors-mediated iPSCs technology has been recognized as a common method for the conversion of cancer cells to benign pluripotent cells, and cancer cells-derived iPSCs can re-differentiate into functional cells with less malignancy and free of tumorigenic potential. Cancer cells also can be directly reprogrammed into benign cells via various reprogramming strategies, such as lineage-specific factors, small molecules, microRNAs, and exosomes. Responsive cellular reprogramming based on EMT contributes to CSCs formation, which mediates the initial, progression, metastasis, and post-treatment recurrence. The role of cellular reprogramming in the formation of CSCs suggests that anti-cellular reprogramming strategies may be considered as a therapeutic alternative in cancer treatment. EMT Epithelial—mesenchymal transition. Created with BioRender.com

metabolic manipulation, stem cells-associated therapy, dietary restriction, immune rejuvenation and heterochronic transplantation, etc. The potential applications of rejuvenation therapy also extend to cancer treatment. Finally, we analyze in detail the therapeutic opportunities and challenges of rejuvenation technology. Deciphering rejuvenation interventions will provide further insights into anti-ageing and ageing-related disease treatment in clinical settings