

**Athenaeum Society of Hopkinsville**  
**Current Medical Breakthroughs – 2023**  
**By Dr. Mitchell Kaye**

**CRISPR/Cas9**

1. What is it? **A tool for cutting and manipulating DNA at specific locations on a chromosome.**
2. Discovered in the DNA of the bacteria *E. coli* by Ishino et al in 1987. Original significance was not understood. 40% of bacterial DNA have Clusters of Regularly Interspaced Short Palindromic Repeats-CRISPR

-----XXXX-----XXXX-----XXXX-----XXXX-----XXXX,

where XXXX is a palindrome and -----is the spacer. The first breakthrough- **the spacer is a match for viral DNA in the bacteria's genome. It was copied from a virus that had infected the bacteria previously (Bacteriophage).** It is the bacteria's record of a previous viral infection. Parts of the viral DNA had been cut from the Bacteriophage by Cas9 protein, copied and saved in the Bacterial DNA for future reference. (Mojica 2005).

3. During a viral infection of a bacteria the viral DNA sequence is copied as a long strand of RNA which is cut into smaller segments of RNA called CRISPR RNA. This binds to the protein CAS 9 which then cuts the invading viral DNA at the point where the sequences match to disable the viral infection.
4. **Scientists have learned to manipulate the CRISPR/Cas9 system to attach and cut at any matching DNA sequence to EDIT GENES. (Charpentier and Doudna 2012, with the Nobel Prize in 2023). Genes can be deleted, added, blocked, turned on and modified in living organisms as well as in the lab. We can control the manufacturing of proteins in living organisms.**
5. Benefits:
  - A. May be possible to treat genetic (inherited) diseases such as Sickle Cell Anemia, Cystic Fibrosis and Duchenne's Muscular Dystrophy.
  - B. Treat diseases caused by certain mutation, e.g. cancers
  - C. Genetic engineering of plants, crops and animals for specific traits such as disease or drought resistance (climate change), better yield or nutritional value etc.
  - D. Can be applied to all living things. **This is a biological revolution.**

6. Risks and Dangers
  - A. Inadvertent damage to other parts of the genome, causing permanent damage to the organism.
  - B. **If changes are made to the Germ cell line** (sperm and eggs) and not the Somatic line of cells (body cells of the organism) modified traits become inherited and **evolution is bypassed**.
  - C. Who controls this technology, and to what extent?
  - D. In 2019, Chinese scientist He Jiankui used CRSPR/Cas9 to delete a region of a receptor on the surface of WBC known as CCR5 with the intention of reducing the likelihood of acquiring HIV later in life. He modified early embryos and implanted two or three. This alters the germ cell line of the child and is passed on to future generations. Little or no Ethics oversight, no consent, poor scientific quality study with no long-term reporting on effects or side effects. Outcome is not known and will likely never be known. Scientist jailed for 3 years.
  - E. Science often has unintended consequences. We cannot predict all the outcomes.

### *mRNA (messenger RNA) Vaccine Technology*

1. mRNA definition: a single stranded molecule of RNA that corresponds to the genetic sequence or a gene and is read by a ribosome in the process of synthesizing a unique protein. For example, mRNA COVID-19 vaccines cause the cell to produce contain viral proteins. This protein triggers your immune system, which then creates the antibodies specific to COVID-19 to prevent infection.
2. Previous vaccines were slow from start of research to FDA approval (Chickenpox-28 yrs, Flu-27yrs, HsPV-17yrs, Polio-13yrs, Mumps-4yrs)
3. Vaccines “teach” your immune system how to respond to a threat.
4. Four traditional methods
  - A. Dead virus vaccine -Flu
  - B. Weakened (attenuated) virus-MMR
  - C. Inert viral toxin, instead of a virus- Tetanus Toxoid
  - D. Vaccines that use only a small portion of the virus to induce immunity-HPV, Hepatitis B and COVID-19 Spike Protein based vaccines

All of the above are difficult and time consuming and require growing live virus in a lab and then killing or modifying the virus. Chicken eggs are often used.
5. **mRNA COVID-19 vaccines contain instructions that your body can read to create a specific viral protein. This viral protein triggers your immune system, which then creates the antibodies specific to COVID-19 to fight viral infection.**

6. mRNA vaccines do not alter the DNA of the recipient. mRNA is broken down quickly by the body. It never enters the nucleus and does not combine with DNA> it does not change the genome.
7. mRNA research: 1971 mRNA from rabbit inserted into frog and rabbit protein was made by frog. Delivery system (lipid nanoparticles) from 1970s-2020 enabling injection delivery and mRNA uptake by cells.
8. The genetic sequence of the COVID-19 virus was decoded within months of the initial outbreak (it keeps changing unfortunately). The Spike Protein is the component of the COVID-19 virus that enables the virus to invade a healthy cell.
9. New vaccines copy the genetic sequence of the virus that makes the Spike Protein (SP) and make an mRNA copy of it. When injected into the body, the mRNA enters cells which then start to manufacture the SP. The immune system then learns to recognize anything with the SP on its surface and destroy it. Examples: Moderna and Pfizer vaccines.
10. **In essence, we are manufacturing the vaccine within our body using our natural cellular machinery to stimulate an immune response.**
11. Drawbacks of mRNA vaccine technology: mRNA breaks down easily and requires a lipid envelope to protect it and super cold storage. Very fussy. Tough to deliver to remote or technology poor areas.
12. DNA based vaccines are more stable but require a viral carrier to introduce the DNA fragments into the cell. The body can develop immunity to the carrier virus, making this type of vaccine less effective with repeated exposure to the patient. Examples: AstraZeneca and Johnson and Johnson COVID-19 vaccines. Does not require ultra cold storage.
13. Future: Rapid development of new or modified vaccines (months) for new or rapidly mutating viral pathogens (New strains of COVID-19, CMV, Varicella Zoster (chicken pox/shingles), Rabies, etc.) Ace in the hole.  
Possible cancer prevention or treatment....  
**We do NOT need to grow the virus or even use the actual virus, just copy parts of its DNA or RNA genome to make mRNA vaccine.**
14. Known dangers of mRNA vaccines: Anaphylaxis, systemic short term side effects, pericarditis/cardiomyopathy in young males.

### *The Human Genome has been fully decoded (2023)*

1. The Y chromosome (male chromosome) was last to be decoded for technical reasons.
2. Major implications for male health care.
3. **If we have the Human Genome decoded, it can be modified using the above technology.**
4. Genetic sequencing now takes hours to days, not months to years due to new advances in technology.

### *New Uses of Psychedelics/Entheogens for Mental Health*

1. Johns Hopkins Studies on Psilocybin (Roland Griffiths et al).  
“Under supported conditions, Psilocybin can occasion mystical type experiences associated with enduring positive changes in attitudes, mood and behavior for extended periods of time ...the results have implications for medical therapeutics, the study of altruism and medical ethics.”
2. Early psychiatric studies of LSD and other Psychedelics in the 1950's showed great promise in treatment of alcohol addiction and other behavioral issues. The CIA saw potential use of LSD for “Mind Control” (Operation MK Ultra) and tested it, without consent in Psychiatric hospitals and on American citizens (without consent) in the 1950s and 1960s. It escaped the lab and became a cornerstone of the Counterculture and anti-Vietnam war movement. War on Drugs (Nixon et al) classified all Psychedelics as DEA schedule 1 (No known legitimate medical use/Felony) along with Heroin, Marijuana and others. Political decision. All research shut down.
3. “The risks of (using these compounds) are real but manageable” RG
4. Johns Hopkins Psilocybin Research Project (20 yrs). 245 participants in > 600 sessions.
  - a. **Healthy volunteers.** Three double blinded studies. Given a capsule of either high dose Psilocybin or a placebo and monitored in a quiet non medical setting.
  - b. Results: a questionnaire 1 month later 80% rated the experience to be among the top 5 most personally and spiritually significant of their lives.
  - c. About 90% reported increased life satisfaction and positive behavioral change, including increased positive mood and better social relationships.
  - d. Results are sustained at least for a year or longer. Social contacts confirm.

- e. Study with 51 patients with **life threatening cancer with clinically significant anxiety or depression**. Double blinded. *Single* Low dose or high Dose.
- f. 92% of high dose and 32% of low dose show significant improvement at one month. 79% of high dose patients show sustained benefit at six months. 70% of this group have reduced symptoms to “normal range”.
- g. Long term smoker study. Very disappointing therapy results in the past (average result 30% abstinence at 6 months). Psilocybin results: 80% at 6 months
- h. **Long Term Meditator study**. The brain imaging studies of meditation and psilocybin effects are very similar to each other. Meditators found the experience very useful, but not a substitute for meditation practice.
- i. Now multiple studies on drug addiction, treatment resistant depression, Tourette’s, OCD are underway.
- j. Mechanism of action: The Default Mode Network (DMN) is structurally and functionally connected for internal processes, such as introspection and imagination. The DMN is *activated* during passive rest and mind wandering such as thinking about others, thinking about oneself, remembering the past or envisioning the future rather than the task being performed. It is *deactivated* by shifts of consciousness to external attention such as social cues, focused attention and external cognitive tasks. Roughly equivalent to the ego. Loss of ego boundaries is frequently seen in mystical states. Unity with the universe and others.
- k. Overactivity of the DMN is seen with depression, anxiety, **Psilocybin temporarily isolates the DMN from the rest of the brain**. It acts like a reset. New neural connections are made during the drug effect. Effects are seen with single doses and can alter obsessive thought patterns.
- l. Other studies using MDMA, an amphetamine like drug (Ecstasy, Molly) in clinical trials have shown major promise for treatment of PTSD. Mechanism of action is completely different. (Doblin et al)
- m. **These remarkable results are seen in clinical trials, under supervision and direction by trained specialists and take place in safe environments. This is not recreational usage, which can carry significant risks for harm in some individuals.**

### ***Superiority of Isometric Exercise to other forms of exercise in blood pressure reduction.***

1. Meta analysis of 270 controlled randomized studies from 1990-2023. 15,827 participant adults with no predetermined limitations on health or disease representing the general population. Exercise regimens lasted > 2 weeks. No other interventions in either group. Systolic and Diastolic blood pressure measured.
2. Isometric exercise (wall squat and hand grip) -8.24/-4.0
3. Dynamic resistance (weight training) -4.55/-3.04
4. Aerobic (running) -4.49/-2.53
5. High Intensity Interval Training -4.08/-2.5
6. All forms of exercise produced reductions in Systolic and Diastolic blood pressure. **Isometric was the most effective.** Not the traditional teaching.

### ***Conclusions***

1. The Human Genome has been completely sequenced.
2. The advent of CRISPR/Cas9 allows scientists to modify the genetic code and the biology of all living organisms. This has profound implications for Human medicine and the rest of life on Earth. Immediate attention is needed to utilize this capacity safely and responsibly.
3. mRNA vaccine technology will be the source for most of our new vaccines and will likely have other applications for disease treatment, outside of Infectious Disease. Rapid development of new vaccines for potential pandemics will probably save millions of lives in the future.
4. Combining AI with numbers breakthroughs 1-3 will alter Human Medicine and Evolution profoundly.
5. Psychiatry is at a breakthrough point in the treatment of many disorders using Psychedelic compounds as medicines. Proper use and clinical study are critical to achieve safe and reproducible results. The potential is enormous. These are often single use or very short-term use therapies, in contrast to long term use of current medicines for the treatment of mental health disorders. It is possible that these substances may improve the quality of life for many people and add to the understanding of Neuroscience.
6. Consider the implications of this discussion. If the genes for mental illnesses such as schizophrenia, ADHA, OCD, etc. are defined could CRISPR/Cas9 be used to treat these devastating disorders?
7. It appears that simple and cheap isometric exercises such as wall squats and hand grip can significantly reduce Systolic and Diastolic blood pressure in the general population. There are no obvious drawbacks.

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Note: Please consider using the above references to visualize CRISPR/Cas9 and mRNA. The animation on YouTube is amazing.