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# WisdomTree Europe

# Enter the BioRevolution

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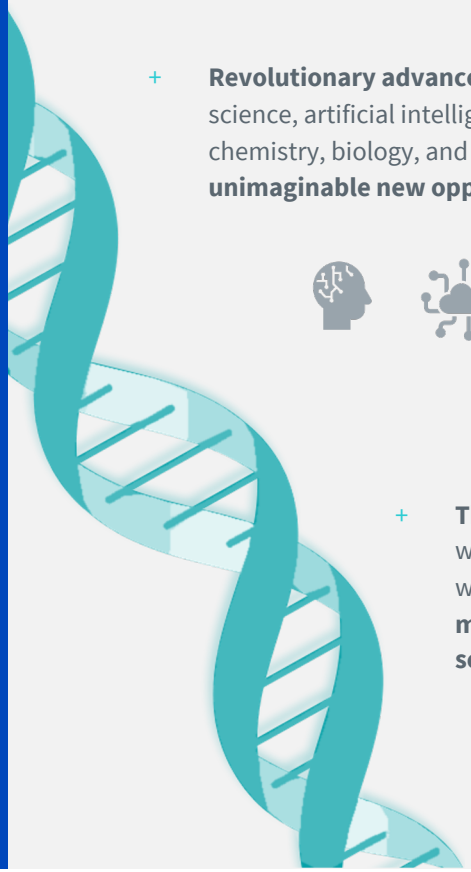
# The Biology Revolution ("BioRevolution")

"We're only a fifth of the way through the 21st century, but we've already sequenced the full human genome, figured out how to turn adult cells into stem cells, discovered ways to rewrite the genetic code of any living cell and brought down the cost of hacking genes by a factor of millions.

If the 19th was the century of chemistry and the 20th that of physics,
**the 21st is the century of biology,**
**in which we will aggressively reengineer biological systems to meet our needs.**"

Jamie Metzl



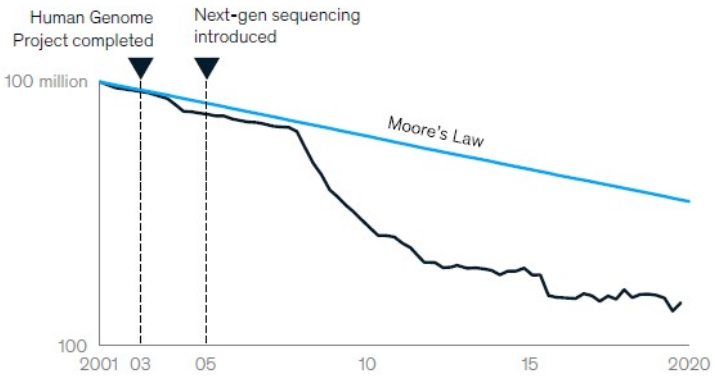
+ **Revolutionary advances across multiple fields** including computer science, artificial intelligence, big data analytics, automation, chemistry, biology, and engineering are **creating previously unimaginable new opportunities to re-engineer biological systems.**

+ **The revolution** in our ability to read, understand, write and hack **DNA, the genetic code of all life**, will transform **healthcare, agriculture, manufacturing, energy production, consumer services, and data storage.**

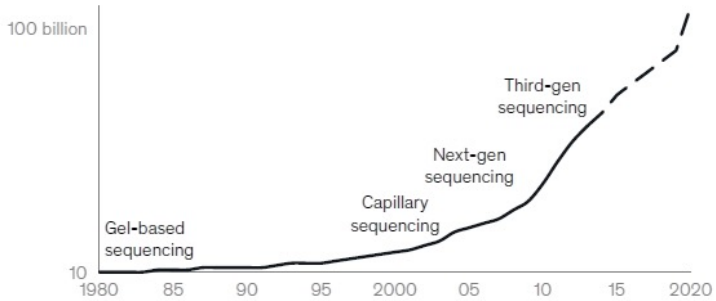
Source: WisdomTree, Jamie Metzl from https://www.newsweek.com/miraculous-mrna-vaccines-are-only-beginning-opinion-1567683

# Genome Sequencing is Faster and Cheaper than Ever

Cost per human genome in $ (log scale)*




Speed of sequencing Kilobytes per day (log scale)



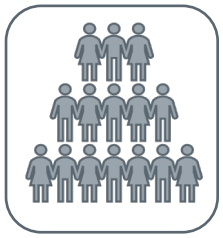

- DNA is made up of four chemical units, called nucleotide bases. The order of nucleotide bases determines the meaning of the information encoded in DNA.
- A genome is an organism's complete set of DNA, which consists of approximately 3 billion DNA base pairs. Genome sequencing determines the exact order of the bases in a strand of DNA.
- Coupled with the reduction in cost of sequencing, parallel advances in genome editing, artificial intelligence, and machine learning have helped us better understand complex biological systems.
- Researchers can sequence DNA (determine the order and information carried in DNA) **more rapidly and cost-effectively than ever before**, which is driving the transformations in healthcare and many other sectors of our global economy.
- The development of **Moderna's COVID-19 vaccine** is just one poignant example – it took the company **only two days to design the sequence for its mRNA vaccine!**

Source: National Human Genome Research Institute; www.yourgenome.org; McKinsey Global Institute analysis. Charts are from the McKinsey Global Institute report "The Bio Revolution: Innovations transforming economies, societies, and our lives " published in May 2020.
* Data do not capture all costs associated with genome sequencing and include only production-related costs (labor, instruments, informatics, data submission).

# The BioRevolution Will Fundamentally Transform Healthcare

We expect our healthcare system to transition from generalized medicine to personalized, or precision, healthcare based on each person's individual biology.

The BioRevolution will pave the way for predictive, preventative healthcare that will help us live healthier and longer lives.

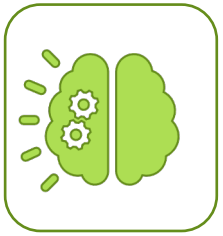


## Generalized Medicine

+ Healthcare and treatments based on population averages.
+ Example: Taking the common prescribed blood thinner Warfarin is effective for most of the population, but for a small percentage of the population it causes negative, potentially fatal, side effects.

## Precision Healthcare

+ Healthcare and treatments based on a person's individual biology to provide the right drug or treatment.
+ Example: Taking a blood thinning medication and dosage level that is prescribed based on how well it will work for your specific genetic makeup.

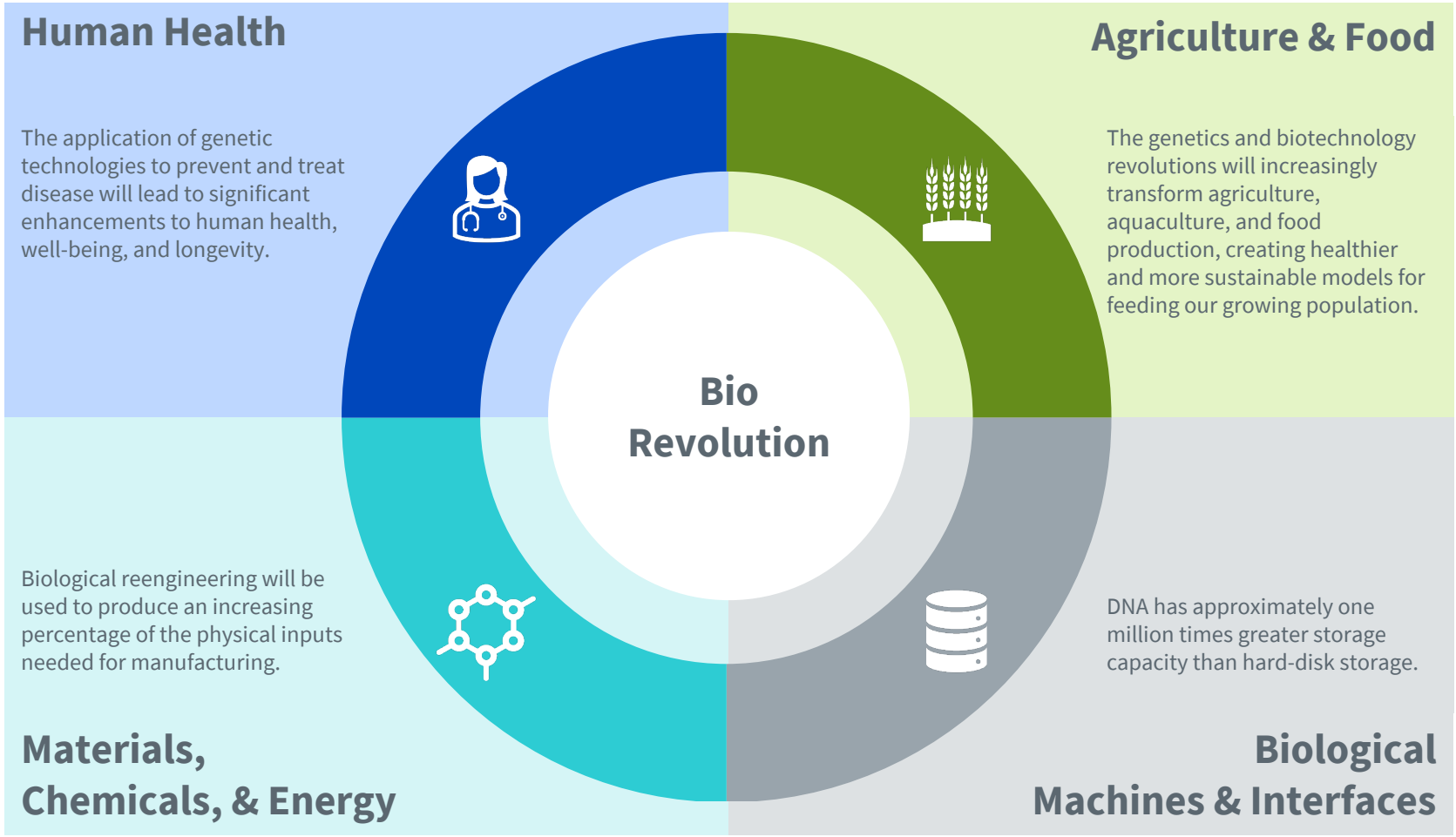


## Predictive Healthcare

+ Anticipating and responding proactively to a person's genetic disposition based on artificial intelligence (AI) generated estimates of a person's future health state.
+ Example: Using AI to predict the genetic risk for a disease, disorder, or trait that may require a person to take blood thinning medication in the future, allowing the individual to take preventative measures early in life.

Source: WisdomTree, Jamie Metzl.

# The Technologies Underpinning the BioRevolution are Connected and Reinforcing Advancements Across Interdisciplinary Fields

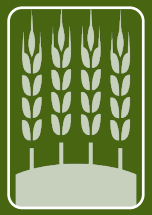



Source: WisdomTree, Jamie Metzl.

# The Applications of the Genetics and Biotechnology Revolutions Will Extend Far Beyond Healthcare

The same **intersection of biology and technology** that is transforming the healthcare sector, is also **driving transformations across many sectors and industry verticals** of our global economy. Although **healthcare is the most mature market** for these technologies, **other sectors will catch up**.

## Agriculture & Food



**Precision Agriculture**

Genome-enabled management of crops and livestock that leads to increased productivity, greater ability to meet demand of a growing population, and increased sustainability.

**Plant-Based Meats**

Vegetarian or vegan alternatives to traditional animal-based meats, derived from protein-rich seeds.

**Cellular Agriculture** "…scientific advances in biology, biochemistry, and engineering that have led to the innovations enabling the growth of animal cells outside of the animal itself, in a controlled environment, for food."[1]

## Materials, Chemicals, & Energy

**Synthetic Manufacturing and Precision Fermentation:** Creating materials at scale by manipulating genetic code, rather than extracting them from nature.

**Biofuels**

"…genomics-based research leading to improved use of biomass and plant feedstocks for the production of fuels."[2]

## Biological Machines & Interfaces

**Biological Machines & Interfaces:** Connection and communication between the biology of humans and computers, including the usage of DNA for computing and storage.

Source: WisdomTree, Jamie Metzl, U.S. Food & Drug Administration, U.S. Department of Energy.
1. https://www.fda.gov/food/food-ingredients-packaging/food-made-cultured-animal-cells
2. https://genomicscience.energy.gov/research/DOEUSDA/index.shtml

# Macro Picture

U.S. Federal Reserve

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# Focus on the U.S. Federal Reserve (Fed) and Related Announcements

+ 22nd November 2021 –J. Powell's renomination as Fed Chair

+ 30th November – Fed Chairman J. Powell testifies before Senate

+ 14th-15th December 2021 – Federal Open Market Committee (FOMC) meeting

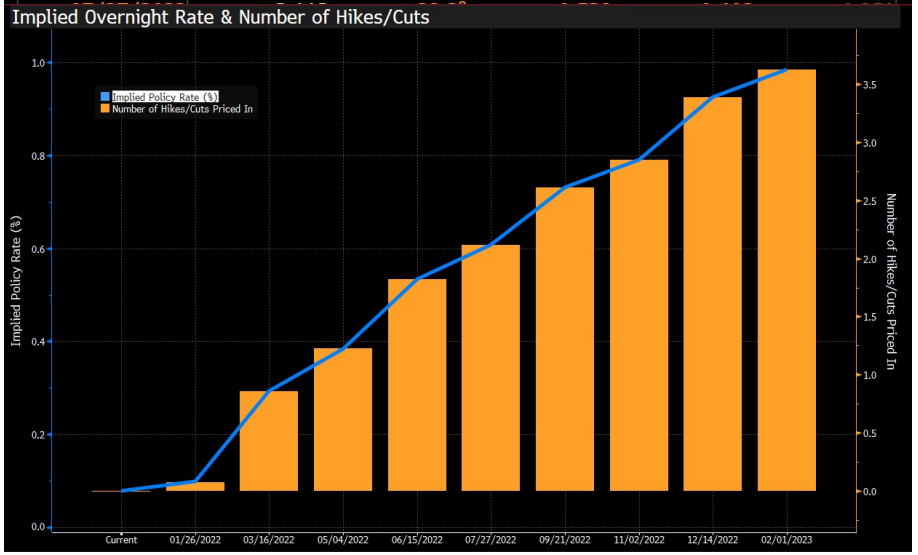
+ 5th January 2022 – Fed's December meeting minutes

+ 7th January 2022 – first jobs report

Region: United States »
Target Rate 0.25
Effective Rate 0.08

Instrument: Fed Funds Futures »
Pricing Date 01/07/2022
Cur. Imp. O/N Rate 0.078

| Meeting | #Hikes/Cuts | %Hike/Cut | Imp. Rate Δ | Implied Rate | A.R.M. |
|---|---|---|---|---|---|
| 01/26/2022 | +0.078 | +7.8% | +0.019 | 0.098 | 0.250 |
| 03/16/2022 | +0.860 | +78.3% | +0.215 | 0.293 | 0.250 |
| 05/04/2022 | +1.225 | +36.5% | +0.306 | 0.384 | 0.250 |
| 06/15/2022 | +1.825 | +60.0% | +0.456 | 0.534 | 0.250 |




Source: Bloomberg, with data as of 7 January 2022.

# Agriculture

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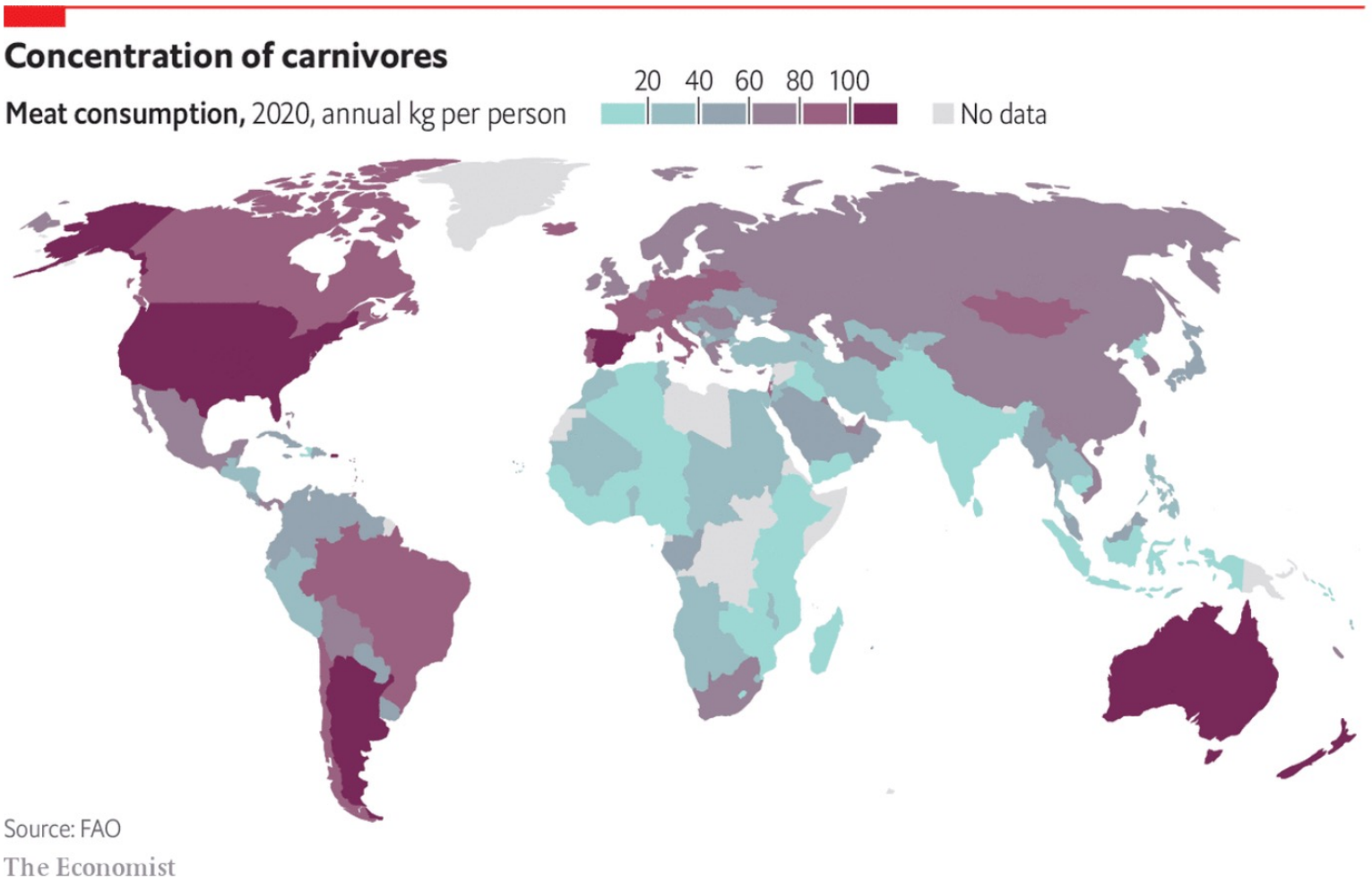
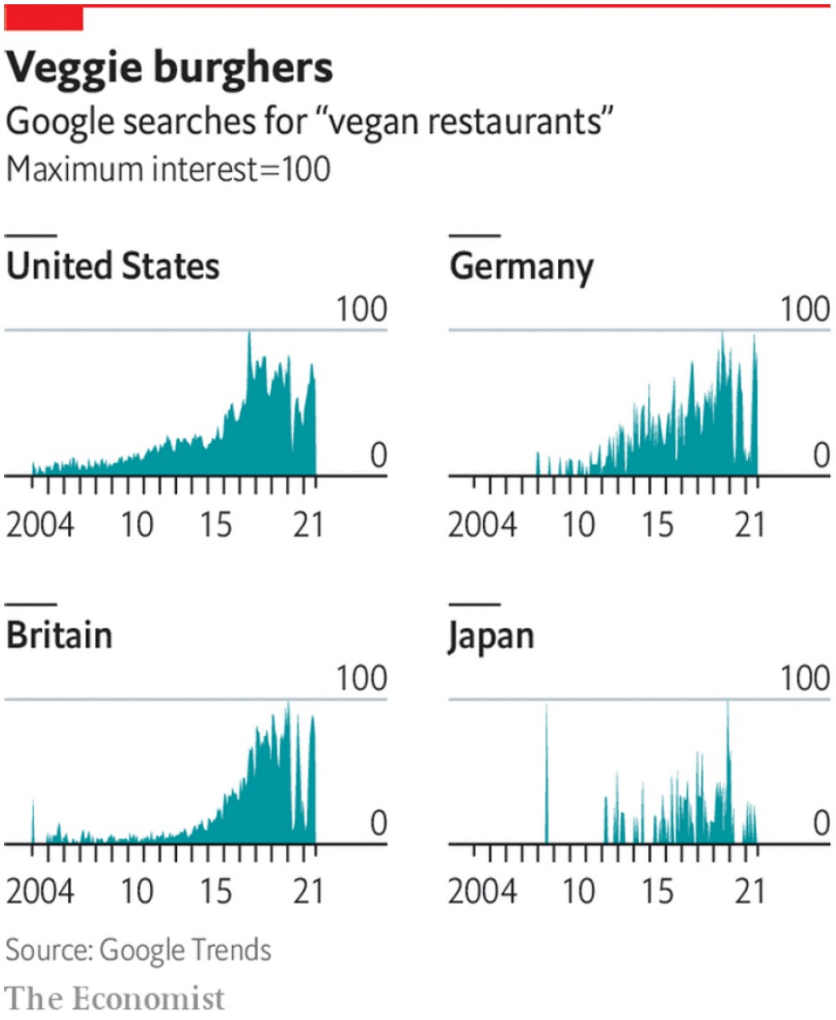
# How will the world feed 9 billion people annually?




Source: "Feeding 9 billion People will Mean Re-Imagining the Edible World." Economist. 28 September 2021.

# Vegan is becoming 'Fashionable'




Source: "Technology Can Help Deliver Cleaner, Greener Delicious Food." Economist. 28 September 2021.

# Why do we need Breakthroughs in Crops? To feed more than 9 billion people…

+ Dr. Borlaug's advances in plant breeding are credited with enhancing the capability of the world to feed millions of people in Asia and Latin America.
+ Mexico & India, for example, through his work, became self-sufficient in feeding the populations through cereal grains.
+ Primary High Level Summary
  - Needed to increase the yield of wheat—led to much larger head on the plant.
  - Needed to strengthen the stalk so that the larger head of wheat would not fall over.

Dr. Borlaug with his wife, Margaret, after being awarded the Nobel Peace Prize in 1970.
STR/AFP/Getty Images

Source: Gillis, Justin. "Norman Borlaug, Plant Scientist Who Fought Famine, Dies at 95." The New York Times. 13 September 2009.

# Will the market learn to love Genetically Modified Organisms (G.M.Os)?

+ Non-G.M.O products have seen market grow from $350 million in 2010 to $26 billion by 2018.
  - How Monsanto introduced its 'Roundup Ready Seeds' for corn and soybeans may have contributed to negative perceptions

+ Golden Rice in 1999 was developed to combat Vitamin A deficiency in Asia

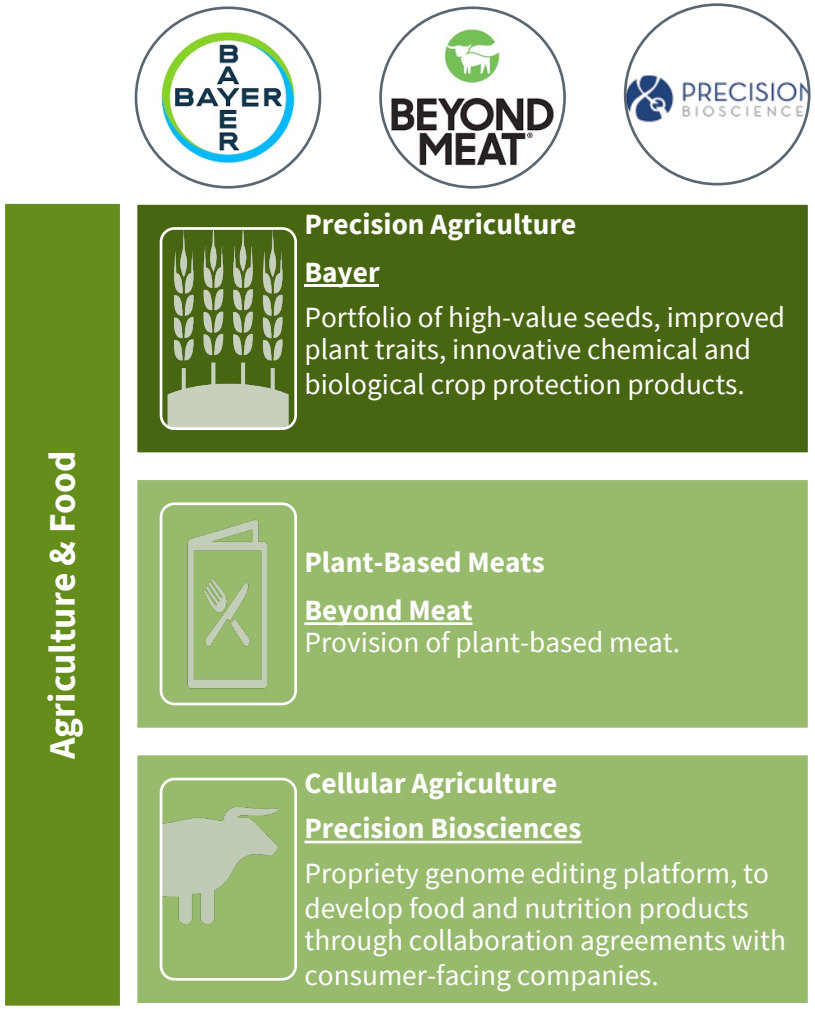
+ Bt corn allows for 30% less insecticide usage per crop

+ Scuba rice allows for 14 days of submersion in water as opposed to 3 days—could lead to 4 million tonnes of rice to be saved annually in India and Bangladesh, which could feed 30 million people

+ A tomato has been grown that produces levodopa, the drug used for Parkinson's disease (cost, side effects—these are some reasons why one would do this)

Source: Kahn, Jennifer. "Learning to Love G.M.O.s" The New York Times Magazine. 20 July 2021.

# Agriculture and Food: Company Examples




Source: WisdomTree, Jamie Metzl, FactSet.
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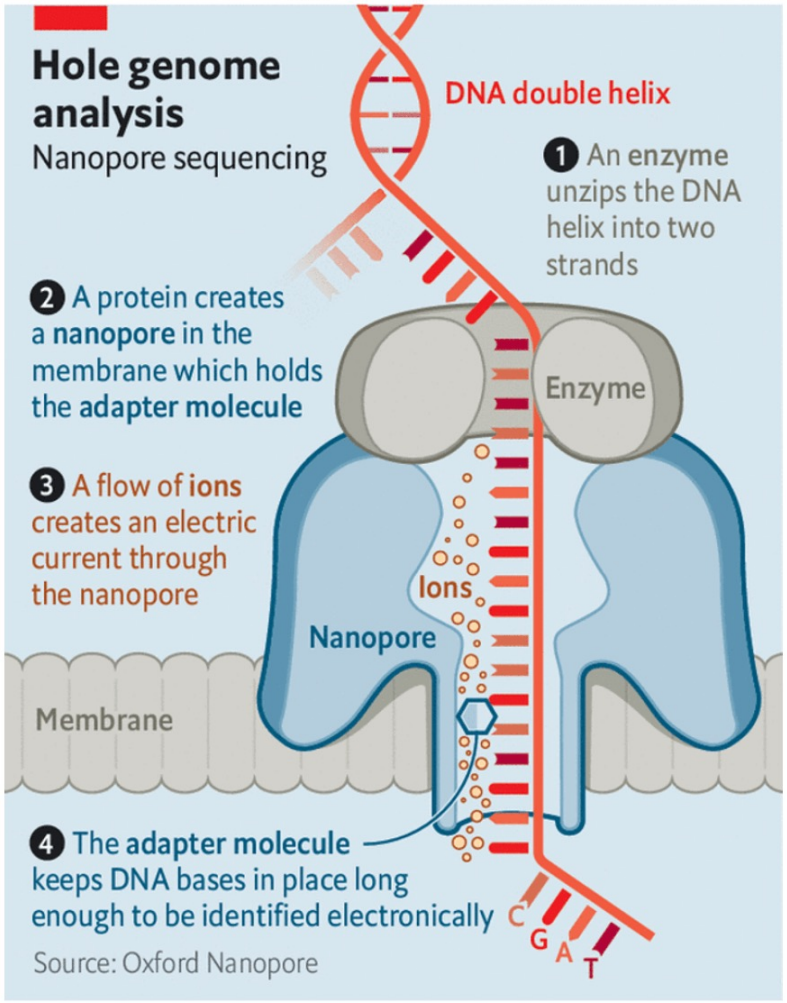
# Nanopore Sequencing Could be Transformative




+ Oxford Nanopore is a company focused on 'nanopore sequencing'
+ The firm's 'Minion' product is the size of a large mobile phone, whereas the typical sequencers are the size of freezers or microwaves
+ The world market for gene sequencing is roughly $7.5 billion, currently growing 10-15% per year

Source: "An Ambitious Unicorn Hopes to Up-end DNA Analysis." Economist. 2 October 2021.

# Human Health

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# A Cure for Type 1 Diabetes?

+ **Disease**
+ Type 1 Diabetes most often occurs around age 13 or 14, when immune cells kill the insulin-producing islet cells on the Pancreas
  - 1.5 million Americans suffer from Type 1 Diabetes
+ **Possible Treatment**
+ A new trial treatment from Vertex Pharmaceuticals gives patients an infusion of insulin-producing islet cells, grown from stem cells
+ **Research Process**
+ Approach took a team of 15 people more than 20 years at a cost of $50 million: Difficulty was to get stem cells to grow into islet cells.
+ On initial success of the process, company Semma was founded in 2014
  - 2019: Vertex acquired Semma for $950 million

Source: Kolata, Gina. "A Cure for Type 1 Diabetes? For One Man, It Seems to Have Worked." The New York Times. 27 November 2021.

# Antibiotics cannot 'Stand Still'—As Bacteria Evolves, Treatments must Evolve

+ Vaccines
+ Clean Water
+ Antibiotics

+ Contribute to Humans Doubling Life Span since 1800's

+ Surgery
+ Transplants
+ Chemotherapy
+ Childbirth

+ The World Health Organisation estimates that, by 2050, 10 million people could die annually from drug resistant bacterial infections

Source: Levy, Max G. "An AI Finds Superbug-Killing Potential in Human Proteins." WIRED. 30 November 2021.

# AI intersects with the Biorevolution

+ **Question: Can peptides naturally-produced by people fight microbes?**
+ Researchers used an AI system to scrutinise the chemical makeup of each and every peptide in the human proteome (complete set of proteins that humans can produce)
  - 43,000 peptides initially screened
  - 2,603 antibiotic candidates
  - Researchers synthesised the most promising 55 for further testing
+ **Results?**
  - Promising capability seen to dissolve bacterial cell membranes
    + Difficult for bacteria to resist this type of antibiotic attack

Source: Levy, Max G. "An AI Finds Superbug-Killing Potential in Human Proteins." WIRED. 30 November 2021.

# Many High-Profile Preliminary Applications of the BioRevolution Have Been Healthcare-Related

## Human Health

| Diagnostics & Surveillance | Precision Health /Gene Therapies | Regenerative Medicine/ Stem Cell | Vaccines | Assisted Reproduction /Fertility | Healthy Aging | Prediction & Prevention |
|---|---|---|---|---|---|---|
| Using biological data to screen and diagnose diseases, disorders, or traits. | Using biological data to screen and diagnose diseases and disorders + to enable more precise and beneficial interventions. | Treatments that repair disease-causing genetic disorders or empower natural defenses. | Using genetic sequencing in vaccine development and administration to enable new platforms and prevent or treat multiple diseases. | The use of assisted reproductive technologies to expand reproduction options and to prevent and treat disease. | Understanding biology of aging and developing genetics and epigenetic-based interventions that increase the potential to live longer and healthier lives. | Anticipating and responding proactively to a person's genetic disposition based on artificial intelligence (AI) generated estimates of a person's future health state. |

Source: WisdomTree, Jamie Metzl, National Institutes of Health.

# Human Health: Company Examples

| Diagnostics & Surveillance | Precision Health /Gene Therapies | Regenerative Medicine/ Stem Cell | Vaccines | Assisted Reproduction /Fertility | Healthy Aging | Prediction & Prevention |
|---|---|---|---|---|---|---|
| **10x Genomics**<br>Life science tools and integrated systems for large-scale analysis of genetic variation and function. | **Moderna**<br>Develops transformative medicines based on messenger ribonucleic acid (mRNA). | **Athersys**<br>Stem cell product which provides biological potency and therapeutic effects for distinct diseases and conditions. | **Regeneron**<br>Discovery, invention, development, manufacture, and commercialization of medicines. | **Natera**<br>**Discovery, development, and commercialization of genetic testing services.** | **Geron**<br>Immuno-oncology committed to improving and extending lives of patients. | **Invitae**<br>Comprehensive panels for hereditary conditions in cancer, cardiology, neurology, pediatrics, and rare diseases. |

Source: WisdomTree, Jamie Metzl, FactSet.
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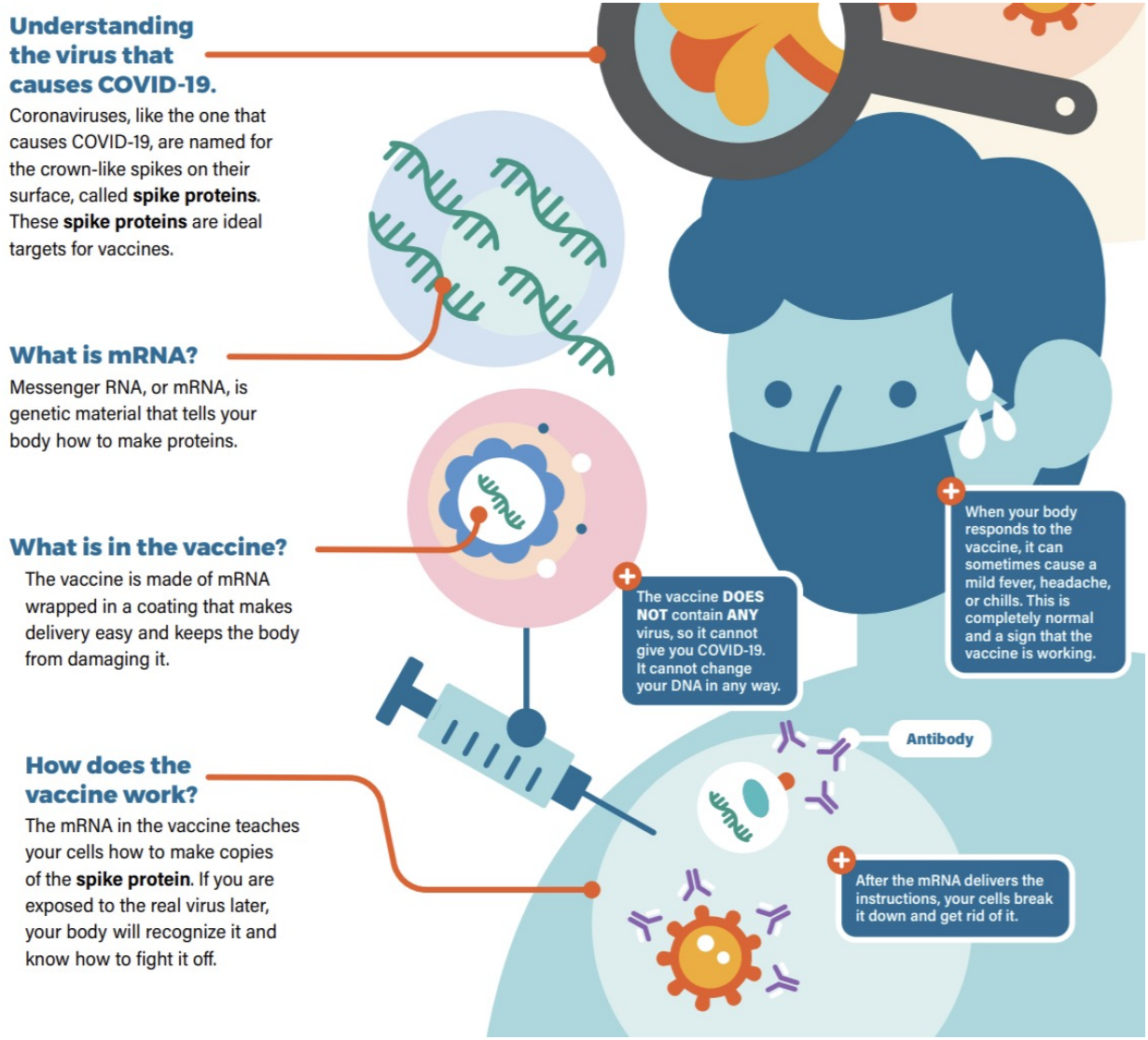
# Zooming In: mRNA Vaccines & Covid-19




Source: https://www.cdc.gov/coronavirus/2019-ncov/downloads/vaccines/COVID-19-mRNA-infographic_G_508.pdf

# mRNA is a Broader Technology than simply 'Vaccines'

+ Omicron had roughly 30 mutations, making it more challenging for existing vaccines to protect against the new variant.
+ BioNTech and Pfizer have indicated they could ship a modified vaccine within 100 days, whereas Moderna is already shipping vaccines to protect against mutations.
+ Conventional vaccine technologies could take six to 36 months to adjust.
+ mRNA technology is also involved in studies to:
  - Regenerate tissue in the heart muscle
  - Reprogram cells, meaning influence what the mature cells evolve into
  - Treatment of autoimmune diseases, like multiple sclerosis
  - Killing cancerous cells

Source: Finley, Allysia. "The Vast Promise of mRNA Technology." Wall Street Journal. 3 December 2021.

# Data Storage

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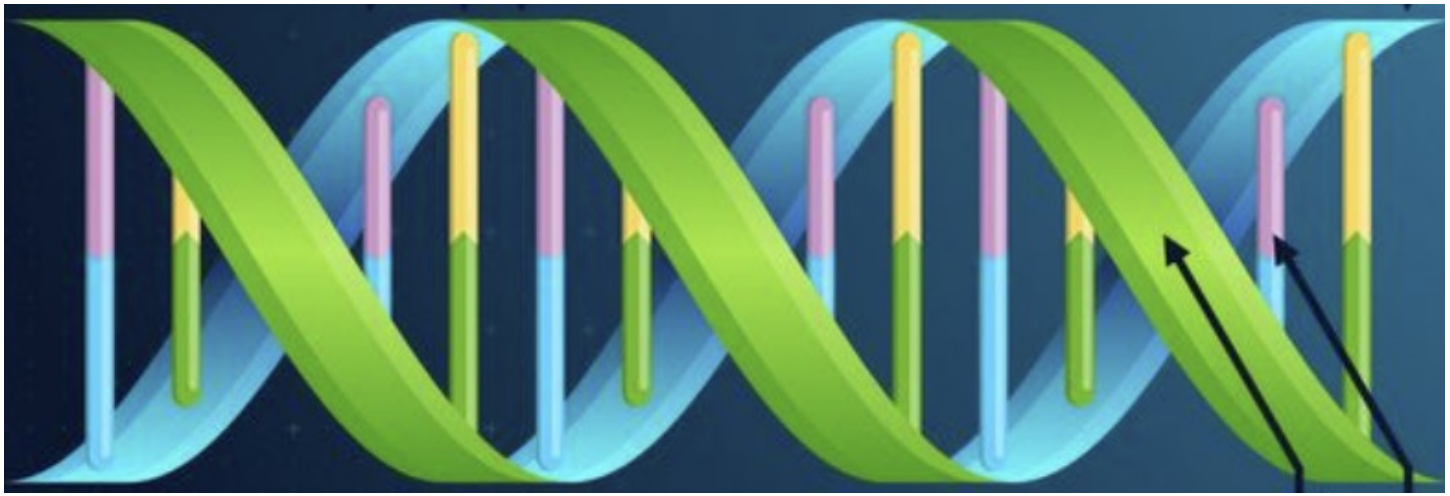
*"…DNA molecules can be the basis for an archival storage system potentially capable of storing all of the world's digital information in roughly nine litres of solution, about the amount of liquid in a case of wine."*

Source: Markoff, John. "Data Storage on DNA Can Keep It Safe for Centuries." The New York Times. 3 December 2015.

# DNA: Taking Data Storage to Unprecedented Levels

+ A hard drive could store something like 30 million gigabytes of data per cubic metre. DNA could store something closer to 600 billion gigabytes per cubic metre[1].
+ DNA can store up to 215 petabytes of data into a single gram—10 million times what a modern hard drive could store[2].
+ DNA is routinely recovered from bones that are thousands of years old—700,000 years is roughly the record. A hard drive warranty rarely exceeds five years[2].



Sources: [1]"DNA may soon be used to store computer data." Economist. 20 October 2018. [2]"DNA could be used to embed useful information into everyday objects." Economist. 12 December 2019.

# Energy & Biofuels

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# Will Supersonic Air Travel Return…
# …with Sustainable Fuel?

+ Concorde
  - Aluminium Alloy Construction
  - Afterburners
  - Conventional jet fuel: burns more than 1 tonne to arrive at the runway prior to take off.

+ Overture Jet
  - Carbon Fibre Composite Construction
  - More efficient turbofan engines.
  - 100% sustainable aviation fuels: comprised of fatty acids to forest cover



Source: Vanderbilt, Tom. "Boom's Quest to Make Supersonic Flights a Reality (Again)." WIRED. 20 December 2021.

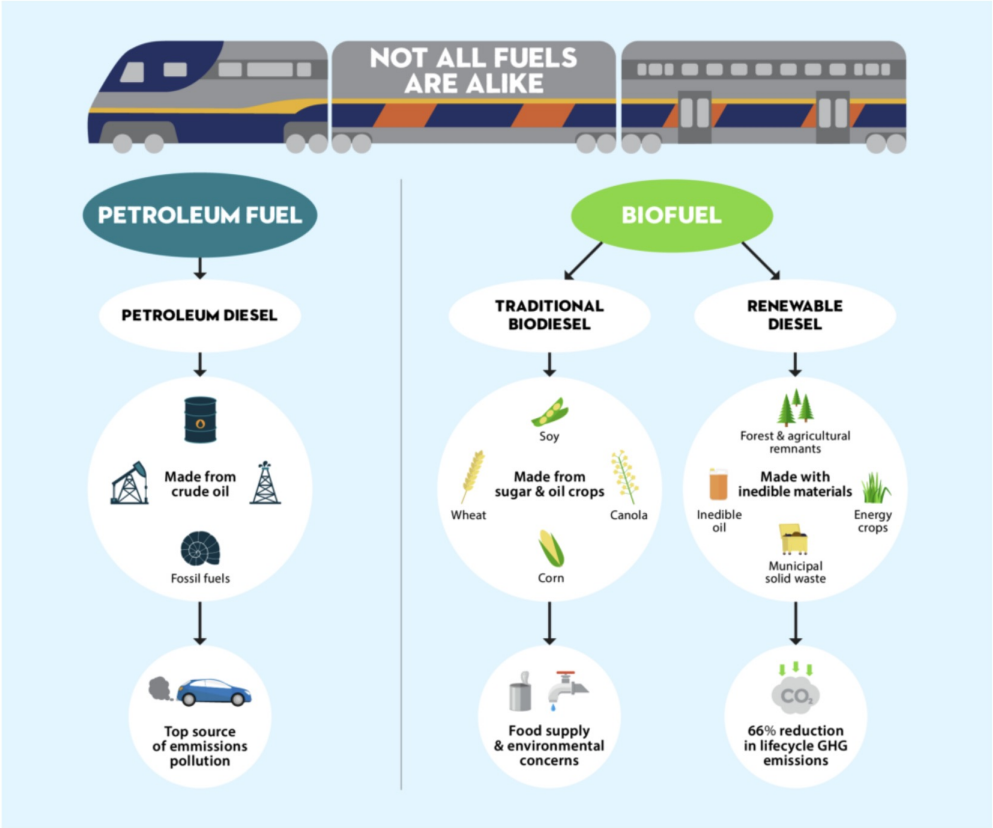
# “Humans dump an estimated 10 billion gallons of potential biofuel into landfills every year. Researchers found a way to capitalise on it.”

- Food wastes, animal manure, sewage
  - Possible to put this in an oxygen-free environment and have bacteria convert it to methane
  - Researchers can interrupt this process
    - Stop at a point where the carbon in bacteria is in chains 4-8 carbons long with a couple of oxygen atoms at the end to form weak acids
    - Two weak acids can merge into a single molecule, so a 7-carbon molecule would have more similar properties to jet fuel
    - Further chemical reactions can bring it even closer to the properties of jet fuel
    - Using different reactions can mix jet fuel from biomass with different properties, getting to 70% total biofuel
  - 200 tonnes of food waste a day could get costs in the neighbourhood of $2.50/gallon

Timmer, John. “How Food Waste Could be Turned Into Climate-Friendly Jet Fuel.” WIRED. 19 March 2021.

# Renewable Diesel

+ Phillips 66, Marathon, HollyFrontier and several others are investing $2 billion to retool refineries: **renewable diesel**
+ If current trends continue: 3.8 billion gallons of renewable diesel by 2025—more than 5% of the total diesel production in 2020.
+ Can be used in existing diesel engines without blending with standard diesel.
+ 50-80% less greenhouse gas emissions.




Source: https://www.capitolcorridor.org/blogs/get_on_board/ccjpa-tests-renewable-diesel/

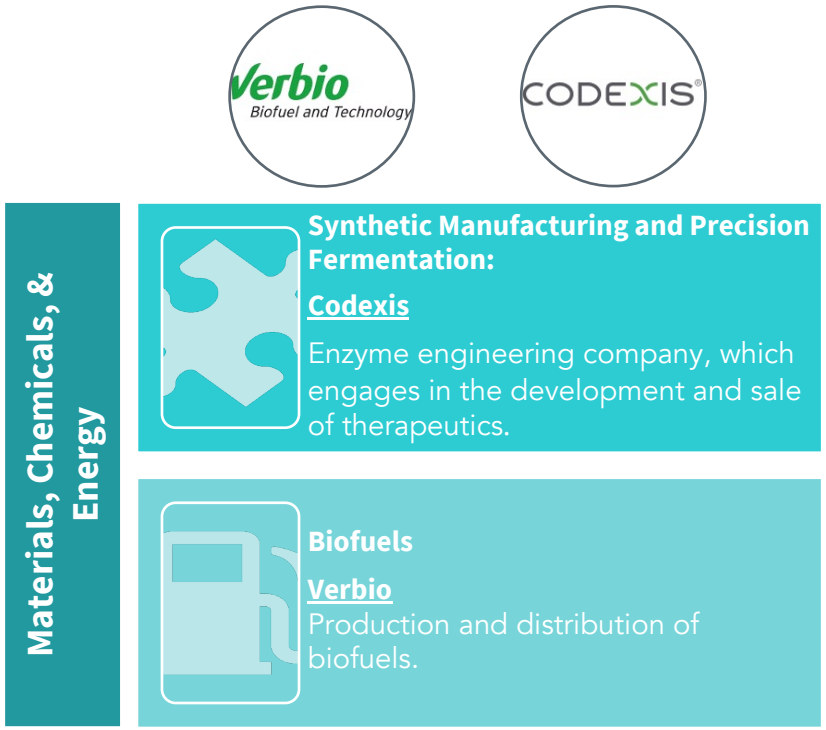
Source: Krauss, Clifford. "Oil Refineries See Profit in Turning Kitchen Grease Into Diesel." The New York Times. 3 December 2020.

# Soybean Oil

- U.S. Agriculture Department estimates the biofuels sector to consume 12 billion pounds of soybean oil (2021-22), up from 9.5 billion pounds in 2020-21.
- Archer Daniels Midland Co. invested $350 million into a new soybean crushing plant—capacity of 150,000 bushels of soybeans a day.
- Cargill will spend $475 million improving its soy crushing facilities across 4 states.
- Animal fats make better renewable fuel but not enough of them
  - 40% of all beef tallow goes to fuel
  - 80% of all yellow cooking grease goes to fuel

Source: Maltais, Kirk. "Renewable-Fuel Push Drives Soyoil Prices to Record High." Wall Street Journal. 6 June 2021.

# Materials, Chemicals, & Energy: Company Examples

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# Conclusions

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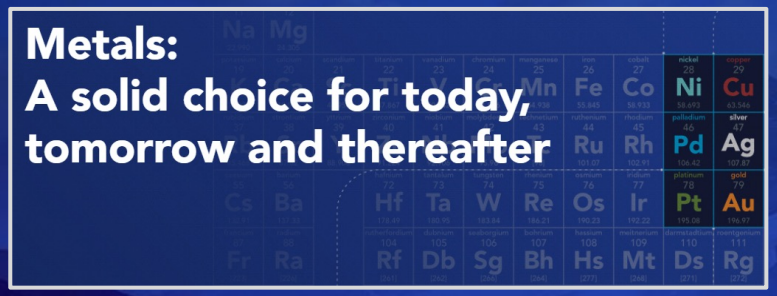
# Conclusions for the Upcoming Biorevolution

+ Costs and speed advantages bring a unique scalability to biological questions and research today (artificial intelligence, cloud computing, etc.)
+ In Agriculture—the driving force for greater research effort is the need to feed 9 billion people
+ In human health, new approaches could lead to different treatments do old diseases
+ While still early in its genesis, DNA may be the most efficient way for the world to store its data
+ Biofuels represent interesting options across the transportation spectrum

# Questions

## For more information and insights please visit: wisdomtree.eu

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