Biotechnology Playbook

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Introduction

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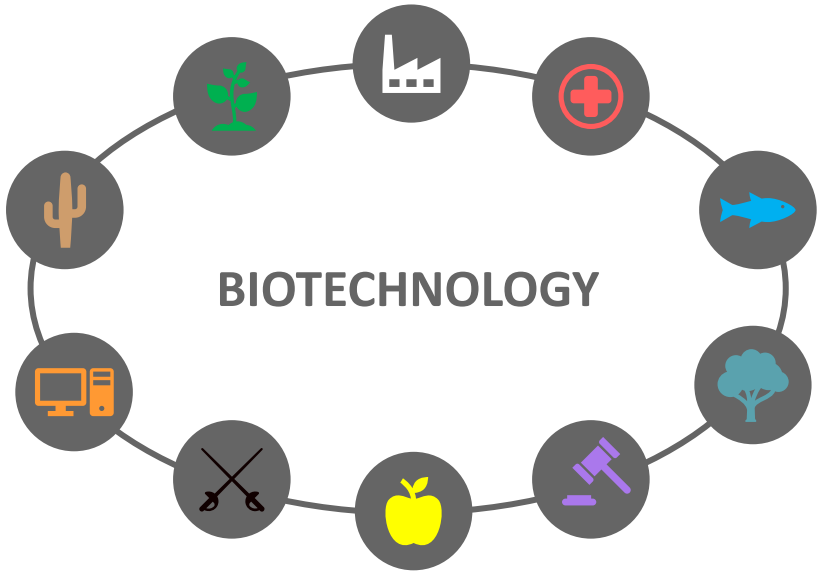
Introduction: The Colours of Biotechnology

Industrial Biotechnology
Use of biological resources for industrial applications e.g. biodegradable polymers; fuel from renewable resources

Agricultural Biotechnology
Collection of scientific techniques used to improve plants e.g. GMOs, resistant crops, improved nutritional content

Medical Biotechnology
Use of biological sources to develop treatments or diagnostic tools e.g. biopharmaceuticals



Desert Biotechnology
Management of arid lands and deserts via biological input e.g. crop management, drought-tolerant plants.

Marine Biotechnology
Exploitation of products from marine animals or plants e.g. aquaculture; GFP

Bioinformatics
Combination of computer science, maths and stats to interpret biological data e.g. sequence, expression, 'omics'

Environmental Biotechnology
Use of biological sources to combat environmental contamination e.g. ground-water treatment, renewal energy sources

Biological Warfare
Use of biological toxins or infectious agents to kill humans, animals or plants
e.g. 'Unlocked'; ricin; anthrax

Law, Ethics, Philosophy
Legal aspects surrounding this science
e.g. gene therapy, animal testing, GMOs

Food Biotechnology
Use of bio-engineering to create or modify foods
e.g. cultured meat; flavours; shelf life

Source: London Strategy, Jeeper

Biotechnology vs Conventional Pharma

What is Biotechnology?
Wikipedia: "any technological application that uses biological systems, living organisms or derivatives thereof, to make or modify products or processes for specific use"

What are Biopharmaceuticals?
Wikipedia: "any pharmaceutical drug product manufactured in, extracted from, or semi-synthesized from biological sources"

What is Bioprocessing?
Pharma IQ: "any process that uses complete living cells or their components to obtain desired products"

Key Differences between Biotech and Conventional Pharma:

	Size	Style	Molecules	Manufacturing	Marketing
Biotechnology	➢ Small, grown out from academic labs	➢ Entrepreneurial, young, cutting edge	➢ Large complex proteins / monoclonal antibodies	➢ Grown and harvested in living organisms	➢ Reliant on pharma to market their drugs
Pharmaceuticals	➢ Large, traditional, big business model	➢ Corporate, secure, traditional	➢ Small molecules / relatively simple synthetic compounds	➢ Produced via chemical synthesis	➢ Strength from phase III to market

Source: London Strategy, Jeeper

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Biotechnology Playbook – Top Biotech Trends & Innovations

- Bioprocessing / Biomanufacturing
- Antimicrobial Resistance
- Stem Cells & Regenerative Medicine
- Precision Medicine
- Vaccine Development
- Longevity / Biology of Ageing
- Genetic Sequencing & Engineering
- Microfluidics / Organ-on-a-Chip
- Synthetic Biology
- Cell & Gene Therapy
- Microbiome
- Big Data & Artificial Intelligence

Source: London Strategy

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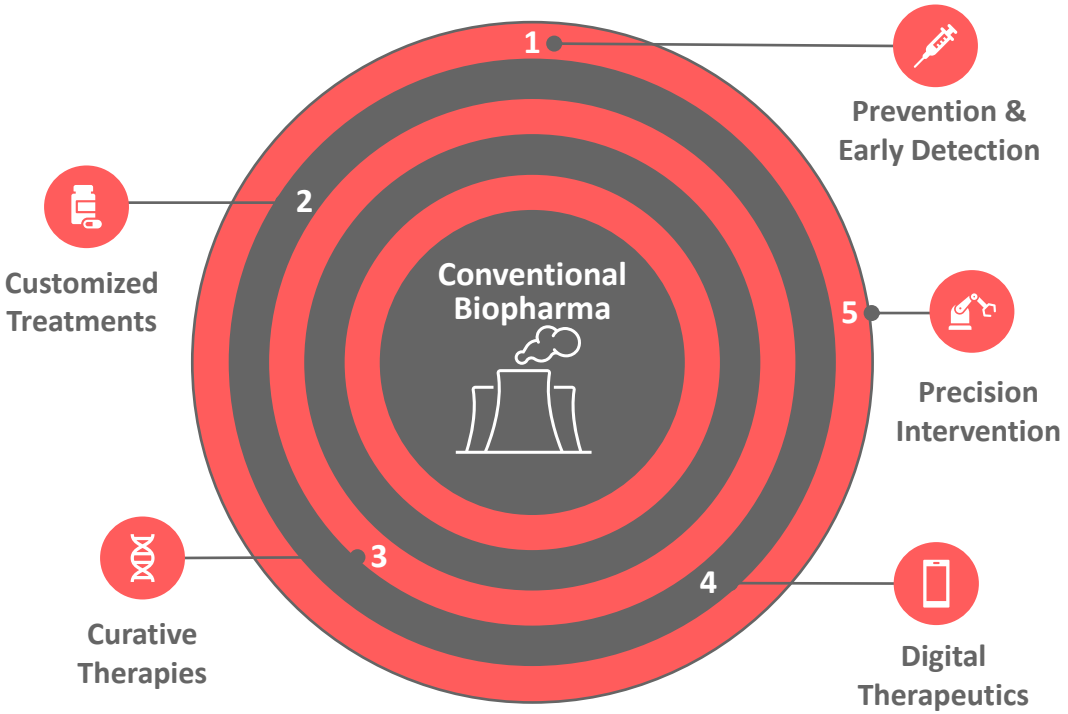
Future Disruptions to the Biopharma Industry

Five forces of disruption to the biopharma industry…

…that may impact the future of bio-pharma companies and the patients they serve.



1. **Prevention & Early Detection**
   - Advances in early detection in conjunction with vaccines and improvements in wellness could help prevent disease, making treatments for some diseases no longer necessary.
2. **Customized Treatments**
   - Personalisation in medicine, driven by data-powered insights, could effectively match patients with customized drug cocktails, or design therapies that would work for just a few people, or even a particular person.
3. **Curative Therapies**
   - As with prevention, treatments that cure disease could reduce or eliminate the demand for some prescription medicines, Developing, marketing and pricing these curative treatments could require the biopharma sector to adopt new capabilities.
4. **Digital Therapeutics**
   - Increasingly effective and scalable non-pharmaceutical (digital) interventions, including those focused on behaviour modification, might also reduce the need for pharmaceutical intervention.
5. **Precision Intervention**
   - Increasingly sophisticated medical technology, such as precise medical intervention by robotics, nanotechnology or tissue engineering, could reduce the need for pharmaceutical intervention.

Source: Deloitte

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Bioprocessing / Biomanufacturing

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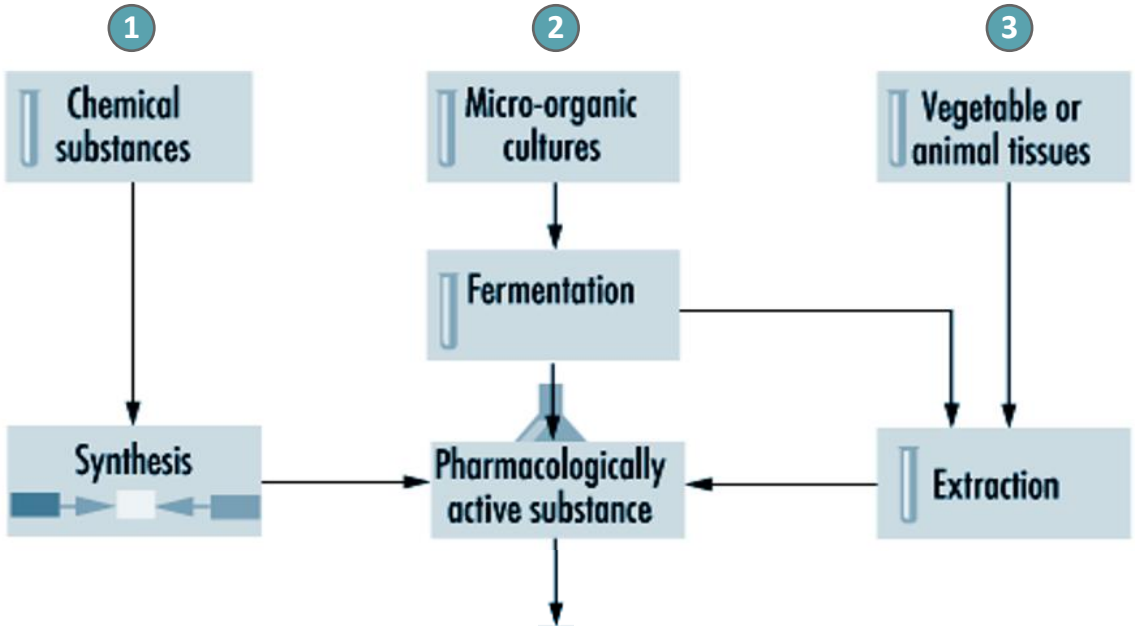
Manufacturing Processes Overview - Biotech vs Conventional Pharma



1. **Conventional Pharma Manufacturing**
   Chemical synthesis for drug manufacturing

2. **Biotechnology Manufacturing**
   Bioprocessing for growth and harvest of biopharmaceuticals

3. **Extraction of natural drug products**
   from vegetable or animal tissues

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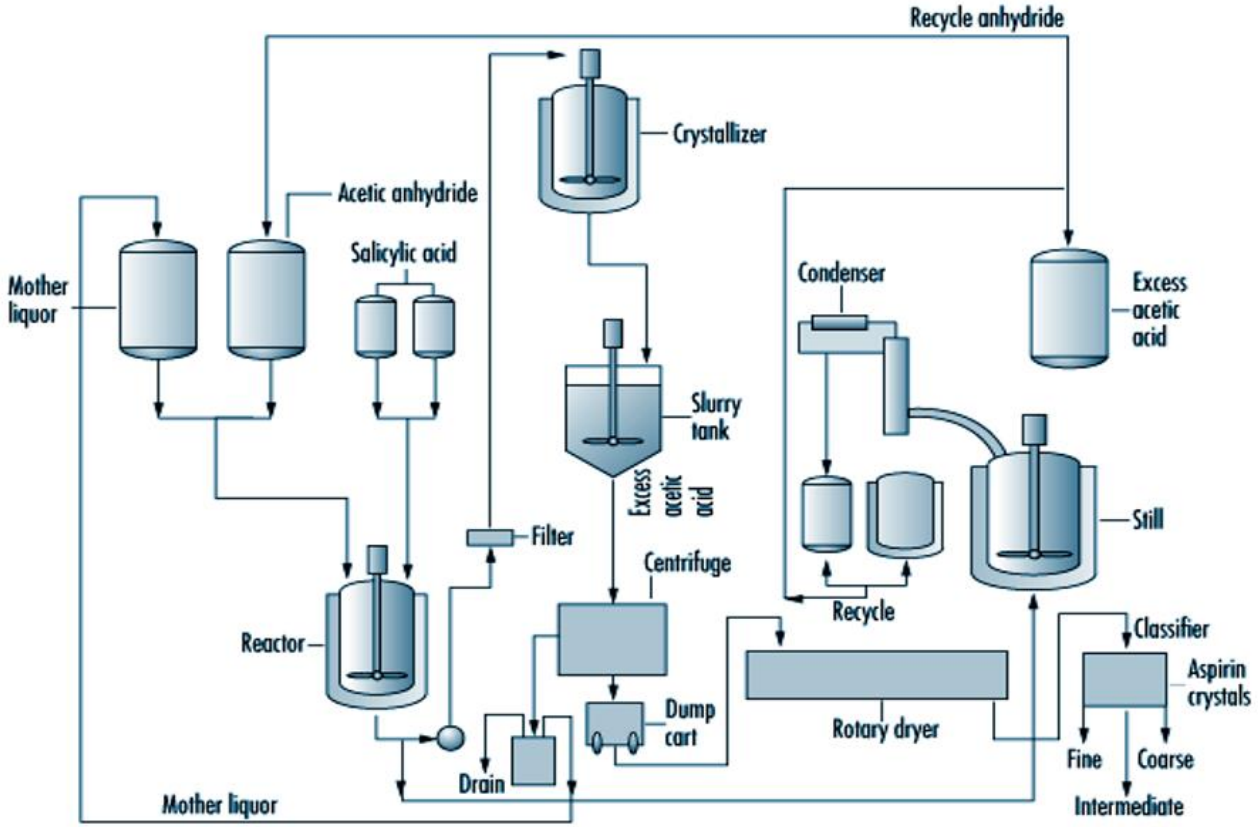
Chemical Synthesis Process Overview

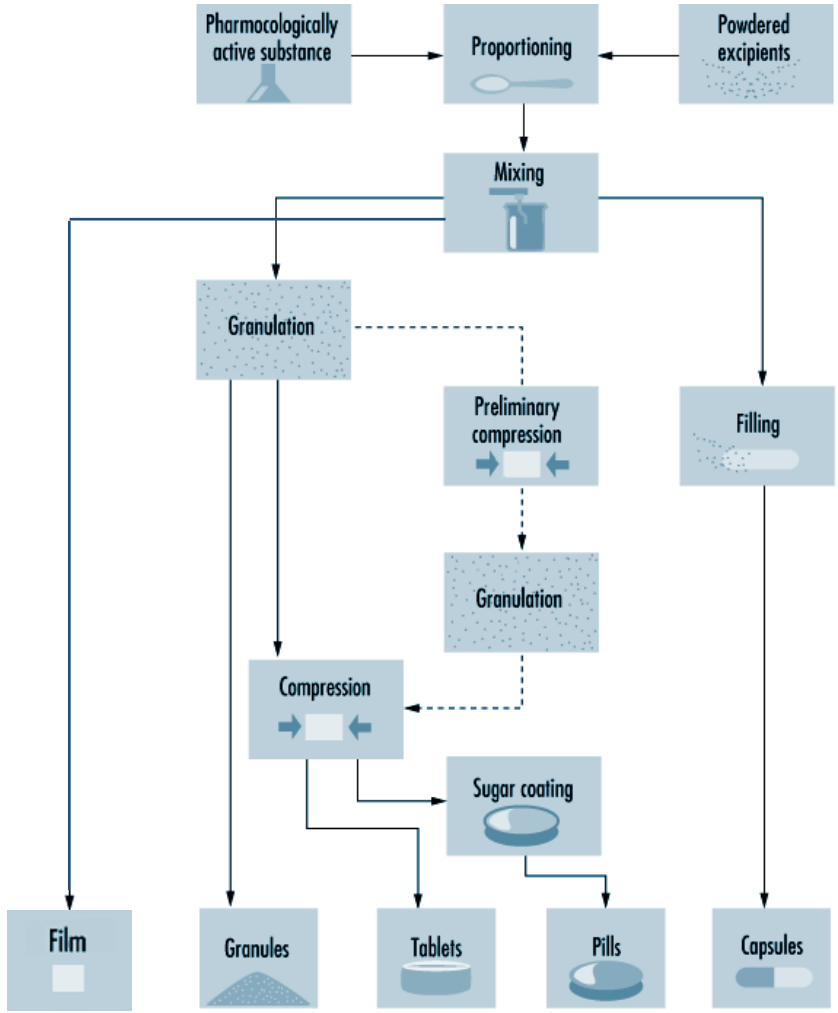


Source: EPA

- Diagram shows an example of bulk aspirin manufacturing process.
- Series of chemical reactions in multipurpose reactors.
- Process flow from reactor to crystallizer, slurry tank, centrifuge, dump cart and rotary dryer.
- The products are isolated by extraction, crystallisation and filtration.

Source: Environmental Protection Agency (EPA).

Process Workflow for Dosage-Form Products



- Drug substances are converted into dosage-form products before administration to humans or animals
- The active drug substances are mixed with excipients and processed to achieve the desired properties for final formulation.
- Tablets, pills and capsules are amongst the most common dosage forms.

Source: London Strategy, Encyclopaedia of Occupational Healthy & Safety

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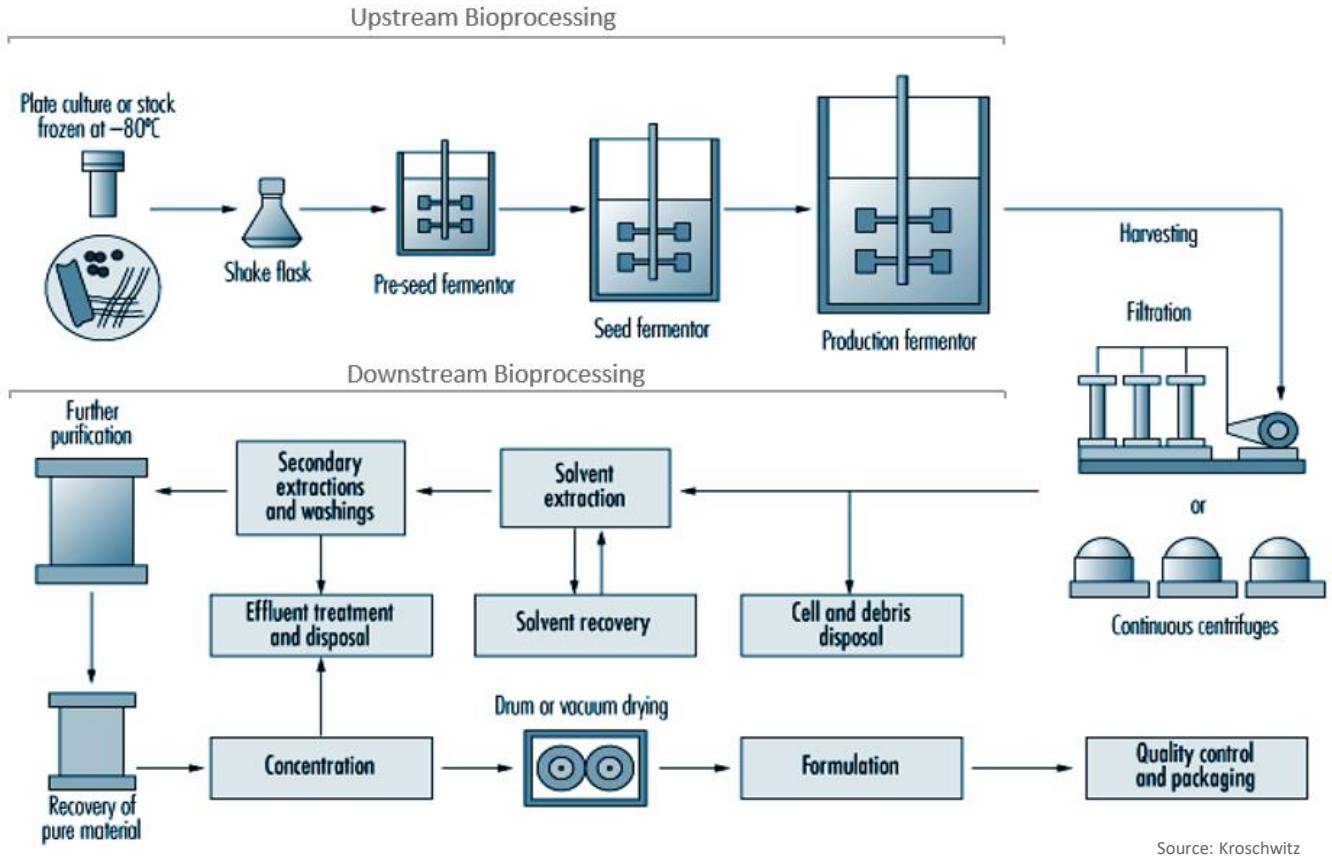
Bioprocessing Overview



Source: Kroschwitz

- Biopharmaceutical manufacturing or Bioprocessing is divided into two broad areas:
  - Upstream Bioprocessing
  - Downstream Bioprocessing
- Microorganisms containing the chemical product are grown up to large scale, the product is them harvested and purified.

Source: London Strategy, Encyclopaedia of Chemical Technology

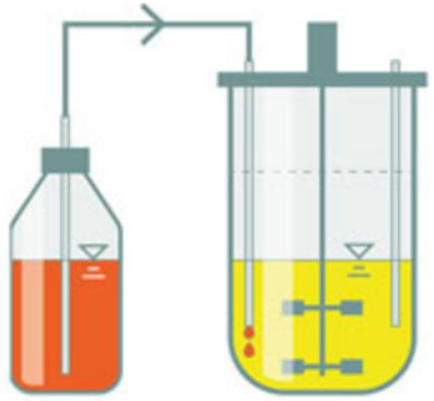
Upstream Bioprocessing: Batch, Fed-Batch, Continuous Cultures

Batch Culture

Source: Eppendorf AG

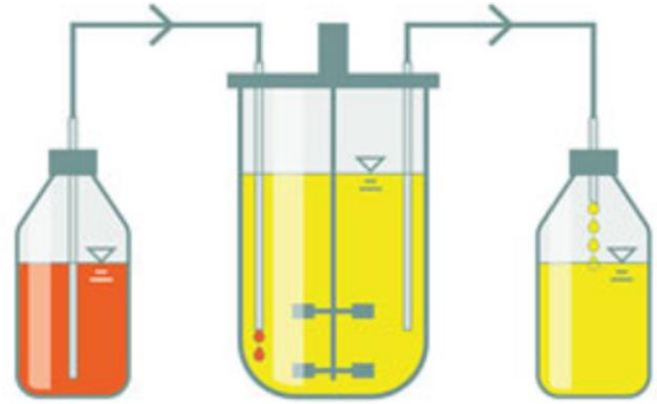
- Medium added once prior to start of culture
- Cells inoculated into fixed volume
- Cells division stops when all nutrients are consumed and toxic by-products build up

Fed-Batch Culture



- Inoculate cells into a small volume of media
- Additional medium or various feed substrates are added periodically to increase or maintain culture
- Duration and cell density of culture can be extended

Continuous Culture



- Initial volume of medium added and cells inoculated
- Cell concentration increases and more media added for steady state
- Perfusion of fresh media and removal of harvested material / waste media

Source: NIBRT

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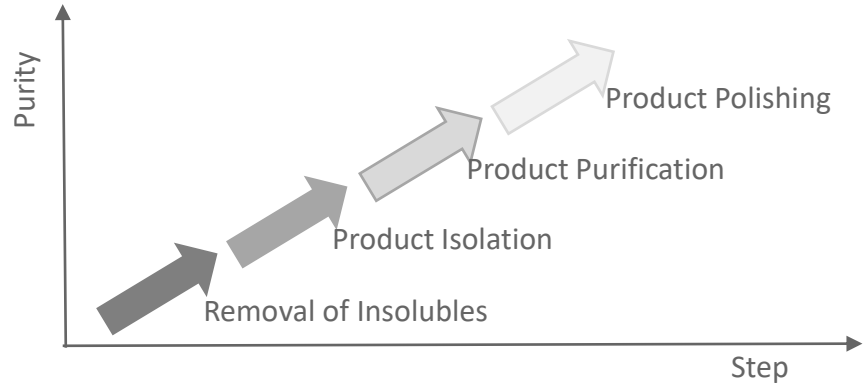
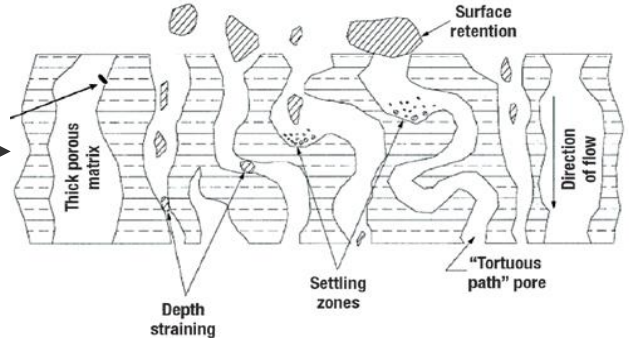
Downstream Bioprocessing: Product Recovery Methods

Filtration

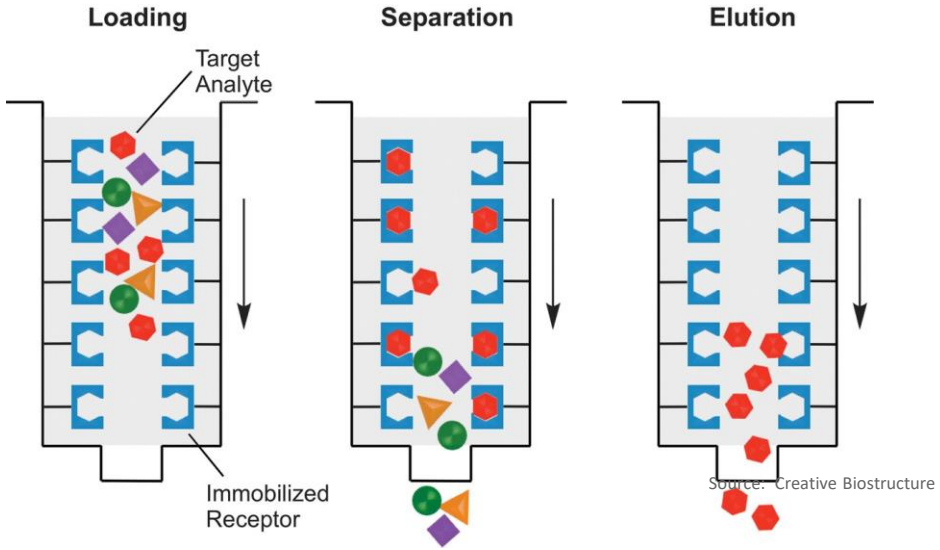


Source: 3M Purification

Depth Filtration removes cell debris due to size exclusion as well as contaminants and unwanted particles



Chromatography



Source: Creative Biostructure

Types of Chromatography:
- Affinity Chromatography
- Ion Exchange Chromatography
  - Cation Exchange
  - Anion Exchange
- Hydrophobic-Interaction Chromatography

Source: NIBRT

Future of Biopharma Manufacturing

Current State & Prospects

- The generic-drug business model is based on high-volume treatments that target large populations, and account for about 90% of all prescription drug purchases.
- There is an increasing shift towards precision medicine, which could have a significant impact on the biopharma supply chain and disrupt the generic volume-based model in the years to come.
- The result of tailored drug regimens and smaller-volume therapies means that new manufacturing capabilities will be required.
- This calls for the emergence of new key trends within the biopharma manufacturing industry, as highlighted below:
    - Smaller Modular Facilities for Niche Products – Precision Medicine
    - Single-Use Technologies – Stainless Steel Vessels
    - Robotics and Automation – Aseptic / Contained Processing
    - Continuous Manufacturing Technologies – Process Analytical Technology (PAT)
    - Portable Manufacturing Facilities – Pfizer PCCM Facility

Additional Material

1 **Pfizer: PCCM Portable Manufacturing Facility**

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Precision Medicine

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Introduction: Personalised vs Precision Medicine?

What is Personalised Medicine?

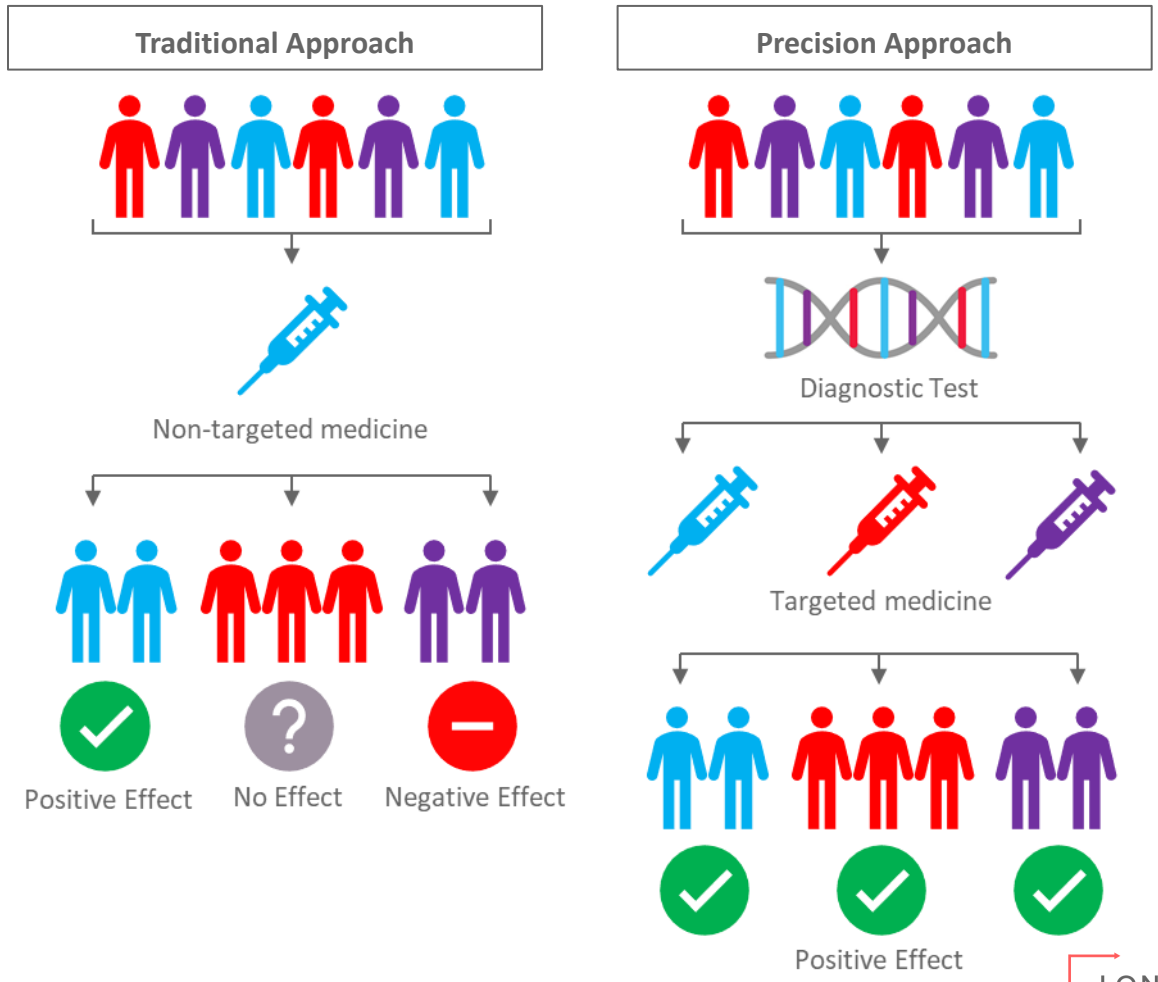
Healio: "A medical model through which health care delivery is tailored to individual patients based on their characteristics, including genetic make-up, disease biomarkers, treatment history and environmental factors."

National Research Council:

Personalised Medicine is sometimes misinterpreted as implying that unique treatments can be designed for each individual.

What is Precision Medicine?

NIH: "An emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person."



Source: NIH

Precision Medicine in Cancer Treatment

Targeted Cancer Therapies:

Background: Drugs or other substances that block the growth and spread of cancer by interfering with specific molecular targets that are involved in the growth, progression and spread of cancer. These differ from standard chemotherapies in different ways:

- These therapies act on **specific molecular targets** associated with the cancer, whereas chemotherapies typically act on all rapidly dividing normal and cancerous cells.
- These therapies are often cytostatic, i.e. they **block tumour cell proliferation**, where as chemotherapies are cytotoxic, i.e. they kill tumour cells

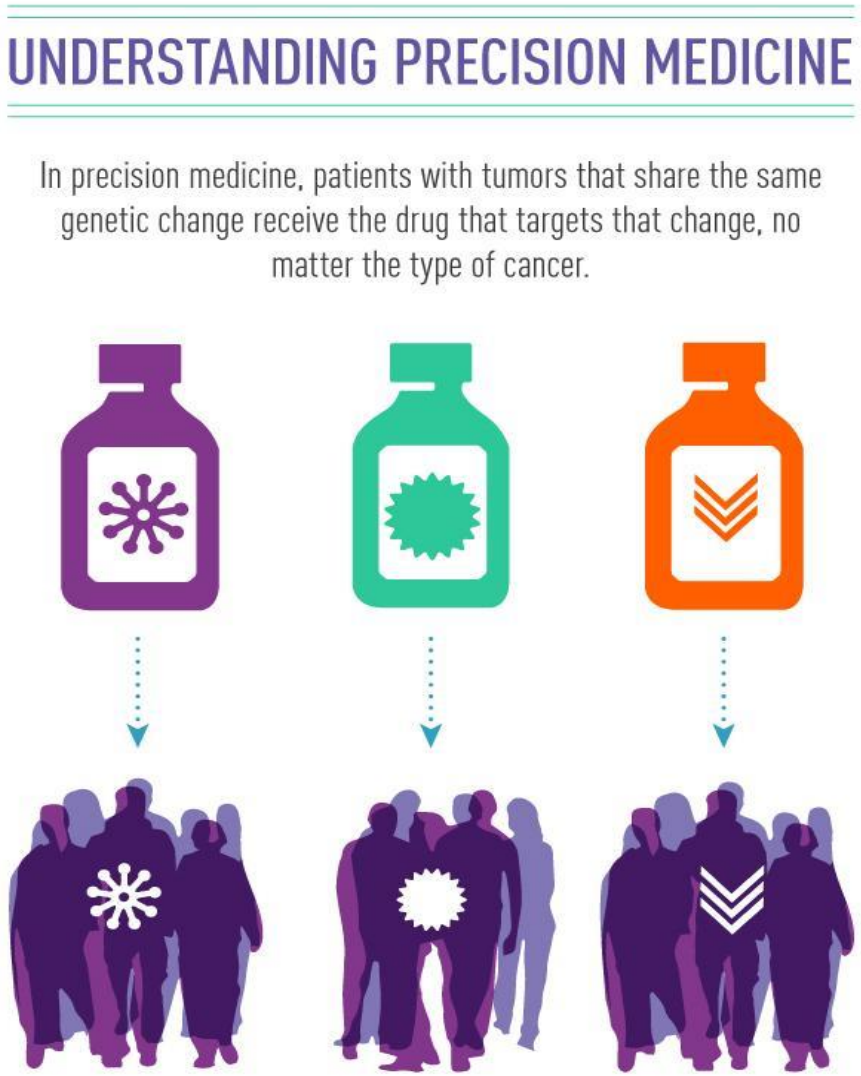
Identification: Standard approached to identify potential targets for these therapies include:

- Identify individual proteins present only or more abundant in tumour cells. These are often involved in growth or survival of the cancer cells (e.g. HER-2).
- Determine whether cancer cells produce mutant (altered) proteins that drive cancer progression
- Identify abnormalities in chromosomes that are present in the cancer cells and not in normal cells, which may create a fusion protein that drives cancer development (e.g. BCR-ABL fusion protein).

Development: Most targeted therapies against specific targets are either:

- Small Molecules: where high throughput-screens allow examination of thousands of test components against a specific target, lead compounds identified and chemically modified for specificity and efficacy.
- Monoclonal antibodies: where animals are injected with purified target proteins that induces production of different antibodies against the target. The lead candidates are then re-tested and humanised (prevent recognition as foreign) before introduction into humans

Summary: These therapies are a cornerstone of precision medicine by using the patient's or cancer's genetic data to prevent, diagnose and treat disease.

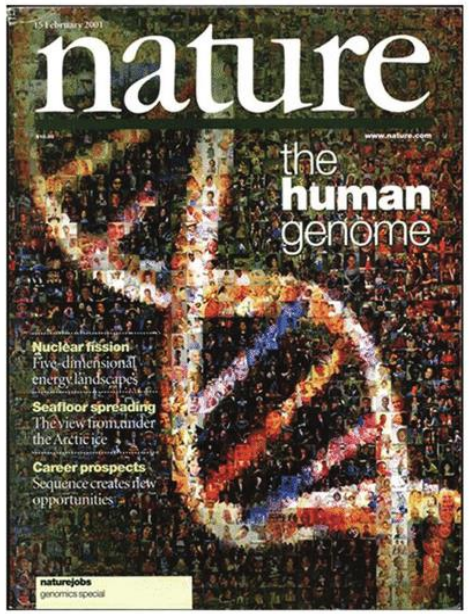


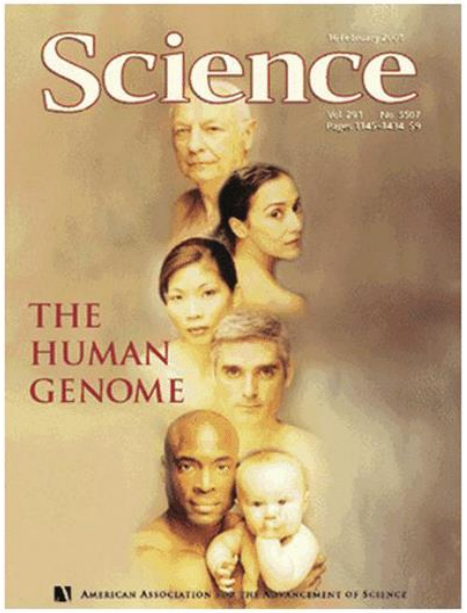
Source: NIH

Human Genome Project & 100,000 Genomes Project

Human Genome Project:

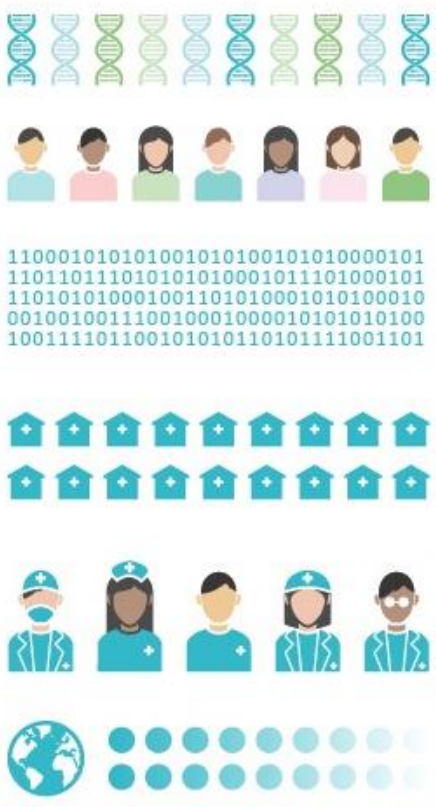
- **Background**: The world's largest collaborative biological project which span from 1990 – 2003 and cost $2.7 bn.
- **Aim:** To determine the identify and sequence of the 3.2 billion base pairs that make up human DNA and mapping these genes from a physical and functional standpoint.
- **Impact:** This has provided a resource of detailed information about the structure, organization and function of the complete set of human genes.





Source: Genomics England

The 100,000 Genomes Project in numbers



Overview:

Background: UK-based project run by Genomics England which span from 2012 – 2018.

Aim: To sequence the whole genomes of 100,000 NHS patients and evaluate the link to rare diseases, cancer and infectious disease.

Impact: The UK has become the first nation in the world to apply whole genome sequencing at scale in direct healthcare

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Precision Medicine Global Initiative: 'All of Us' Research Program

All of Us Research Program - Overview:

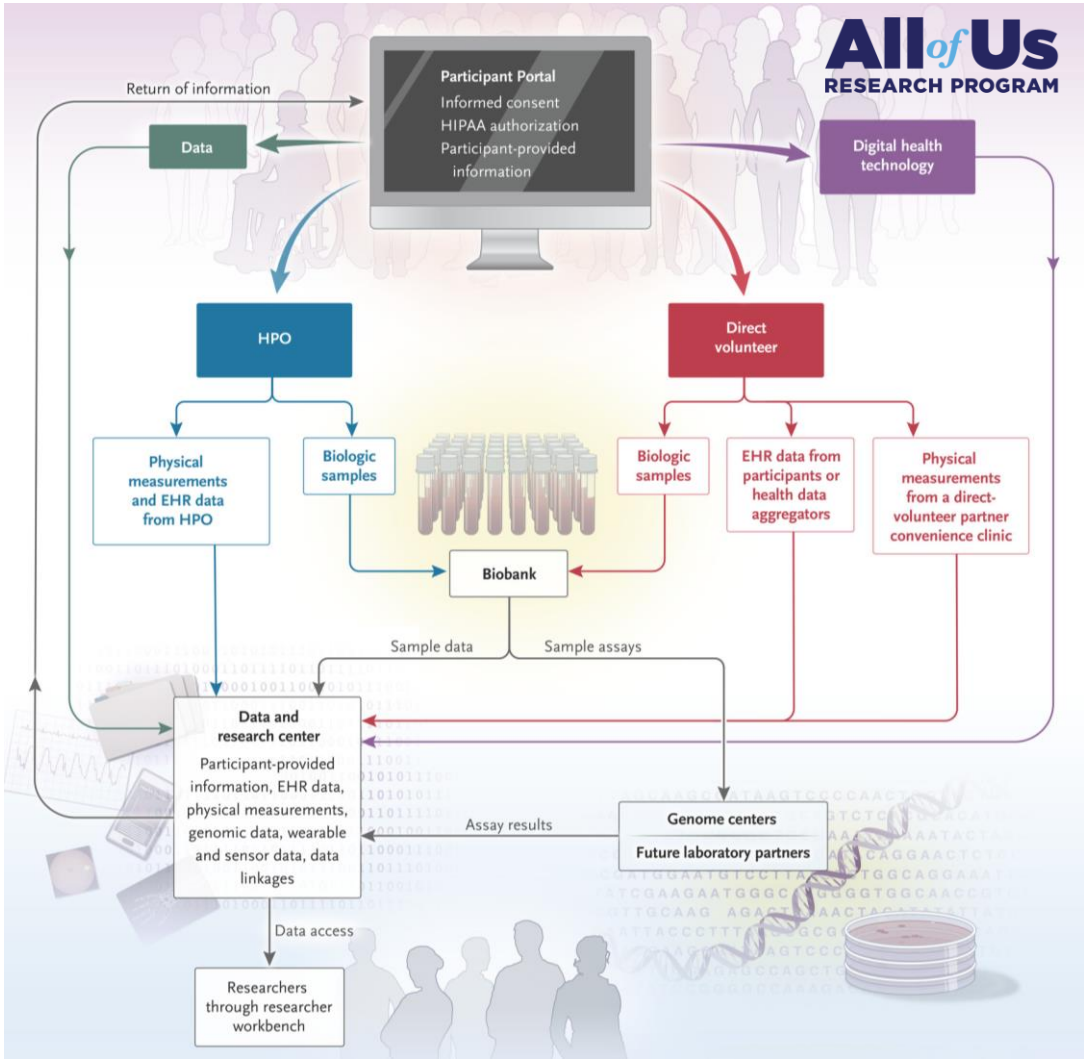
Background: A research initiative created in 2015 under the tenure of Barack Obama with $130 million in funding to make advances in tailoring medical care to the individual.

Aim: To collect genetic and health data from one million volunteers or more living in the United States.

Method: The protocol ranges from health questionnaires, electronic health records (EHRs), physical measurements, the use of digital health technology, and the collection and analysis of biospecimens

Progress: The program had opened for enrolment in 2018 and one year later met 1/5th of its recruitment goal. Enrolment is expected to last for up to 10 years.

Result: This will form the basis of a longitudinal cohort studies for advancing characterizing natural histories of diseases, identifying their risk factors, and revealing new biomarkers as part of the movement towards precision medicine.

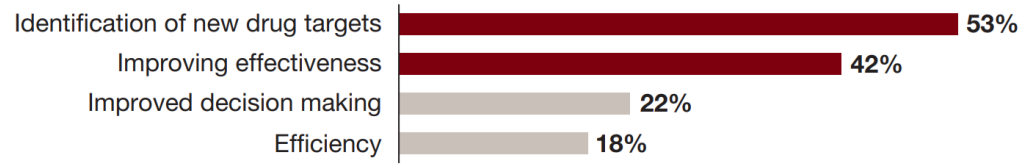


Source: NIH

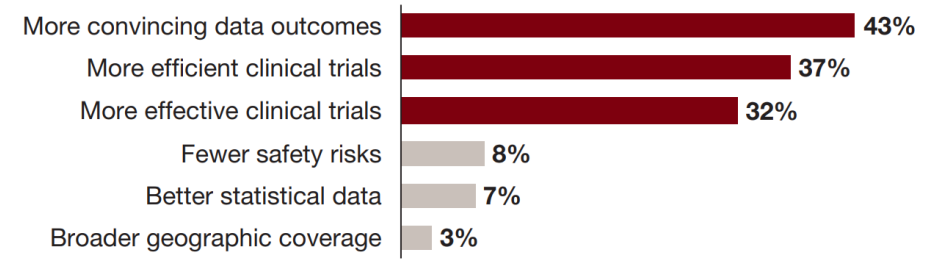
Promise of Precision Medicine: Strategy&

Benefits of Precision Medicine to the Pharmaceutical Value Chain:

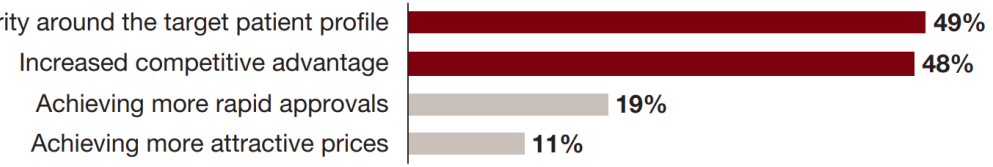
Research



Development

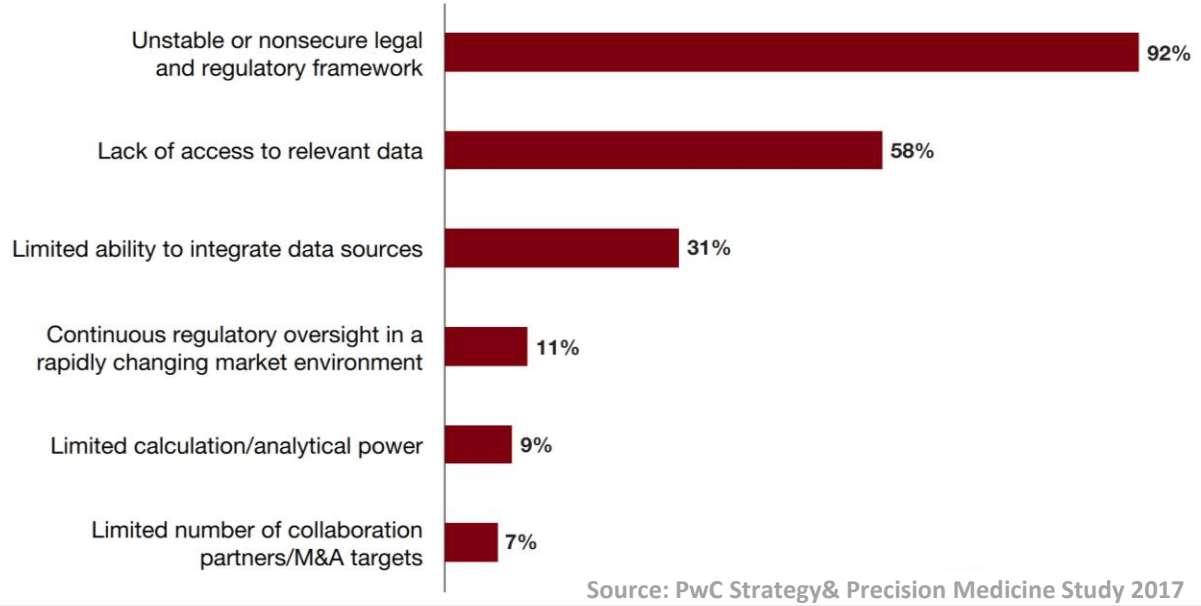


Market authorization



Source: PwC Strategy& Precision Medicine Study 2017

Key External Barriers for Precision Medicine



Source: PwC Strategy& Precision Medicine Study 2017

Closing Remarks on Precision Medicine

- Precision medicine can help physicians tailor medicines to patients needs with a deeper understanding of diseases with richer patient data and advanced analytics, leading to better outcomes at potentially lower costs.
- This initiative has the potential to transform the pharmaceutical value chain, from early development through to go-to market models, despite the external barriers that remain.
- Many global leaders in the pharmaceutical industry are aware of the promise and recognise the opportunities that this brings to this sector.
- The next few years are critical for pharmaceutical companies to capitalise on this promise.

Genetic Sequencing & Engineering

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Introduction: What is Genetic Engineering?

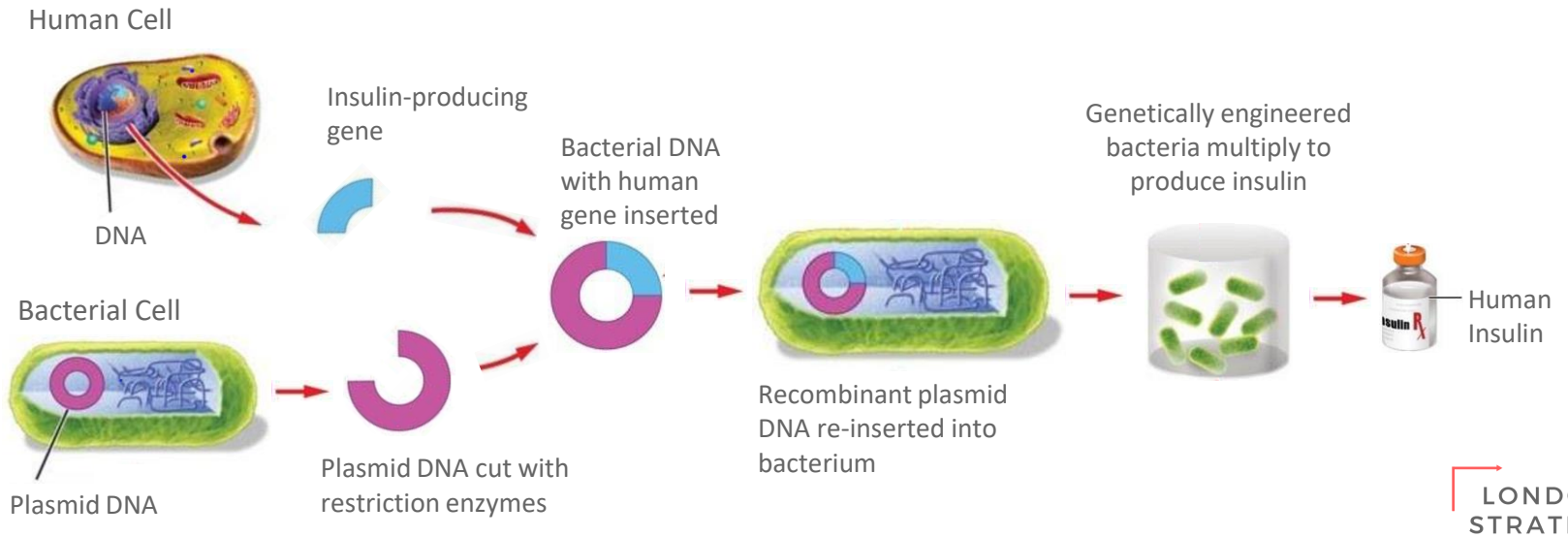
What is Genetic Engineering?
Wikipedia: "also called genetic modification or genetic manipulation, is the direct manipulation of an organism's genes using biotechnology"

What is Genome Editing?
Wikipedia: "a type of genetic engineering in which DNA is inserted, deleted, modified or replaced in the genome of a living organism at site specific locations"

What is Gene Therapy?
GHR: "a type of gene editing, involving the introduction of genetic material into cells to compensate for abnormal genes or to make a beneficial protein"

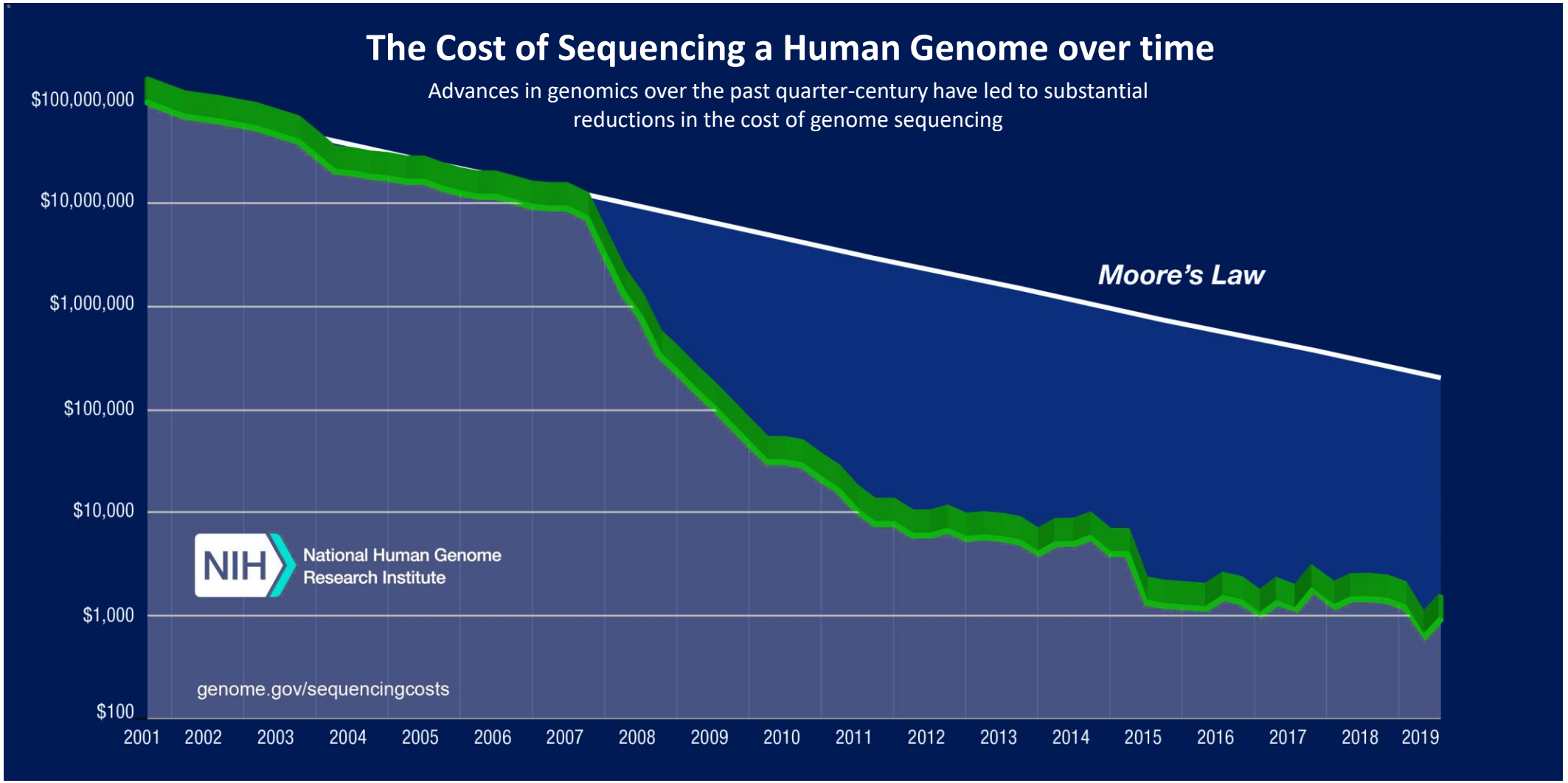
- All organisms generated through genetic engineering are considered to be **GMOs.**
- There are several applications of genetic engineering:
  - Agriculture
  - Medicine
  - Research
  - Industry

Outline of the genetic engineering process to produce human insulin using bacterial cells



Source: A Star Biology

Costs of Genome Sequencing



Source: NIH

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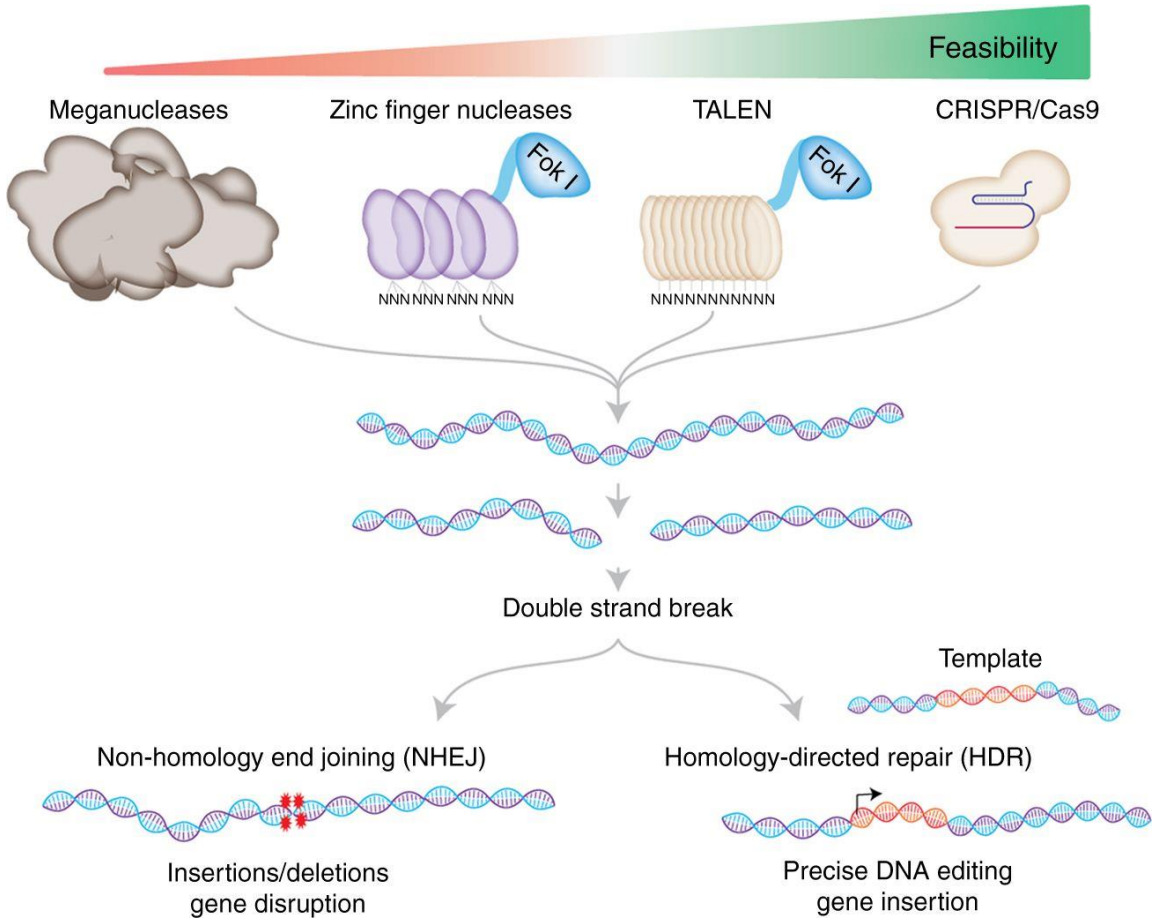
Genome Editing Techniques

The basic working principle of major genome-editing technologies



Toolkits

1. **Meganucleases**
   - These are engineered restriction enzymes that recognize long stretches of DNA sequences.
2. **Zinc Finger Nucleases**
   - These are restriction enzymes that are engineered to recognise specific desired triplet DNA sequence
3. **TALENs**
   - These are restriction enzymes that are engineered to recognise any location via protein-DNA interaction
4. **CRISPR/Cas9**
   - This is a natural defence mechanism in bacteria adopted for simple RNA–DNA base pairing and the PAM sequence determine CRISPR targeting specificity

Source: Nature Communications

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CRISPR – The Biggest Science Story of the Decade

Discovery

- CRISPR was first discovered in 1987 by Yoshizumi Ishino at Osaka University Japan.
- This technology was proposed for programmable gene editing in 2012 by Jennifer Doudna and Emmanuelle Charpentier at UC Berkeley

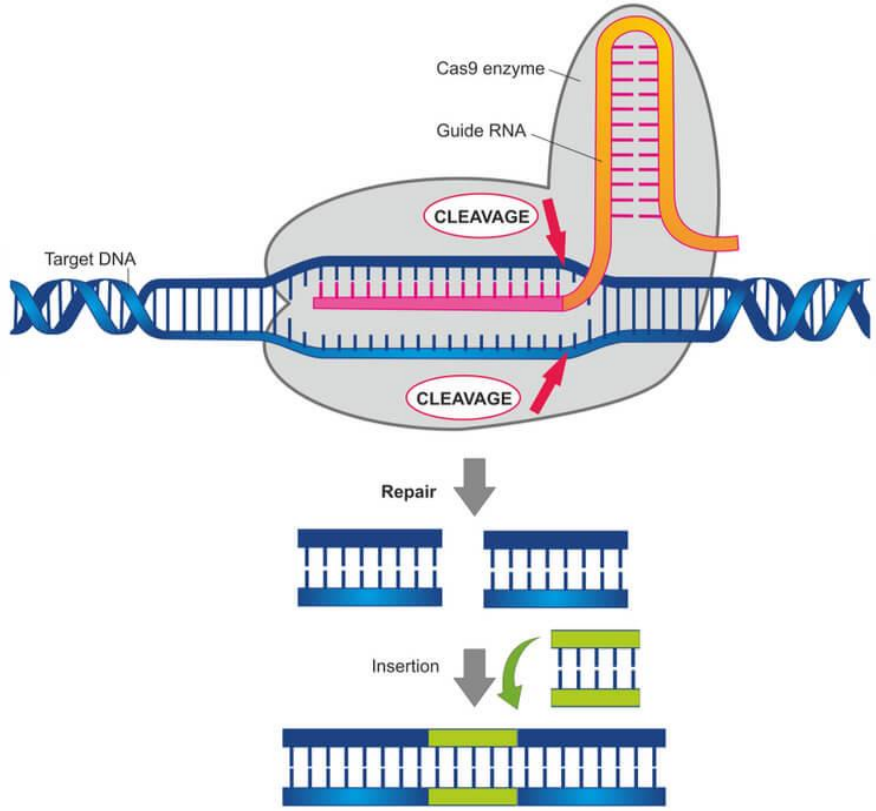
Method

- Viral DNA is injected into the bacterial cell to cause infection.
- When the bacterial cell detects the presence of foreign DNA, it produces a RNA-Protein (Cas-9) complex, that matches that of the viral DNA.
- Cas-9 is a nuclease, a type of enzyme that cuts the DNA, therefore rendering the viral DNA ineffective.

Application

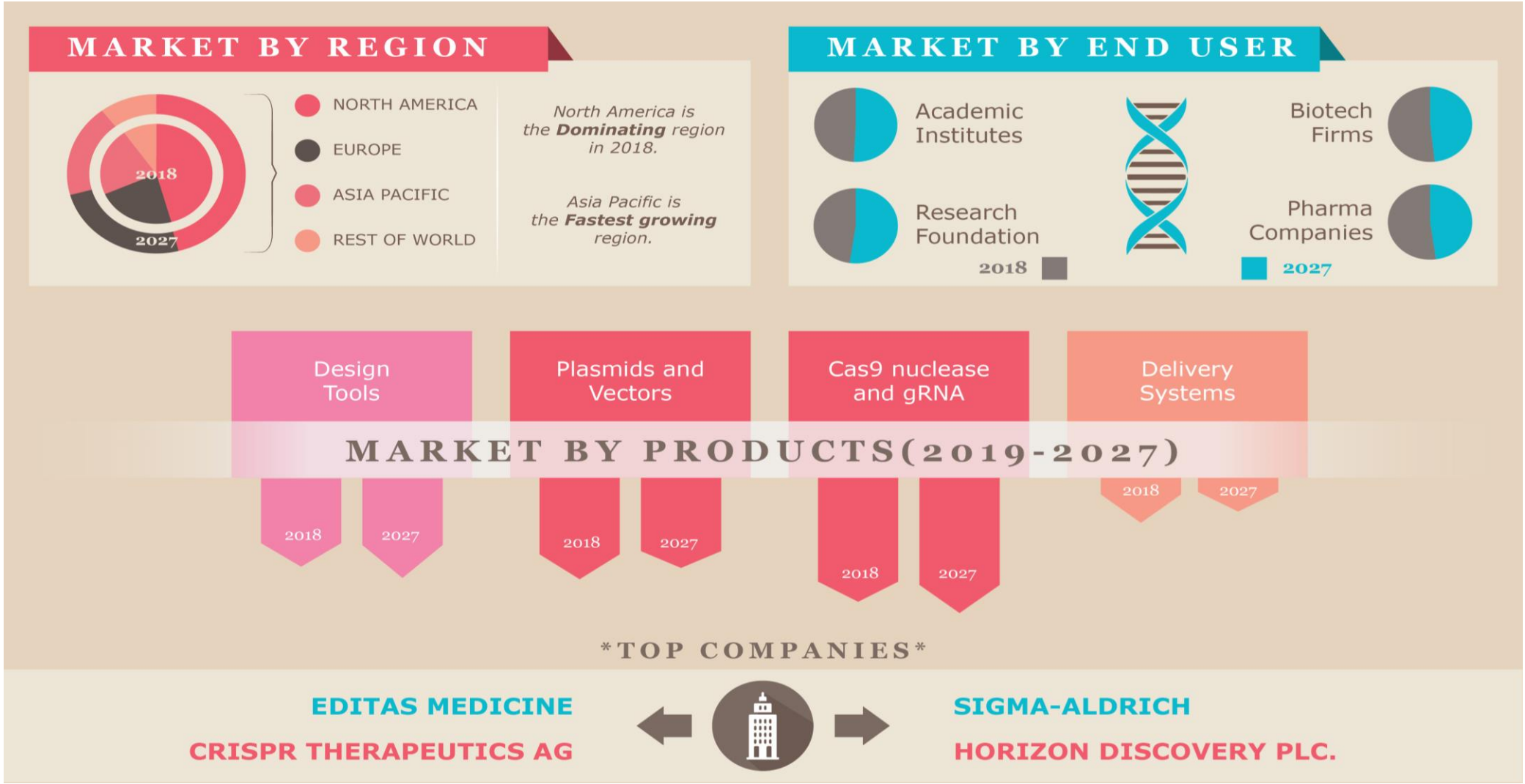
- Researchers found that this complex can be engineered to cut any DNA sequence at a precisely chosen location in vivo.
- The cut strand is then repaired by insertion of new nucleotides, either randomly or by with a desired sequence.
- This method will have applications in basic research, drug development, agriculture and human disease

CRISPR: Mechanism of Action *



Source: London Strategy, Labiotech EU

Global CRISPR Market Forecasts (2019-2027)



Source: Inkwood Research

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Cell & Gene Therapy

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Introduction: Gene Therapy vs. Cell Therapy

Gene Therapy

Definition

- An approach of treating disease by modifying gene expression by:
  - Replacing a mutated gene
  - Inactivating or knocking out a mutated gene
  - Introducing a new gene

Mode of Action

- Therapeutic genetic material could be transferred to in vivo or ex vivo to somatic or germline cells
- A vector, often a virus (AAV) or physical / chemical methods to deliver a new working gene or genetic material into the cell.

Examples

- 20 Gene Therapy Products approved (FDA) e.g. Luxturna (Novartis), Macugen (Pfizer), Glybera (AMT)
- 2000 + human gene therapy clinical trials worldwide

Cell Therapy

Definition

- An approach of treating disease whereby cellular material (i.e. living cells) is injected, grafted or implanted into a patient.

Mode of Action

- Cells that are pluripotent / multipotent stem are injected into the site of injury, where they replace damaged tissue and facilitate improved function of the organ / tissue
- Cells that are able to release soluble factors like chemokines, cytokines or growth factors act in a paracrine or endocrine manner to facilitate self-healing

Examples

- Stem Cell Therapy – Embryonic, Mesenchymal, Neural, Hematopoietic
- CAR T-Cell Therapies – Kymriah (Novartis) & Yeskarta (Gilead)

Source: American Society of Gene & Cell Therapy

Overview: CAR T-Cell Therapy

What are T-cells?

- T-cells are a type of **white blood cell** (immune cells) that are able to search and destroy any foreign invaders.
- These cells recognise '**non-self antigens**' and generate responses to eliminate the pathogen or pathogen-infected cells

What does 'CAR' stand for?

- CAR refers to **chimeric antigen receptors**, which are proteins that have been engineered to give the T-cell the ability to target a specific protein
- These receptors are **chimeric** as they combine both antigen-binding and T-cell activating functions into a single receptor.

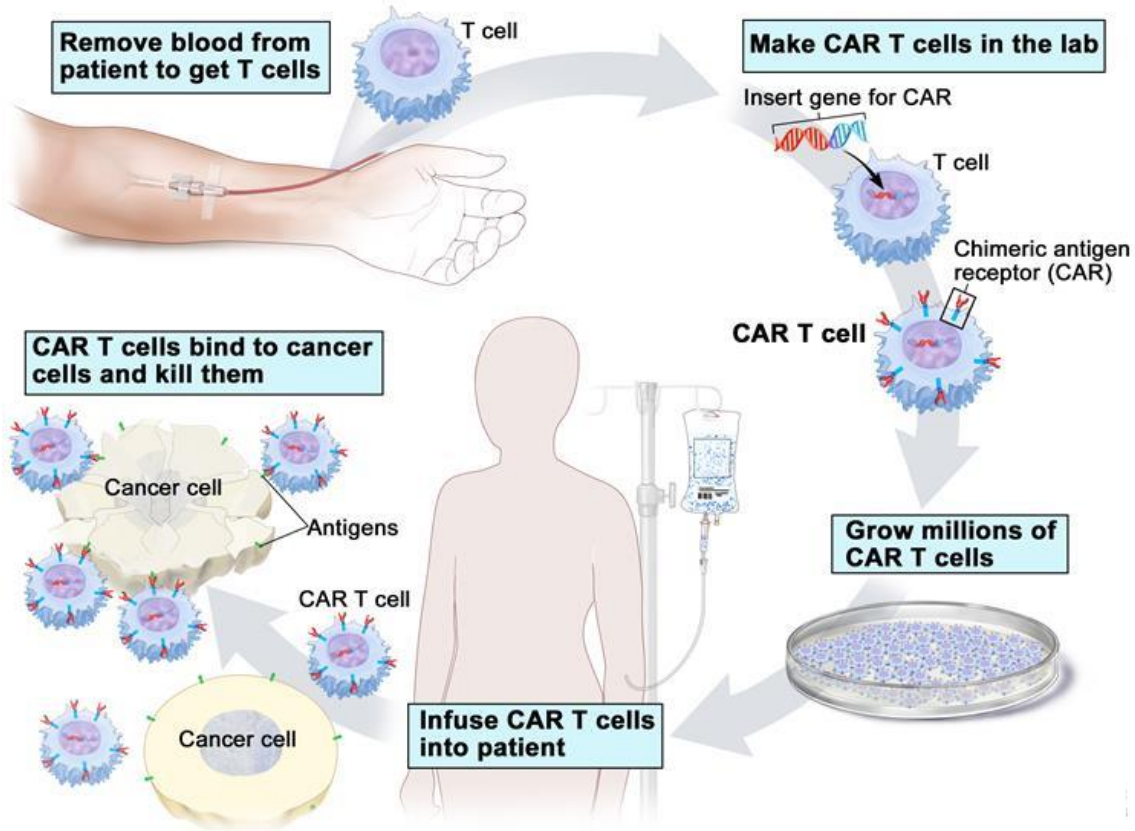
BBC NEWS

Immune discovery 'may treat all cancer'

By James Gallagher
Health and science correspondent

20 January 2020 | 136 Share

Overview of CAR T-Cell Therapy Mechanism of Action



Source: National Cancer Institute

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Antimicrobial Resistance

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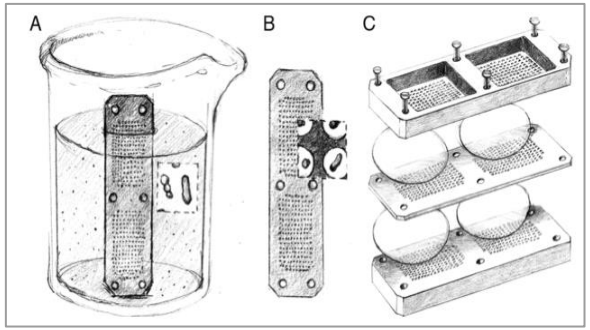
The History of Antibiotic Discovery Methods

There is a Pressing Need for Novel Platforms of Antibiotic Discovery



Penicillin

Golden Age of Antibiotics

Discovery Void

Great Plate Count Anomaly

iChip

1930 1940 1950 1960 1970 1980 1990 2000 2010 2020 2030

Waksman Platform

Diffusion Chamber

Metagenomics

Silent Operons

isChip

Source: Nature Reviews Drug Discovery

Antibiotic Resistance: One of the Biggest Threats to Global Health?

What are Antibiotics?
WHO: "antibiotics are a type of medicine used to prevent and treat bacterial infections."

What is Antibiotic Resistance?
Wikipedia: "the ability of a microbe to resist the effects of medication that once could successfully treat the microbe"

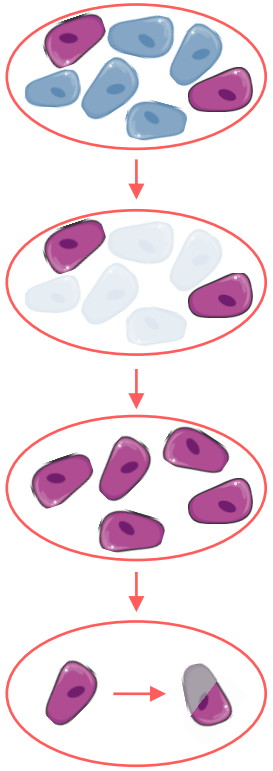
What are the implications of Antibiotic Resistance?

- Emergence of "**super-bugs**" or ultra-resistant bacteria which are much more difficult to treat
  - Well known examples include *MRSA*, *MSSA*, *E.coli*, *C.Difficile*
- Increased **costs to healthcare** due to prolonged hospital stays and more intensive care required
  - Estimated to cost the NHS around £180 million per year
- Increased death and **mortality rates** globally
  - Estimated that at least 700,000 deaths per year worldwide from AMR. (NICE)
- Surge to discover new types of antibiotics or explore **alternatives to antibiotics**
  - New strategies include Bacteriophage therapy, bacteriocins, predatory bacteria etc.

How can microorganisms acquire resistance?

- **Natural resistance**: when the microorganism already has the genes that confer resistance, but were inactive prior to exposure to the antibiotics
  - Genes that were **always** expressed in the species (e.g. reduced permeability of the cell membrane)
- **Acquired resistance**: when the microorganism acquire genetic material which confers a resistant trait against specific types of antibiotics.

How does Antibiotic Resistance occur?



A population of microbial cells with some resistant bacterial cells

Exposure to antibiotics kills all bacterial cells that do not confer antibiotic resistance

The resistant bacterial population have preferred conditions and are able to grow and multiply

Resistant bacterial cells are able to pass on this favourable gene to other bacterial cells.

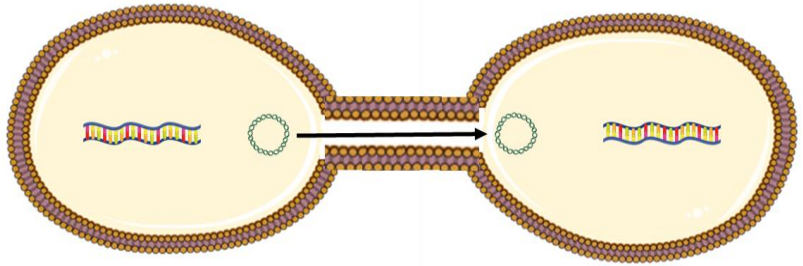
Source: AIMS Microbiology, WHO

How is Antibiotic Resistance Transferred to other Bacteria?

There are two principal routes of antibiotic resistance transfer called Horizontal and Vertical Gene Transfer

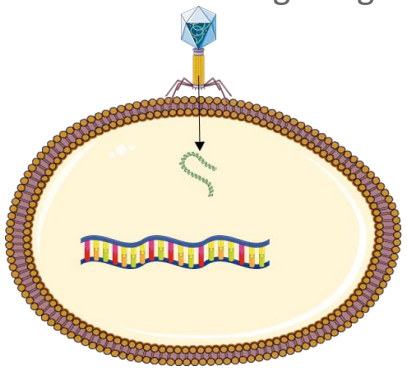
Horizontal Gene Transfer - antibiotic resistance genes transferred from an organism that is not its parent and is typically a member of a different species

1. Conjugation: Exchange of genetic material (plasmid) from one bacteria to another



The donor bacterial cell transfers genetic material through direct contact (via a structure called pilus) to the recipient bacterial cell.

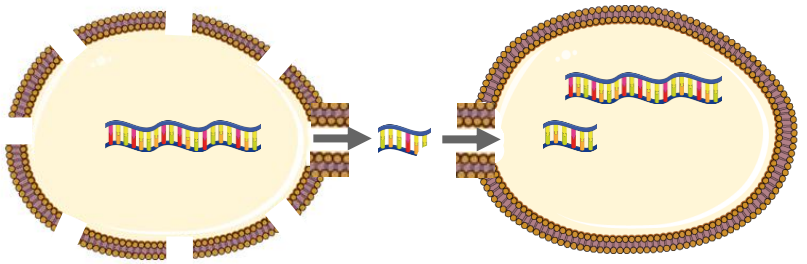
2. Transduction: Exchange of genetic material via a bacteriophage



Viral genetic material is injected into the bacterial cell and results in genetic recombination to confer antibiotic resistance

Source: AIMS Microbiology

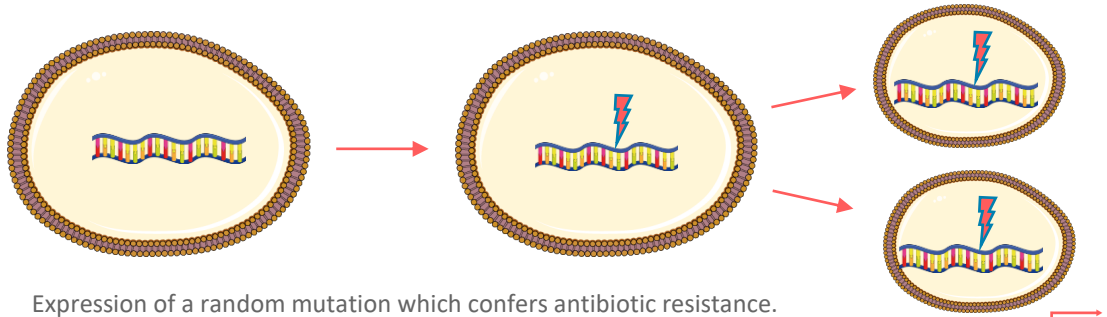
3. Transformation: Uptake of genetic material directly from the bacterial cell's environment



Bacterial cells lyse and release genetic material into the environment which is taken up by other bacterial cells

Vertical Gene Transfer - antibiotic resistance genes transferred down generations i.e. from parents to offspring

1. Random Mutation: Mutation of the bacterial cells genetic information can confer antibiotic resistance



Expression of a random mutation which confers antibiotic resistance. This mutation is passed on to the next generation.

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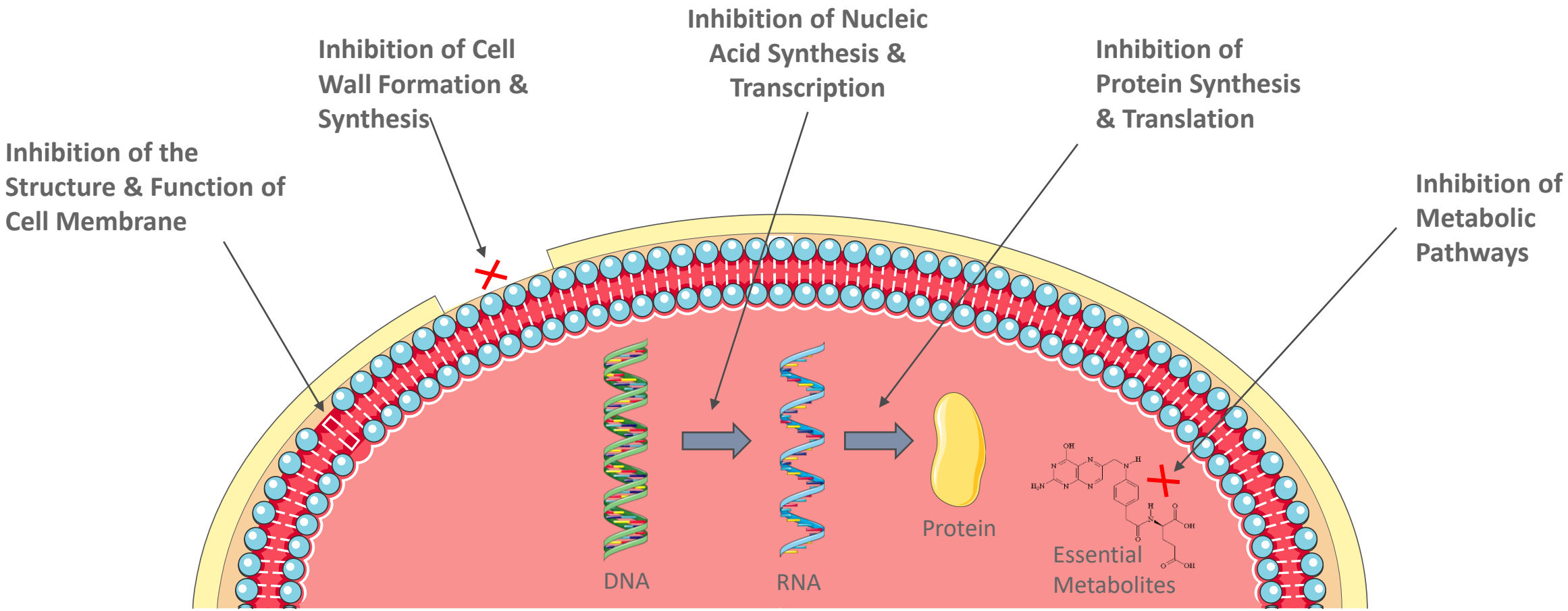
Mechanisms of Action: Antibiotics

There are five principal antibiotic mechanisms of action to kill bacterial cells



Source: AIMS Microbiology

The Future of Antibiotic Discovery

There is a pressing need for novel platforms of antibiotic discovery

Big pharma failing to invest in new antibiotics, says WHO

Health body says there are alarmingly few drugs in the pipeline to deal with growing resistance

▲ The reports say that most antibiotics being developed are hardly any improvement on existing drugs. Photograph: Helen Sessions/Alamy Stock Photo

Source: Wellcome Trust News

CEO of Bugworks, Anand Anandkumar says: *"This is the only field within pharmaceutical science where you come out with a drug and you don't want it to be used too much"*

Wellcome Trust News: *"There are currently between 40 and 50 antibiotics in clinical development. Many of these will only bring limited benefits compared to existing treatments."*

What is the Future?

- Untapped Sources of Novel Antibiotics
- Combination Antibiotic Treatments
- Artificial Intelligence to Identify Novel Antibiotic Candidates
- Alternatives to Antibiotics: Bacteriophage Therapy, Bacteriocins, Predatory Bacteria

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Vaccine Development

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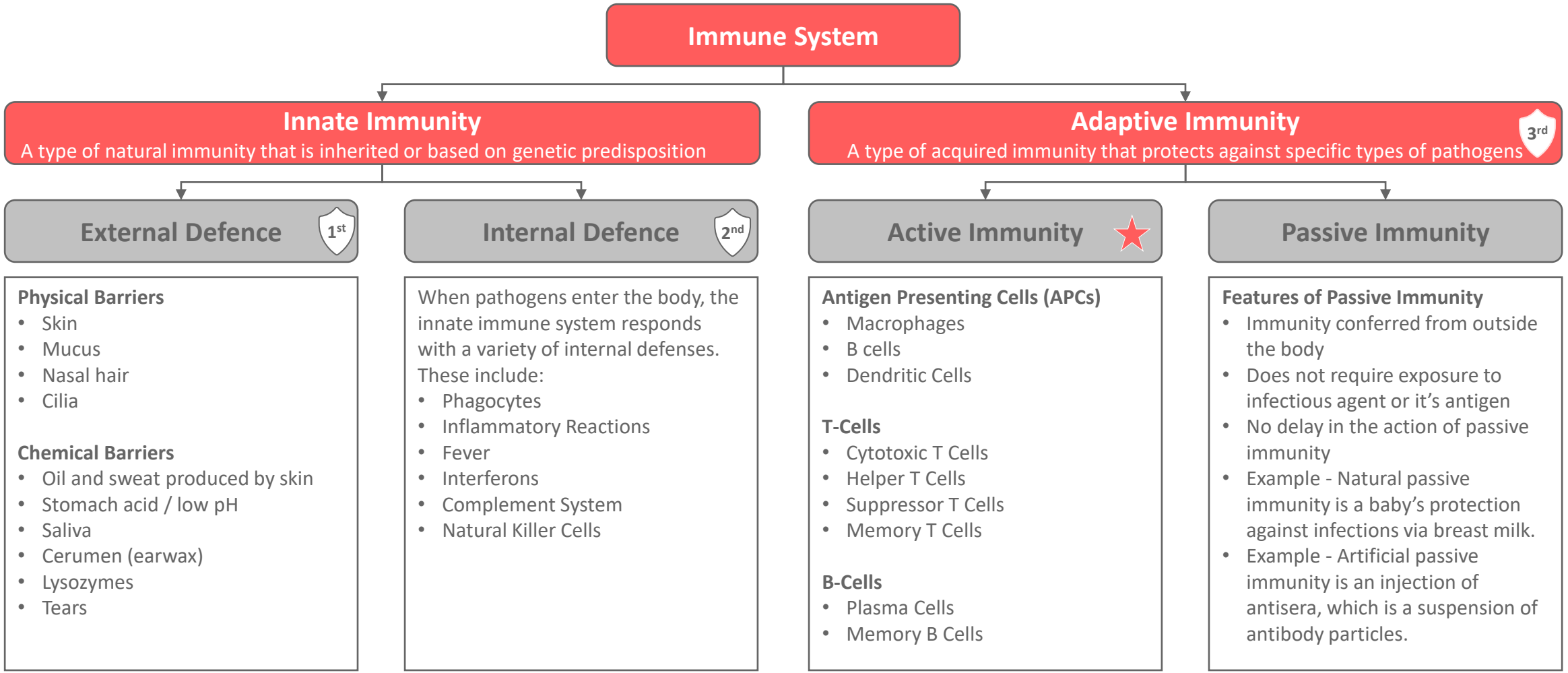
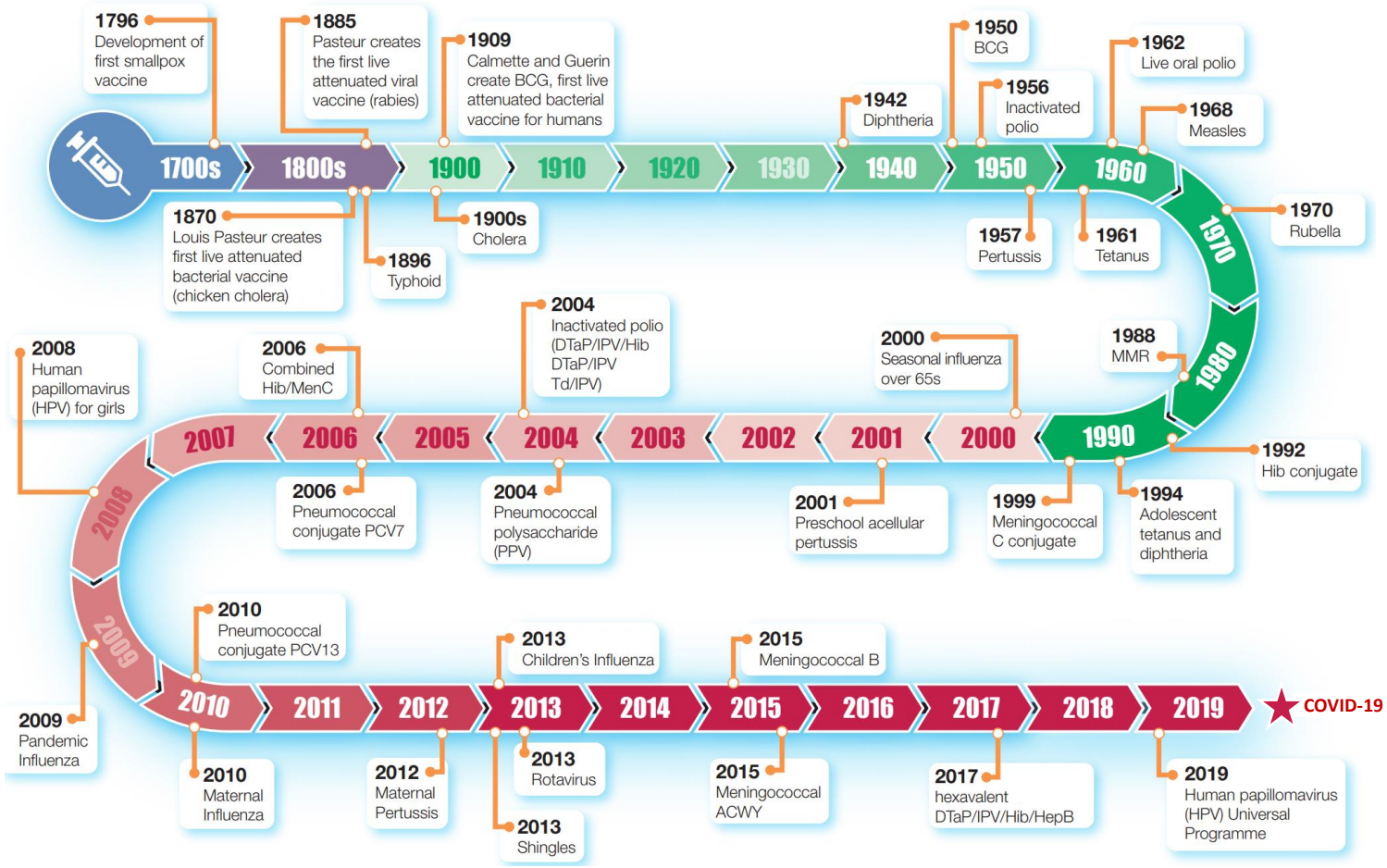
Introduction: Overview of the Immune Defence System



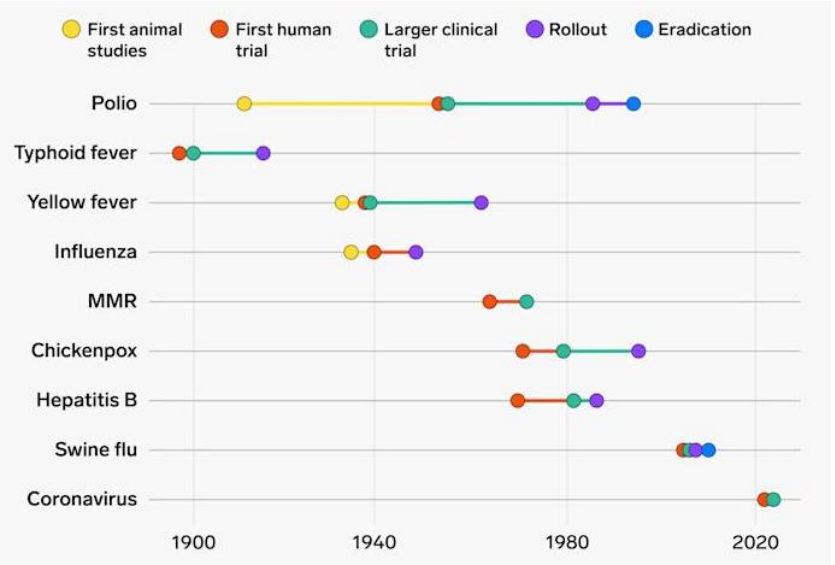
Source: London Strategy, Public Health England

Introduction: History of Vaccines

Historical Vaccine Development and Introduction of Routine Vaccine Programmes in the UK



Comparing Vaccine Development throughout History



- Vaccine research and development has improved massively throughout history.
- Nearly 200 years passed between the creation of the first successful vaccine and the eventual eradication of smallpox.
- The influenza virus was isolated in a lab in 1933, and the first flu vaccine wasn't licensed until 1945.
- Coronavirus vaccine research began just a few months after the first case of COVID-19 was observed, and it has progressed at a rapid pace.

Source: London Strategy, Public Health England, Business Insider

Immunisation and Vaccination

What is immunisation?
WHO: "process wherein a person is made immune or resistant to an infectious disease, typically by the administration of a vaccine."

What is inoculation?
Google: "the action of immunizing someone against a disease by introducing infective material, microorganisms, or vaccine into the body."

What is a vaccination?
WHO: "a simple, safe and effective way of protecting people against harmful diseases, before they come into contact with them."

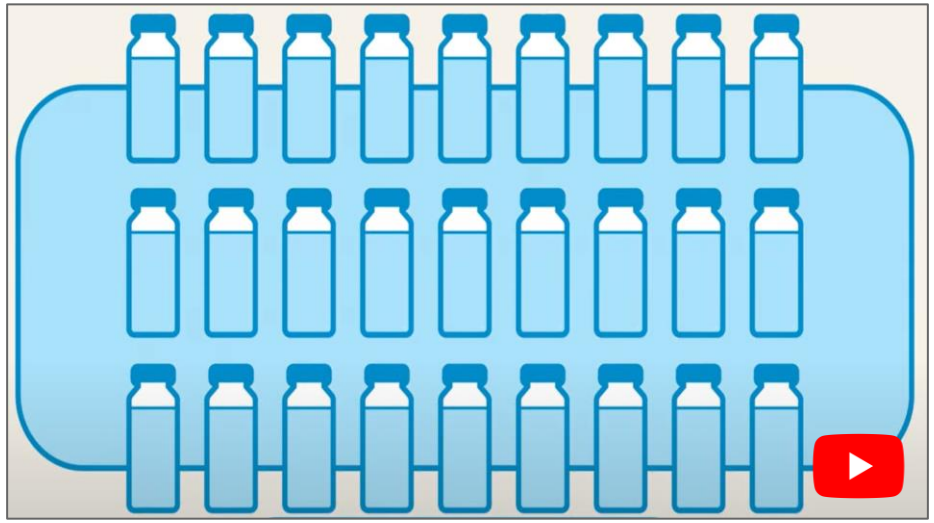
How does a vaccine work? Fundamental steps of vaccination

1. A biological preparation is introduced into the patient, typically by injection.
2. White blood cells recognise the antigens introduced by the vaccination.
3. This elicits an immune response, whereby antibodies are produced at high-levels.
4. These antibodies are able to prevent the antigen from entering a cell or mark the antigen for destruction.
5. The immune system is now primed to respond with speed and strength if the body encounters the pathogen.

What are the key ingredients of a vaccine?

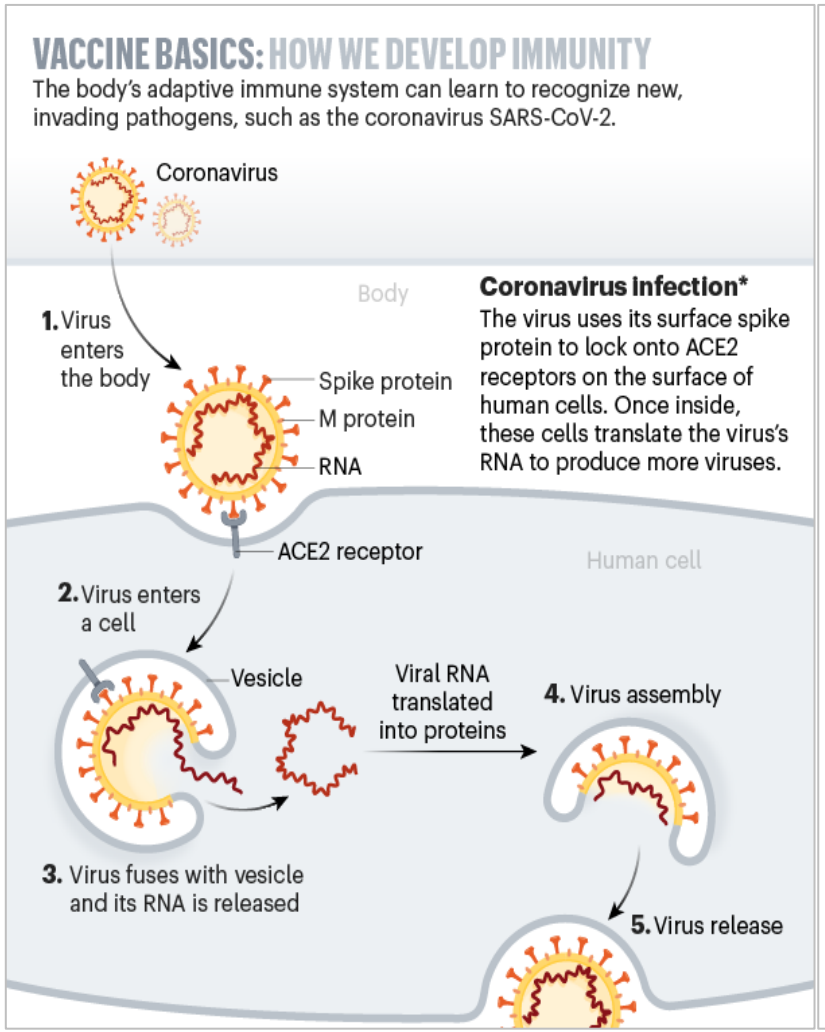
- **Antigen:** Active component / foreign substance which induces an immune response in the body.
- **Adjuvants:** They help boost the body's immune response to vaccine
- **Diluents:** Liquid used to dilute a vaccine to the correct concentration immediately prior to use.
- **Stabilizers:** They prevent chemical reactions from occurring within the vaccine.
- **Surfactants:** They prevent settling and clumping of elements that are in the liquid form of the vaccine.
- **Residuals:** Substances used during the manufacturing process that are not active ingredients in the final product.

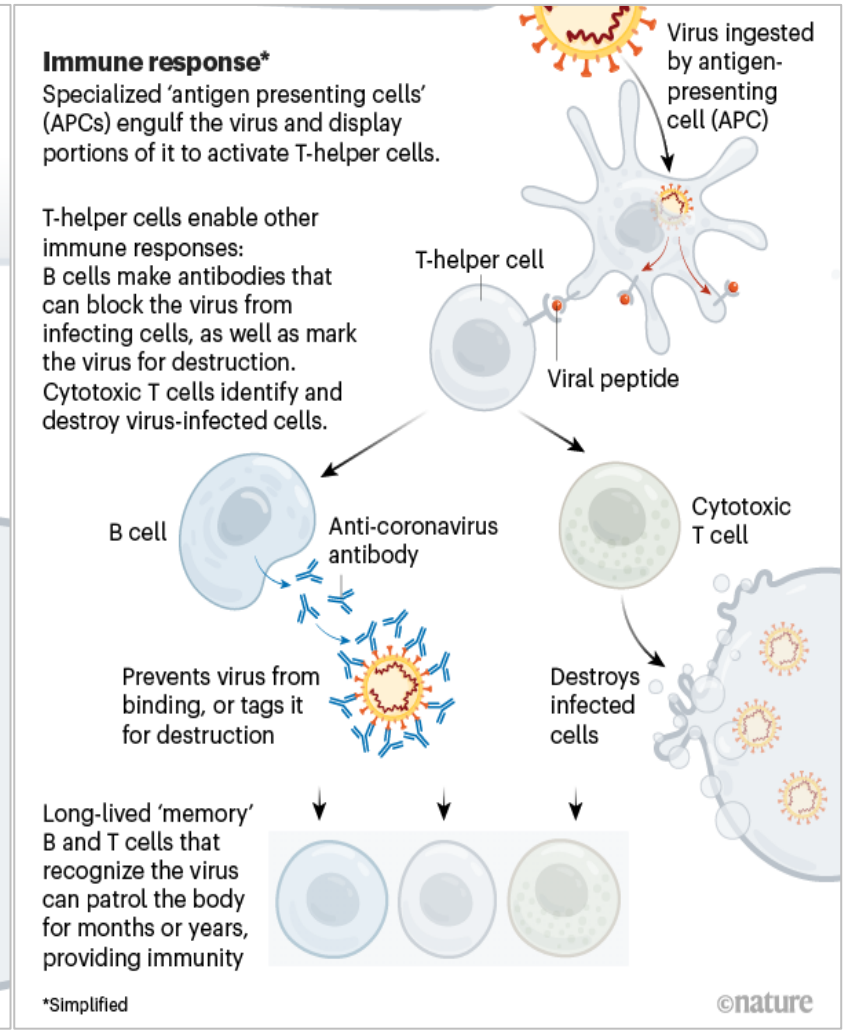
The Journey of a Vaccine: From Lab to Patient

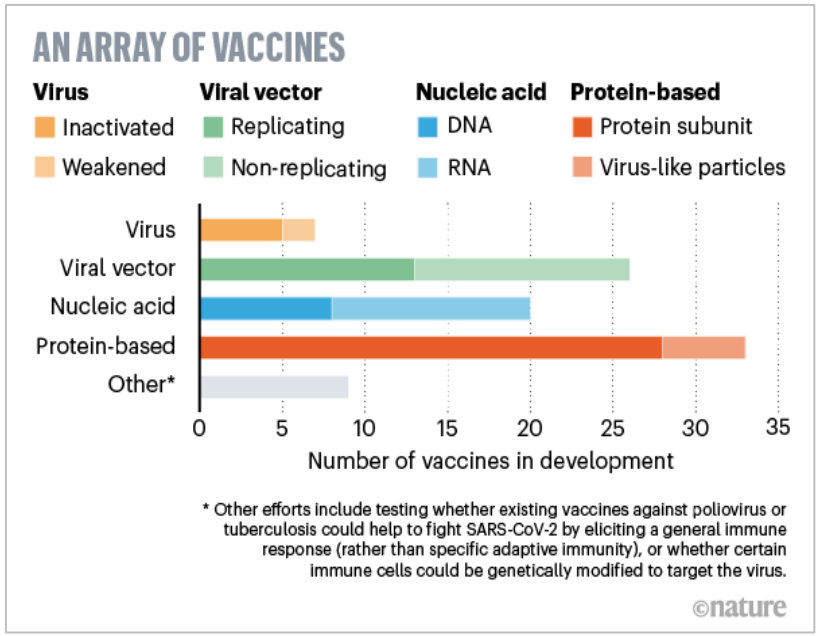


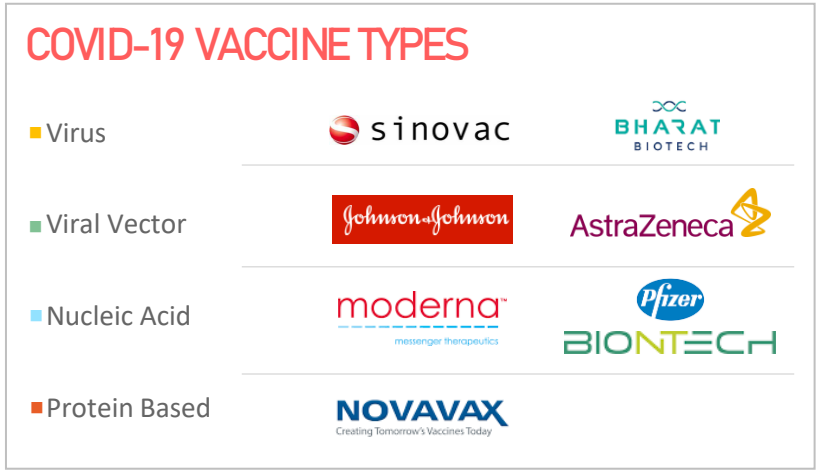
Source: CDC, WHO

Vaccine Classification & Development: COVID-19





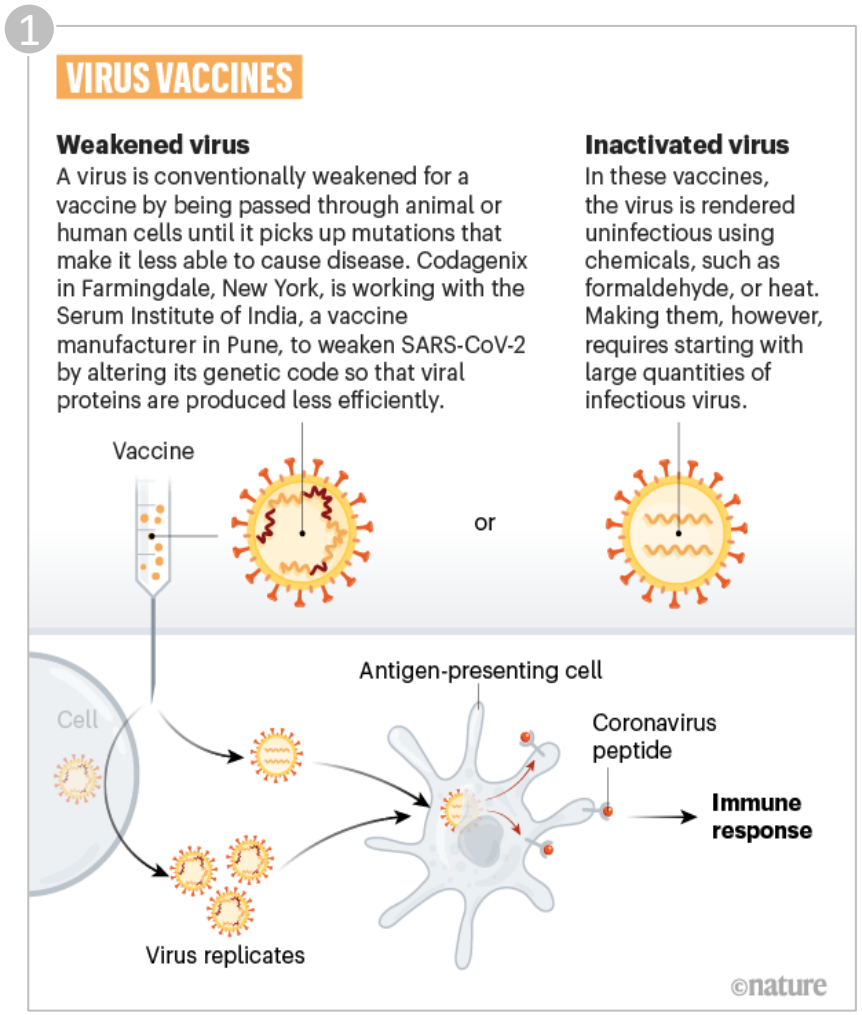


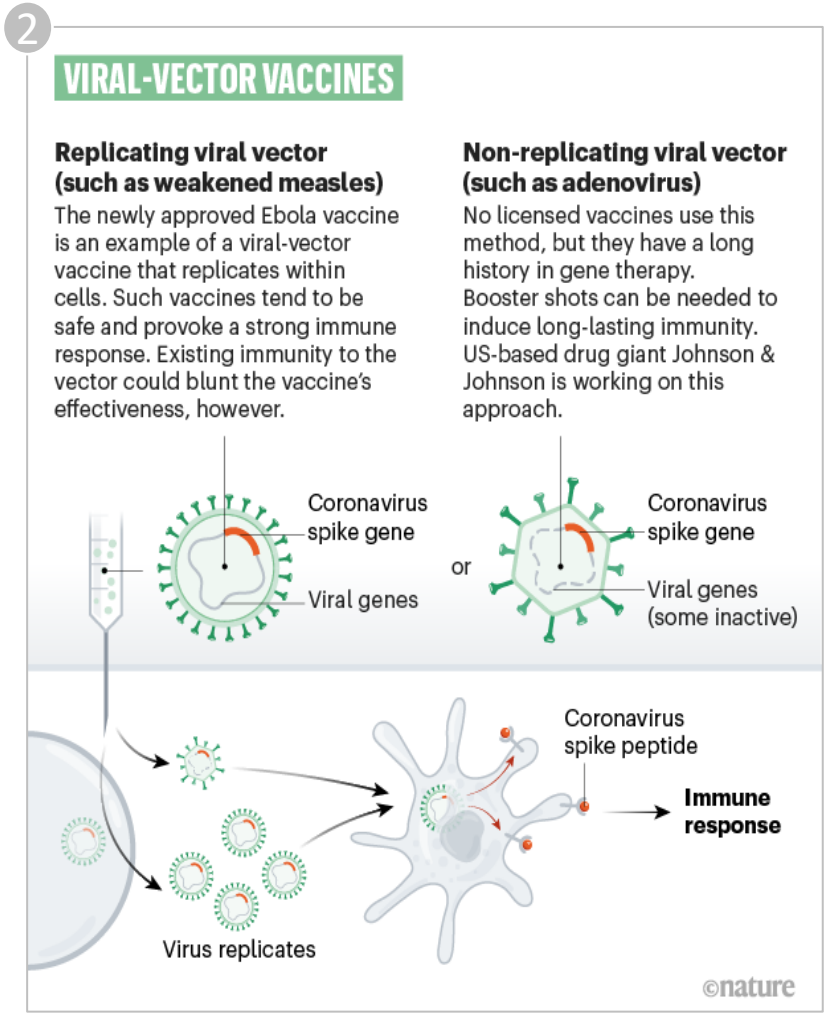


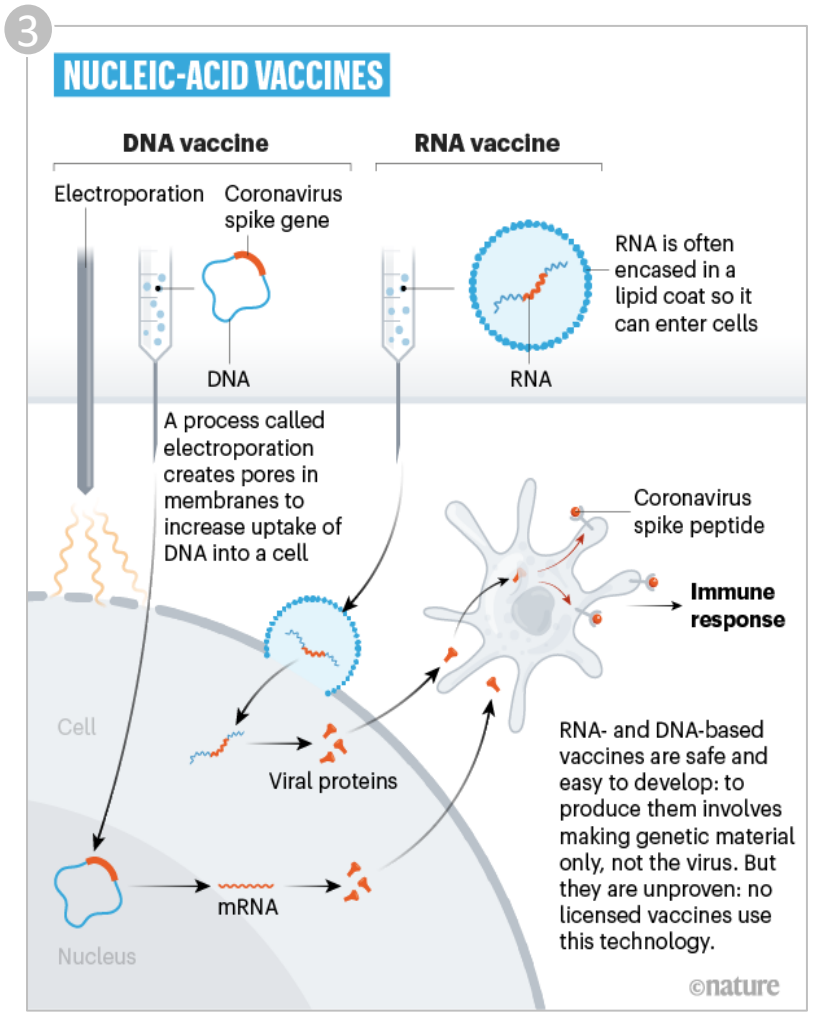
All vaccines aim to expose the body to an antigen that will not cause disease, but will provoke an immune response that can block or kill the virus if a person becomes infected. There are at least eight different types of vaccines that are being tried and tested against the coronavirus, and each one will rely on different viruses or viral parts. – Nature 2020

Source: London Strategy, Nature

Vaccine Classification & Development: COVID-19







Source: Nature

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Vaccine Classification & Development: COVID-19

4

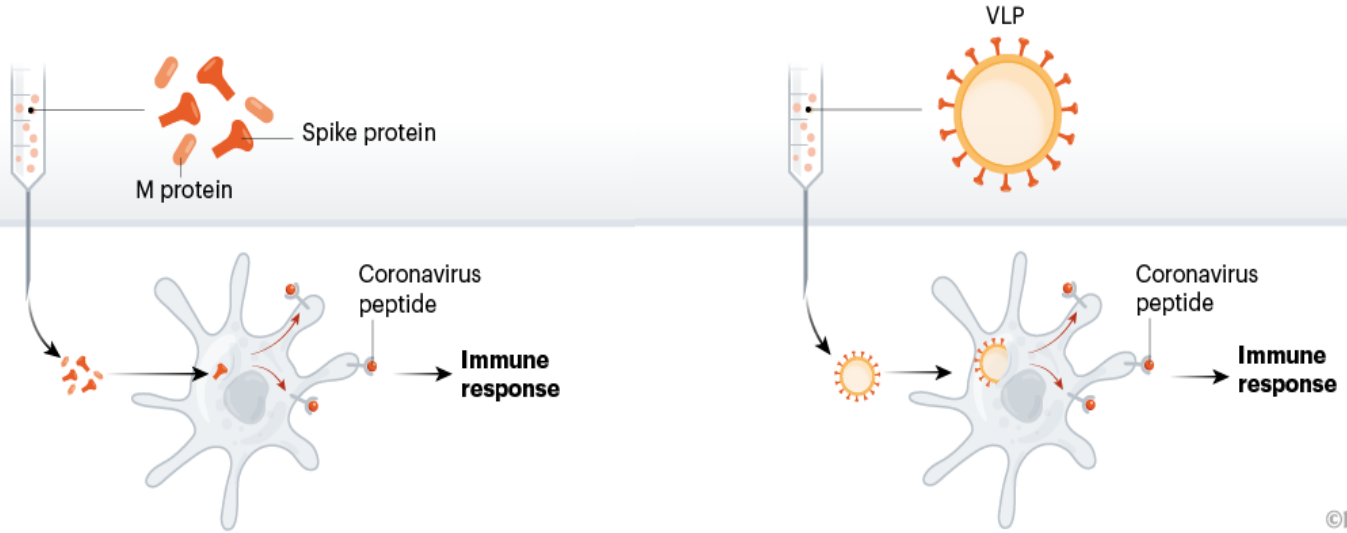
PROTEIN-BASED VACCINES

Protein subunits

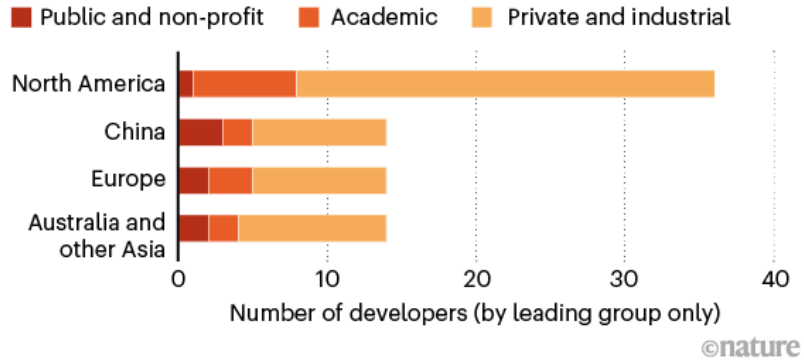
Twenty-eight teams are working on vaccines with viral protein subunits — most are focusing on the virus's spike protein or a key part of it called the receptor binding domain. Similar vaccines against the SARS virus protected monkeys against infection but haven't been tested in people. To work, these vaccines might require adjuvants — immune-stimulating molecules delivered alongside the vaccine — as well as multiple doses.

Virus-like particles

Empty virus shells mimic the coronavirus structure, but aren't infectious because they lack genetic material. Five teams are working on 'virus-like particle' (VLP) vaccines, which can trigger a strong immune response, but can be difficult to manufacture.



PUBLIC AND PRIVATE DEVELOPMENT LANDSCAPE



More than 70% of the groups leading vaccine research efforts are from industrial or private firms. Clinical trials start with small safety studies in animals and people, followed by much larger trials to determine whether a vaccine generates an immune response. Researchers are accelerating these steps and hope to have a vaccine ready [soon]. – Nature 2020

Source: Nature

Future of Vaccines & Development

COVID-19: Implications on Vaccine Development

- The search for a COVID-19 vaccine has forced the scientific community to consider new ways of developing vaccines.
- Government agencies and Biopharmaceutical companies have entered unprecedented public-private partnerships to fund research in this area.
- We have seen the development of new vaccine technologies based on the decades of previous research on how cells can translate mRNA into proteins.
- The research and development behind these vaccines and other COVID-related vaccines will provide valuable information about how to create more effective vaccines in the future.
- Traditional vaccine development methods will continue to prove essential to fighting disease, but new platforms and technologies are becoming available.
- Increased investment and leadership should boost research, modernize processes, and decentralize manufacturing, facilitating advances in this field greater than most would have anticipated.

Challenges of Traditional Vaccinations

Key Challenges of Vaccinations

Cold-Chain

- A series of links from manufacture to patient are required to keep the maintains product quality
- The COVID-19 pandemic has highlighted the disparities in vaccine rollout around the world, due to costs and infrastructure around cold-chain supply chain

Fear of the Needle

- Vaccine hesitancy has been listed as a top 10 threat to global health by WHO and fear of needles plays a significant part in this.
- The number may seem small, but this can have large implications on global health can be

Alternative Routes of Delivery

Patch Application

- Non-invasive method of delivering vaccines via wearable skin patches
- These patches contain thousands of dissolvable needles that can reach immune cells in the skin
- No requirement for specialised storage and transport

Mucosal Vaccines

- Administration via the mucosal sites (e.g. nasal, oral, ocular, rectal, vaginal)
- Elicits immune defence in both mucosal entry points, where pathogen invasion is common, and systemic tissues

Source: Nature

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Appendix: COVID-19 Vaccine Flashcards

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COVID-19 Vaccine Flashcards (1/3)

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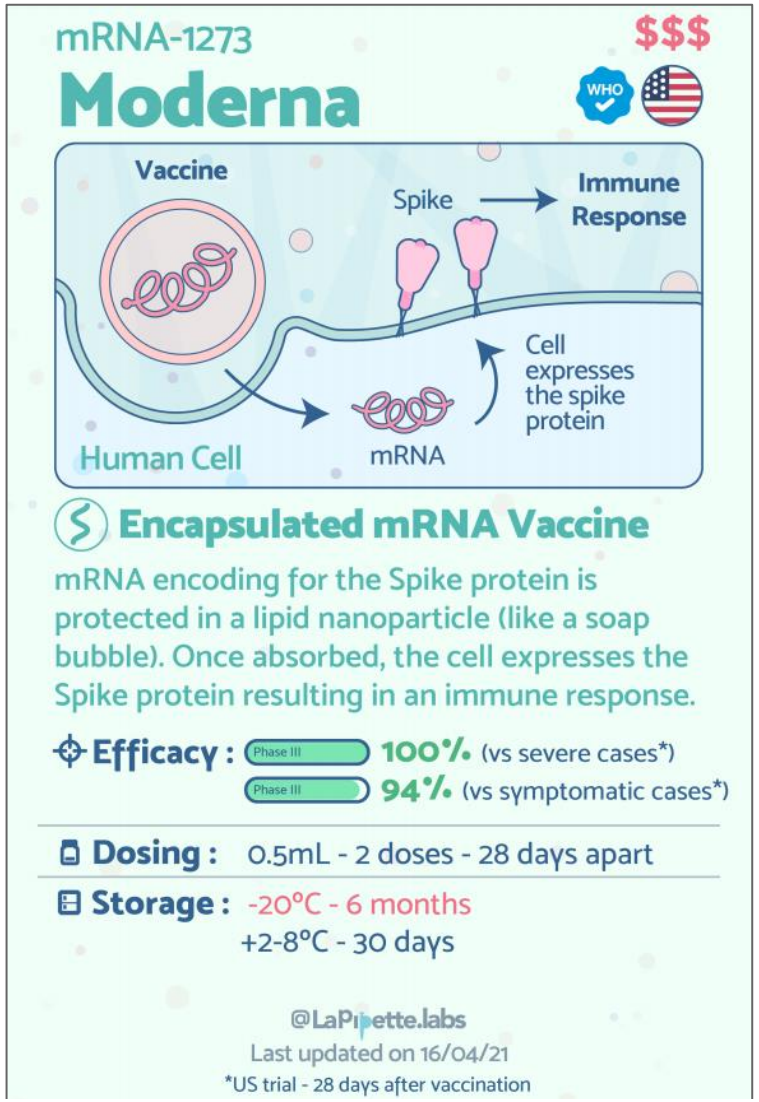

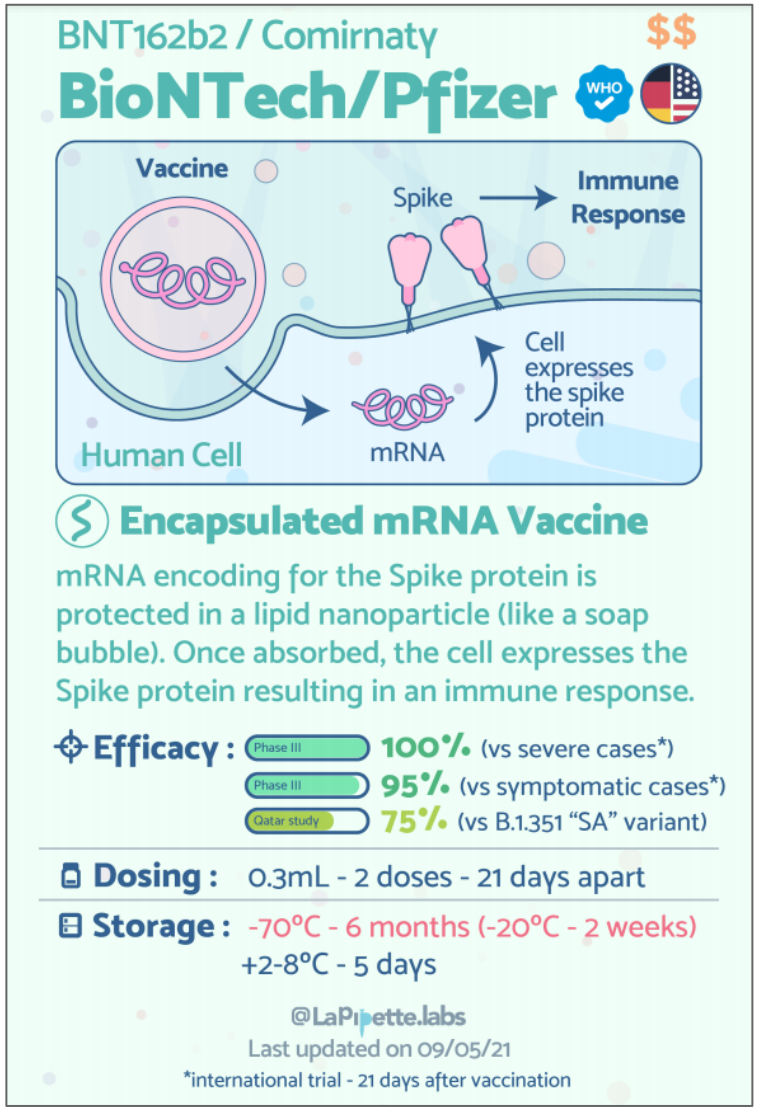

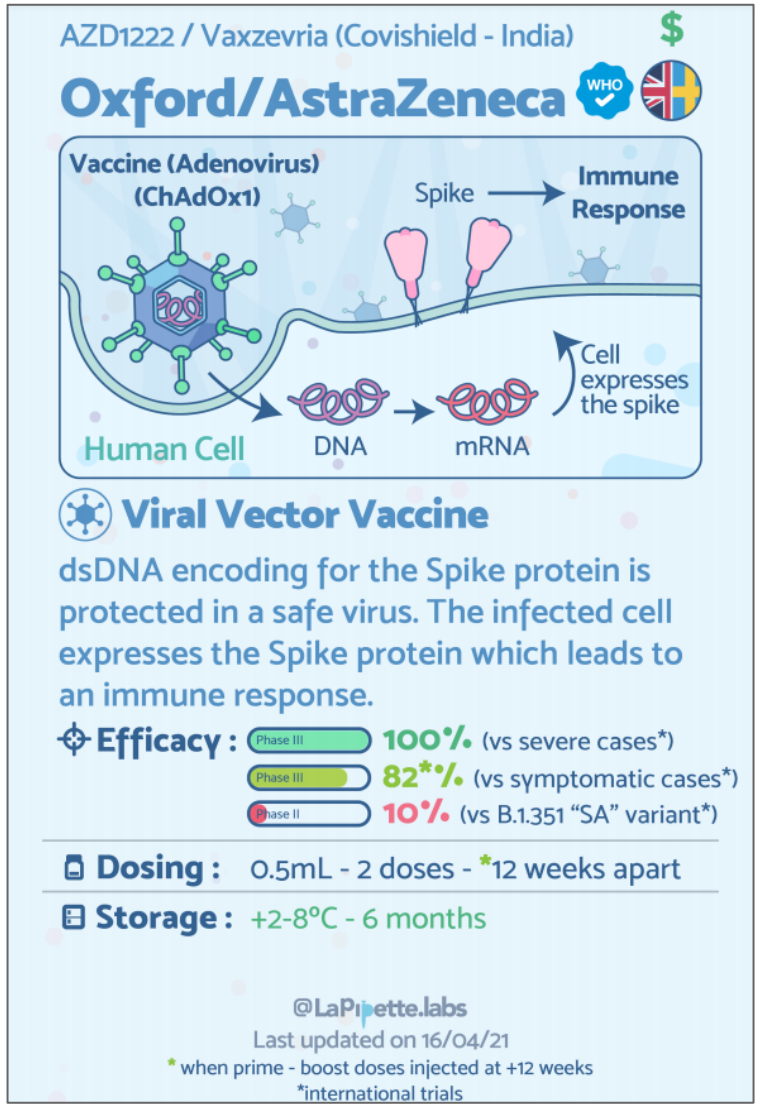

Source: LaPipette Labs

COVID-19 Vaccine Flashcards (2/3)

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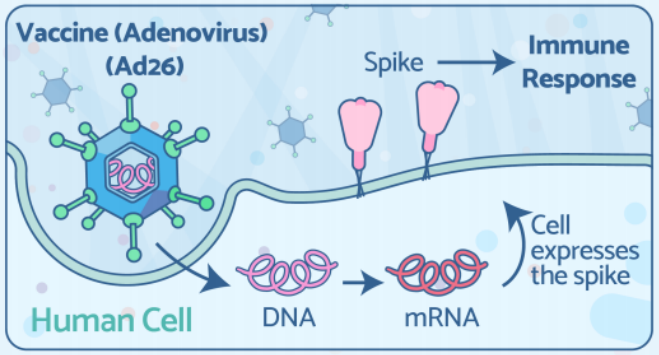
JNJ-78436735 / Ad26.COV2.S
Janssen / J&J



Viral Vector Vaccine

dsDNA encoding for the Spike protein is protected in a safe virus. The infected cell expresses the Spike protein which leads to an immune response.

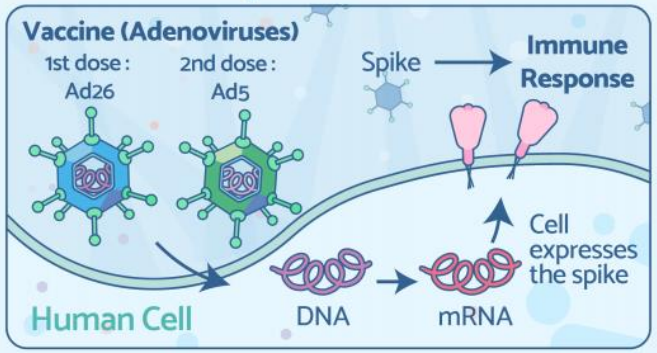
Efficacy : Phase III **100%** (vs hospitalisation*)
Phase III **74%** (vs symptomatic to severe*)
Phase III **64%** (vs B.1.351 "SA" variant*)

Dosing : 0.5mL - 1 dose

Storage : +2-8°C - 3 months
-20°C - 2 years

@LaPipette.labs
Last updated on 09/05/21
*US trial - 28 days after vaccination - CDC report

Sputnik V /Gam-Covid-Vac
Gamaleya



Viral Vector Vaccine

dsDNA encoding for the Spike protein is protected in a safe virus. The infected cell expresses the Spike protein which leads to an immune response.

Efficacy : Phase III **100%** (vs severe cases*)
Phase III **92%** (vs confirmed cases*)

Dosing : 0.5mL - 2 doses - 21 days apart

Storage : +2-8°C - 6 months
-20°C - 2 years

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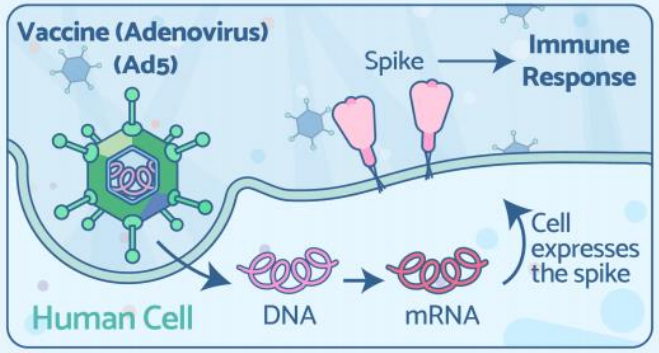
Last updated on 16/04/21
* Russian trial - 21 days after vaccination

Convidecia / Ad5-nCoV
CanSino Bio



Viral Vector Vaccine

dsDNA encoding for the Spike protein is protected in a safe virus. The infected cell expresses the Spike protein which leads to an immune response.

Efficacy : Phase III **90%** (vs severe cases*)
Phase III **65%** (vs symptomatic cases*)

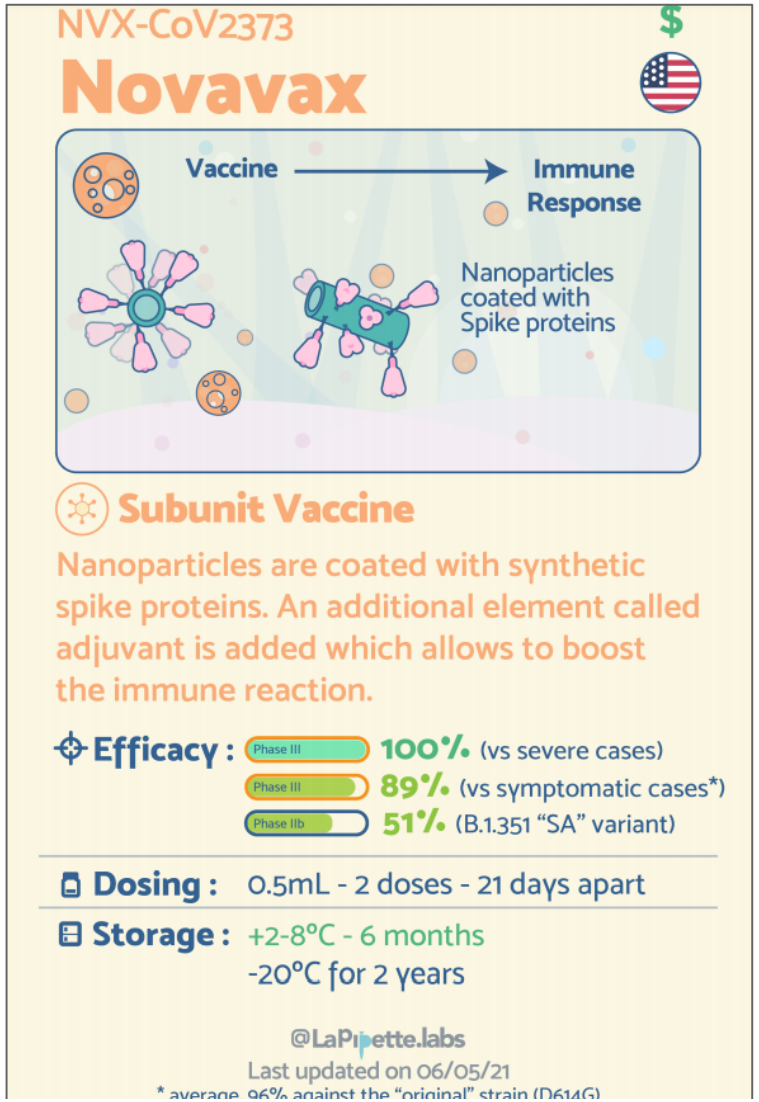
Dosing : 1 dose

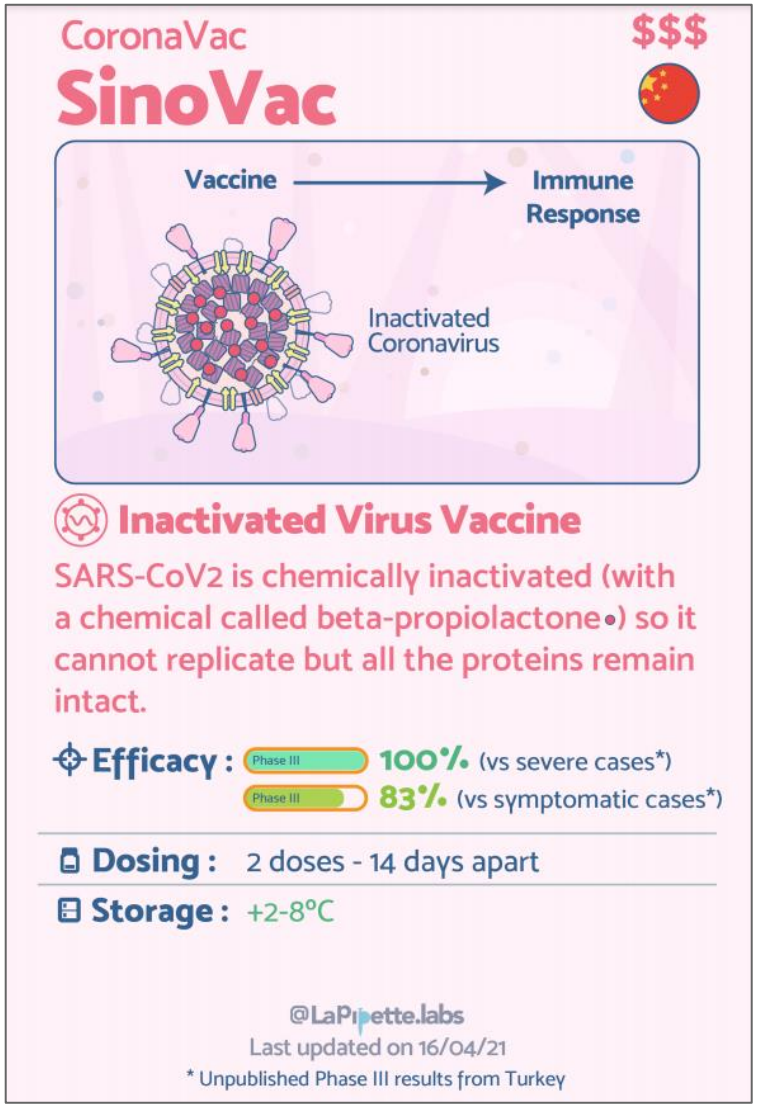
Storage : +2-8°C

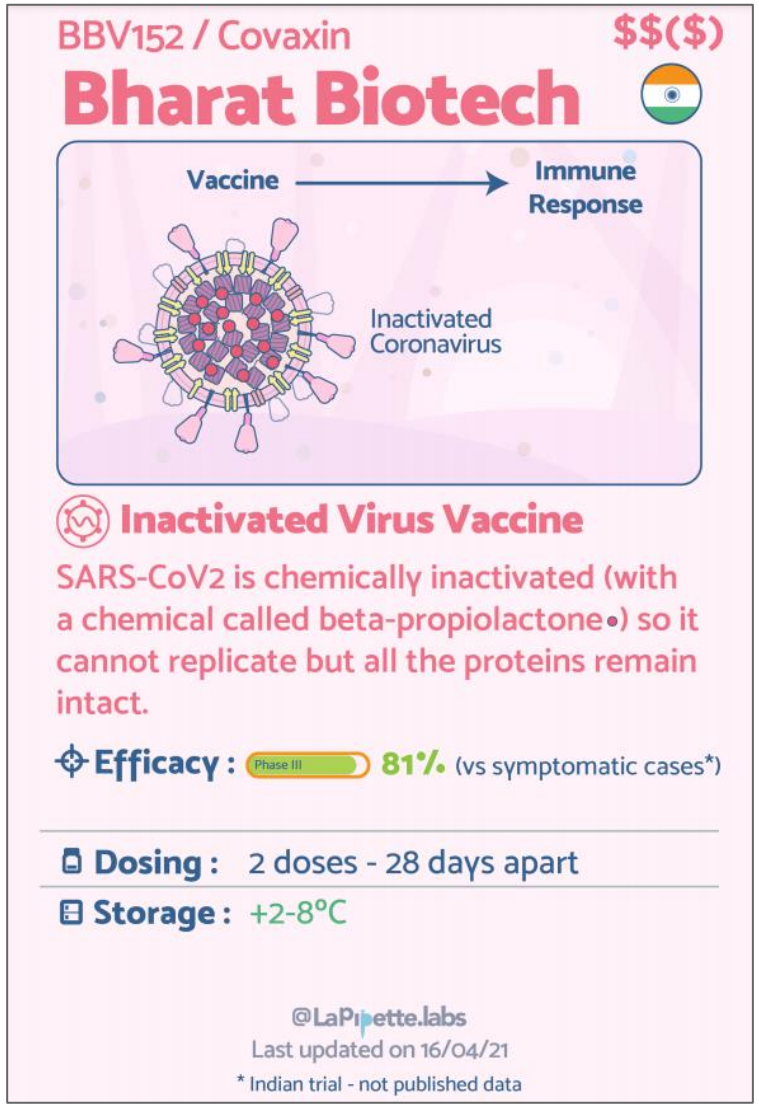
@LaPipette.labs
Last updated on 16/04/21
* International trial - not published data

Source: LaPipette Labs

COVID-19 Vaccine Flashcards (3/3)







Source: LaPipette Labs

Microfluidics

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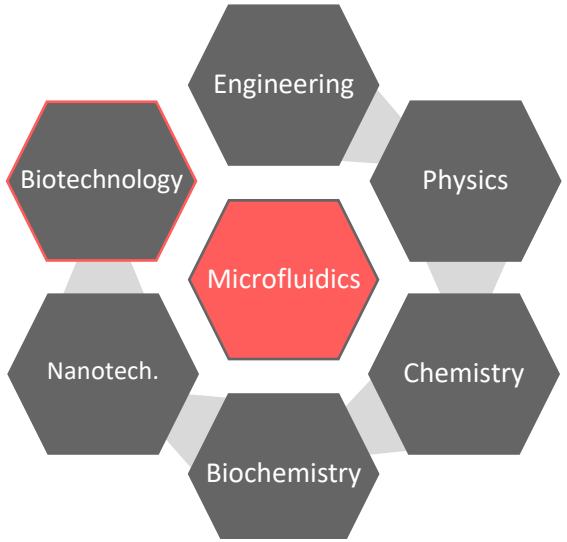
Introduction: What are Microfluidics?

What are Microfluidics?

Science Direct: "the science of manipulating and controlling fluids, usually in the range of microliters to picolitres, in networks of channels with dimensions from tens to hundreds of micrometers."

Applications of Microfluidics

Microfluidics is a multi-disciplinary field with various practical applications. Advances in microfluidic technologies have enabled applications in the medical field, most notably immunoassays, biological assays, chemical synthesis, drug testing etc.



Microfluidics in the Medical / Healthcare Field

- The miniaturization of conventional laboratory equipment and technologies through microfluidics has led to several advancements including:
  - Minimal usage of reagents with short & simple assay protocols
  - Improved parallel processing of samples & screening approaches
  - Accurate control of cell microenvironments
- Microfluidics has not only been proven beneficial in benchwork but also in several medical and pharmaceutical applications, including diagnosis of infectious diseases to treatment of cancer, as well as in fabrication of functional living tissues and artificial organs.

Key Players in The Field of Microfluidics

illumina, Roche, Abbott, SAMSUNG, emulate, Cepheid, BIO-RAD, DANAHER, Thermo SCIENTIFIC

Source: London Strategy, Science Direct

Applications of Microfluidics: Lab-on-a-Chip

Lab-on-a-Chip Model

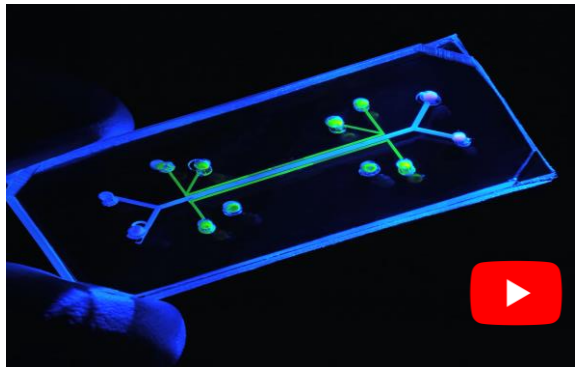
- A lab-on-a-chip is a miniaturized device that enables **integration of one or several analyses** to be performed *in vitro* onto a single circuit (commonly called a chip).
- Microfluidics technologies used in lab-on-chip devices enable the **fabrication of millions of microchannels** to conduct laboratory functions.
- This technology generally enables automation and high-throughput experiments to be conducted, however comes with challenges such as **complex micro-manufacturing processes** and only **proof-of-concept applications** given its infancy.

Advantages of Lab-on-a-Chip Models

Low Cost	Faster Response Time
High Parallelisation	Low Volume Samples
Ease of Use	Real-Time Control
Reduced Human Error	Expandability

Organ-on-a-Chip Model

Microfluidic devices used for culturing living cells in a micrometer-sized and continuously perfused chambers to model physiological functions of organs and tissues.



Spotlight on Applications in Global Health

- Lab-on-a-chip technology may soon become an important part of efforts to improve global health, particularly through the development of **point-of-care testing devices**.
- Many researchers believe that this technology may be the key to powerful new **diagnostic instruments**.
- The goal of these researchers is to create microfluidic chips that will allow healthcare providers in poorly equipped clinics to perform diagnostic tests such as microbiological culture assays, immunoassays and nucleic acid assays with no laboratory support.

Source: London Strategy, Science Direct

Microfluidics: Market Trends & Forecast

Microfluidics Technology: SWOT Analysis

Strengths:
It is expected that soon, more commercially available integrated microfluidic systems will be used in Point-of-Care (POC) settings, reference laboratories and hospital laboratories.

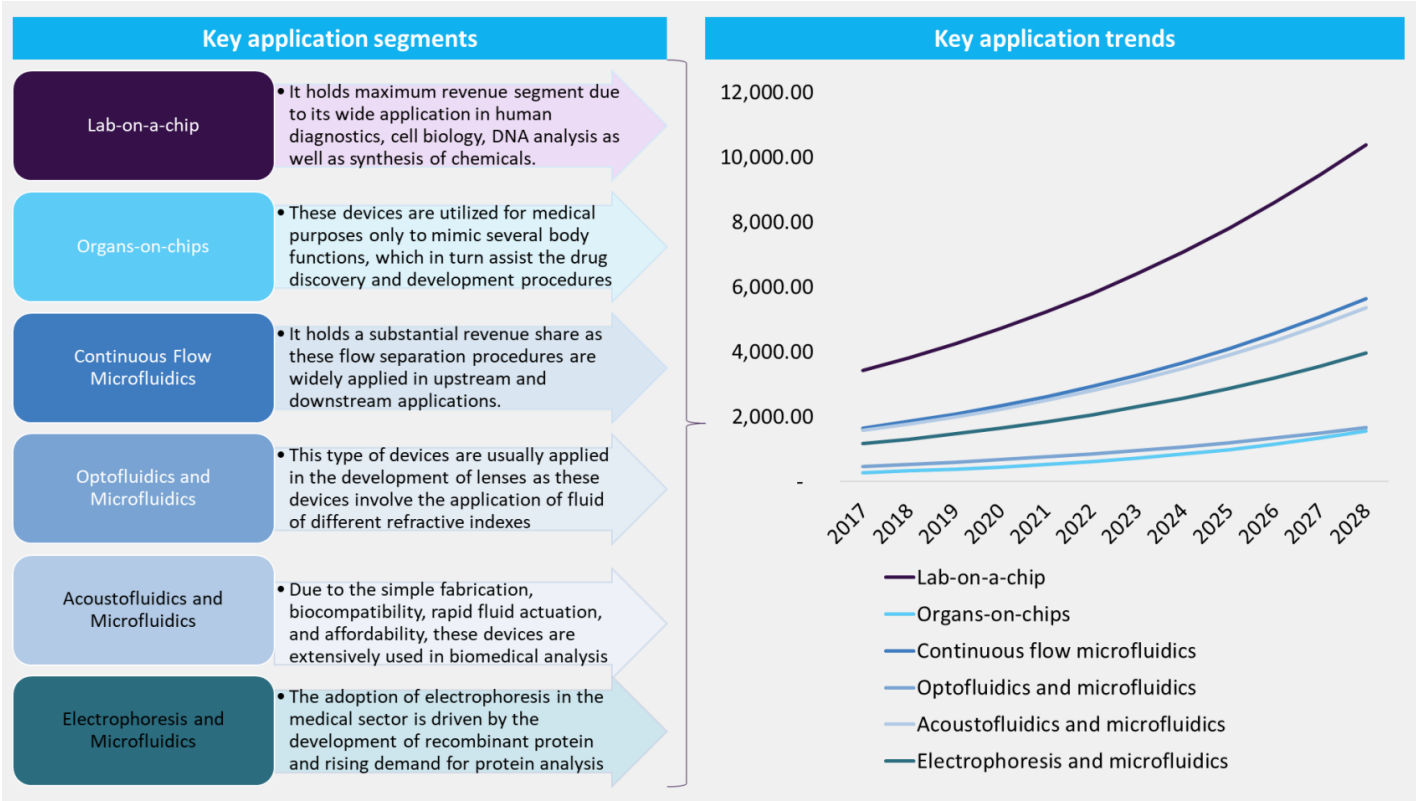
Weaknesses:
Introduction of new technologies and the launch of more effective devices has been challenging and with the advent of newer products the demand for existing devices declines.

Opportunities:
There are lucrative opportunities to market players. Droplet digital microfluidics for detection of cancer markers, clinical & environmental detection using paper-based microfluidics etc.

Threats:
If the patent of the device is issued for an innovative incremental step to an existing invention, the patent owner does not necessarily hold rights over selling or using the product.

Source: Grandview Research

Microfluidics Market: Key Application Take-Aways



Source: Grandview Research

Microbiome

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Introduction: What is the Microbiome?

What is the Difference between 'Microbiota' & 'Microbiome'?

Microbiota: the microorganisms of a particular site, habitat or geographical location.

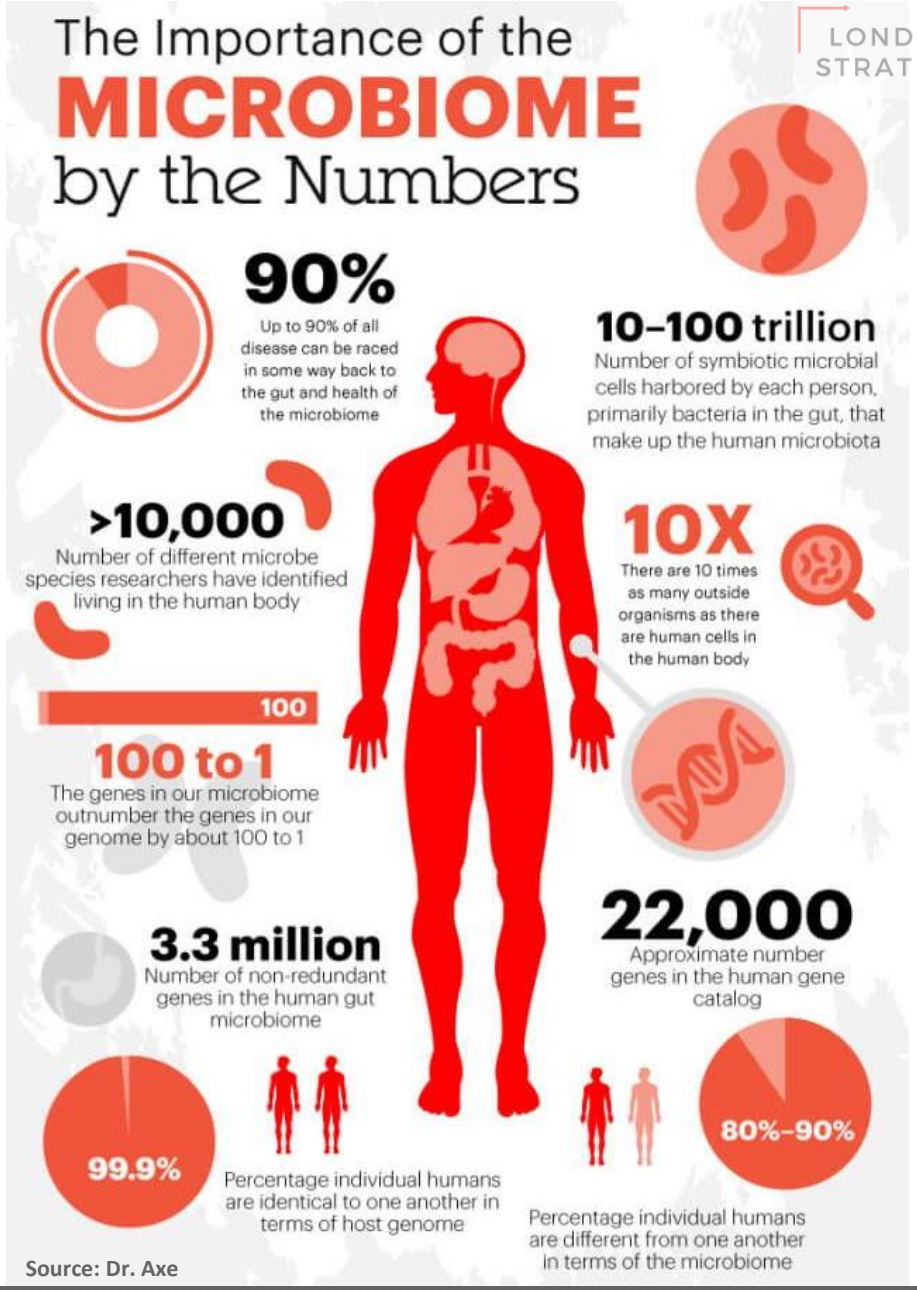
Microbiome: the collection of microbes and their genetic material in an environment.

What is the Importance of the Microbiome?

- The critical role of the microbiome is not surprising considering that the metagenome of the gut microbiome alone exceeds our own by about **100-fold**
- Microorganisms live in the human digestive system and affect our health – and scientists are trying to work out how.
- The microbiome contributes to human health and wellness in various ways:

Resistance to Pathogens	Development of Immune Cells	Break-down of Food Compounds	Metabolism of Therapeutics	Protection Against Epithelial Injury
Biosynthesis of Vitamins & Amino Acids	Modulation of Bone Mass Density	Promotion of Fat Storage	Modification of Nervous System	…

Source: London Strategy, Dr. Axe



The Human Microbiome: Types & Functions

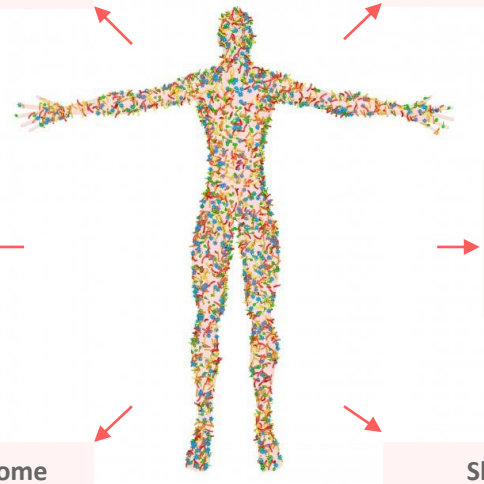
Key Microbiome Niches of the Human Body

Each microbiome niche has a unique microbial composition and a specific function within the body.

Oral Microbiome
- **Functions:** digestion of food and good dental health.
- **Imbalance**: effects beyond the mouth (common sign is gingivitis).

Nasal Microbiome
- **Functions:** shapes olfactory function, protection to pathogens
- **Imbalance**: emergence of pathogens and subsequent effects

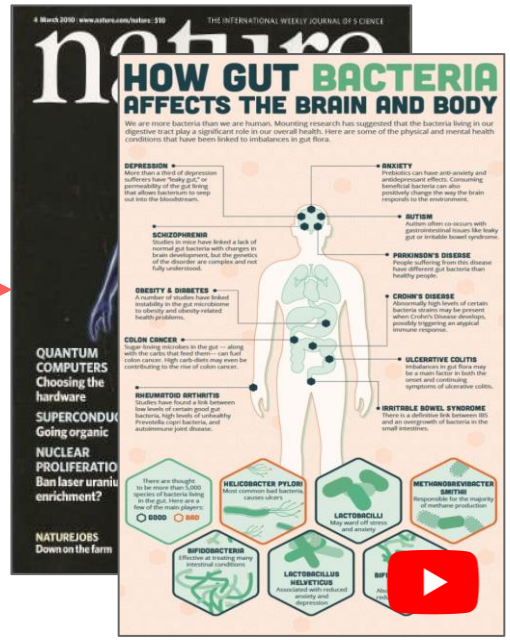
Lung Microbiome
- **Functions:** protective barrier and maintain normal functions
- **Imbalance**: progress inflammation and respiratory disorders



Gut Microbiome
- **Functions:** food digestion, immune regulation and mental health
- **Imbalance**: conditions including IBD, Obesity and Autism

Urogenital Microbiome
- **Functions:** maintain normal functions and predispose disease
- **Imbalance:** urinary tract infections and diseases

Skin Microbiome
- **Functions:** protective barrier to skin infections and other skin ailments.
- **Imbalance**: conditions including eczema, dandruff, acne etc.



What's Next? Metagenome of the Microbiome

- The **Human Microbiome Project (HMP)** has greatly advanced the metagenomic analysis of the microbiota in the human body.
- By understanding all the 'meta-omics' **(genes, proteins and metabolites)** of the microbiome, we can further understand the mechanisms and interactions that define the effects of the microbiome on the host.
- The current status of microbiome research is growing at **a rapid pace**, with a wide variety of studies looking at microbiomes in humans and their respective environments.

Source: London Strategy, Science Direct

The Human Microbiome Project

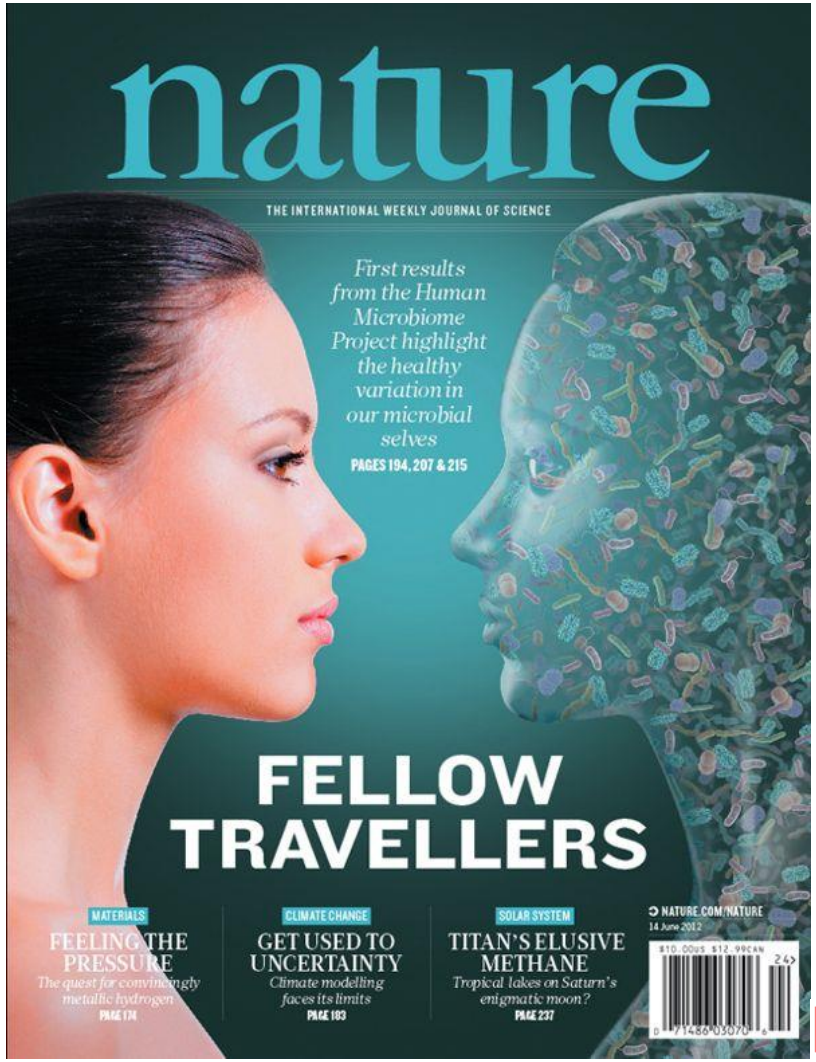
Overview: The Human Microbiome Project (HMP)

Background
A research initiative launched in 2007 by the United States National Institute of Health (NIH) with $170 million in funding to improve understanding of the microbial flora involved in human health and disease.

Aim
Phase 1: (2007-2014) Identifying and characterising human microbial flora.
Phase 2: (2014-2016) Characterising the microbiome and elucidating the roles of microbes in health and disease states.

Milestones
Over 650 peer-reviewed publications were listed on the HMP website from June 2009 to December 2017 and had been cited over 70,000 times. Major milestones accomplished include:

- **Reference Database**
  - HMP data used to understand the boundaries of normal microbial variation in humans
- **Clinical Applications**
  - HMP data used to identify the role of the microbiome in health and various diseases
- **Pharmaceutical Applications**
  - HMP data used to understanding microbial presence in manufacturing processes and implications in sterile and non-sterile settings.

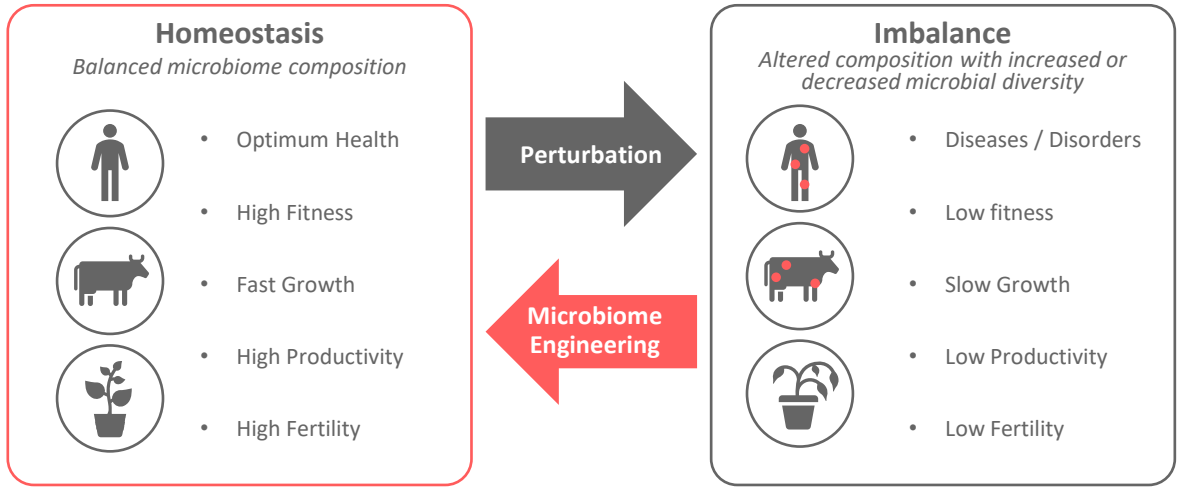


Source: London Strategy, NIH Human Microbiome Project

Microbiome Engineering & Microbiome-Based Therapeutics

Microbiome Engineering

- **Perturbation to balanced microbiomes** of ecosystems in homeostasis will result in an imbalance, which brings about **deleterious effects** such as increased rates of diseases and disorders, and reduced host fitness, growth, productivity and soil fertility.
- These negative influences can be alleviated or eradicated by employing **microbiome engineering**.
- Microbes can be engineered to **restore ecological balance** and **promote human health**. For example, probiotic benefits can be amplified, preventing infections, resolving inflammation, or treating metabolic disorders.
- To date, engineering of microbiomes has been achieved in **humans, animals, plants** and **soil.**
- Through microbiome engineering, the unbalanced microbiome will be equilibrated, and the ecosystems will be restored to their balanced states or even improved, leading to **enhanced phenotypes**.



Microbiome-Based Therapeutics

Modulatory
Used for altering the composition or activity of endogenous populations of microbiota

Additive
"Addition to microbial population"

Examples
- Usually in the form of administration of prebiotics or probiotics
- Tailored probiotics based on individual microbiota sequencing data
- Fecal Microbiota Transplant (FMT) used to relieve chronic intestinal infection

Subtractive
"Subtraction from microbial population"

Examples
- Synthetic phages to modulate certain populations of bacteria that have negative effects on human health
- Bacteriophages to manipulate the gut microbiome to prevent malnutrition in children in developing countries

Key Players

SERES THERAPEUTICS · VEDANTA BIOSCIENCES · Kaleido BIOSCIENCES · zymergen · EVELO · GINKGO BIOWORKS

Source: London Strategy, Plug & Play Tech Centre

Future Prospects: Microbiome in Health & Disease

LONDON STRATEGY

Current State

- Advances in **metagenomics**, **genome sequencing** and **bioinformatics** tools has allowed a greater proportion of the microbiome to be characterised than previously possible.
- We are transitioning from **associations to appreciation** of the mechanisms of action and developing clinical interventions based on these understandings.

What's Next?

- There is a future where "smart" cell-based therapeutics, synthetic biology, and autonomous sensors will rule the microbiome realm.
- Fully autonomous "smart" cell-based therapeutics will be able to restore the health of a human host through the help of clinically relevant sensors.
- These biosensors with luminescent, fluorescent, or colorimetric outputs could eventually lead to transcriptional regulation, or even permanently coupled to genomic alterations.
- Through synthetic biology engineering, smart microbes and phages will have the ability to modulate populations within the microbiota community – increasing the productivity or amounts of secondary molecules or destroying harmful bacteria that are negatively affecting the host's health.
- With the advancements of these technologies and applications, the possibilities are endless.

Additional Material

1 Overview: What is the Microbiome?

2 TEDx: Importance of Gut Microbiome

Source: London Strategy, Plug & Play Tech Centre

Stem Cells & Regenerative Medicine

LONDON STRATEGY

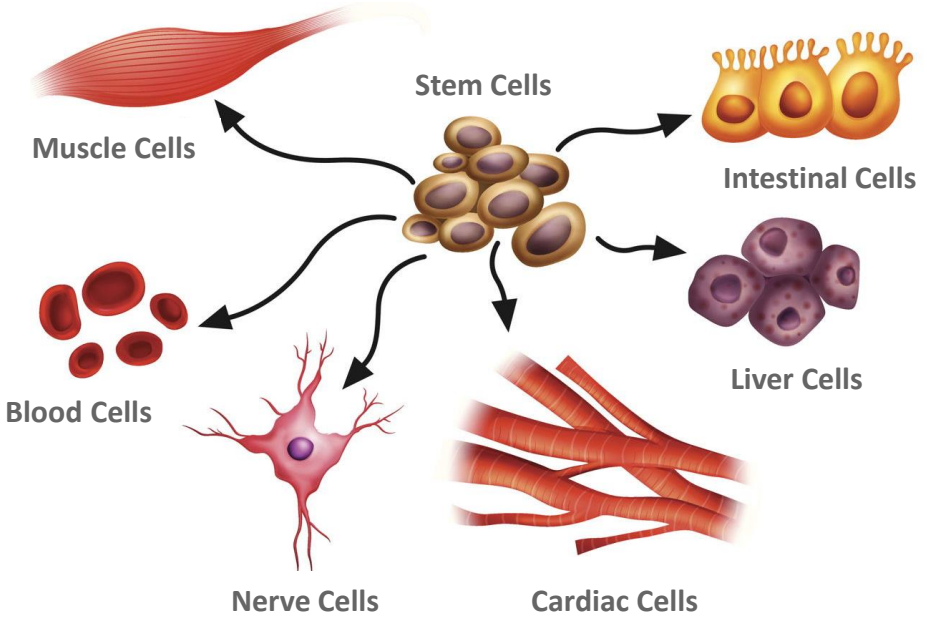
Introduction: Stem Cells & Regenerative Medicine

What is Regenerative Medicine?
Regenerative medicine refers to methods that replace or regenerate human cells, tissues or organs in order to restore or establish normal function.

What are Stem Cells?
Stem cells are undifferentiated or partially differentiated cells that can **differentiate into various types of cells** and **self-renew** / proliferate indefinitely to produce more of the same stem cell.

Stem Cells & Regenerative Medicine: Overview

TED Ed
Lessons Worth Sharing



Source: London Strategy, TEDx

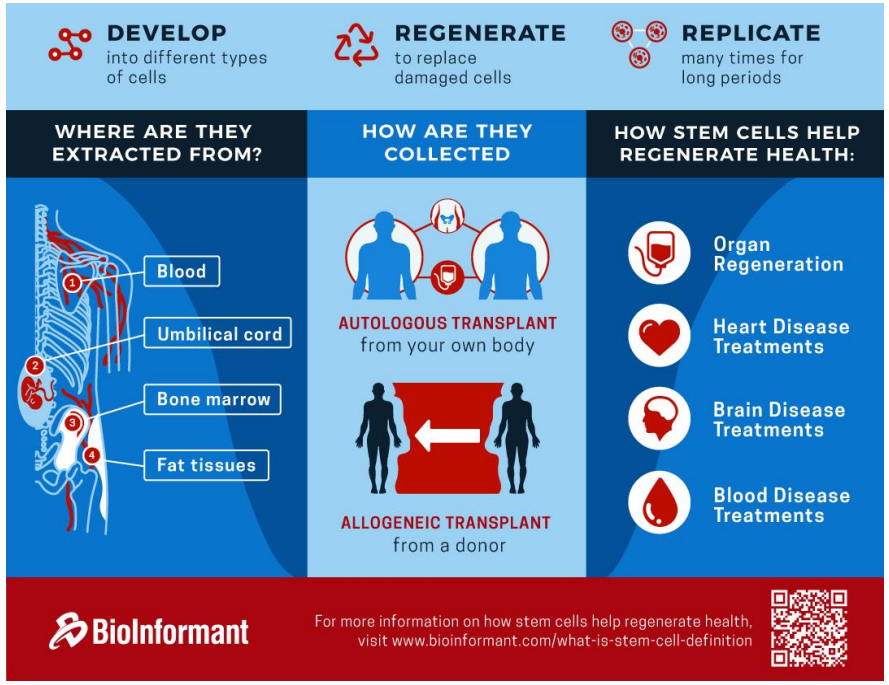
Classification & Types of Stem Cells

LONDON STRATEGY

Classification of Stem Cells

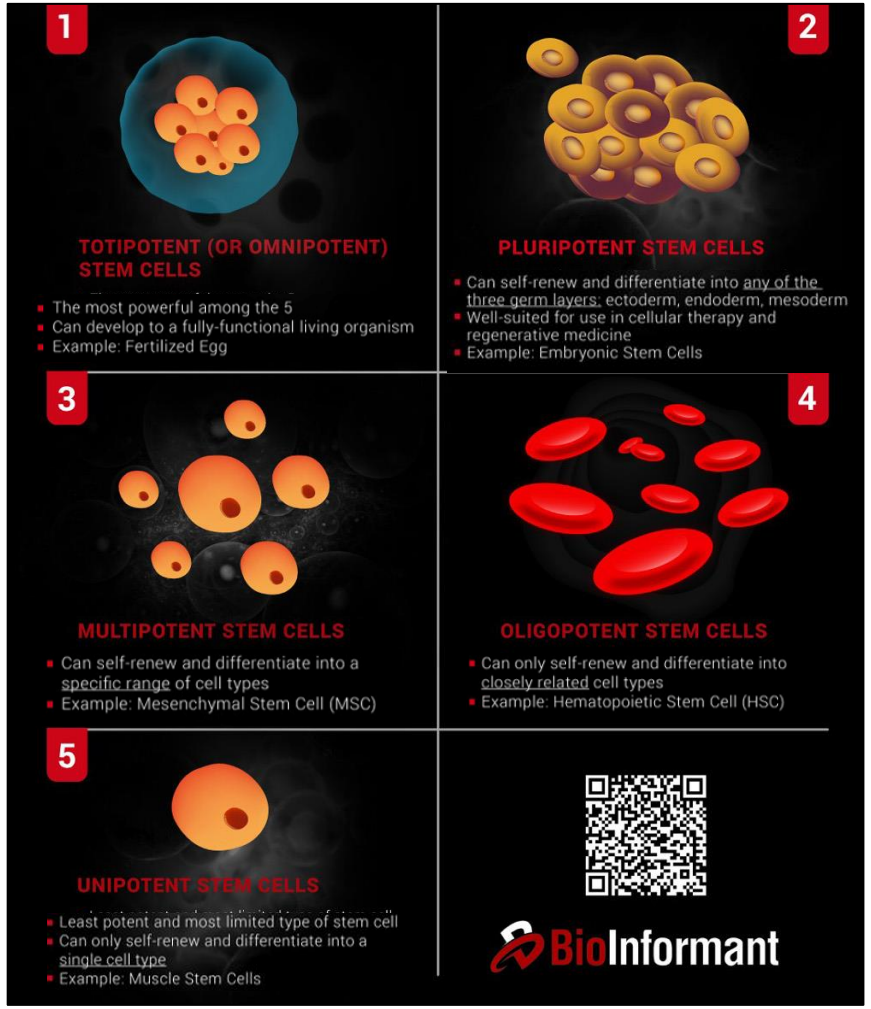
- The defining characteristic of a stem cell is that it can **self-renew** or **differentiate**.
- Stem cells can differentiate into specialized cell types based on their **cell potency** (number of stem cells they can produce).

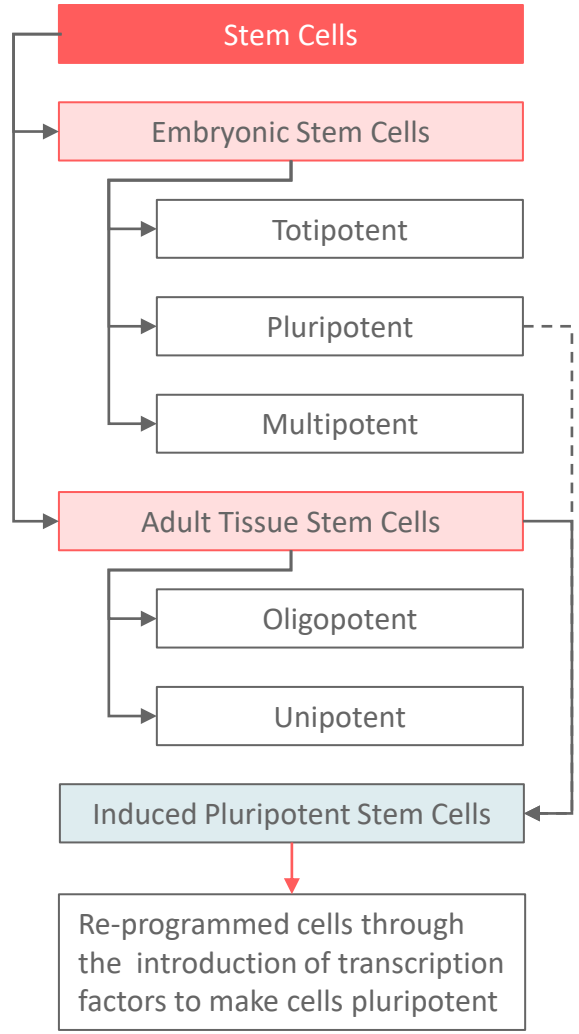
Function of Stem Cells



Source: BioInformant

Types of Stem Cells

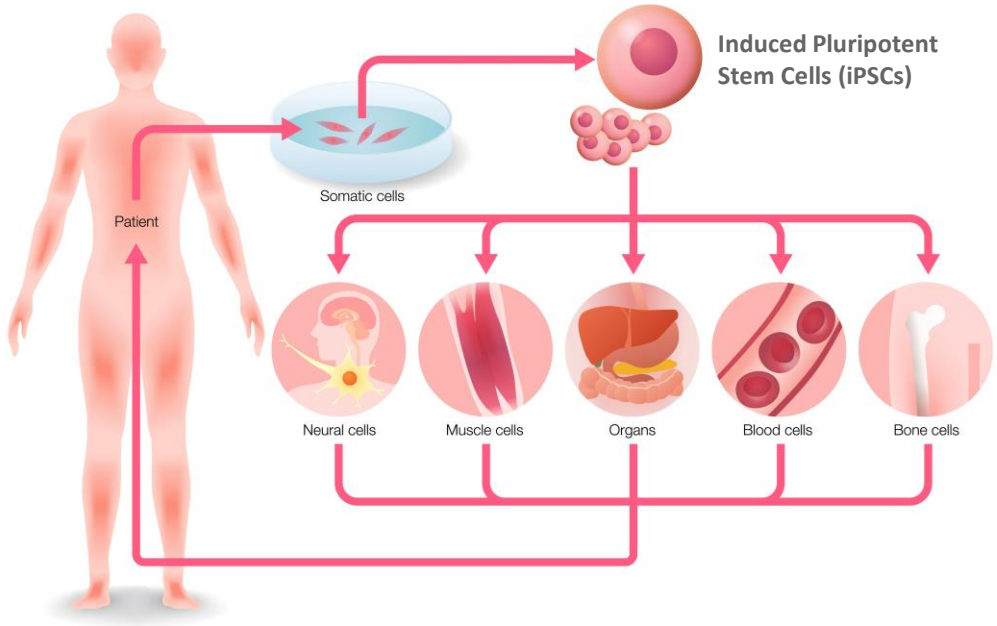




Induced Pluripotent Stem Cells (iPSCs) in Regenerative Medicine

Overview: Induced Pluripotent Stem Cells

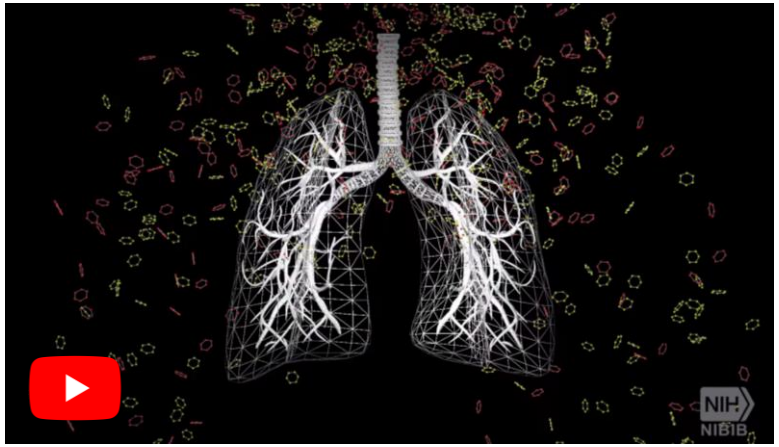
- iPSCs are type of pluripotent stem cell that can be artificially generated directly from somatic cells.
- These cells were first generated in 2006 by Shinya Yamanaka at Kyoto university, Japan (2012 Nobel Prize).
- Somatic cells are introduced with specific genes / transcription factors (Yamanaka factors) to convert the cells into pluripotent cells.



Source: London Strategy, NIH

iPSCs in Tissue Engineering & Regenerative Medicine

- **Tissue engineering** is a rapidly evolving discipline that **seeks to repair, replace or regenerate tissues or organs** by translating fundamental knowledge in science into practical and effective materials, or devices and clinical strategies.
- The terms **tissue engineering** and **regenerative medicine** have become largely **interchangeable**, as the field hopes to focus on cures instead of treatments for complex, often chronic, diseases.
- Pluripotent stem cells hold promise in the field of regenerative medicine, as they can propagate indefinitely and give rise to other cell types in the body (neurons, heart, pancreatic etc.), thereby replacing cells lost to damage and disease.



Future Prospects: Stem Cells & Regenerative Medicine

Current State & Prospects

- The past few years witnessed an exponential advancement in clinical trials revolving around stem cell-based therapies.
- To date, the most established stem cell treatment is bone marrow transplants to treat blood and immune system disorders, but advancements have been made in understanding applications in neurogenerative disease, organ disorders as well as aging and longevity .
- iPSCs are conquering the field of stem cells research with endless possibilities of treating diseases using patients own cells.
- There are currently tremendous efforts exerted globally towards setting up regulatory guidelines and standards to ensure patients safety.
- Scientists study the genetic and biochemical mechanisms that drive axolotl tissue regeneration in hopes that deeper understanding may bridge the gap between regenerative biology and medicine.
- Translation of stem cell therapies to patients have enriched the hope that such regenerative strategies may one day become a treatment for a wide range of diseases.

Additional Material

1. **TEDx: Stem Cell Therapy**

2. **Axolotol: Masters of Regeneration**

Source: London Strategy, NIH

Longevity / Biology of Ageing

LONDON STRATEGY

Introduction: Longevity & Biology of Ageing

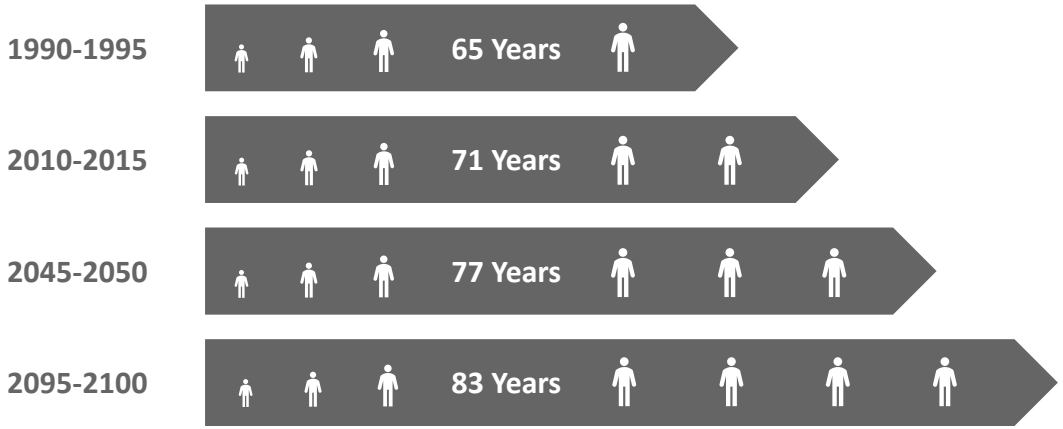
What is the definition of 'Biological Ageing'?
The gradual and progressive changes in physical function that occur in all species, beginning in adulthood and culminating with death.

What does the field of 'Biology of Ageing' involve?
Research on the biology of aging focuses on understanding the cellular and molecular processes underlying these changes as well as those accompanying the onset of age-related diseases.

What are the implications of this research?
As scientists learn more about these processes, experiments can be designed to better understand when and how pathological changes begin, providing important clues toward developing interventions to prevent or treat disease.

What are the future directions of this field?
Continued efforts to find biologic interventions to promote healthy aging, to understand the genetic basis of aging, and to explore the potential of adult stem cells and cell replacement for reducing disease and improving function.

Ageing has always been considered as a **natural 'wear and tear' process** and never seen as a '**disease**'. However, that view is changing as scientists begin to understand the **complex interactions** between our **genes, metabolism** and implications on how these **regulate our lifespan**.



What is the importance of this field?
The world population is ageing, and predictions show that this trend will continue. Age-related diseases, such as cancer or dementia, are therefore increasingly present and impacting our healthcare systems. Further understanding the ageing process will allow us to increase healthy ageing and reduce this overall burden on our quality of life and healthcare systems.

Source: London Strategy, World Population Prospects

Biological Processes that Influence Ageing

LONDON STRATEGY

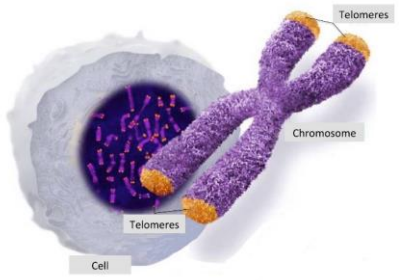
Telomere Shortening

What are telomeres?

- Repetitive sequence of non-coding DNA located at both end of chromosomes.

What is telomere shortening?

- As the cells replicate, chromosomes end shortens. Telomeres protect the coding DNA from being affected by this shortening.
- When telomeres become too short, cell death is triggered.
- Telomeres shortening has been associated with ageing including cancer development.



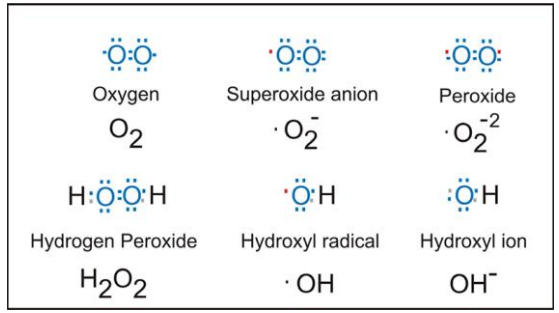
Oxidative Stress

What are Reactive Oxygen Species (ROS)?

- ROS are chemicals formed from O_2 and are produced as a by-product of oxygen metabolism.

What is the role of ROS in ageing?

- Studies have shown that ROS production increases with age
- ROS can damage the DNA sequence and therefore create mutations detrimental to the human body.
- Such mutations can lead to disease of ageing including cancer.



Caloric Restriction

What is caloric restriction (CR)?

- Caloric restriction is a reduction of the daily caloric intake (note: CR differs from fasting).

What is the link between CR and ageing?

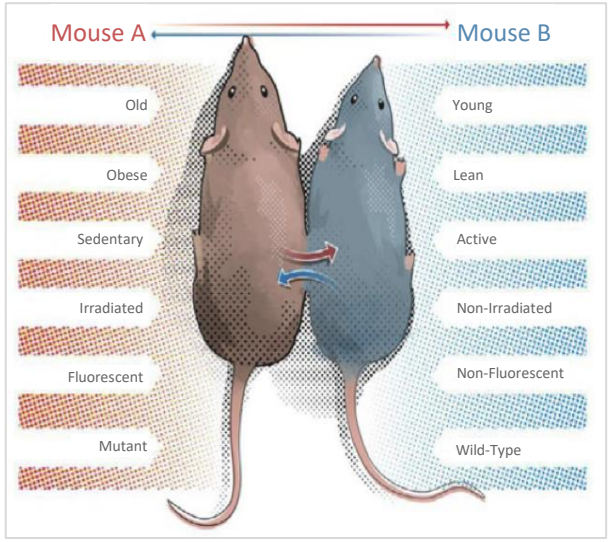
- Several studies on various models (yeast, worms, rodents, monkeys, etc) have demonstrated a significant link between CR and increased lifespan.
- Okinawans (Japan) who practice the *Hara Hachi Bu* (eat until 80% full), have the highest proportion of centenarians in the world.

Source: London Strategy, NIH, Science Direct

Reversing the Ageing Process

Reprogramming Cells to be Young Again

- **Parabiosis** refers to the union of two living organisms by surgical operation, leading to the development of a **shared circulatory system**.
- It enables researchers to explore whether circulating factors in the bloodstream can alter tissue function.
- Pairing **young and aged organisms** together provides a unique experimental design to assess the effects of **systemic environment** on the **age-related processes**.



Scientists are beginning to explore the rejuvenating effects of young blood on age-related impairments. The nature of the circulating molecules that mediate pro-youthful effects remains to be understood.

Animal Models for Human Ageing

- Several species are recognized for their significant enhanced lifespan. **The naked mole rat** is a classic example. Naked mole rats, which rarely develop cancer, can live beyond 30 years whereas other rat species maximum life expectancy is ~ 6 years.
- The naked mole rat is used in the laboratory to understand what anti-ageing mechanisms these rodents have developed. Studies have shown that these rodents have high DNA repair mechanisms.

- The **bowhead whale** is another example of species with significant increased lifespan. Studies suggests that these whales may live for over 200 years.
- Genome studies on these whales have given clues on how these animals lifespan is significantly longer compared to other whale species.

Source: London Strategy, Harvard Business School (Sinclair Lab)

Longevity Genes & Drug Development for Ageing

Longevity Genes & Implications on Ageing

What are longevity genes?

- Scientists have discovered a family of genes that are directly associated with life-span and longevity.
- Six major gene families have been shown to play a role in the genetic regulation of longevity, with SIRTUINs & FOXO gene families being the most predominant.

What role do they play in the ageing process?

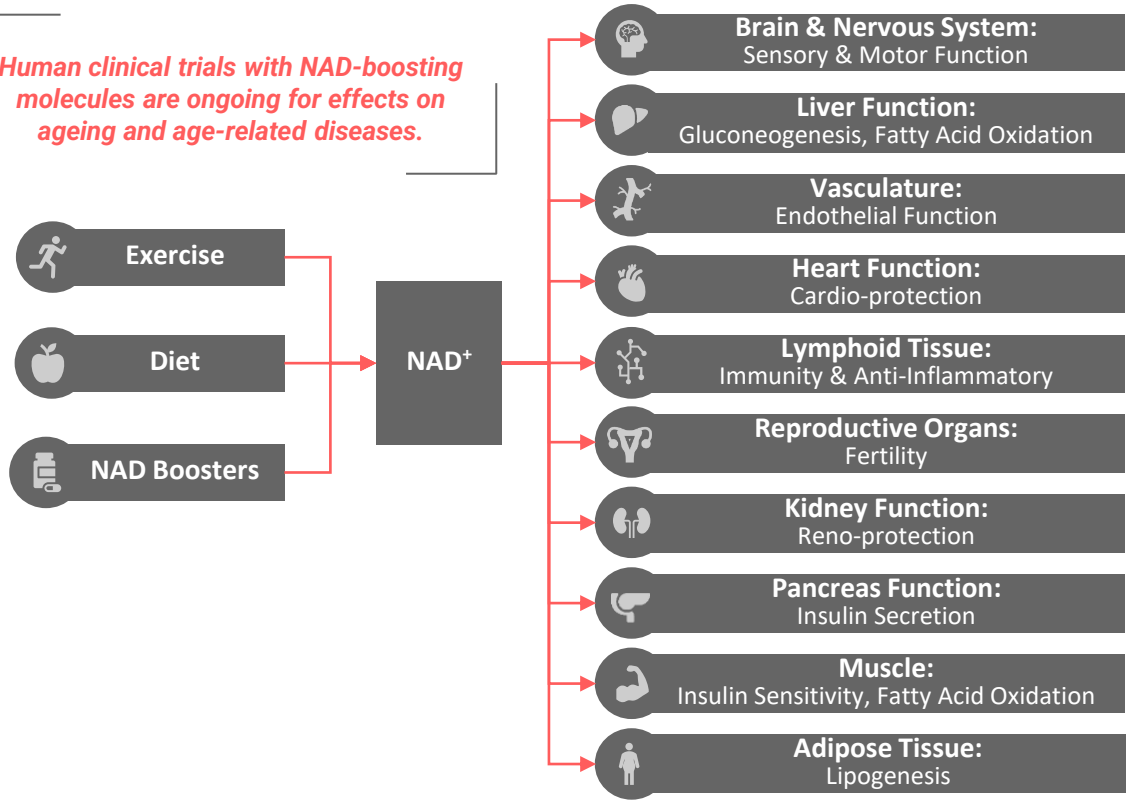
- Overtime, DNA inevitably suffers from double-strand breaks (DSBs) which cause genes to mutate, therefore triggering ageing and diseases like cancer.
- Scientists have found that these genes are involved in DNA repair from these DSBs.

What are the implications of this discovery?

- The discovery of longevity genes showed that it is possible to greatly slow the pace of aging and disease by manipulating just one central pathway.
- This raises the possibility that we can find small molecules that can treat multiple, seemingly unrelated diseases, with a single medicine.

Developing Drugs that Slow Ageing

Human clinical trials with NAD-boosting molecules are ongoing for effects on ageing and age-related diseases.



Source: London Strategy, Harvard Business School (Sinclair Lab)

Synthetic Biology

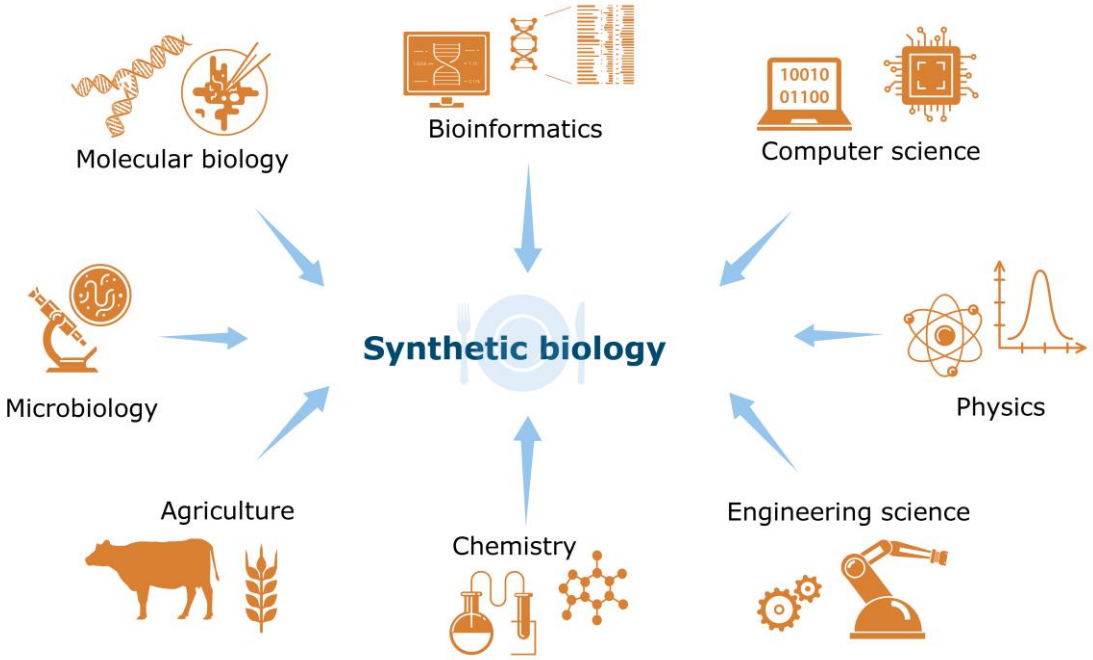
LONDON STRATEGY

Introduction: What is Synthetic Biology?

LONDON STRATEGY

What is Synthetic Biology?

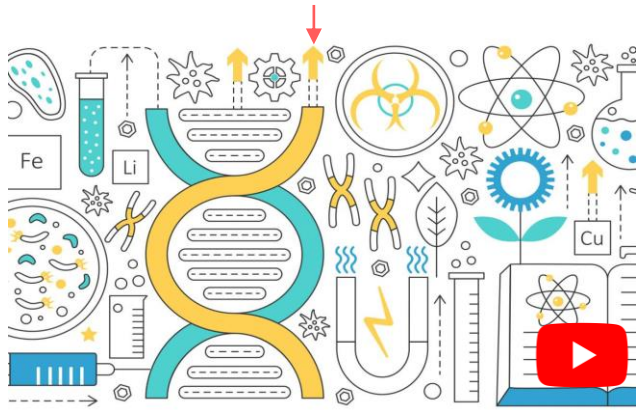
"A multidisciplinary area of research that seeks to **create new biological parts**, **devices**, and **systems**, or to **redesign systems** that are already found in nature."



Synthetic Biology vs Genetic Engineering?

- Synthetic biology has many times been called "**extreme genetic engineering**" and there is still, in social and scientific media, confusion about the differences between genetic engineering and synthetic biology.
- Synthetic biology aims to **design and create full genetic systems** that can be implemented in an organism in order to perform a self-regulated task.
- This does not imply just recombining DNA but designing and modeling a **novel pathway** by assembling many different pieces of genetic material collected and characterized from natural organisms.

"Synthetic biology allows the standardization and automation of the genetic engineering process, making it more precise and faster."



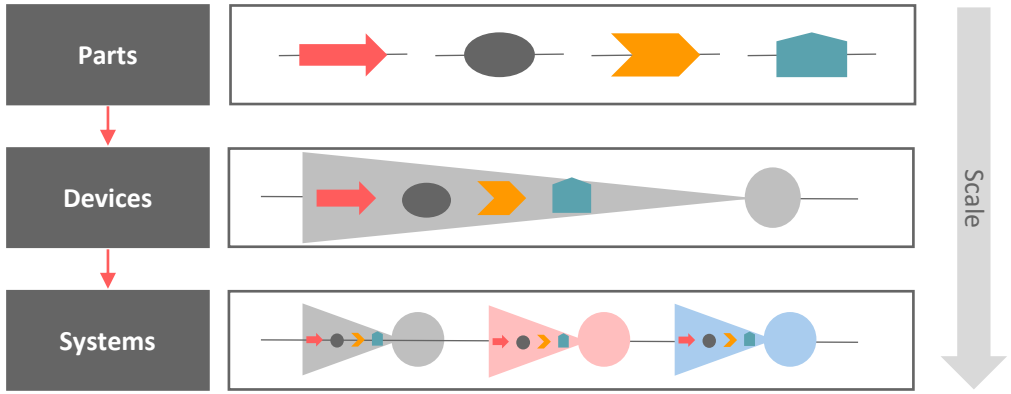
Source: London Strategy, McKinsey

Foundation & Applications of Synthetic Biology

LONDON STRATEGY

BioBricks in Synthetic Biology

- BioBricks form the base of the hierarchal system on which synthetic biology is based.
- These parts or modules encode biological functions and are used in thee assembly of devices or systems.
- These include key DNA elements such as promoters, terminators, protein coding sequences, ribosome-binding sites and so on.



BioBricks FOUNDATION

- The BioBricks Foundation was formed in 2006 as a not-for-profit organization to standardize biological parts across the field.
- The Foundation focuses on improving in areas of Technology, Law, Education and the Global Community as they apply to synthetic biology.

Applications of Synthetic Biology

Synthetic biology could provide a platform for disruptive innovation and growth. Some high-level applications include:

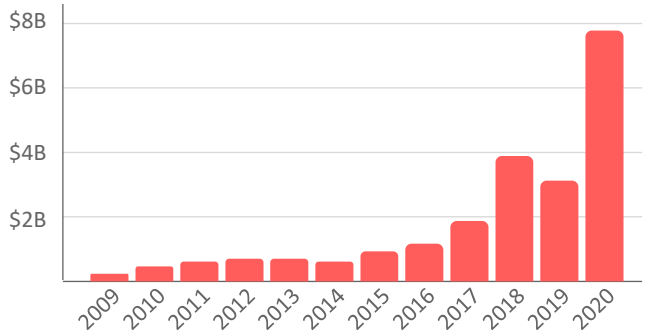
Industry	Examples	
Healthcare	Novel potent antibiotic compounds	Artificial production of by antimalarial compounds
Agriculture	Engineered cattle to reduce waste and env. impact	Self-regulating pest-resistant crops
Food	Crops with increased nutritional value	Crops requiring fewer chemical inputs
Industrial / Energy	Novel industrial ingredients with reduced env. impact	Engineered bacteria that convert CO_2 into fuel
Other	Novel biochemical pathways to produce new perfumes	Sense-respond systems in infection and disease

Source: London Strategy, BioBricks

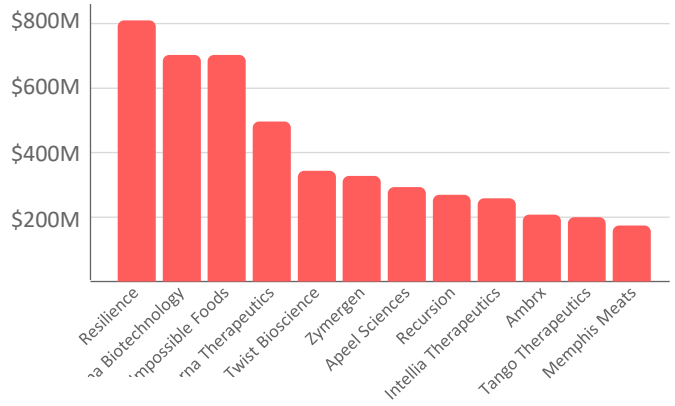
SynBio Market Trends & Forecast

- Synthetic Biology companies received an astounding **$7.8B in private and public financing** in 2020.
- This amounts to nearly two-and-a-half times the amount of funding the industry received in 2019, and nearly twice as much as 2018.
- The market is expected to grow to up to **$28.8B** by 2025 according to market forecasts

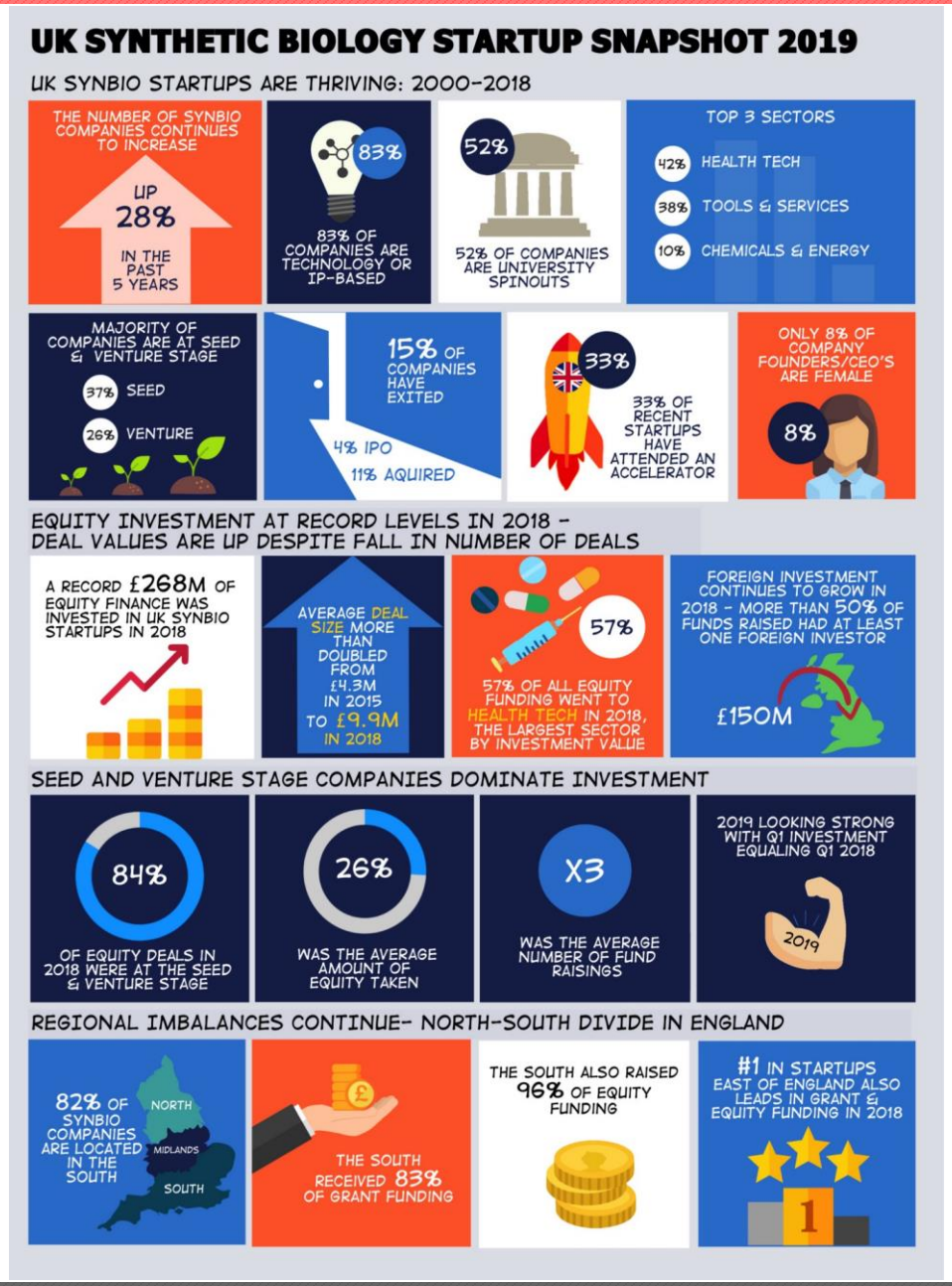
Total Global Funding for Synthetic Biology from 2009-2020
Financing sources include private, public and non-dilutive government grant financing.



Top Synthetic Biology Companies Funded in 2020
More money was available to early-stage biotech companies through the public markets and venture funds.



Source: London Strategy, Synbiobeta, BIA



Big Data & Artificial Intelligence

LONDON STRATEGY

Introduction: What is Big Data all about?

What is the definition of 'Big Data'?
A field that treats ways to analyze, systematically extract information from, or otherwise deal with data sets that are too large or complex to be dealt with by traditional data-processing application software.

Does this also apply to the Biopharma industry?
As one of the world's most information-intensive industries, biopharma has much to gain from big data and analytics. The industry has become more data-driven in recent years as new technologies become more affordable and widely available.

What some examples that we see today?
The cost of genome sequencing has dropped from more than $10 million per genome about 20 years ago to less than $1000 today. As a result, the amount of genomic data that is available for biopharma R&D has increased significantly.

What are the future implications of Big Data in Biopharma?
Many biopharma companies have invested billions into technologies, capabilities and processes to exploit big-data possibilities. We are now seeing an increasing number of applications across all aspects of the biopharma value chain.

Big Data has implications across all aspects of the Biopharma industry

Discovery Research
- Identifying new drug targets and validating mechanisms of action.
- Predicting properties of drug molecules.
- Using innovation networks to drive science.

Regulatory Approval & Access
- Analyzing complex clinical data for regulatory submission.
- Mining real-world effectiveness data to demonstrate the value of products to payers.

Clinical Development
- Analyzing clinical data to understand efficacy and safety in patient populations.
- Integrating real-world evidence with data from randomized controls.

Sales & Marketing
- Predicting prescribing behavior.
- Developing prioritized prescriber detailing.
- Optimizing sales force structure and organisation.

Manufacturing
- Forecasting demand.
- Identifying bottlenecks and optimizing equipment efficiency.
- Predicting and preventing equipment failure.

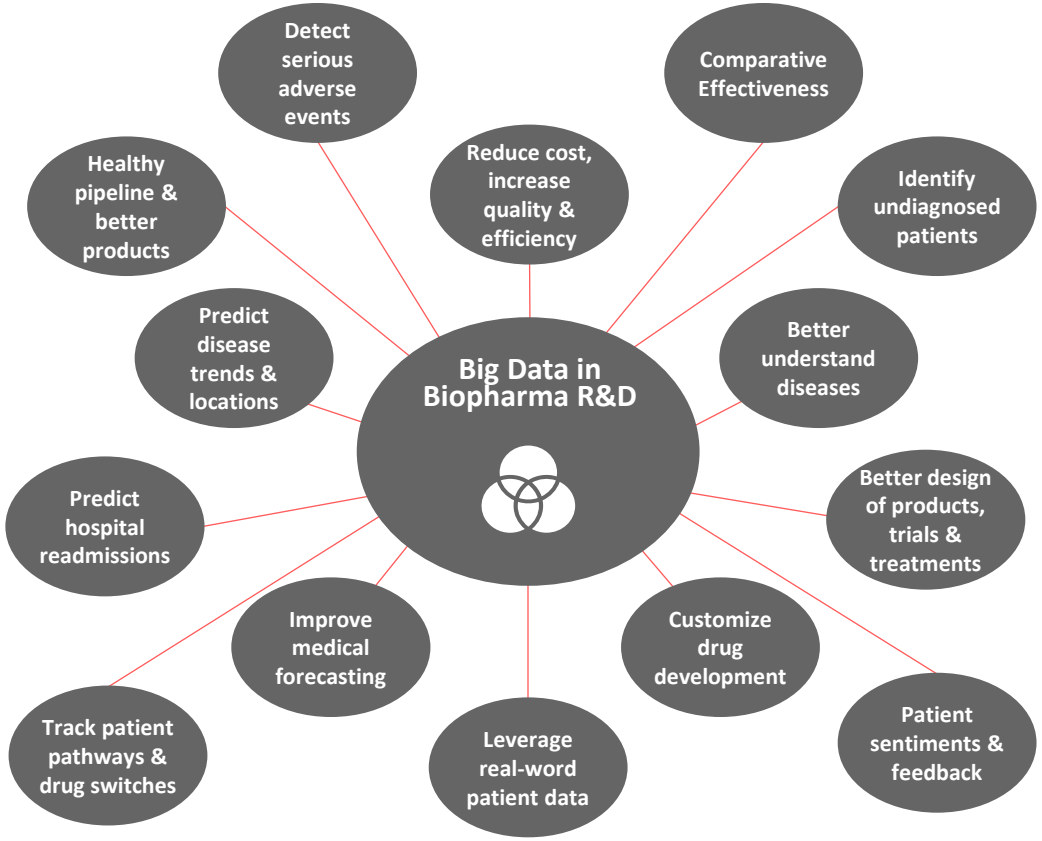
Real-World Evidence
- Studying medication effects.
- Segmenting patients to better target medicines.
- Assessing the impact of post-launch activities (such as marketing and phase IV trials).

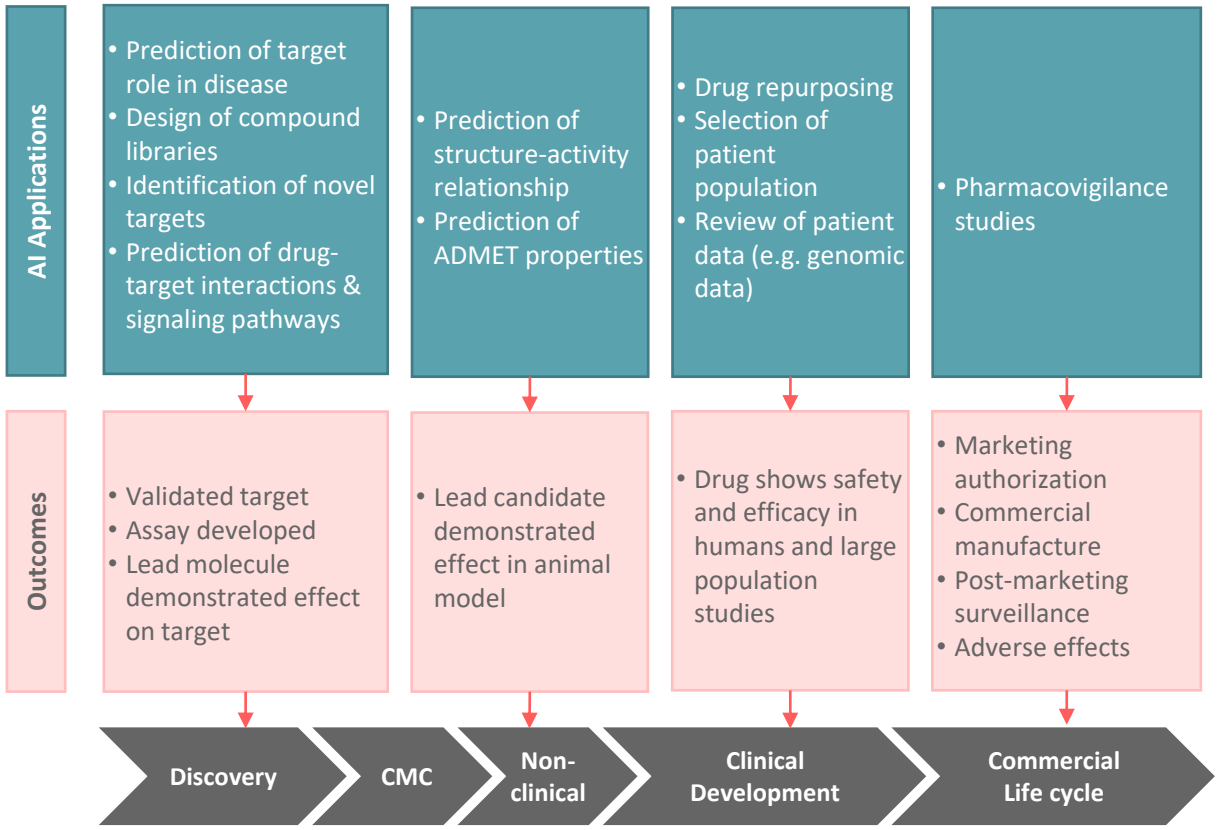
Source: London Strategy, Boston Consulting Group (BCG)

Big Data & Artificial Intelligence (AI) in Biopharma R&D

There is increasingly more data cross all aspects of the R&D processes…

…we are leveraging AI to enhance each stage of the end-to-end drug life cycle.

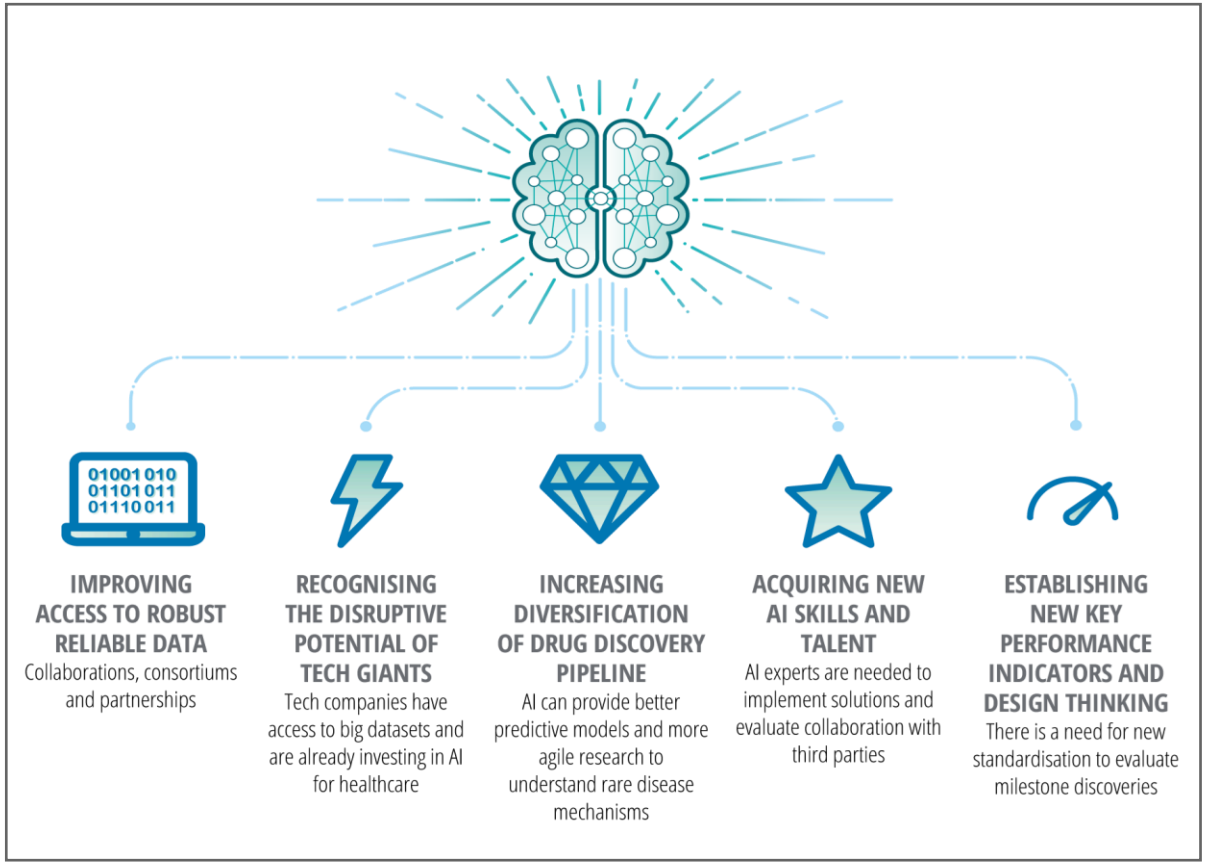




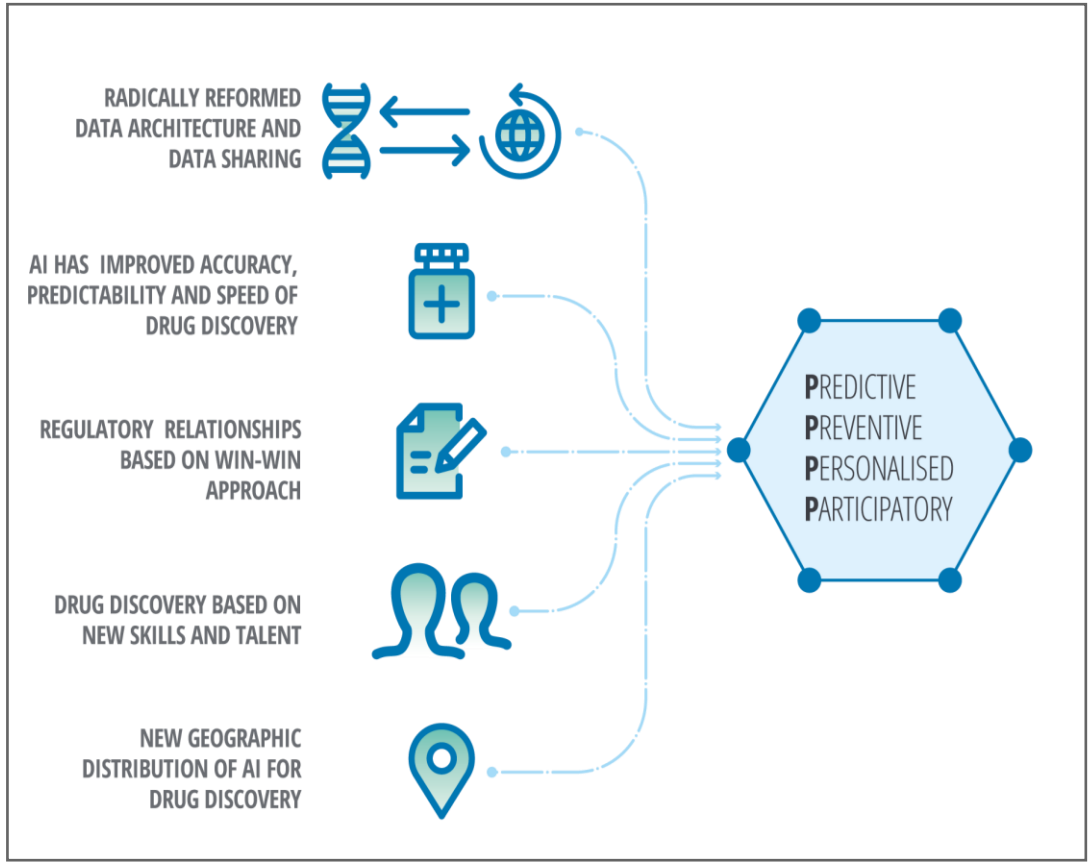
Source: London Strategy, Biopharma Excellence

Key Considerations for Adopting AI Solutions in Drug Discovery

Some key considerations for the adoption of AI solutions must be overcome…



…to enable intelligent drug discovery and deliver '4P' medicine



Source: London Strategy, Deloitte Insights

Current Use Cases and the Future of AI in Biopharma

LONDON STRATEGY

Examples of companies leveraging AI capabilities to better the drug discovery and development processes

NOVARTIS

- Novartis uses AI to predict untested components researchers should explore to **find new and improved cures**.
- Research teams use images from machine learning algorithms to predict which untested compounds might be worth exploring in more details, thus **speeding up the screening process**.

MERCK / **BAYER**

- Merck & Bayer use AI software that aims to **support clinical decision-making** of chronic thromboembolic pulmonary hypertension (CTEPH).
- This technology enables radiologists to detect certain patterns easier, quicker and more accurately, leading to **earlier treatment and better patient outcomes**.

VERGE GENOMICS

- Verge Genomics uses AI to predict the effect **of new treatments** for patients suffering from **ALS & Alzheimer's**.
- Research teams use automated data gathering and analysis to identify potential drug targets for neurological diseases, thereby **reducing cost** and **time** of the development process.

CYCLICA / **BAYER**

- Cyclica & Bayer use AI to **discover drugs faster, cheaper** and **safer**.
- Their technology, Ligand Express, screens drugs against repositories of structurally-characterized proteins to determine pharmacological profiles, identify targets and study drug-protein interactions to develop **more affordable drugs**.

mission therapeutics

- Mission uses AI to develop **treatments for Alzheimer's**
- They are developing Deubiquitinase (DUB) inhibitors to regulate the degradation of misfolded, toxic proteins and preventing their accumulation in patients suffering from Alzheimer's disease, there potentially **delaying the progression of this disease.**

The future of AI in the pharmaceutical industry holds lots of promise in the years to come

Investment

- The McKinsey Global Institute estimates that AI and machine learning in the pharmaceutical industry could generate nearly $100B annually across the US healthcare system alone.
- About 50% of global healthcare companies plan to implement AI strategies and broadly adopt the technology by 2025.
- The market is expected to grow from $699.3 million in 2020 to $2,895.5 million in 2025 at a rate of 32.9%.

Focus

- Specifically, global pharmaceutical and drug development companies will invest more in discovering new drugs for **chronic** and **oncology diseases**.
- Chronic diseases are the leading causes of death in the US. Therefore, organizations are increasingly leveraging AI to improve chronic disease management, drive down costs, and enhance patient health.

Application

- AI and machine learning will continue to help boost all aspects of the pharmaceutical industry, from more intelligent clinical trials, drug discovery and manufacturing process through to regulatory processes, real-world evidence sales and marketing.
- As AI tools become more accessible over the years, they will become part of the natural process within the end-to-end process in our industry. The future will be AI-enabled.

Source: London Strategy, Digital Authority Partners