THE SCIENCE OF CELL CULTURE

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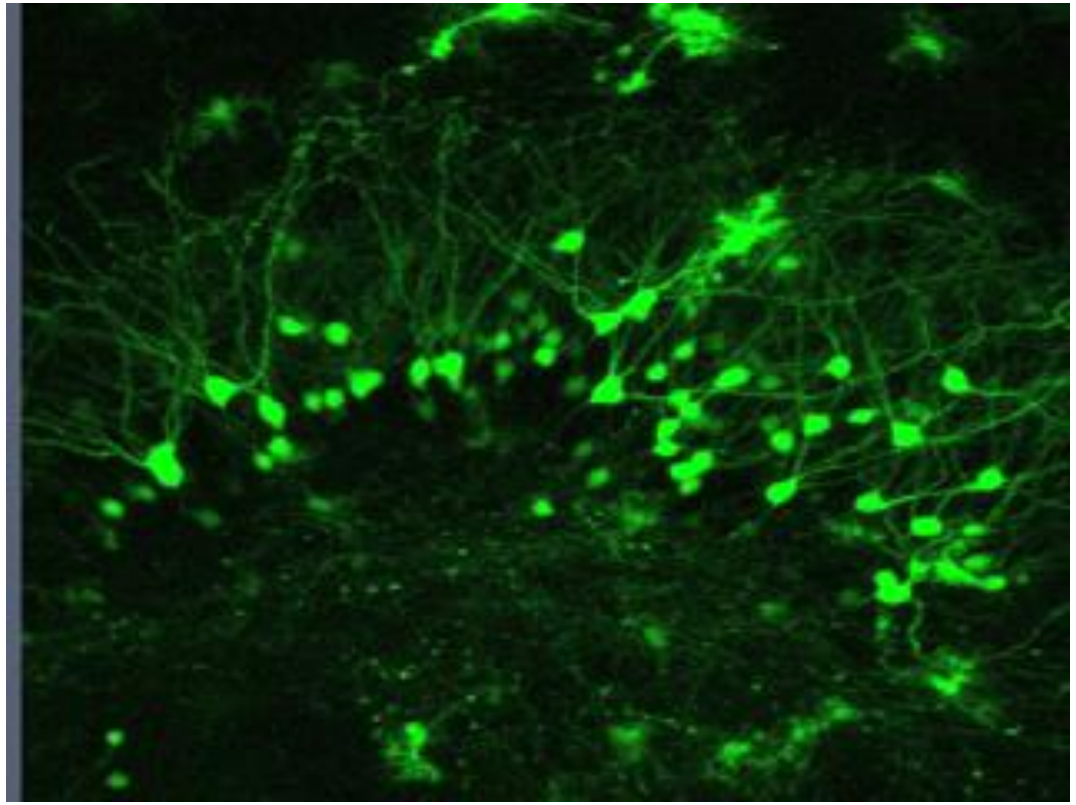
WHY I'M TALKING ABOUT THIS

- fascinated by biology in high school
- loved lab work & microscopy
- studied biochemistry to understand mechanisms
- worked at the cellular scale during PhD & postdoc



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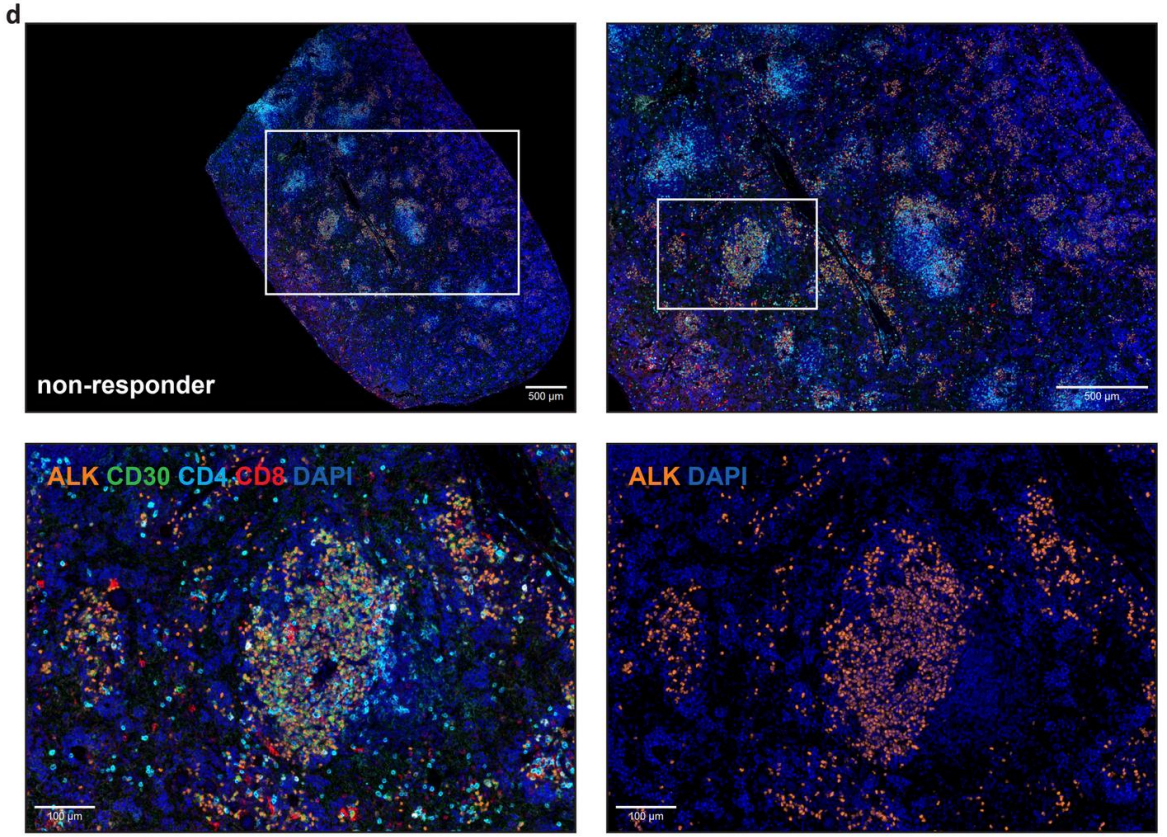

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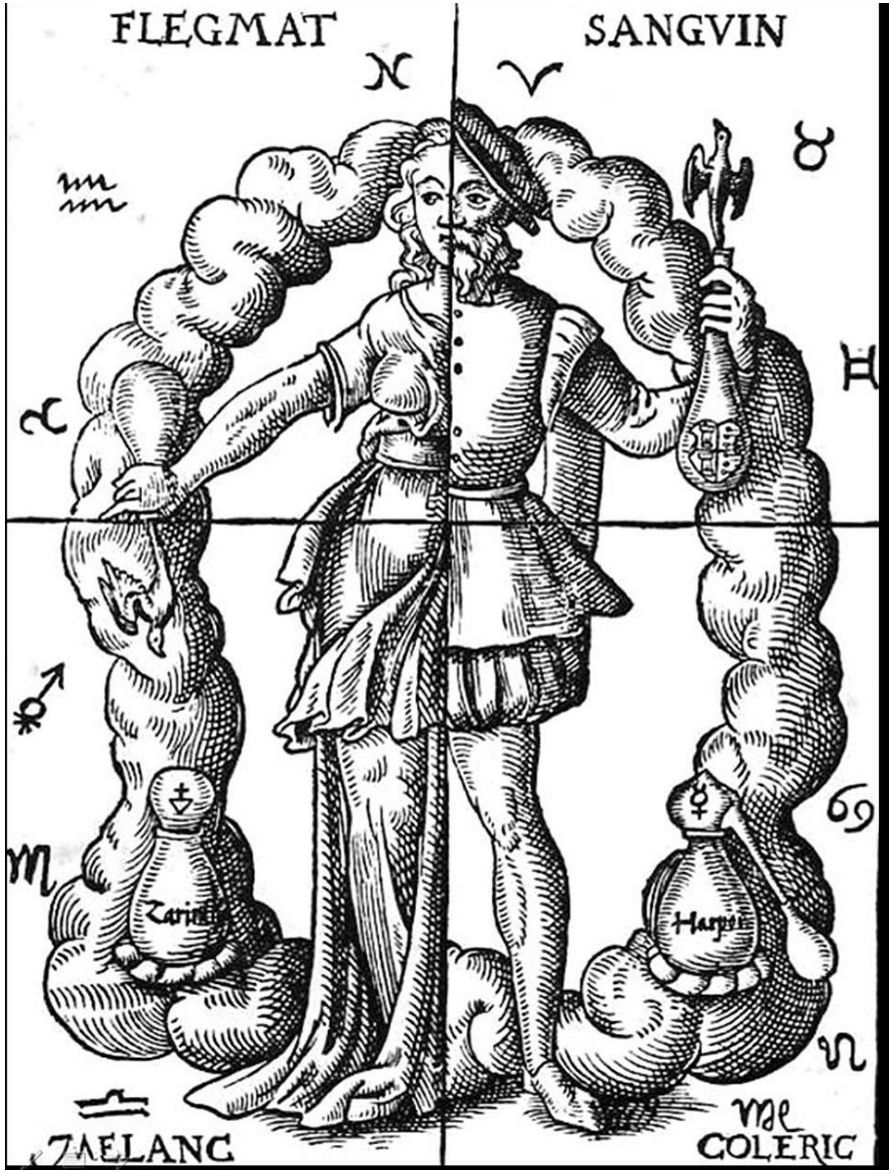
- huge implications for medicine
- most of it is hidden from public view

WHAT WE WILL EXPLORE

- how cells became visible
- what cells are & what they need
- how we grow cells outside the body
- what we learn from cultured cells
- how this enables new therapies



16th-century German illustration of the four humors: *Flegmat* (phlegm), *Sanguin* (blood), *Coleric* (yellow bile) and *Melanc* (black bile), divided between the male and female sexes

BEFORE CELLS WERE VISIBLE

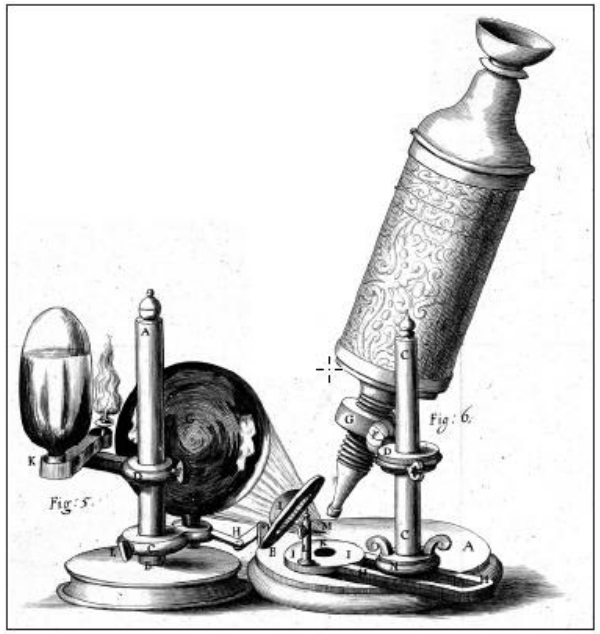
- cells too small to see
- tissues seen as continuous
- disease explained by “humors”

  Humorism, the humoral theory, or humoralism, was a system of medicine detailing a supposed makeup and workings of the human body, adopted by Ancient Greek and Roman physicians and philosophers.

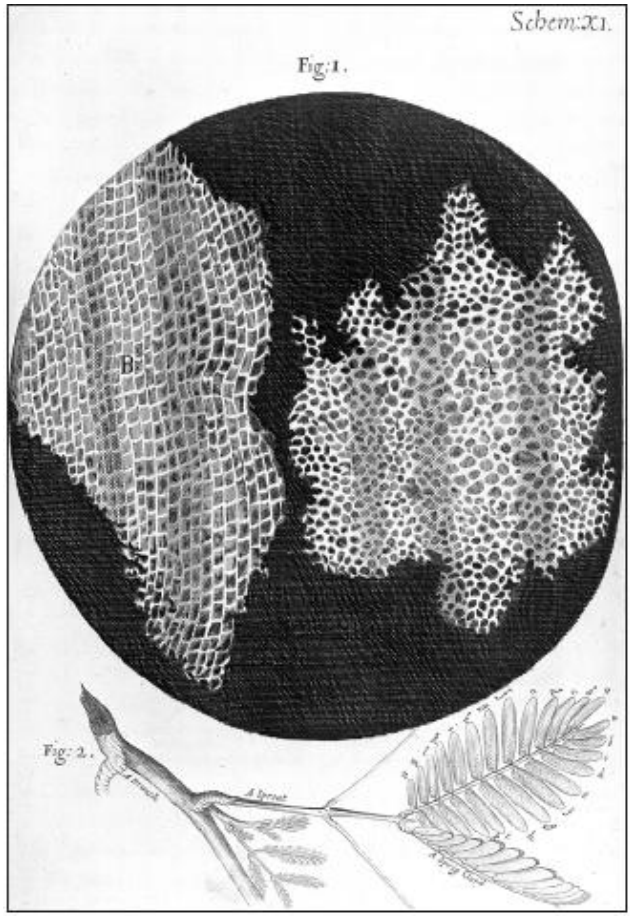
- no microscopic mechanisms

MICROSCOPES REVEAL NEW WORLD

- lenses enable magnification
- tiny compartments seen in cork



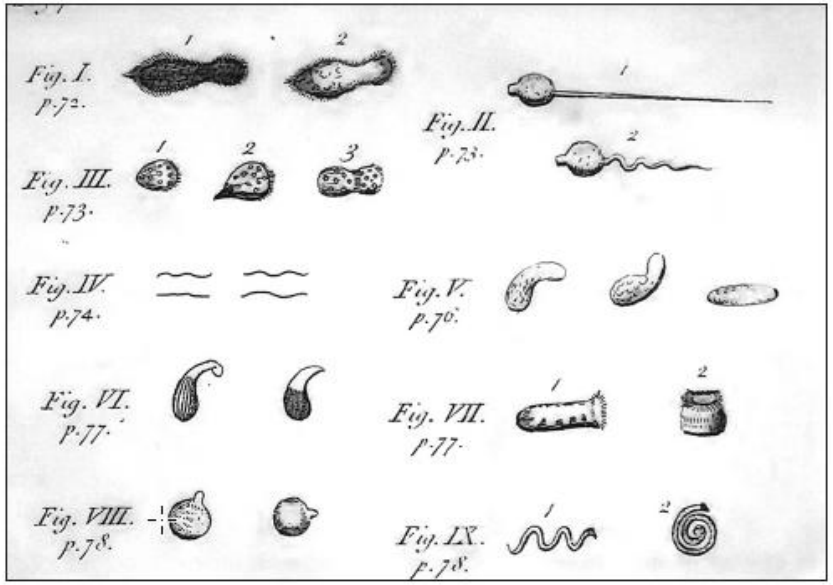
An illustration of compound microscope invented by dutch spectacle makers Hans and Zacharias Janssen (c. 1590).



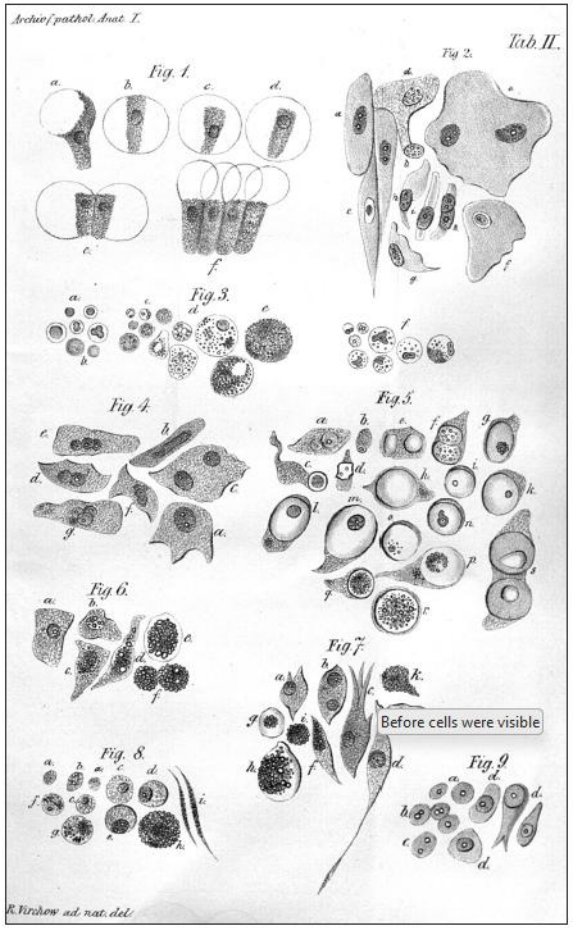
Robert Hooke's drawing of a section of a piece of cork from *Micrographia* (1665). The book generated enormous and unlikely attention, becoming popular all over England for its magnified images of small animals and plants.

MICROSCOPES REVEAL NEW WORLD

- lenses enable magnification
- tiny compartments seen in cork
- microorganisms discovered
- tissues are not continuous



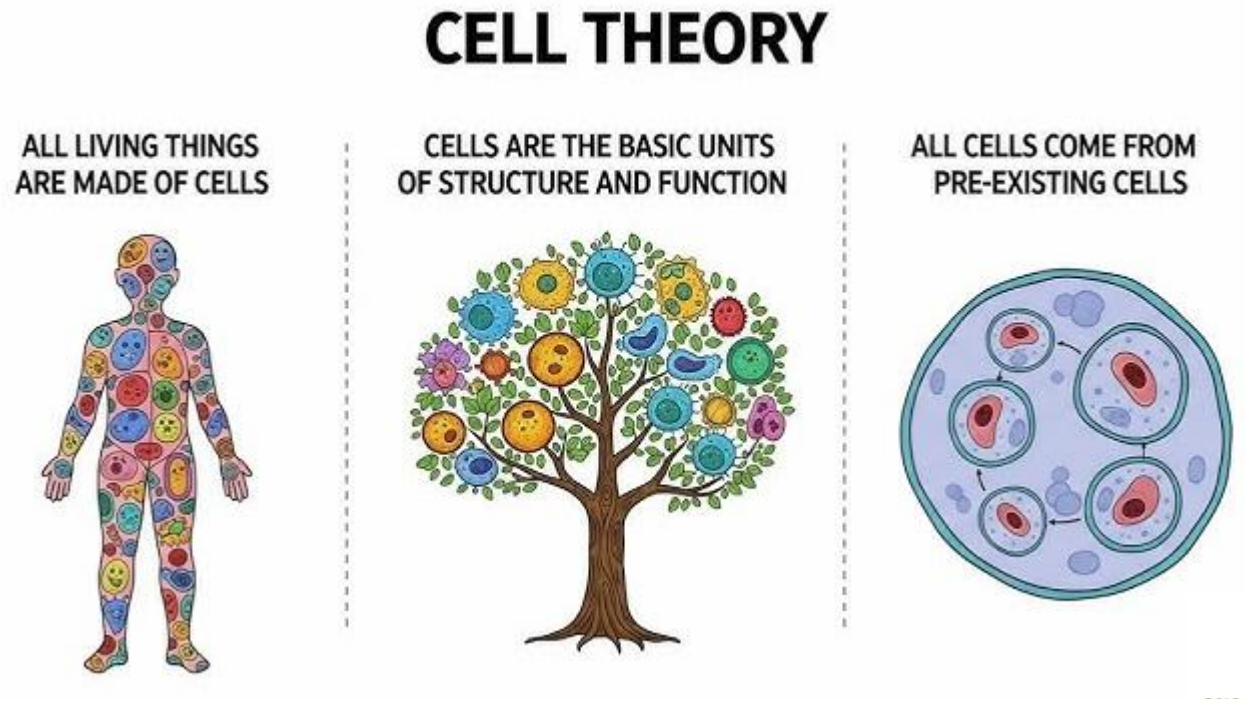
Some of the “animalcules” observed by Leeuwenhoek through his single-lensed microscope (1670).



A drawing from Virchow’s Archives, ca. 1847, illustrating the organization of cells and tissues. Note the multiple abutting or adhering cell types in figure 2. Figure 3f shows the various cells found in blood.

THE CELL THEORY FORMS

- organisms are made of cells: cell = basic structural and functional unit of all forms of life
- cells are basic units of life
- cells arise from other cells
- no spontaneous generation



FROM OBSERVATION TO CULTURE

- seeing cells was not enough
- scientists wanted to keep cells alive

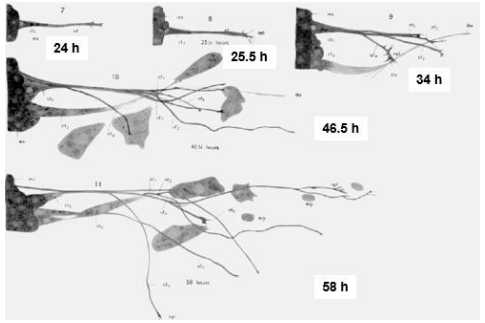
Wilhem Roux
(1850 -1924)

Pioneer of cell culture – kept embryonic chicken cells alive for several days in a warm saline solution in 1885

Important principle of cell culture: mimicking the environmental conditions of the cells within the original organism

Ross Harrison
(1870 -1959)

Established culture of frog nerve fibers in 1907

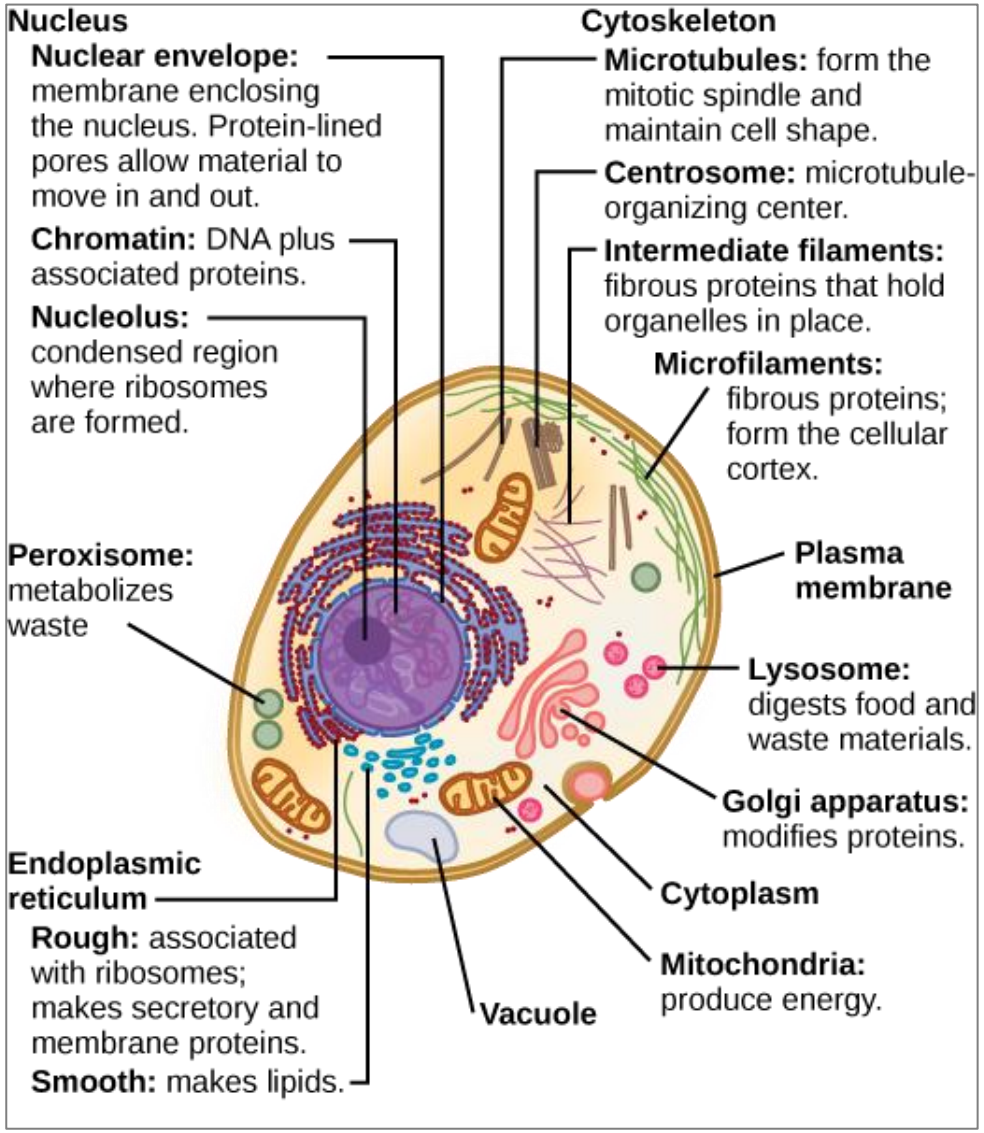


FROM OBSERVATION TO CULTURE

- seeing cells was not enough
- scientists wanted to keep cells alive
- early culture attempts succeed
- foundation for modern research

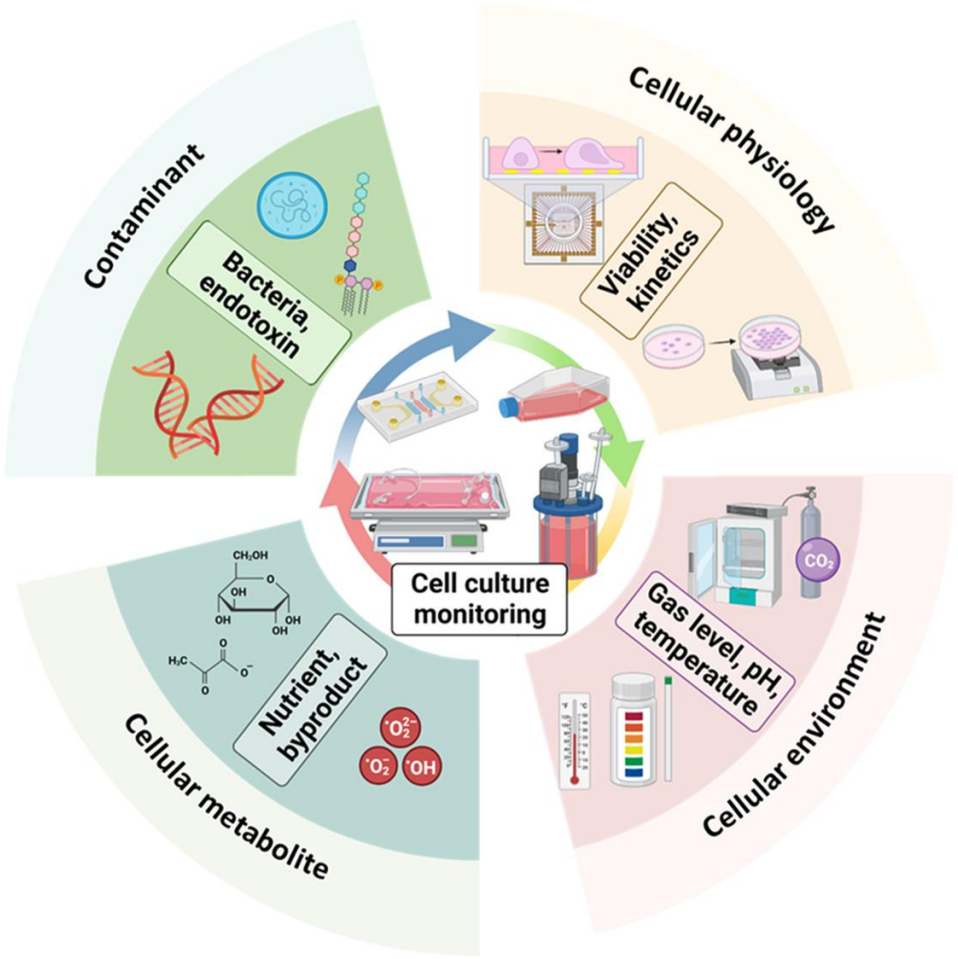
WHAT IS A CELL?

- basic unit of life
- membrane separates inside/outside
- stores information (DNA)
- uses energy & resources
- can grow + divide + specialize



Scheme and legend detailing the main organelles found in a eukaryotic animal cell and their functions.

CELLS NEED A HABITAT



- nutrients for energy & building
- chemical signals to guide behavior
- correct temperature
- physical support & space
- protection from microbes

WHAT CELLS EAT

- glucose for energy
- amino acids for proteins
- salts & ions for balance
- vitamins & co-factors
- growth factors = instructions

TEMPERATURE & STERILITY

- cells kept at ~37°C
- incubators provide CO_2 & humidity
- sterile cabinets prevent contamination
- bacteria divide faster than cells

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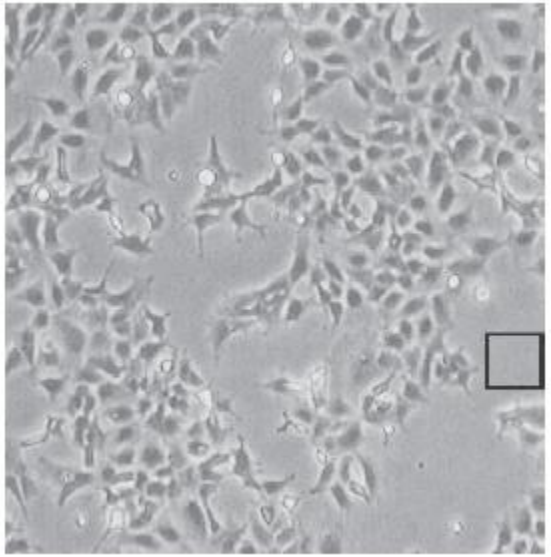
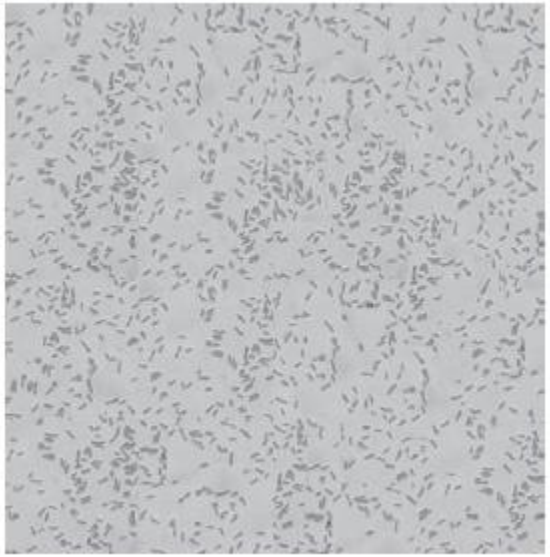
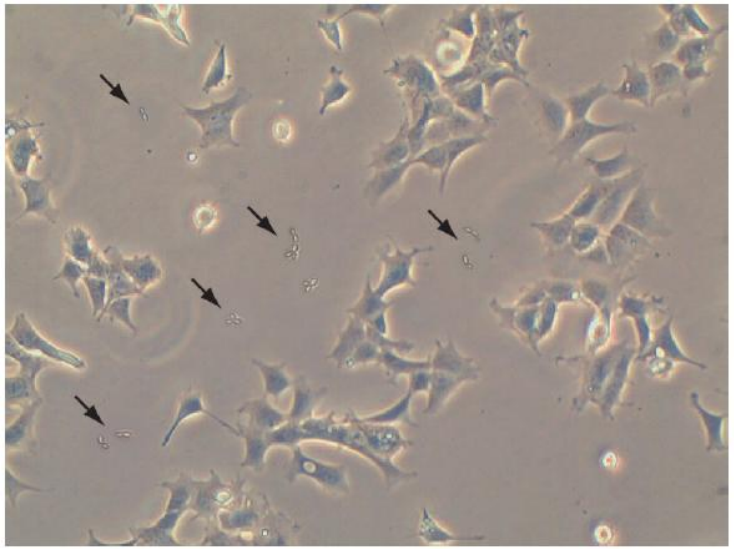
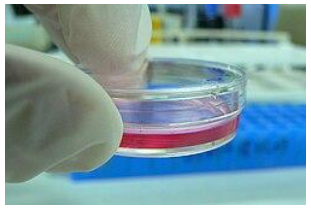
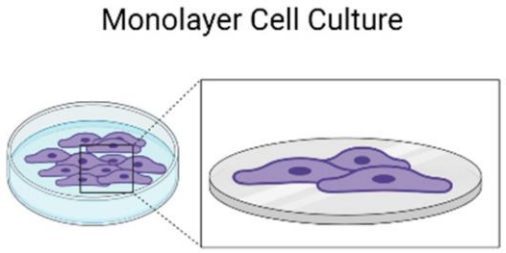




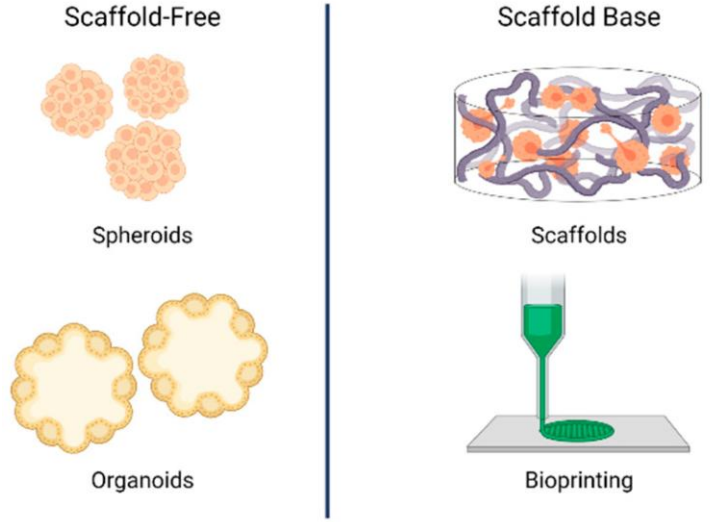


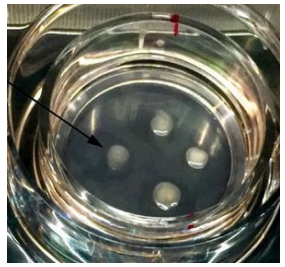
2D, 3D & TINY TISSUES





3D Cell Culture





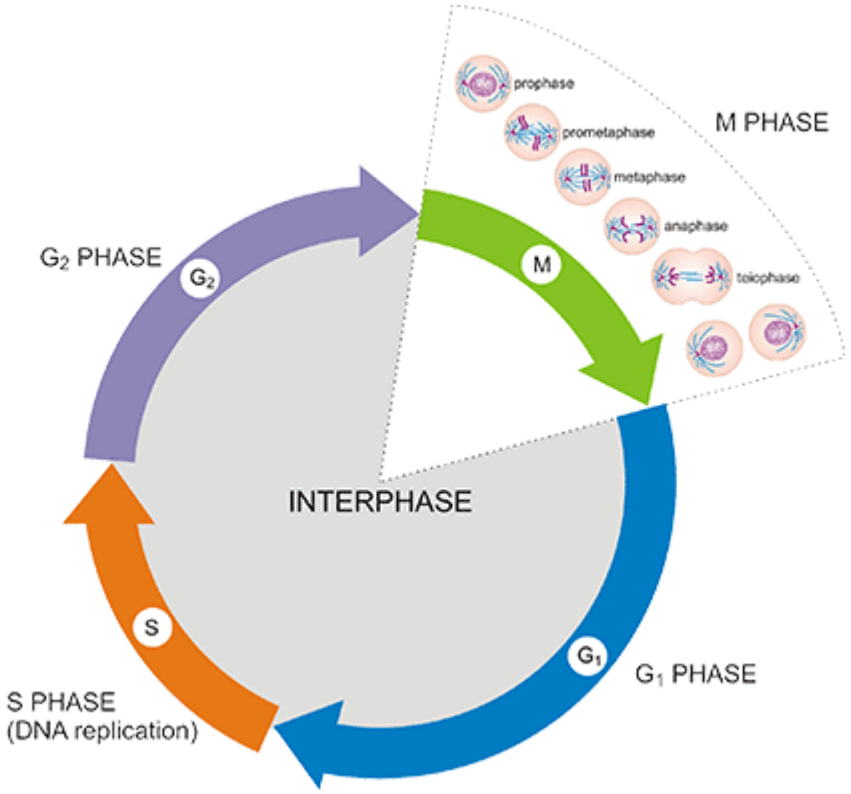
- 2D monolayers: flat, easy to observe
- 3D cultures: more realistic structure
- scaffolds support organization
- organoids self-organize from stem cells

WHAT CELLS DO WE GROW?

- primary cells – fresh from tissues
- cell lines – immortal & stable
- stem cells – can specialize
- patient-derived cells – match individuals
- choose based on research goals

DISCOVERING THE CELL CYCLE

- cells divide in stages
- checkpoints regulate progression
- signals start/stop division
- foundation for cancer insights



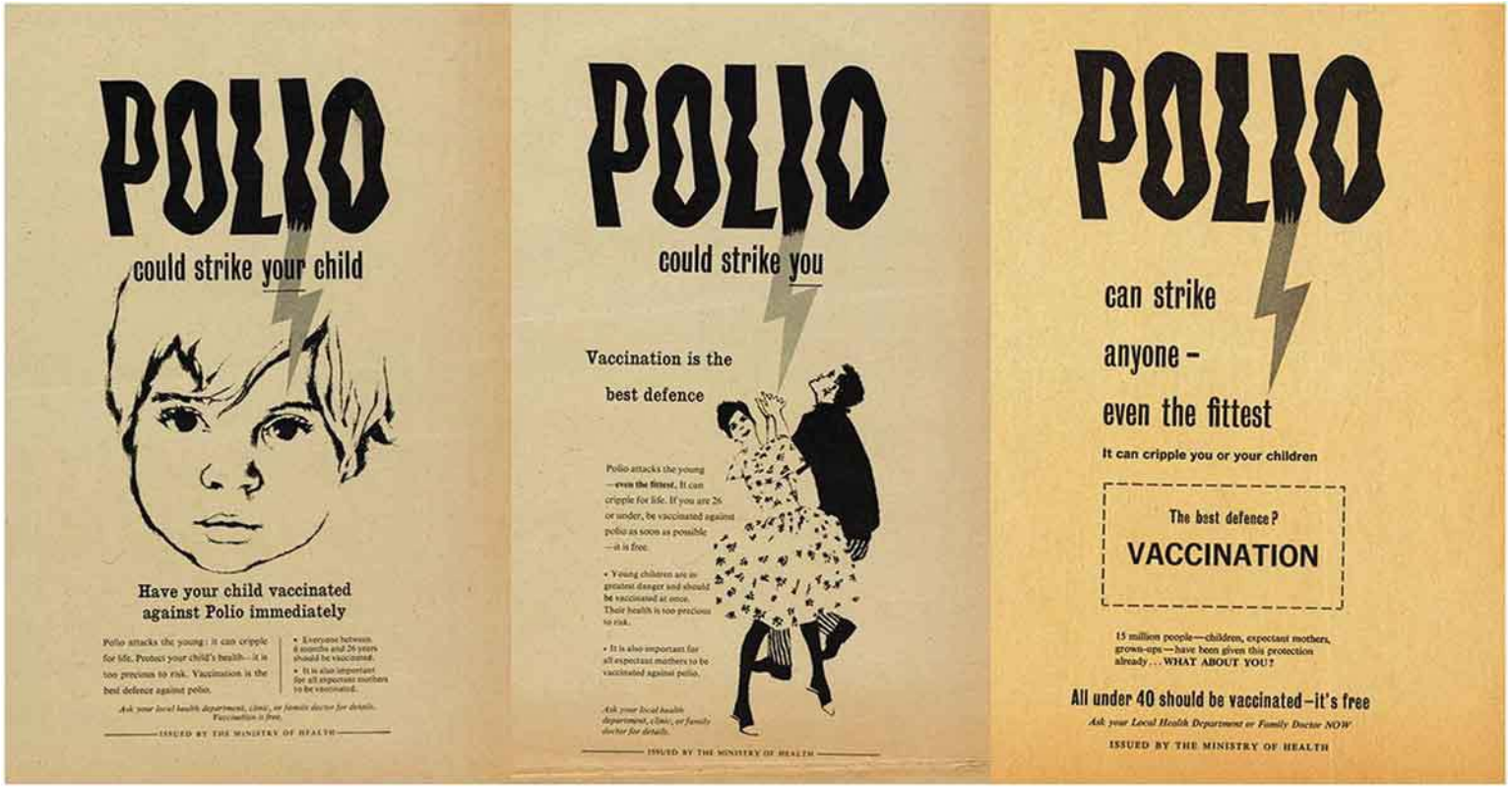
FROM ORGANS ▸ TISSUES ▸ CELLS ▸ PROGRAMS

- Past: treat organs
- Present: treat tissues

- Immunotherapy: train the immune system
- Regeneration: replay development
- Cancer: treat tumors as evolving systems

POLIO VACCINE

- polio caused paralysis & fear
- virus could not be grown safely
- cell culture enabled mass production
- vaccines ended outbreaks
- transformed global public health



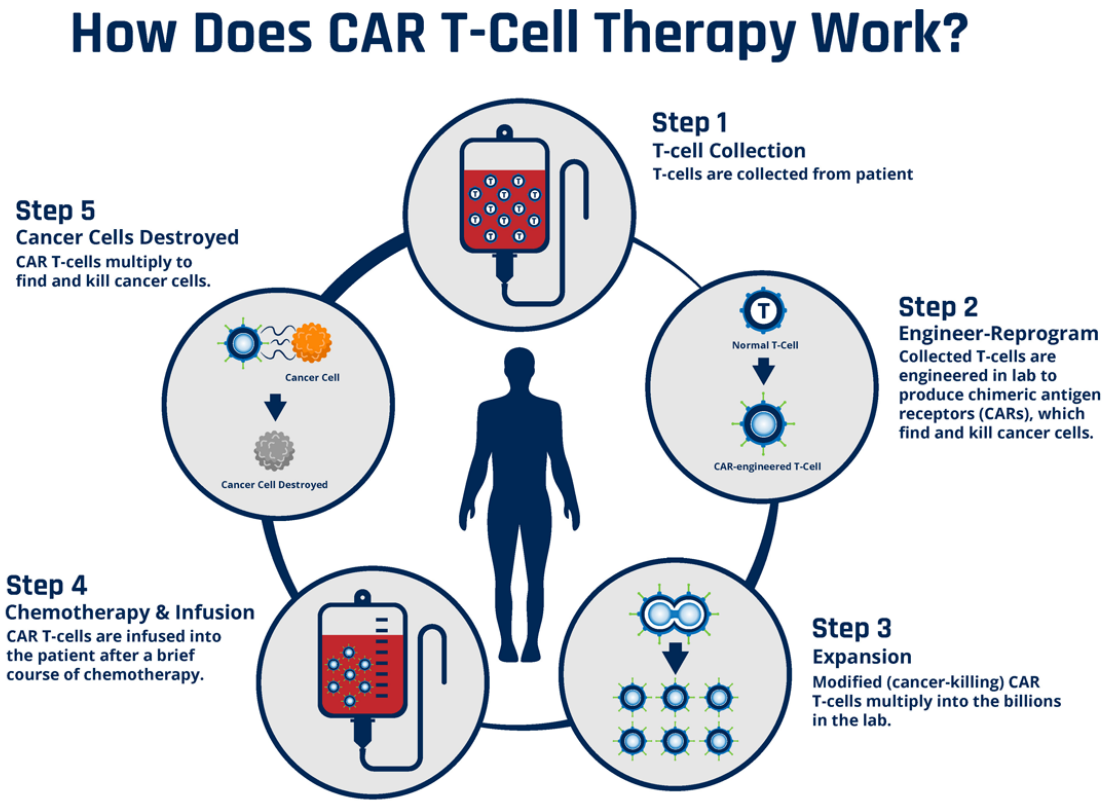
Set of ‘Polio could strike’ posters aimed at ensuring different cohorts were vaccinated (1960)

IVF - *IN VITRO* FERTILIZATION

- fertilization outside the body
- early embryo grows in culture
- transferred at blastocyst stage
- pioneered in 1978
- millions of births since then

CAR-T - TRAINING IMMUNE CELLS

- patient's T cells extracted
- modified & expanded in culture
- reinfused to attack cancer
- dramatic remissions in leukemias
- first FDA-approved cell therapy



MONOCLONAL ANTIBODY DRUGS

Targeted disease	Target antigen	Monoclonal antibody
Immunological		
Autoimmune disorders	Inhibition of TNF-α signaling	Adalimumab Infliximab
Allergy-related asthma	Immunoglobulin E (IgE)	Omalizumab
Ankylosing spondylitis (other indications—rheumatoid arthritis, Crohn's disease, psoriasis, hidradenitis suppurativa, and refractory asthma)	TNF-α inhibitor	Golimumab
Cardiovascular disease	Inhibition of glycoprotein IIb/IIIa	Abciximab
Cryopyrin-associated periodic syndromes (CAPS)	IL-1β	Canakinumab
Crohn's disease	Inhibition of TNF-α signaling	Certolizumab pegol
Macular degeneration	Vascular endothelial growth factor A (VEGF-A)	Ranibizumab
Multiple sclerosis (other indications—Crohn's disease)	Alpha-4 (α4) integrin	Natalizumab
Paroxysmal nocturnal hemoglobinuria	Complement system protein C5	Eculizumab
Psoriasis	CD11a	Efalizumab
Rheumatoid arthritis	Anti-IL-6R	Atlizumab
Transplant rejection	IL-2Rα receptor (CD25)	Daclizumab Basiliximab
	T cell CD3 receptor	Muromonab-CD3
Oncological		
Acute myelogenous leukemia	CD33	Gemtuzumab
Breast cancer	ErbB2 or HER2	Trastuzumab
Chronic lymphocytic leukemia	CD52	Alemtuzumab
	CD20	Ofatumumab
Colorectal cancer	Epidermal growth factor receptor	Panitumumab Cetuximab
	Vascular endothelial growth factor (VEGF)	Bevacizumab
Hodgkin and non-Hodgkin lymphomas	CD30	Brentuximab vedotin
	CD20	Rituximab Tositumomab Ibritumomab tiuxetan
Melanoma	Blocks CTLA-4	Ipilimumab
Postmenopausal osteoporosis (other indications—solid tumor's bony metastases)	RANK ligand inhibitor	Denosumab
Systemic lupus erythematosus	Inhibition of B-cell activating factor	Belimumab
Anti-infective		
Respiratory syncytial virus	Epitope of the RSV F protein	Palivizumab

Note: This table lists monoclonal antibodies approved by the US FDA as of this writing. There are more than 150 other monoclonal antibodies in clinical trials worldwide

- cells act as protein factories
- require immortal cell lines
- treat cancer & autoimmune disease
- top-selling drug class today
- manufactured via culture

COVID-19 VACCINES & VIRAL TESTING

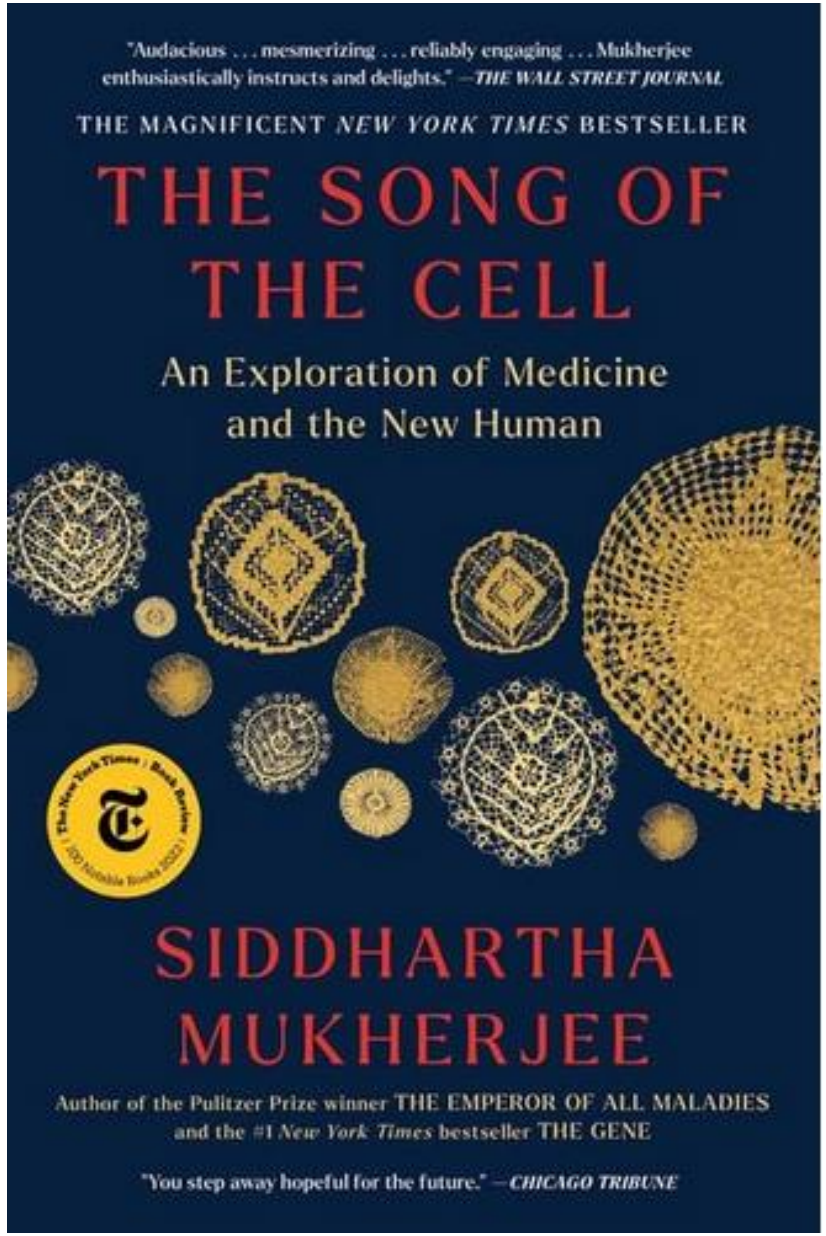
- virus needed to be cultured
- neutralization assays required cells
- validated vaccine responses
- accelerated global rollout
- saved millions of lives

WHY CELL CULTURE MATTERS

- gives access to the cellular level of life
- makes cells visible, measurable, and controllable
- expands the action surface of medicine
- enables new ways to diagnose, prevent, and treat disease

NEW CAPABILITIES ▸ NEW QUESTIONS

- what should we allow?
- who gets access?
- who decides?
- who benefits (and who doesn’t)?
- what are the long-term consequences?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