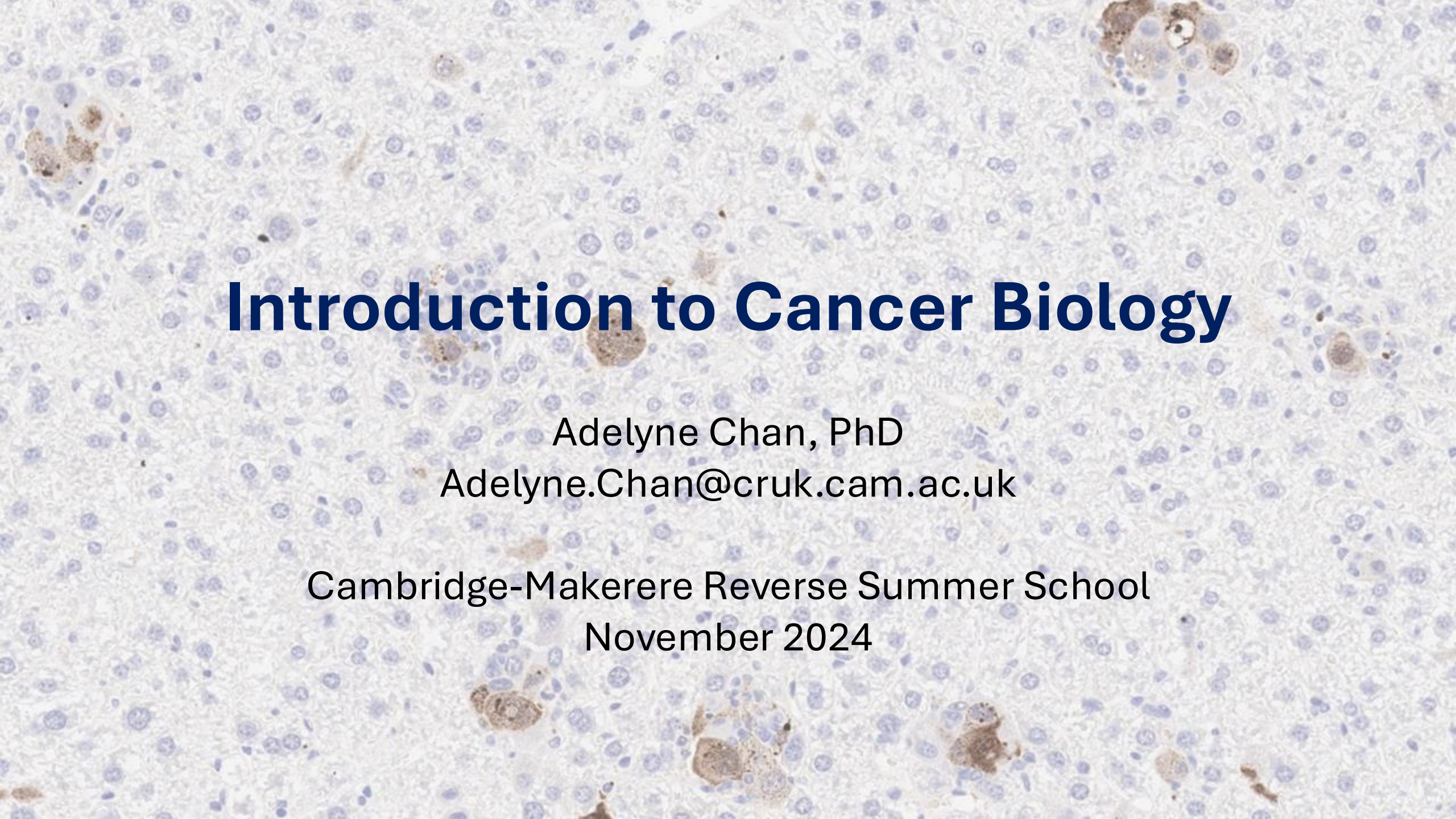
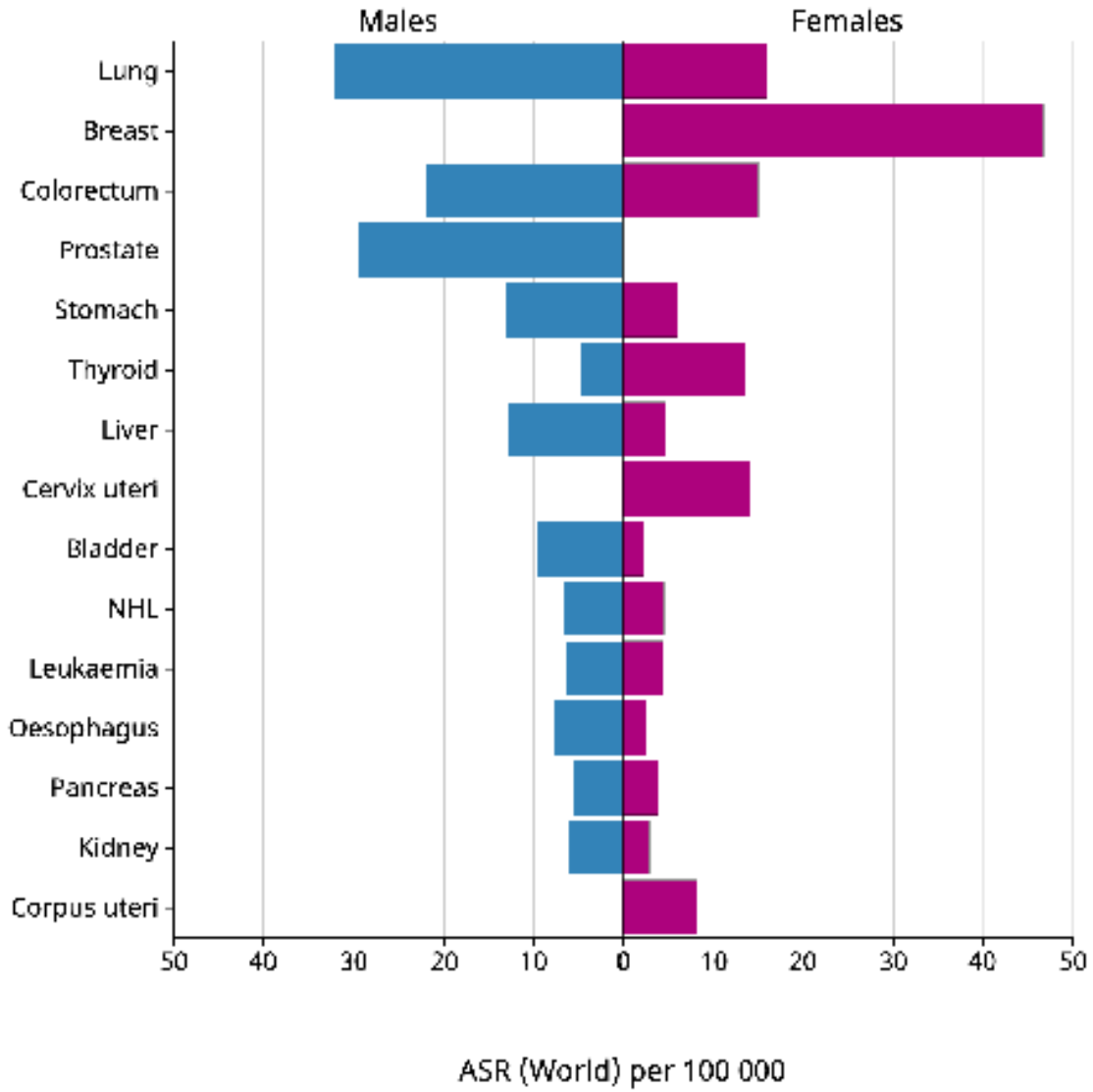


Introduction to Cancer Biology

Adelyne Chan, PhD
Adelyne.Chan@cruk.cam.ac.uk

Cambridge-Makerere Reverse Summer School
November 2024

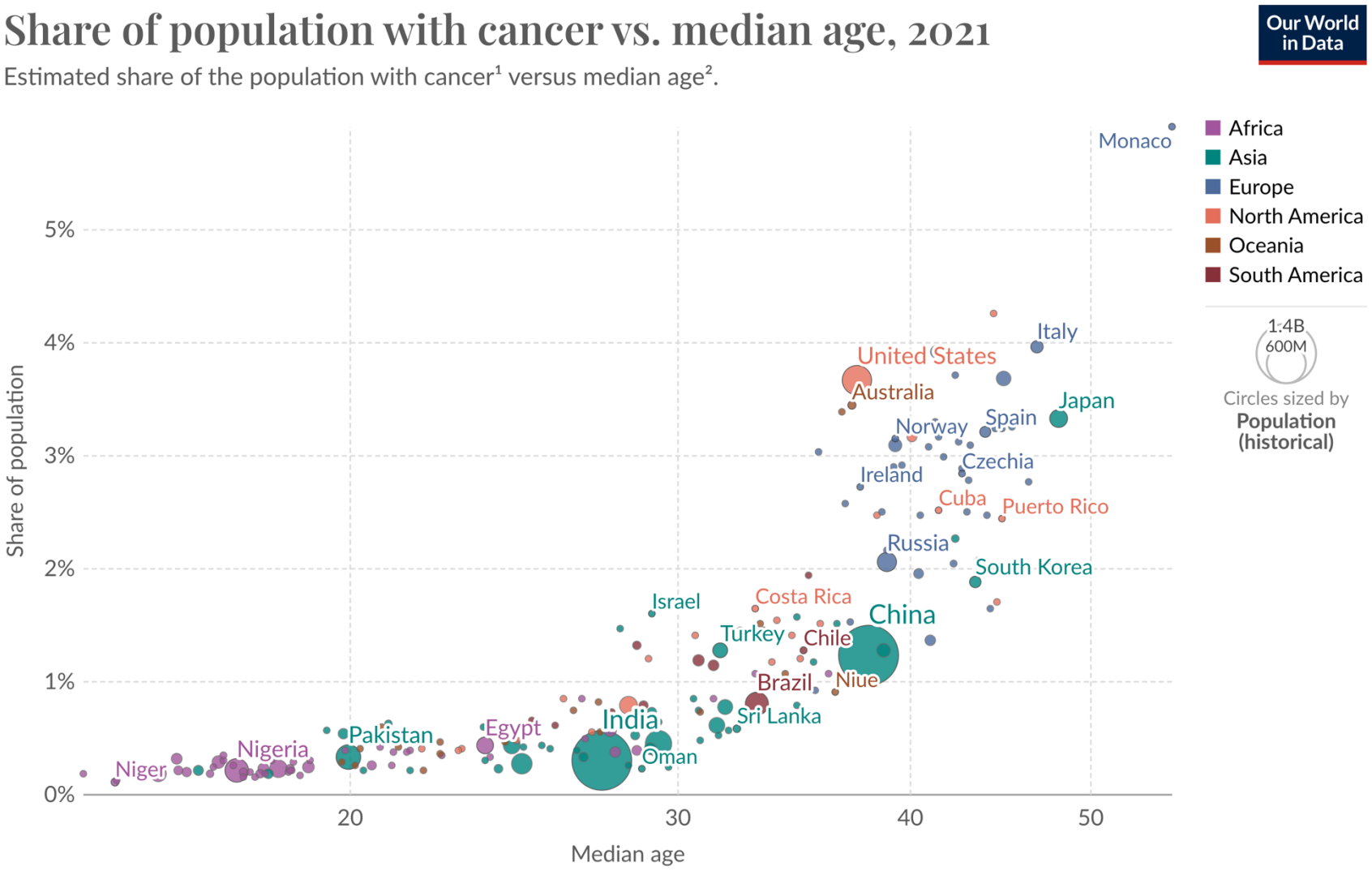
Global Burden of Cancer



Cancer TODAY | **IARC** - https://gco.iarc.who.int/today
Data version : Globocan 2022 (version 1.1)

International Agency for Research on Cancer
World Health Organization

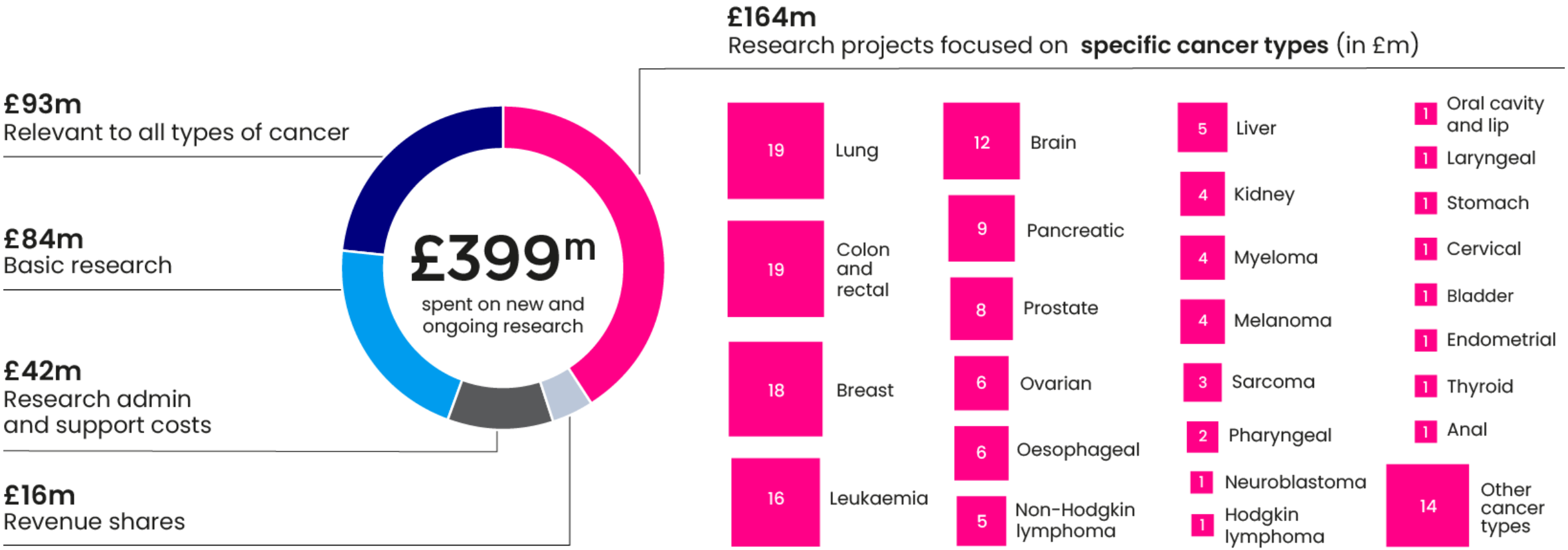
Burden of Cancer is Region-Dependent



Data source: IHME, Global Burden of Disease (2024); UN, World Population Prospects (2024) OurWorldinData.org/cancer | CC BY

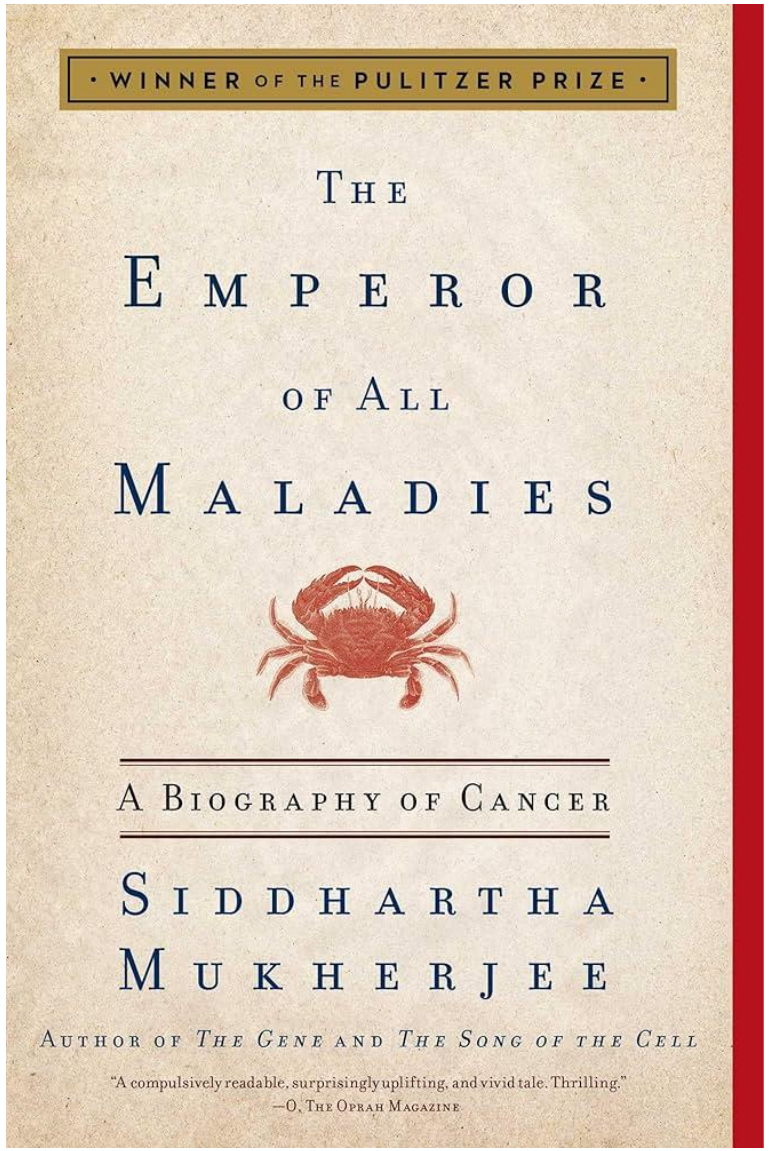
Note: Non-melanoma skin cancers[3] are excluded due to potentially incomplete records and inconsistent registry practices.

Cancer Research Today



Cancer Research UK Annual Spend 2023/2024

What is Cancer?



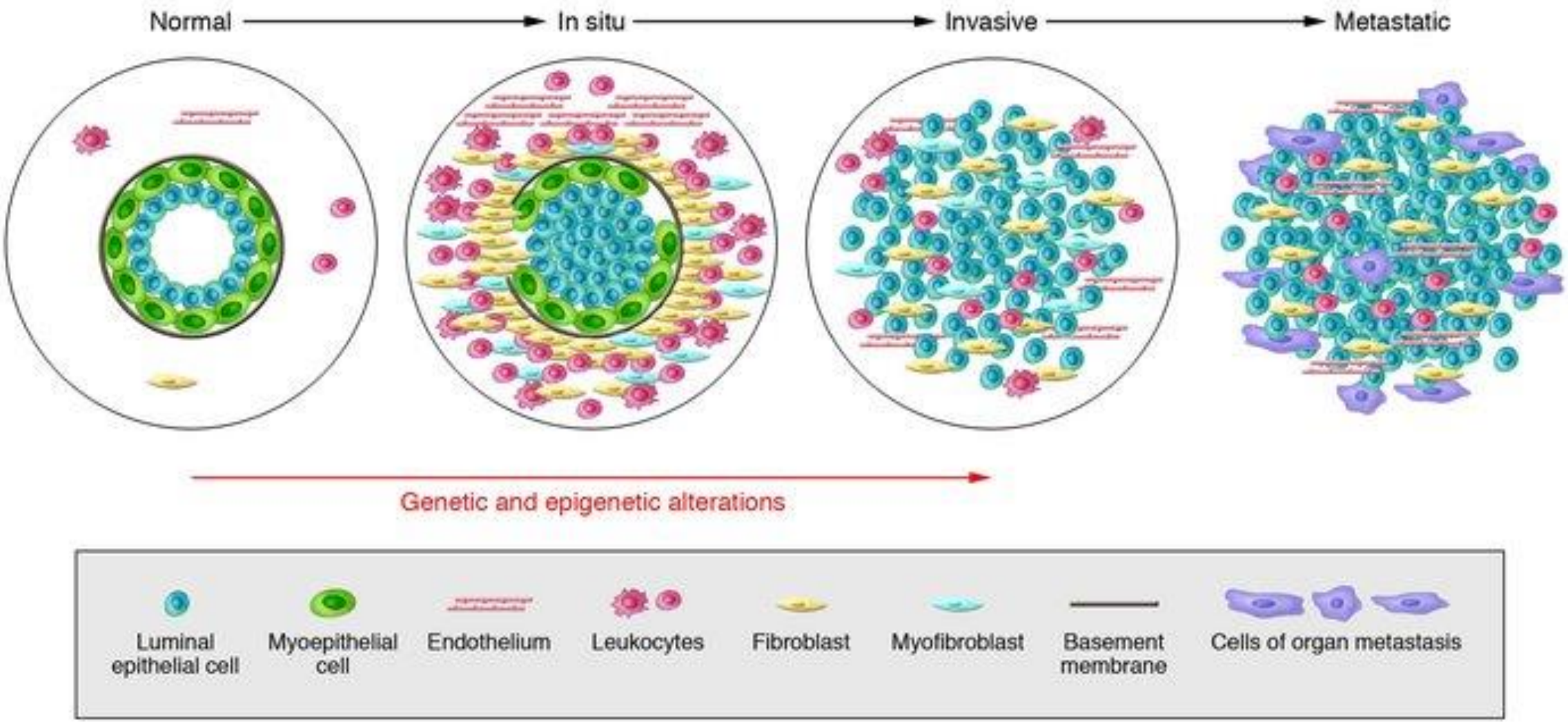
"Down to their innate molecular core, cancer cells are hyperactive, survival-endowed, scrappy, fecund, inventive copies of ourselves."

- Siddhartha Mukherjee, The Emperor of All Maladies

"Tumors: Wounds that do not heal"

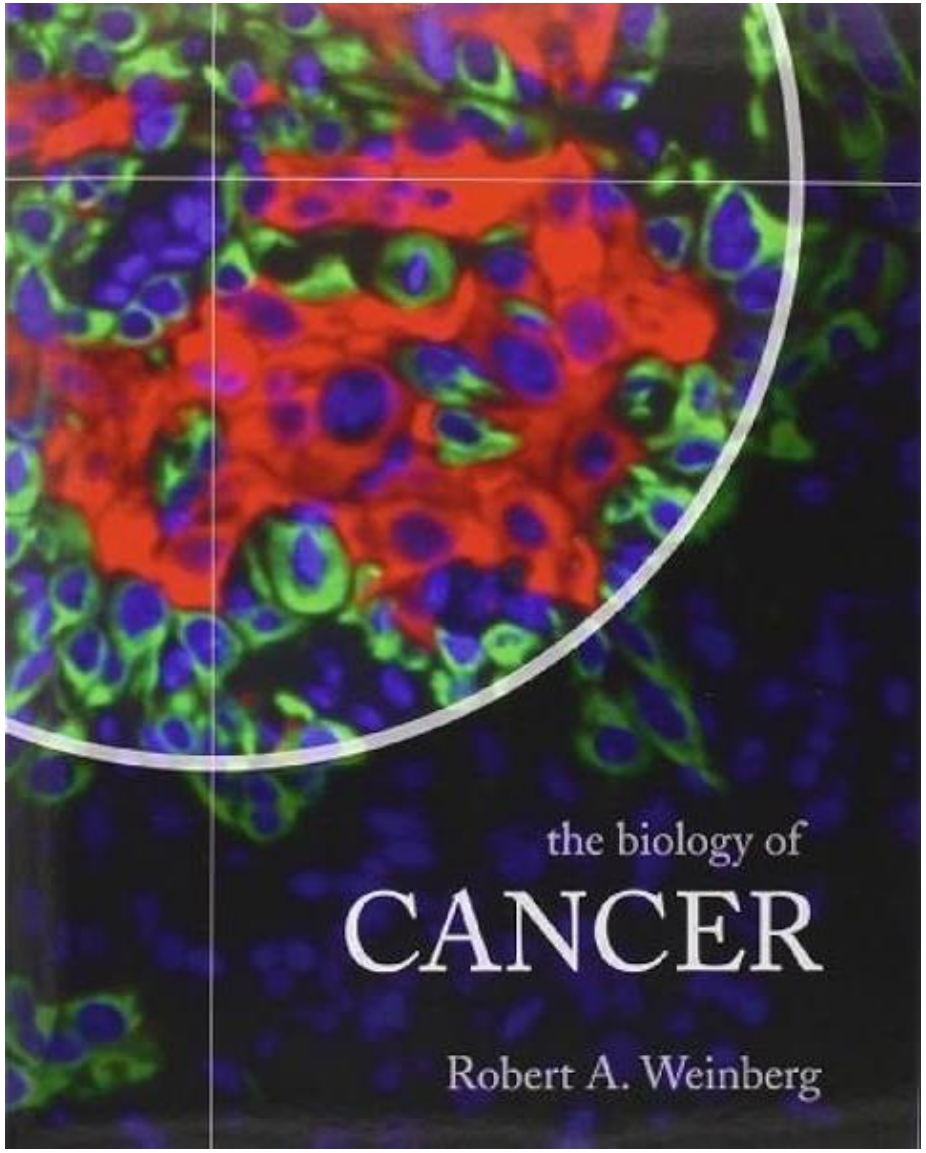
- Harold F. Dvorak, Harvard Medical School Professor of Pathology (1986) NEJM

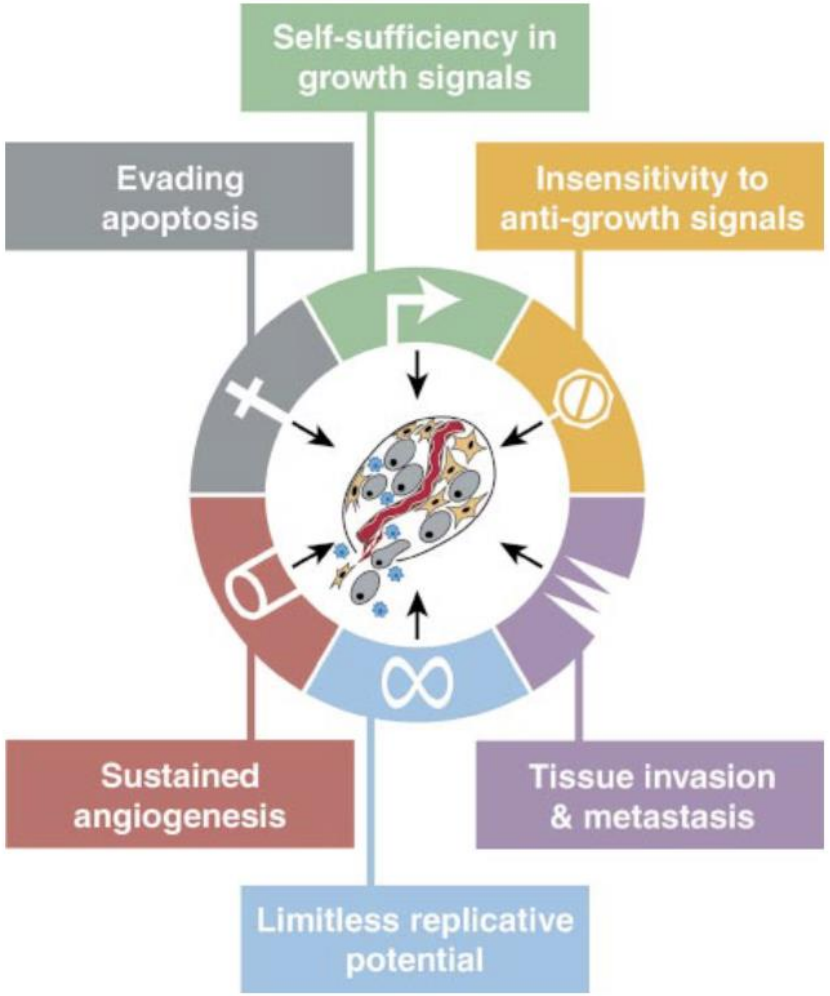
The Cancer Continuum



Polyak (2007) J Clin Invest

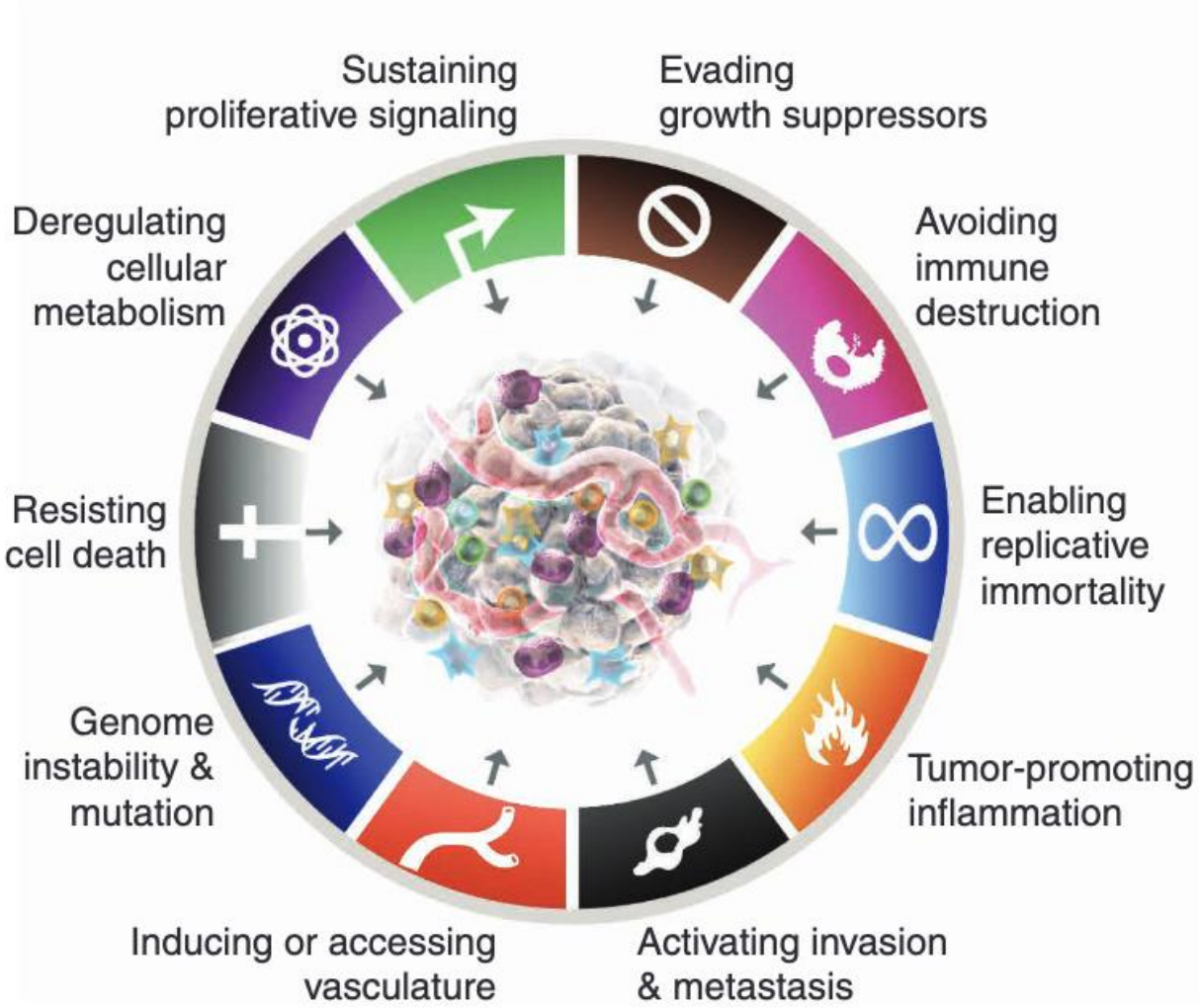
The Biology of Cancer



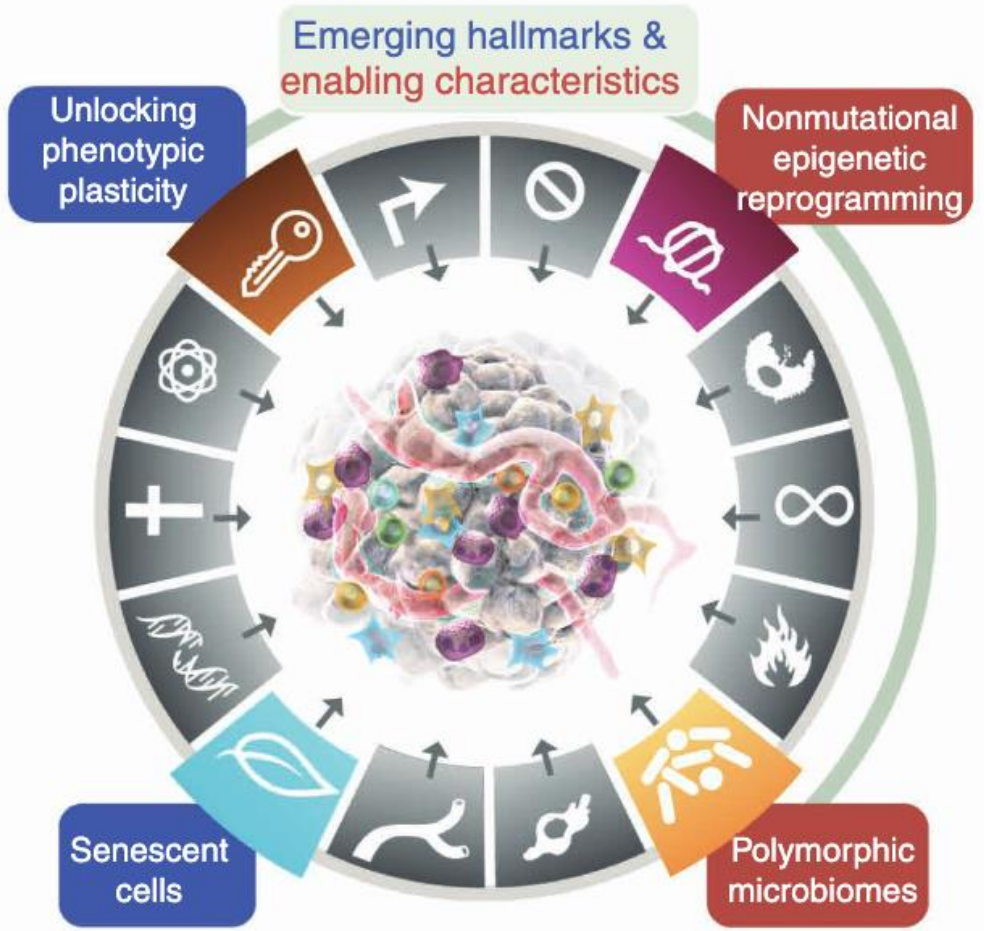


Hanahan & Weinberg, The Hallmarks of Cancer (2000)

Hallmarks of Cancer: Updated

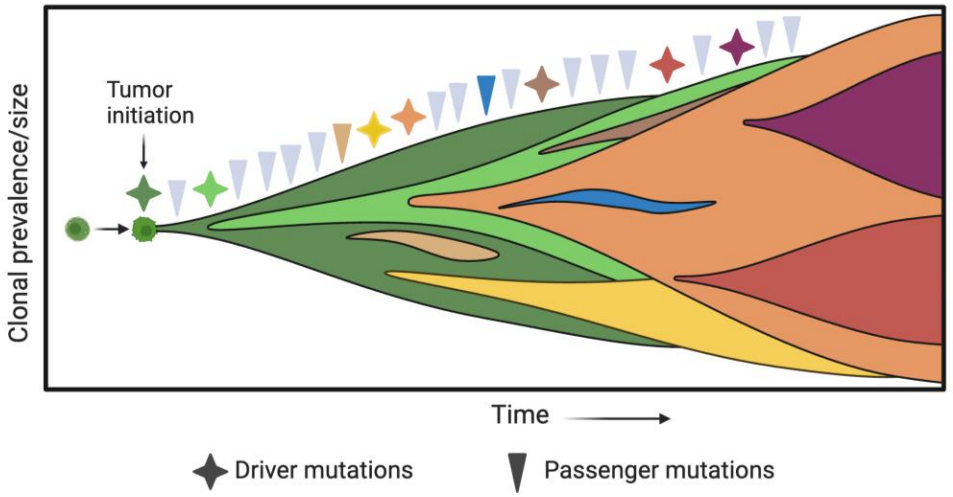


Hanahan & Weinberg (2011),
The Hallmarks of Cancer: The Next Generation

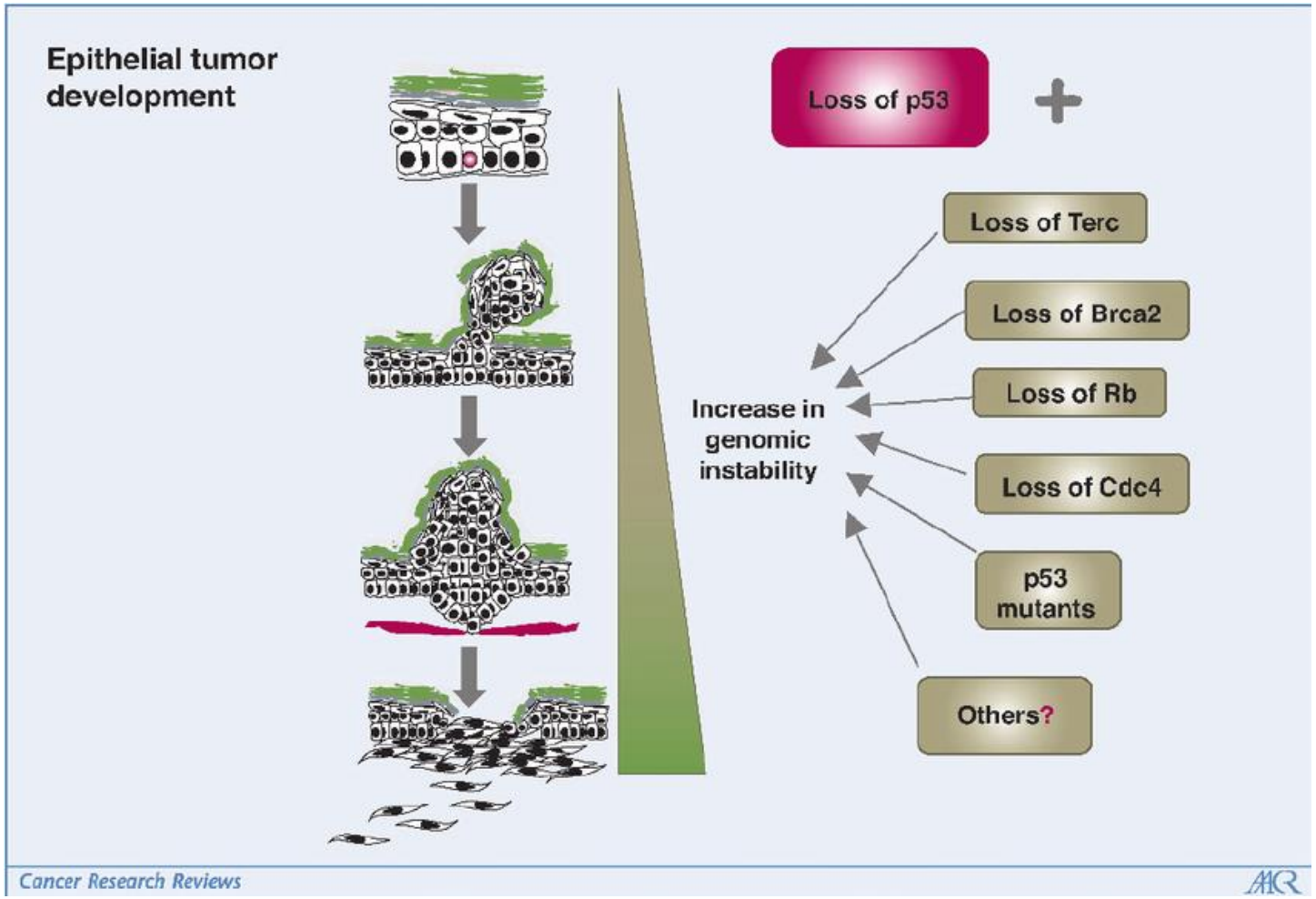


Hanahan & Weinberg (2022),
The Hallmarks of Cancer: New Dimensions

Genomic Instability

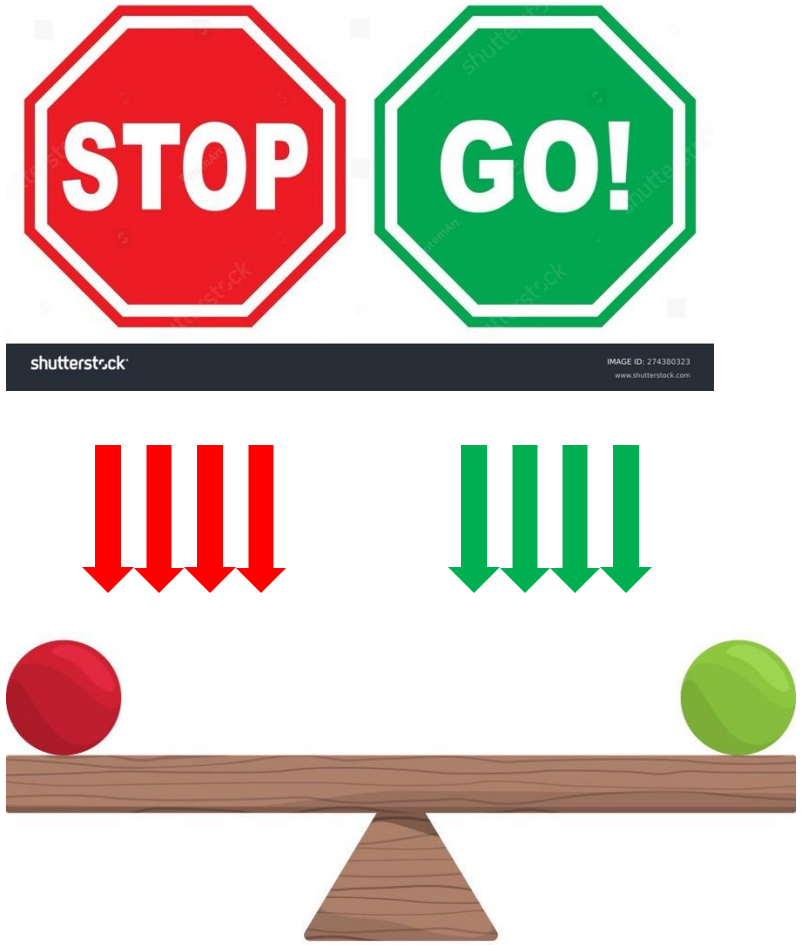


Jigyansa Mishra, Biorender



Cell-autonomous Immortality

+ Replicative Immortality



Cell-autonomous Immortality

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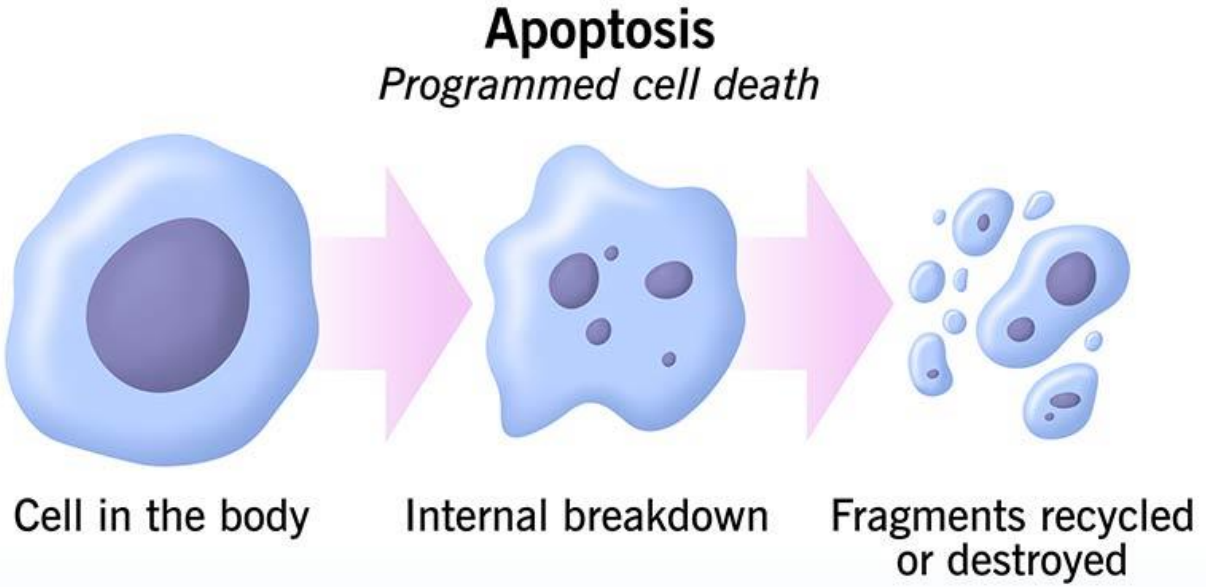
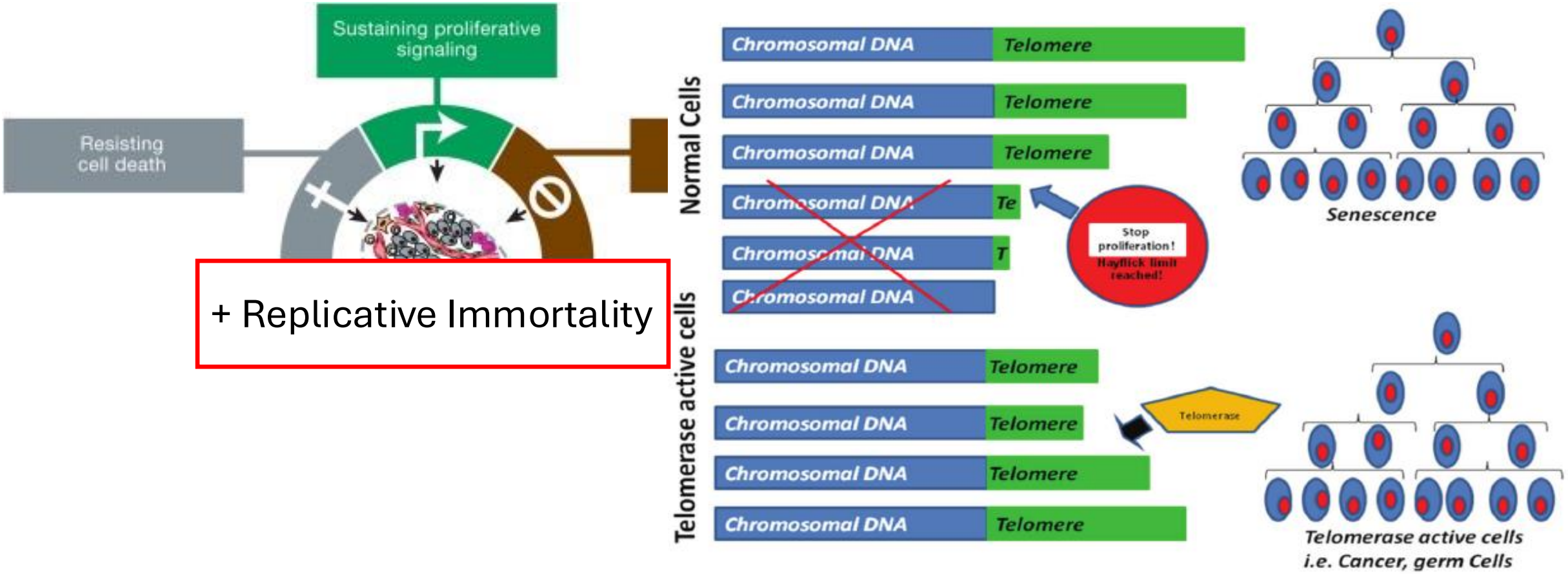


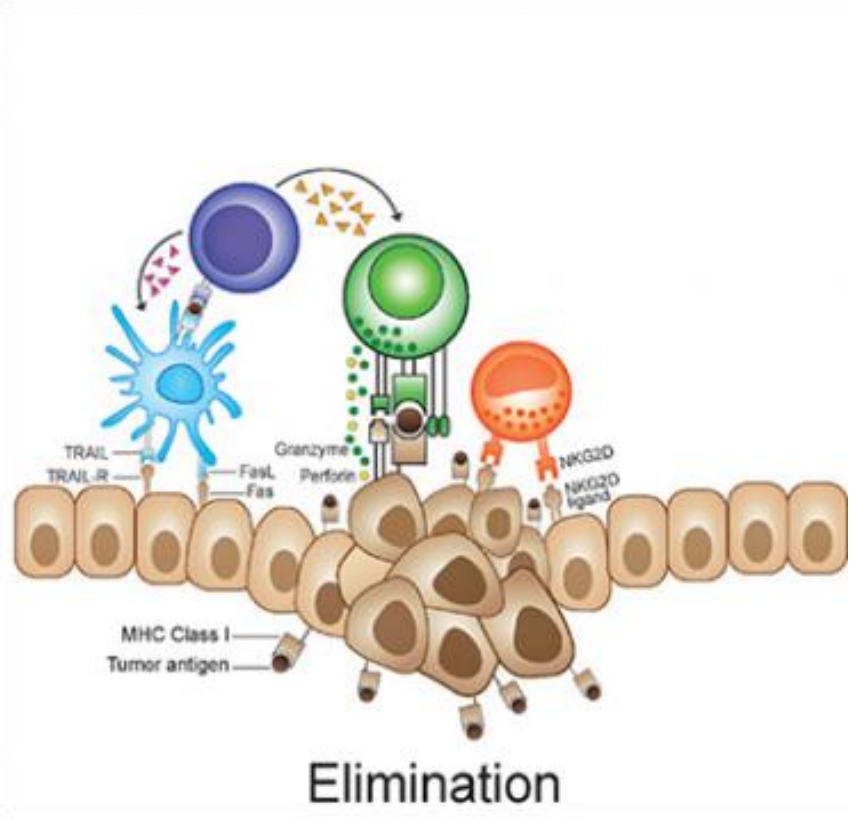
Cell-autonomous Immortality

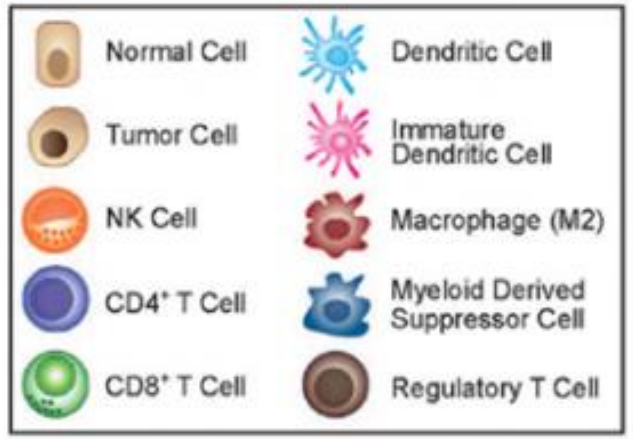


Serakinci (2011), Cancer Stem Cells – The Cutting Edge

What about non-cell autonomous aspects?

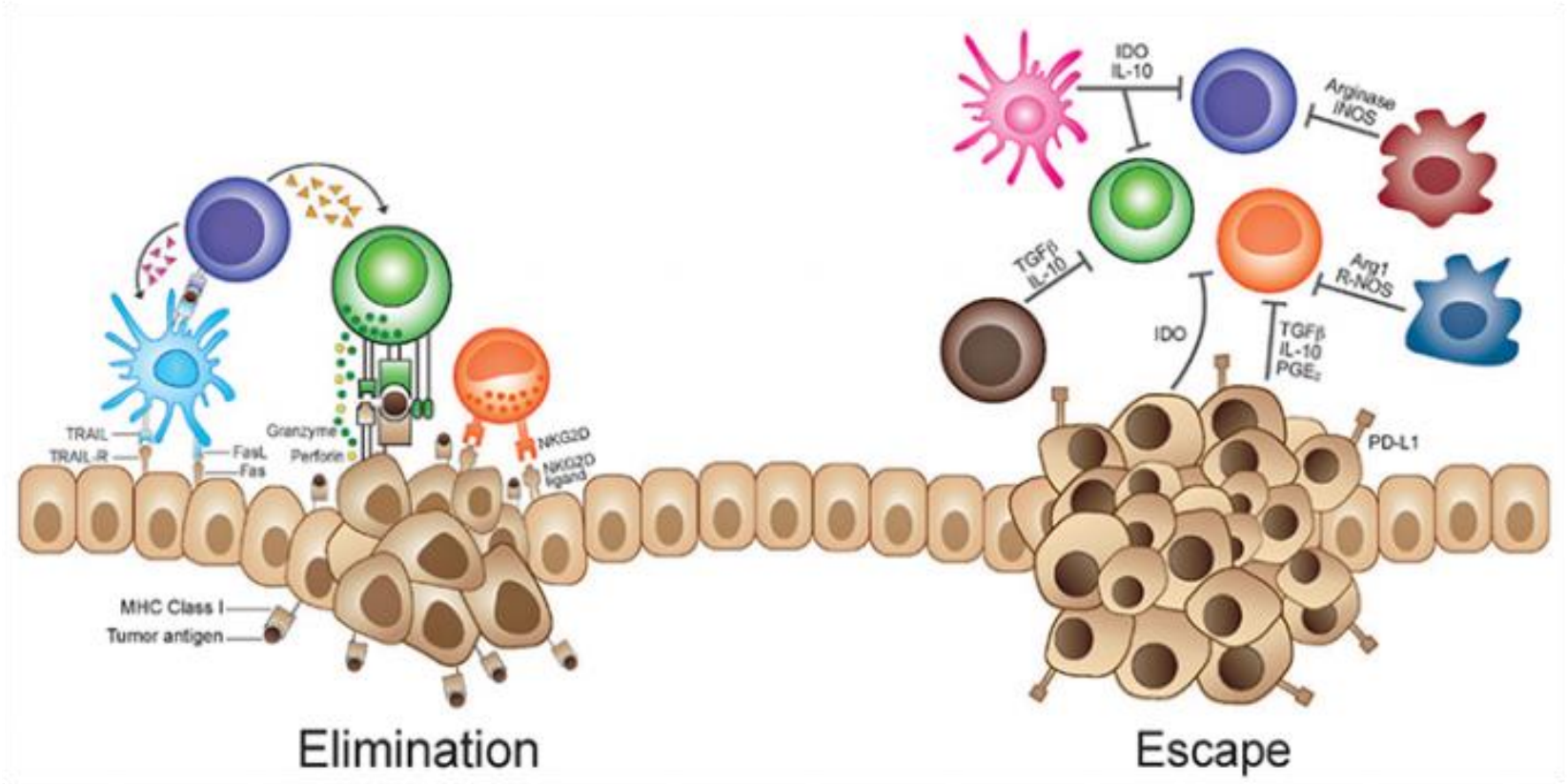
Immune Evasion

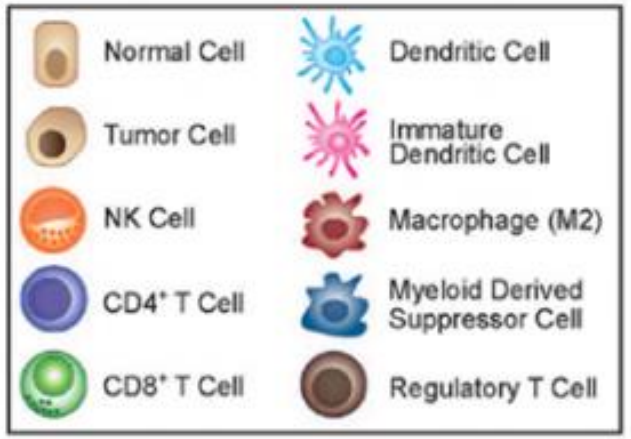




Tebu Bio

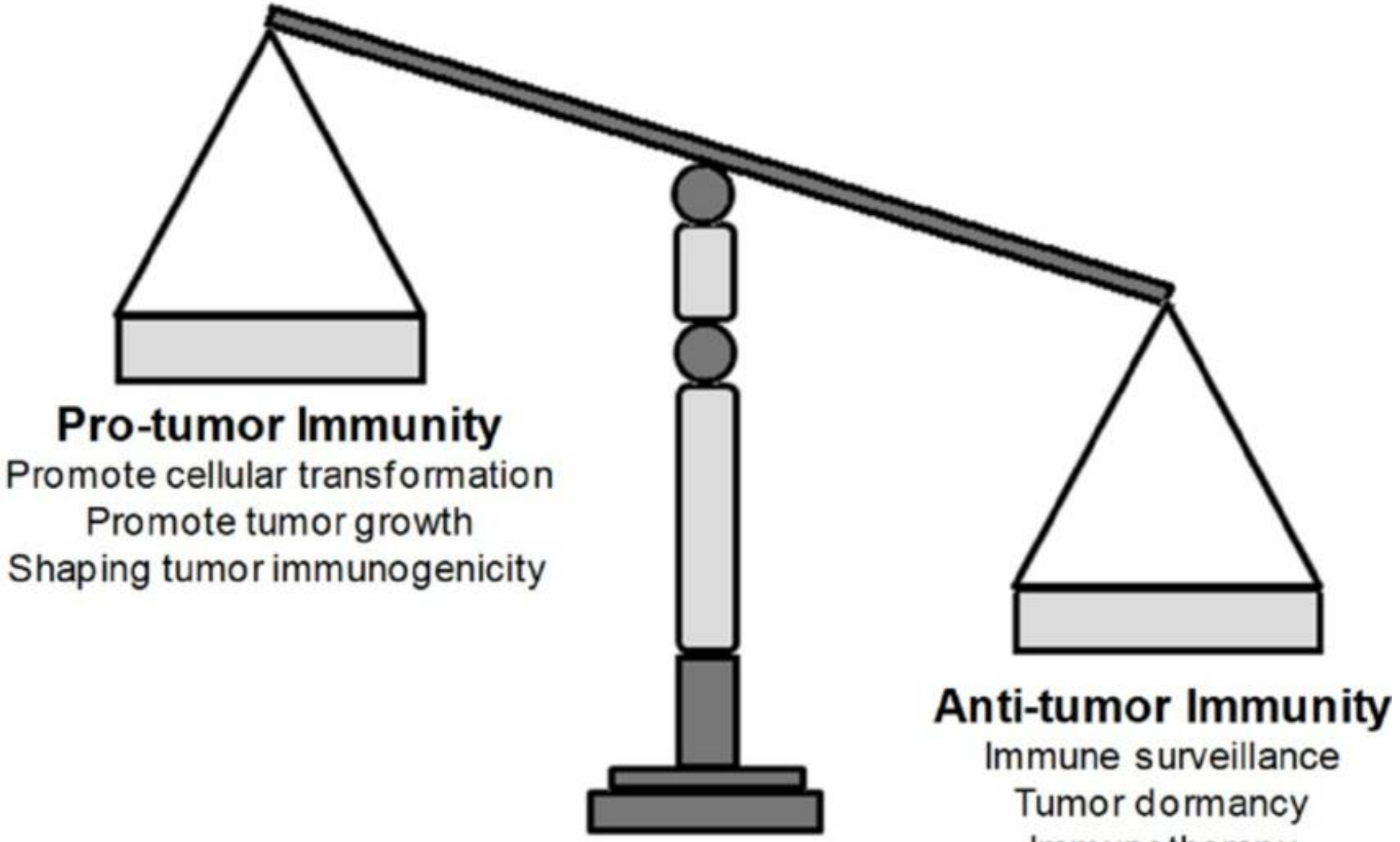
Immune Evasion





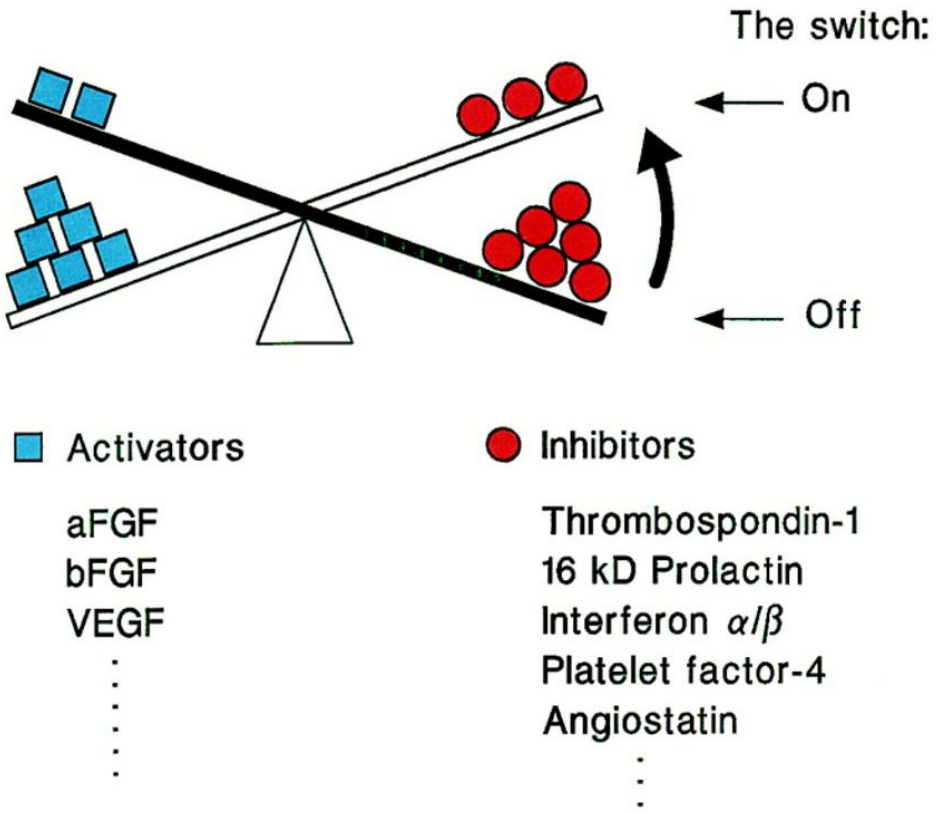
Tebu Bio

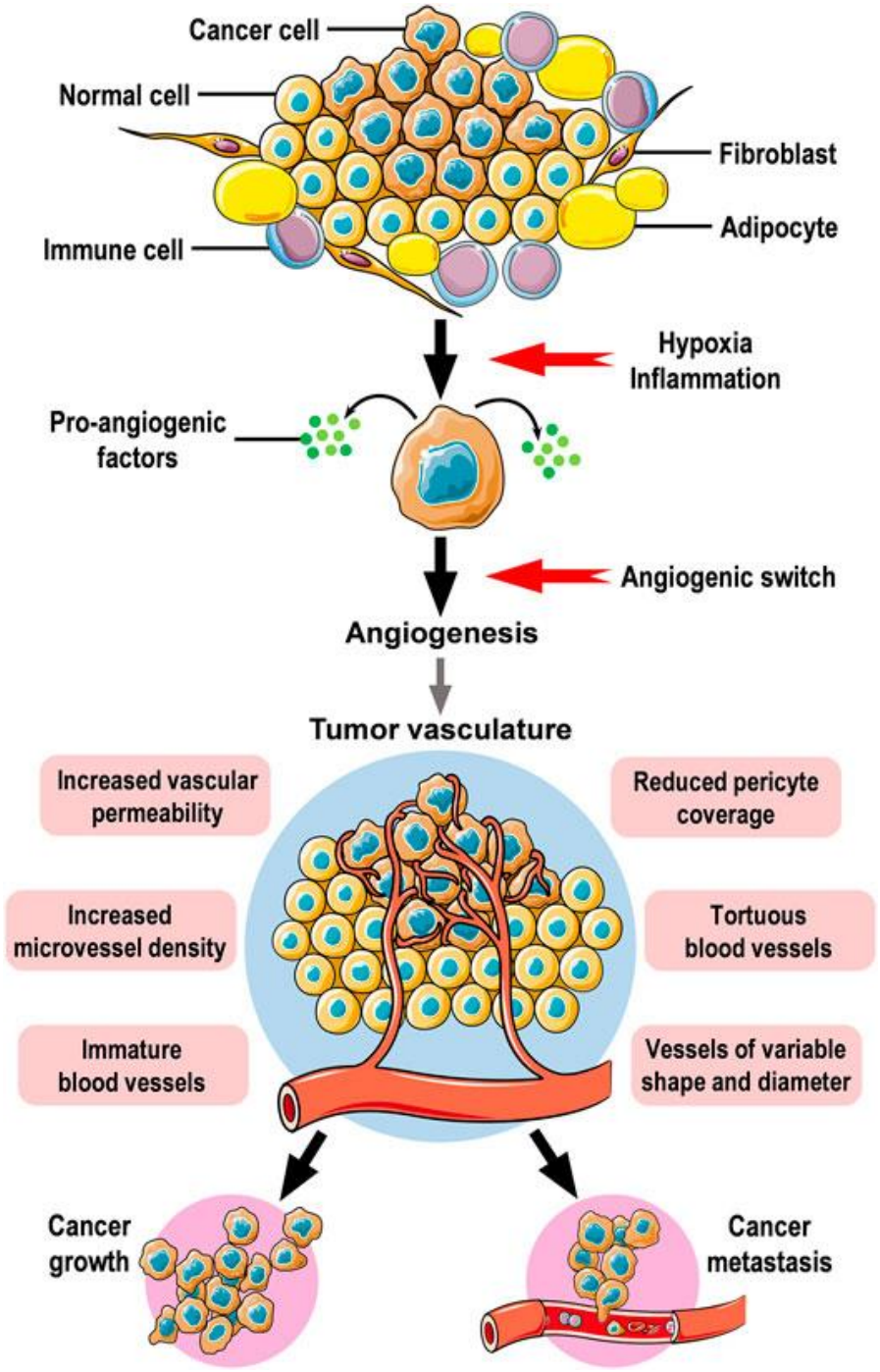
Immune Evasion



Sustainability

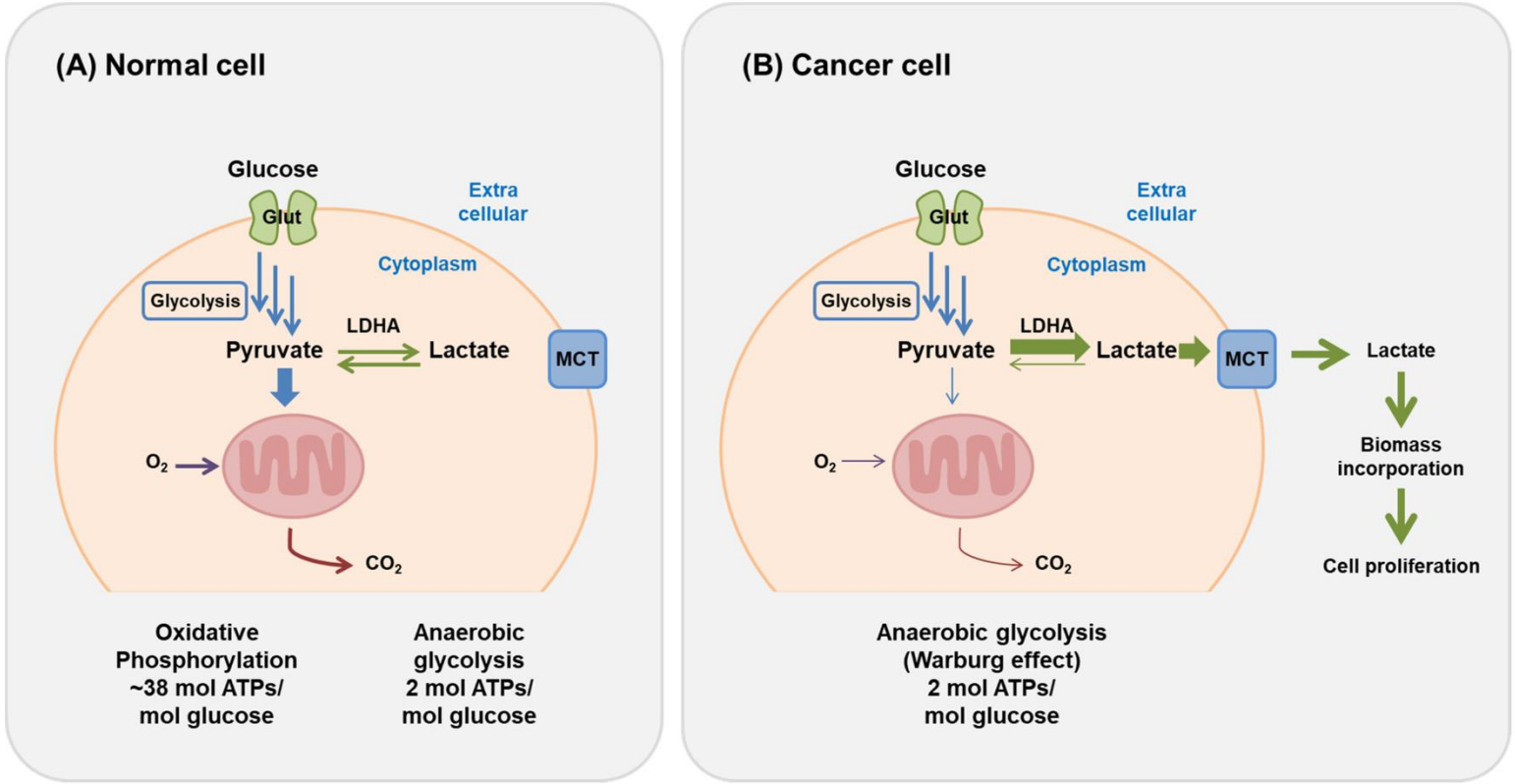
Angiogenesis: Ensuring nutrient supply

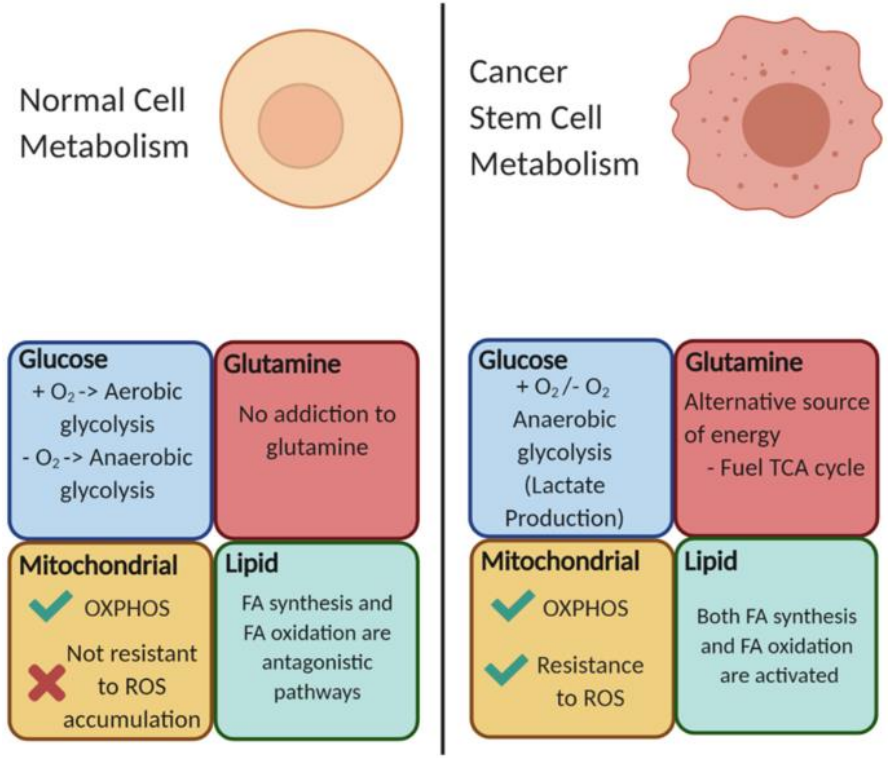




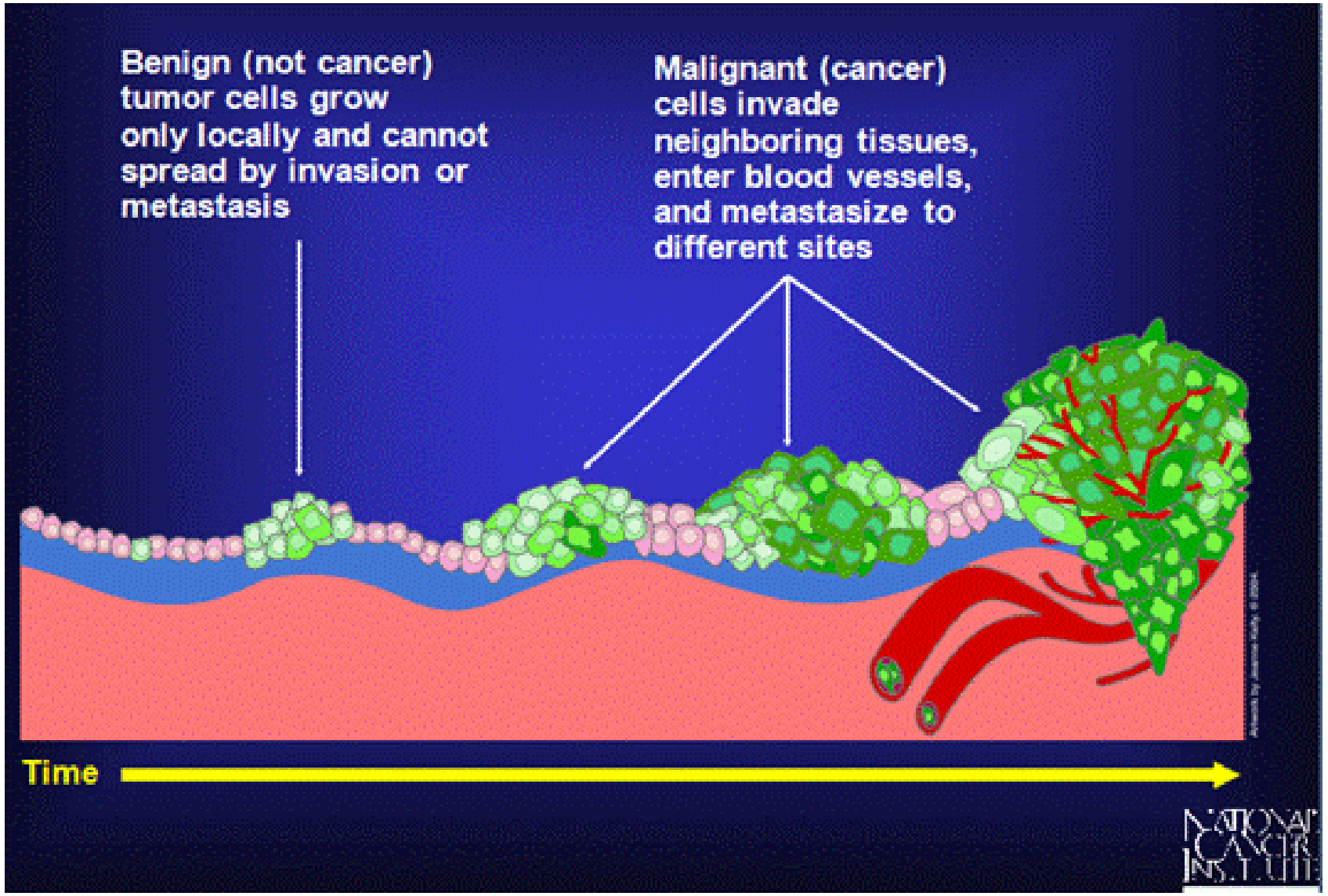
Sustainability

Deregulated cellular metabolism: Ability to adapt to available nutrient supply



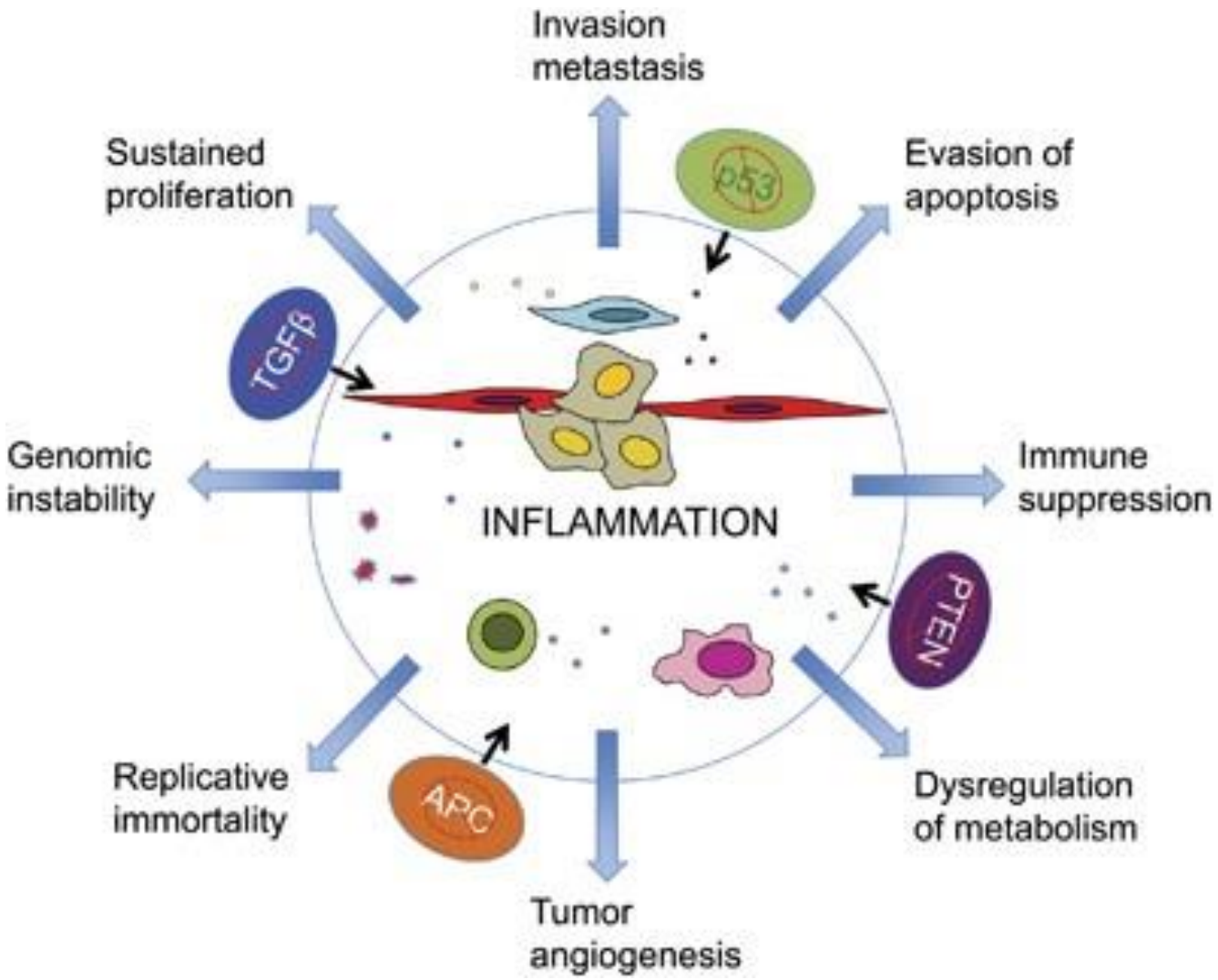


Expanding Beyond Tissue-of-Origin



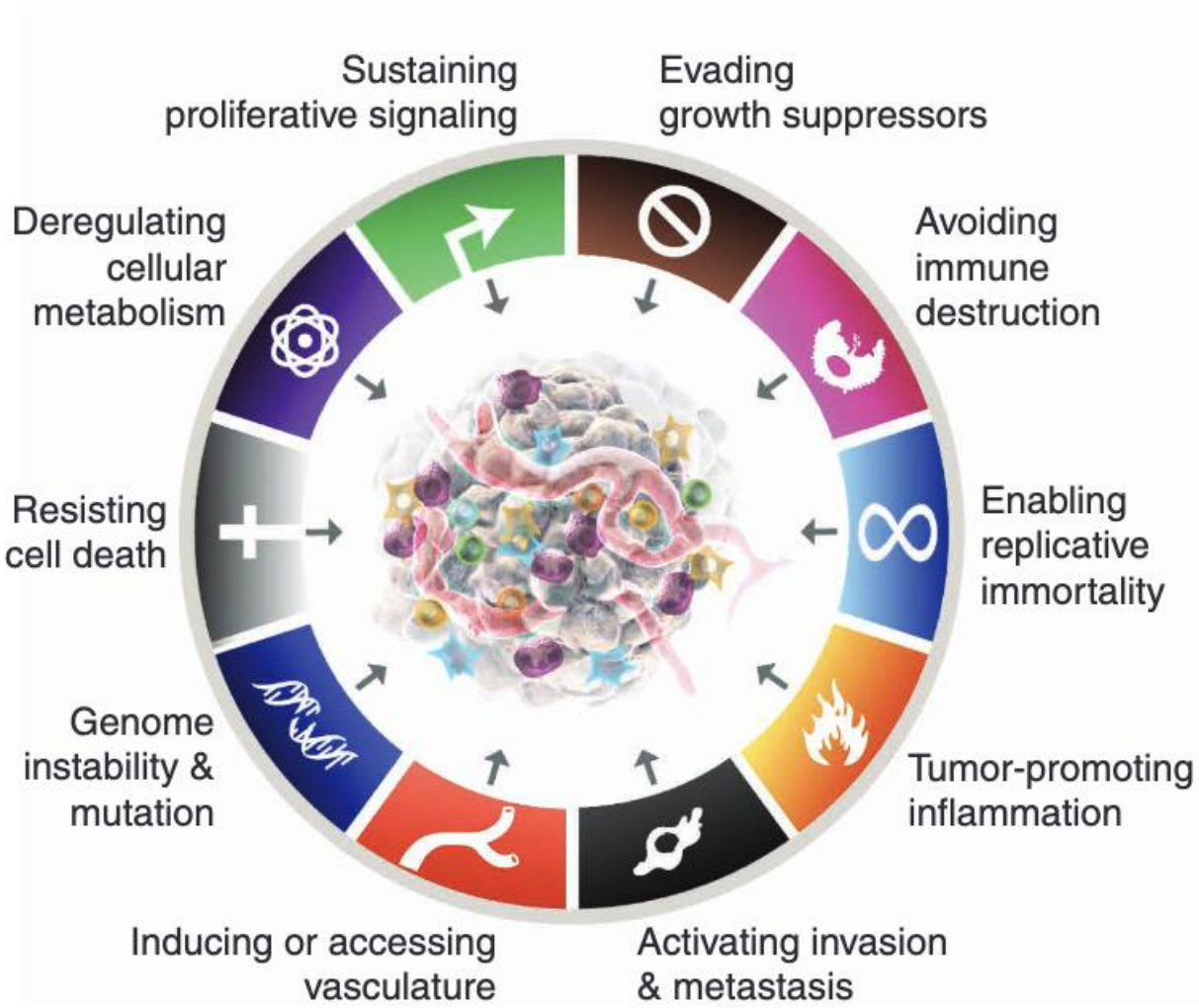
Shaping a Permissive Microenvironment

Chronic inflammation:
“Wounds that do not heal”

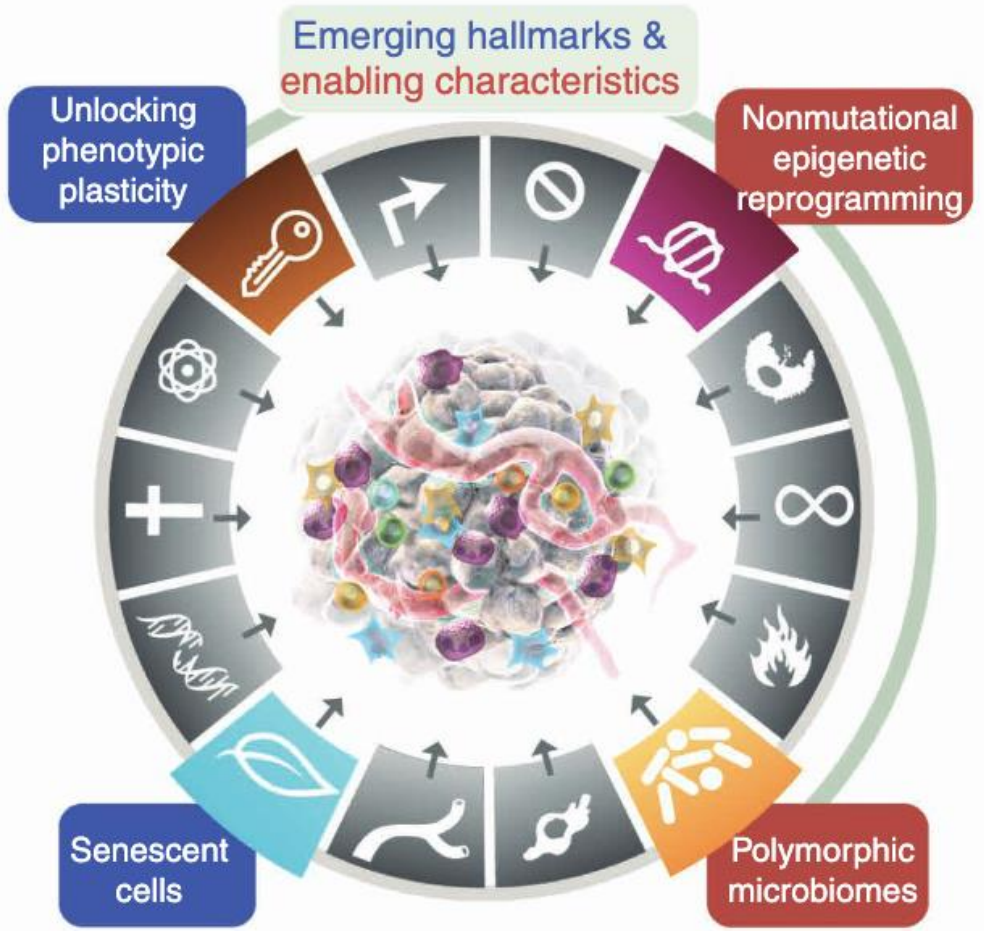


Yang (2014) Cell Death & Differentiation

Hallmarks of Cancer: Updated

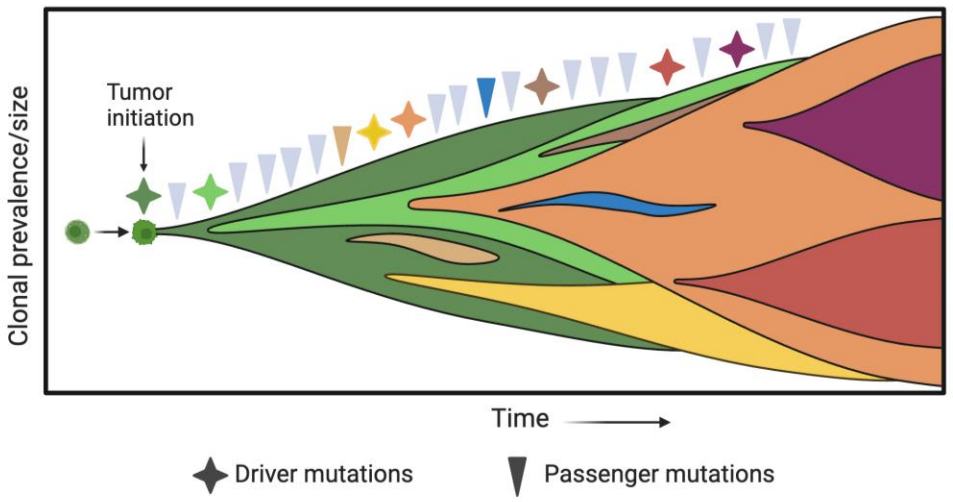


Hanahan & Weinberg (2011),
The Hallmarks of Cancer: The Next Generation



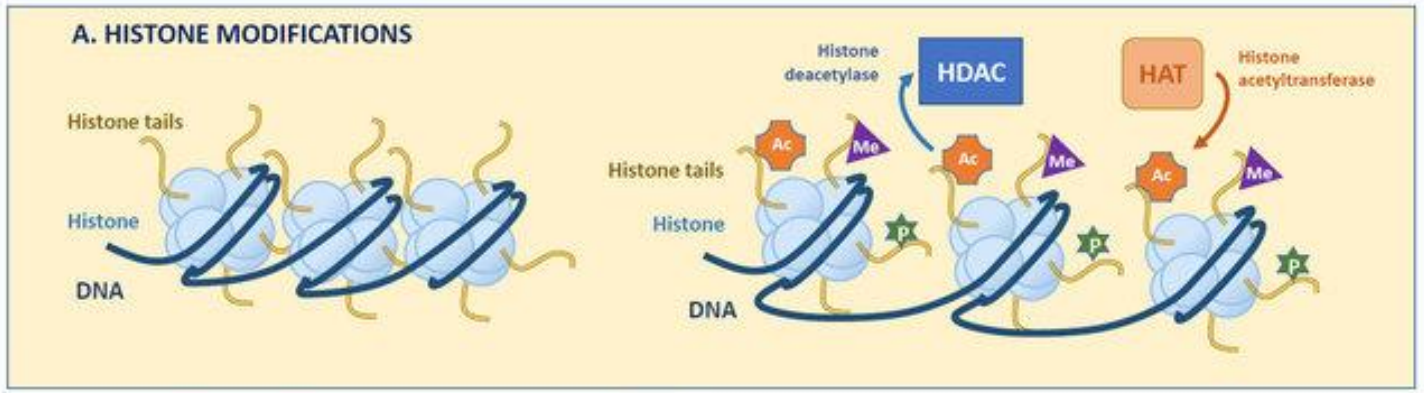
Hanahan & Weinberg (2022),
The Hallmarks of Cancer: New Dimensions

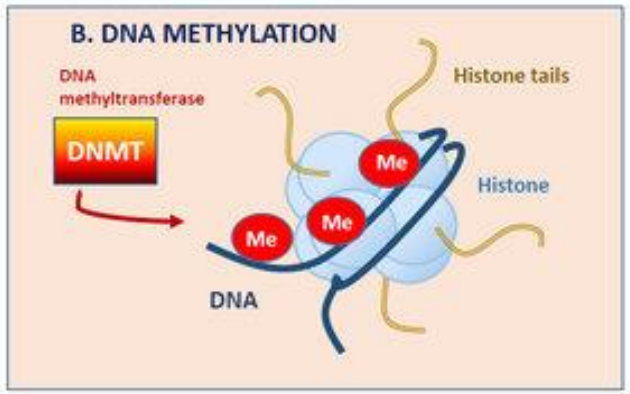
Epigenetic Reprogramming

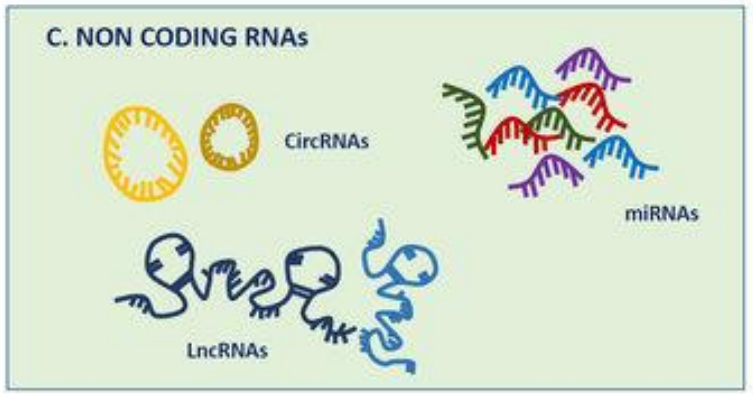


Jigyansa Mishra, Biorender

Central dogma of molecular biology





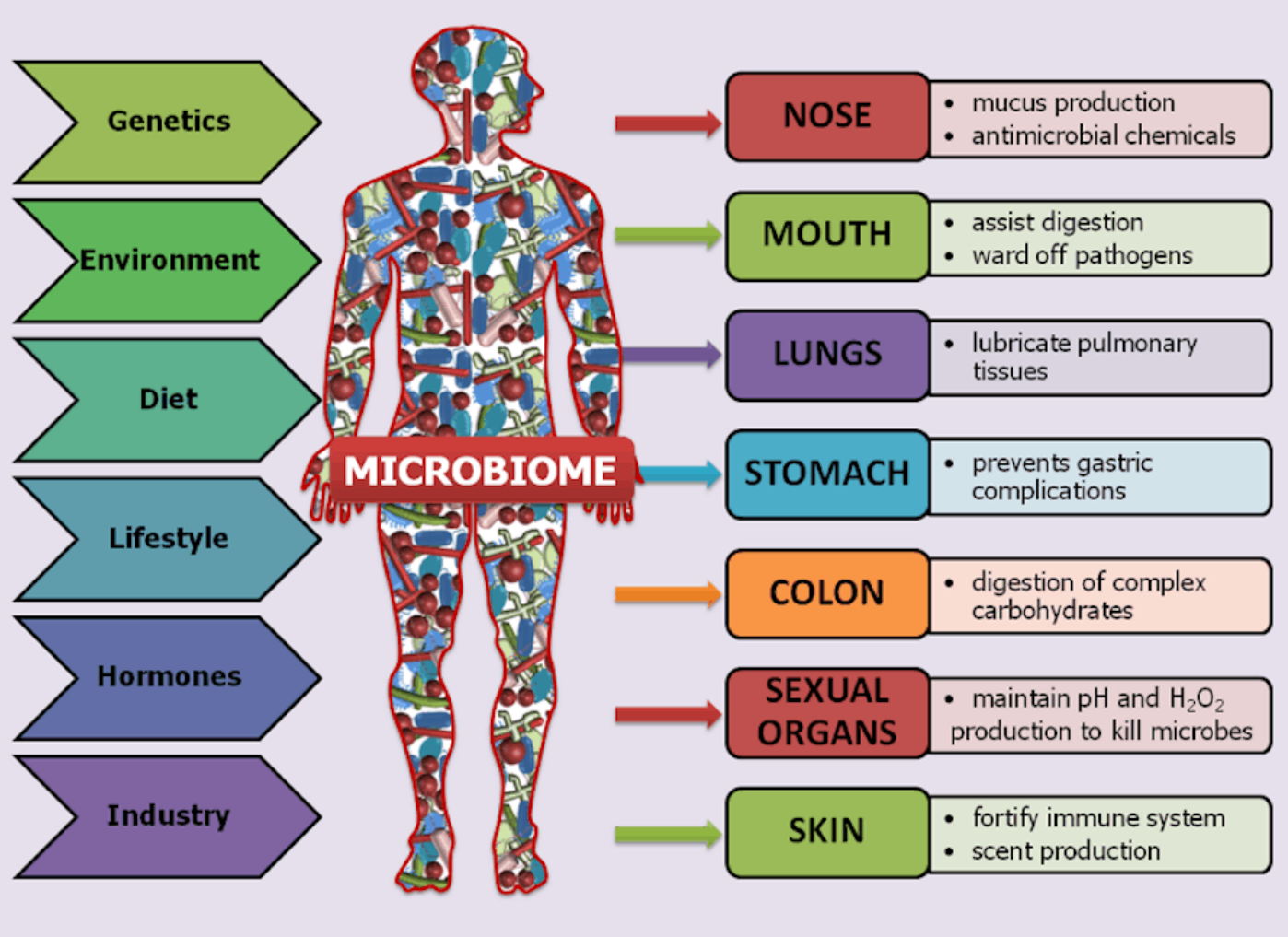


Epi = On top of

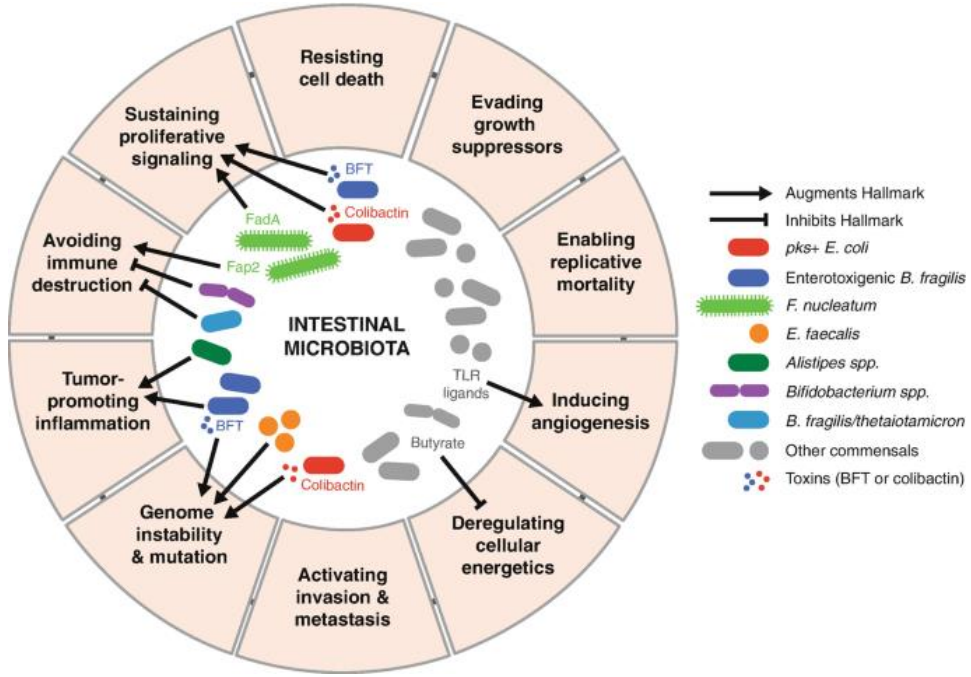
Epigenetics = Non-genetic changes that affect expression of genes

Coco (2019) International Journal of Molecular Sciences

Microbes

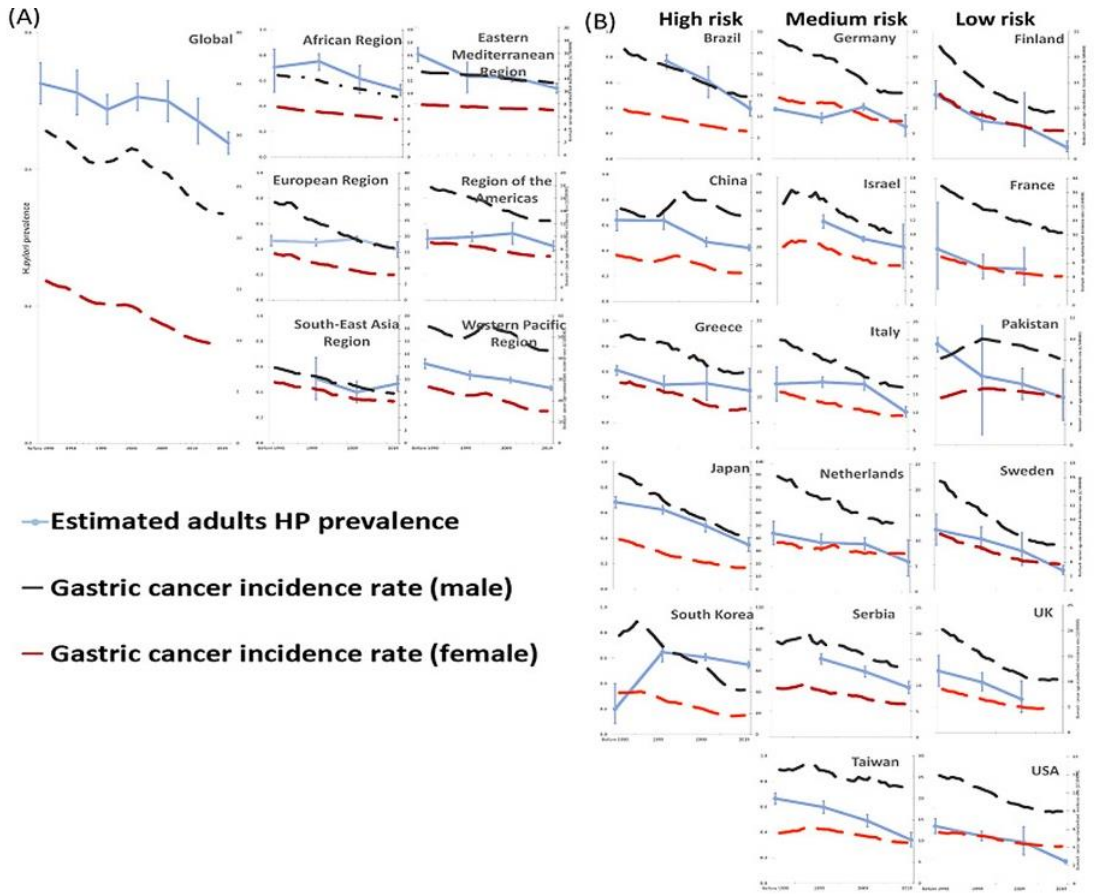


Behaviour of the cancer

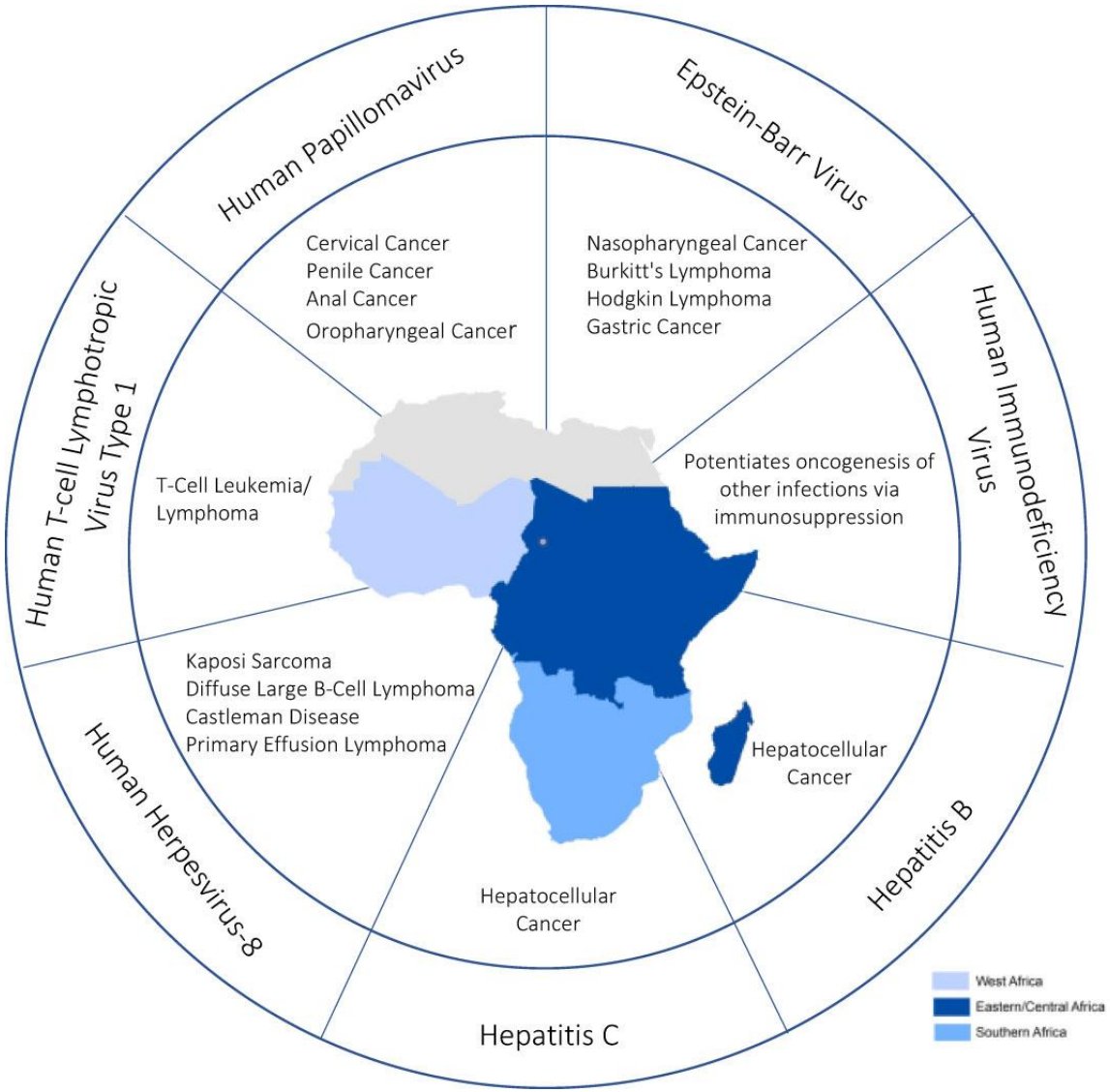


+ Therapy response

Microbes

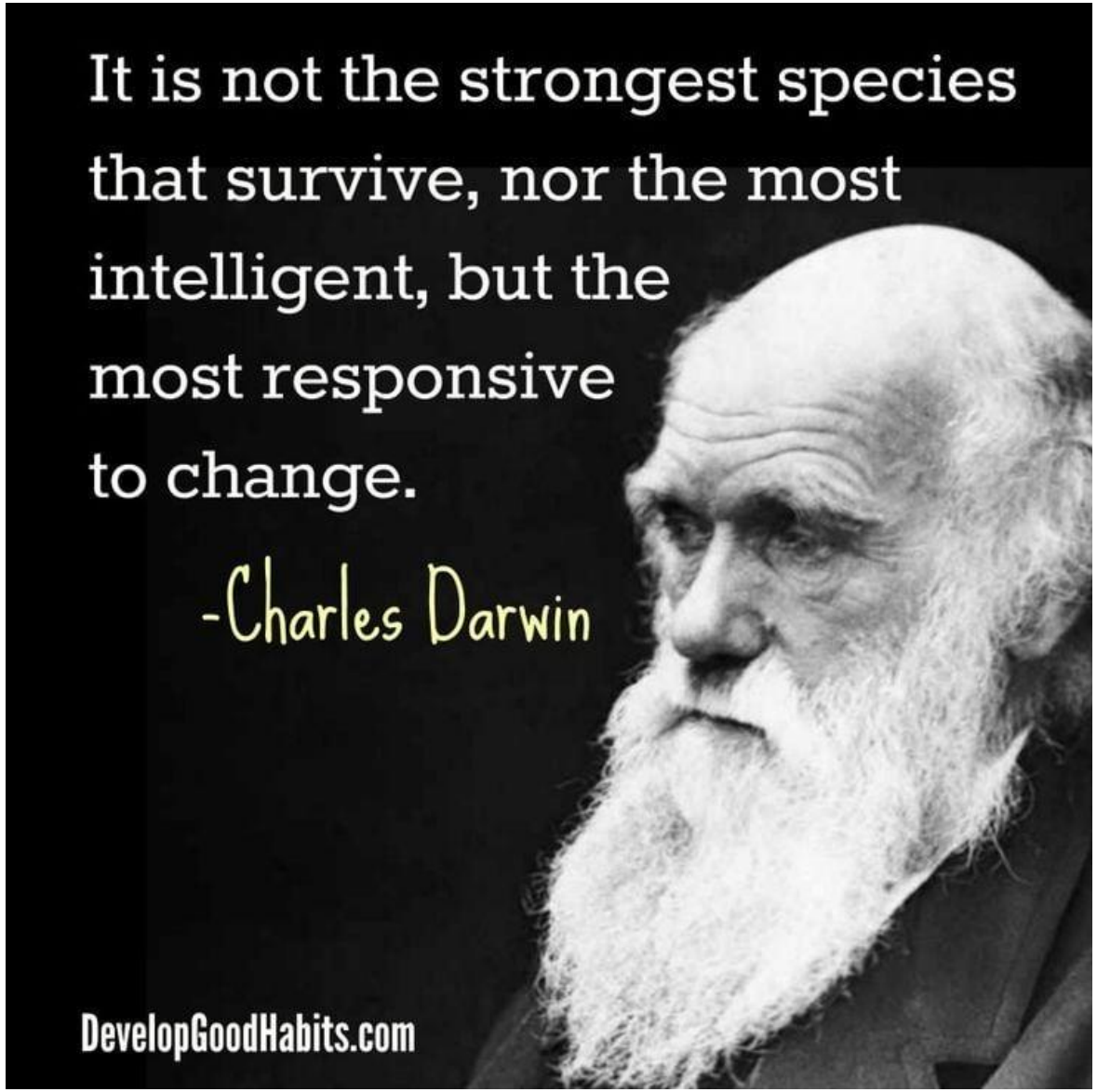


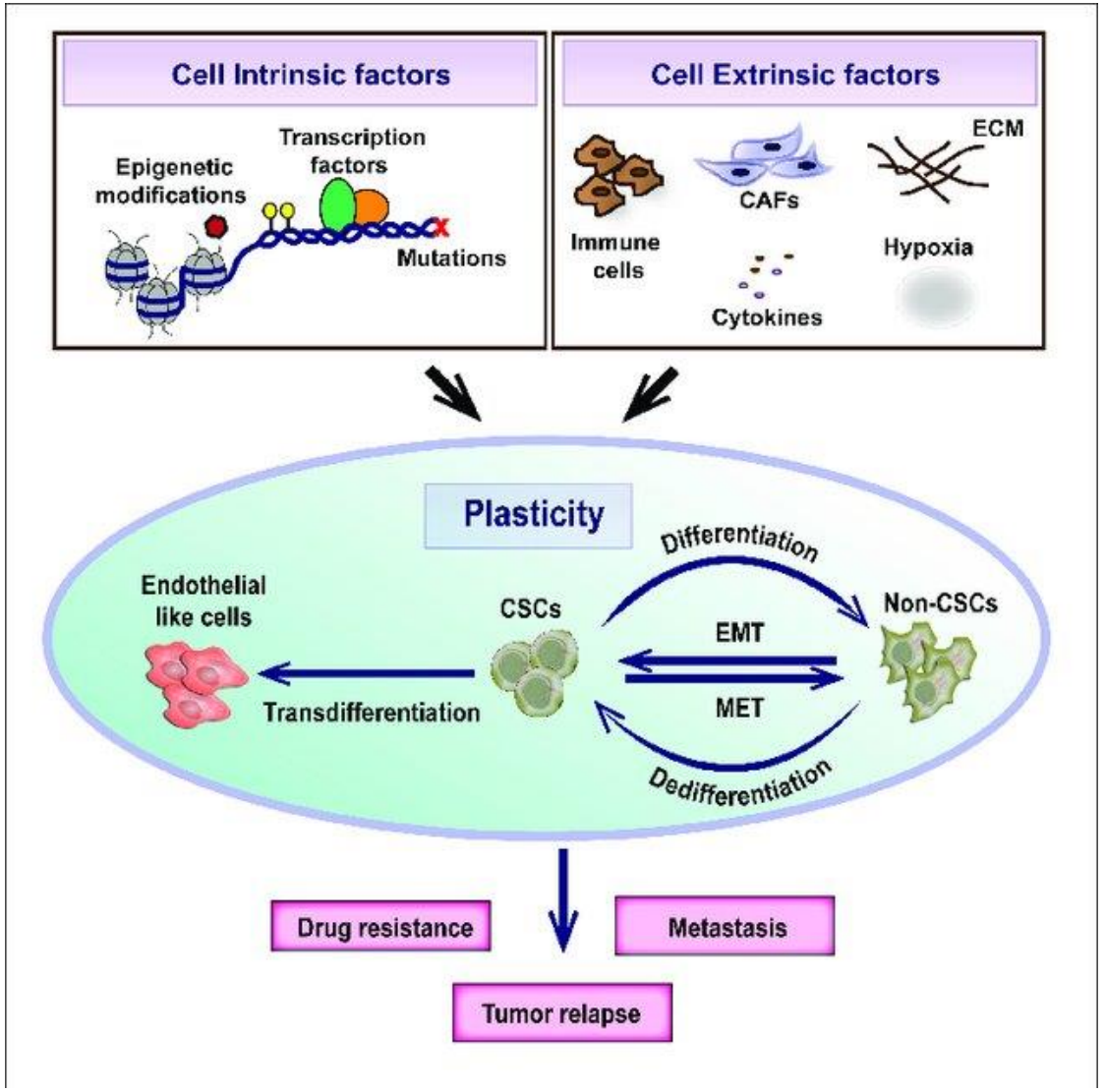
Chen (2024) Gastroenterology



Diakite (2023) Front. Virol.

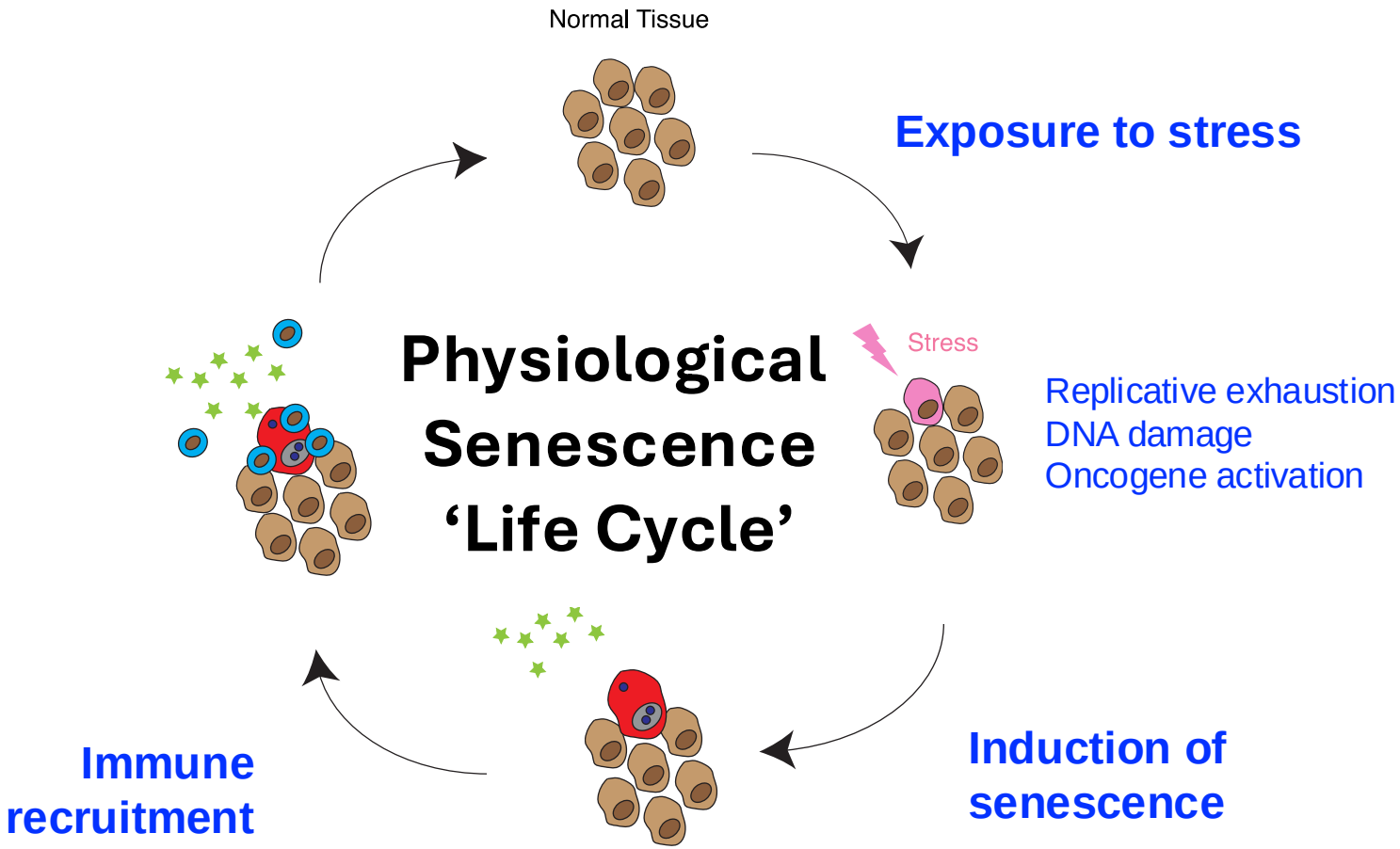
Phenotypic Plasticity



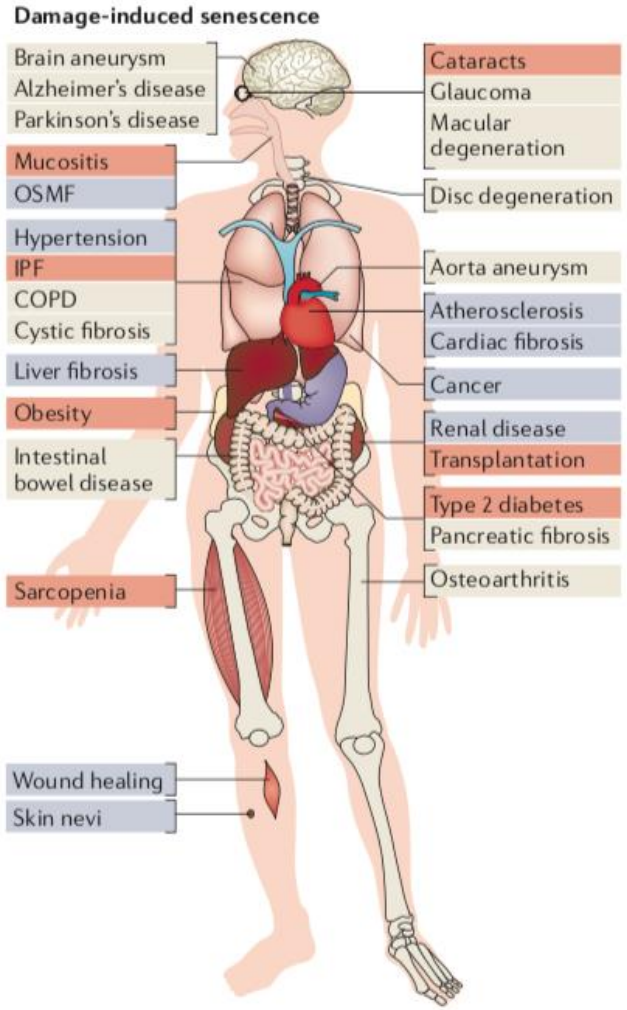


Thankamony (2020) Frontiers in Molecular Biosciences

Senescence

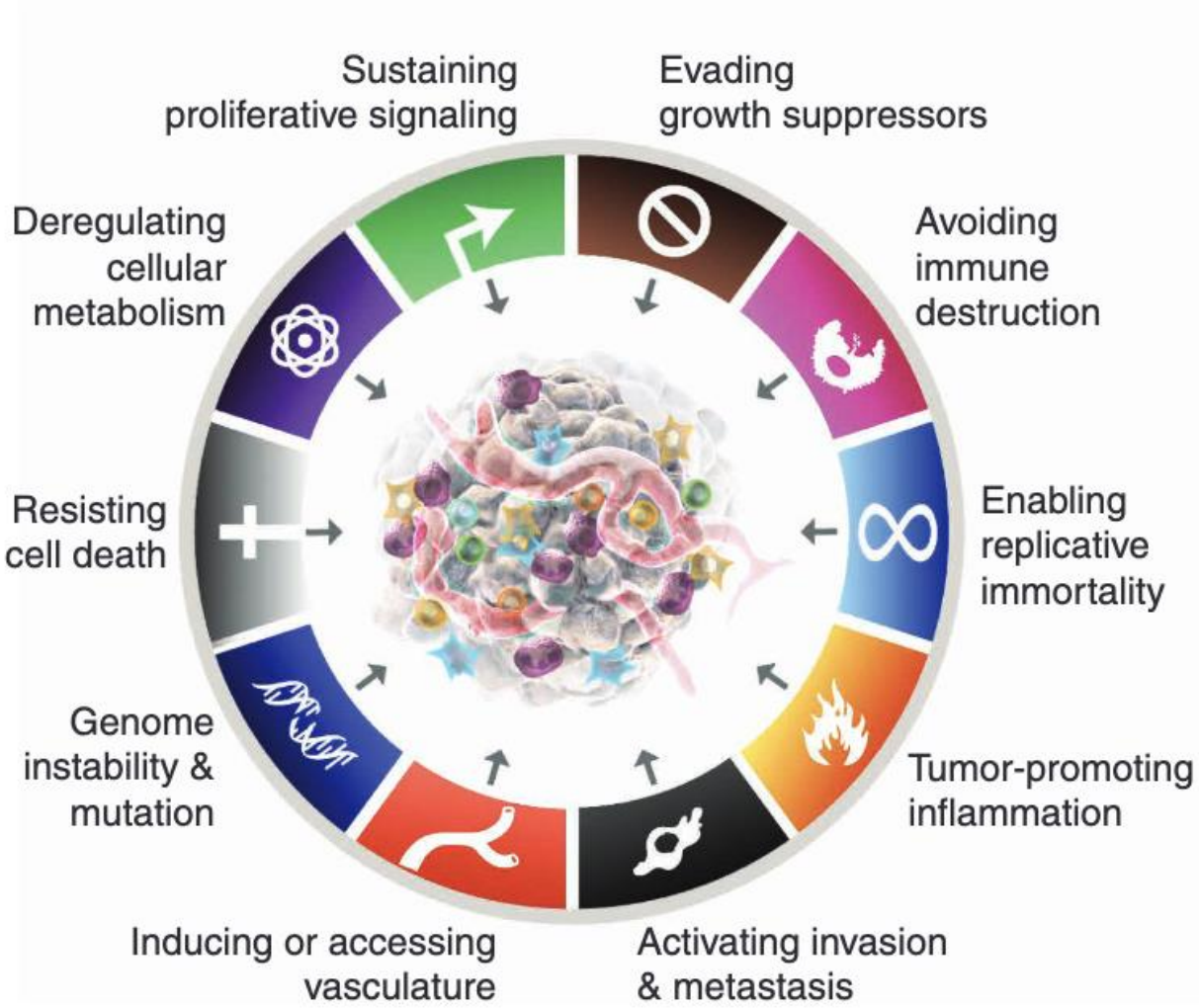


Chan & Narita (2019) Genes Dev.

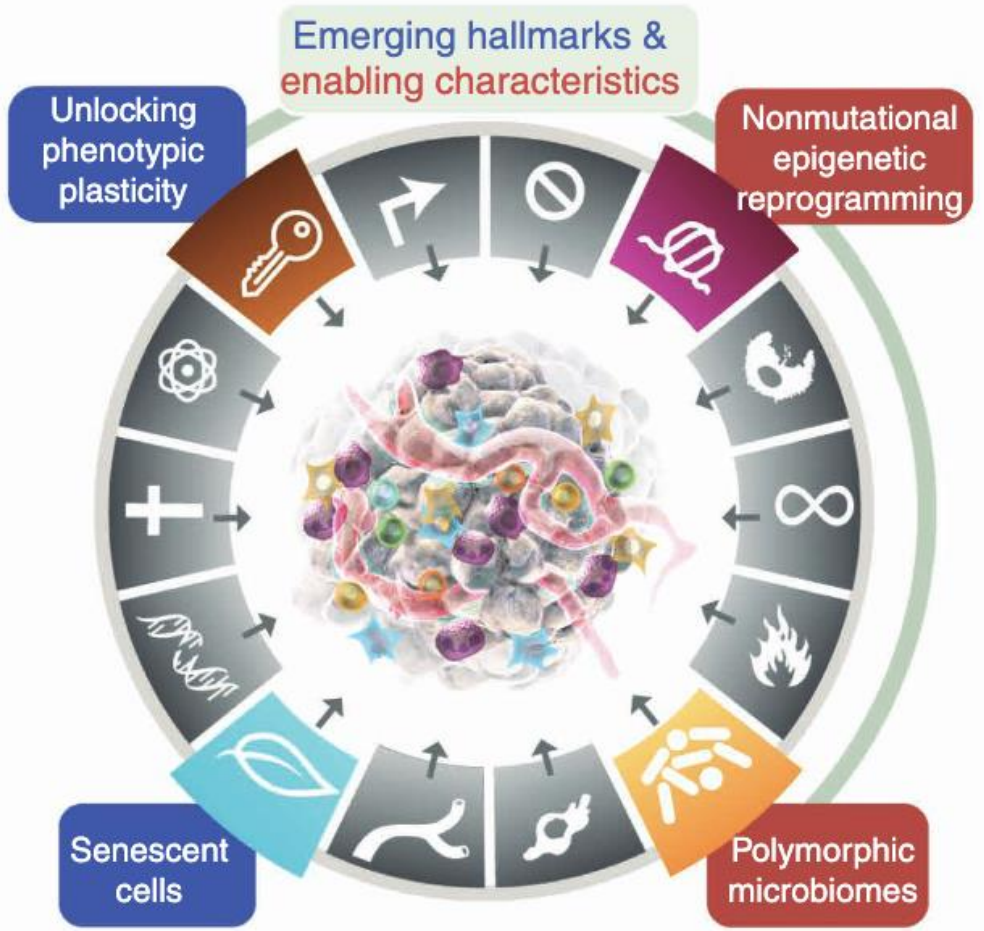


Munoz-Espin (2014) Nat. Rev. Mol. Cell Biol.

Hallmarks of Cancer: Updated



Hanahan & Weinberg (2011),
The Hallmarks of Cancer: The Next Generation



Hanahan & Weinberg (2022),
The Hallmarks of Cancer: New Dimensions

Tools for Studying Cancer Biology

In vitro

Translates directly to "in glass" meaning the study takes place in a test tube, rather than in a model organism.

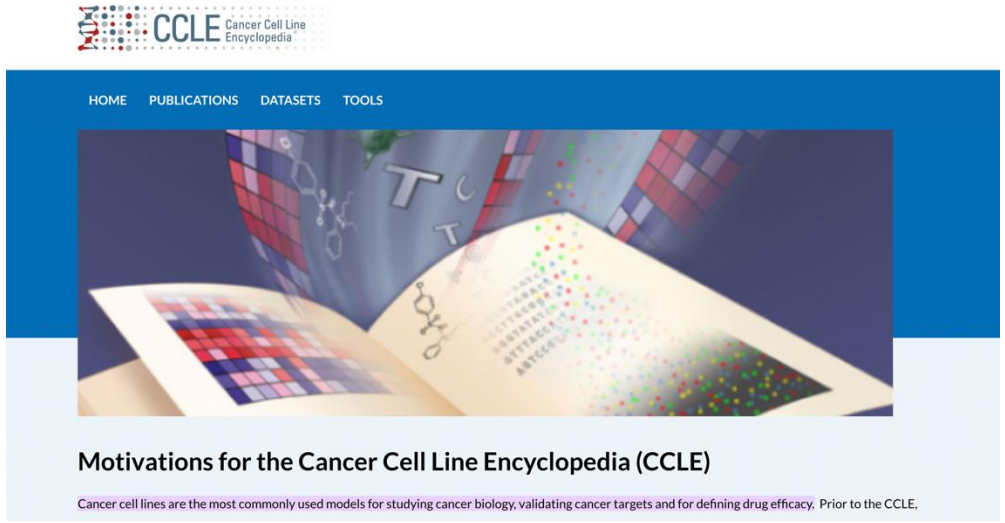
In silico

An *in silico* experiement is one done in a virtual setting, such as a computer or virtual simulation.

In vivo

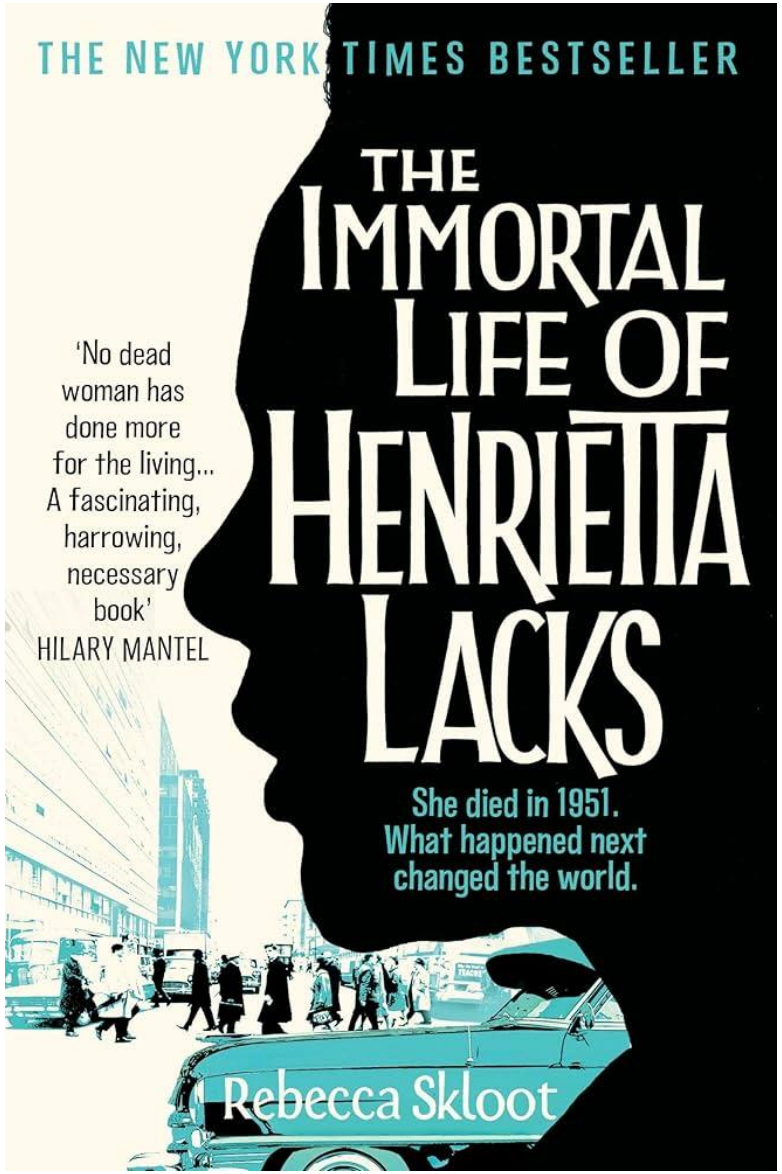
Translates directly to "in life", meaning the study takes place in a living cell or model organism.

Cell Lines



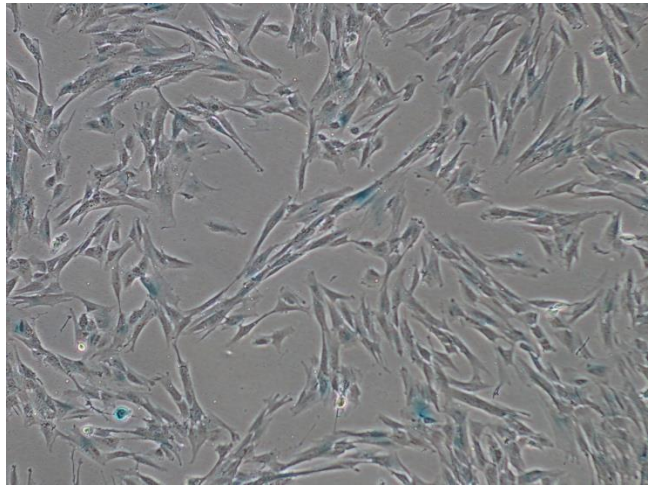
Cancer cell line	Species		Morphology
HeLa	*Homo sapiens*	Cervix adenocarcinoma	Epithelial
MCF-7	*Homo sapiens*	Breast adenocarcinoma	Epithelial
U87MG	*Homo sapiens*	Glioblastoma-astrocytoma	Epithelial
HT-29	*Homo sapiens*	Colon adenocarcinoma	Epithelial
A549	*Homo sapiens*	Lung carcinoma	Epithelial
HEP-G2	*Homo sapiens*	Hepatocellular carcinoma	Epithelial
K-562	*Homo sapiens*	Chronic myeloid leukaemia	Lymphoblast
Cos7	*Cercopithecus aethiops*	SV40 transformed - kidney	Fibroblast
PC3	*Homo sapiens*	Prostate adenocarcinoma	Epithelial
A375	*Homo sapiens*	Malignant melanoma	Epithelial

Table 1 Examples of some widely used cancer cell lines with origin in different cell types. These data

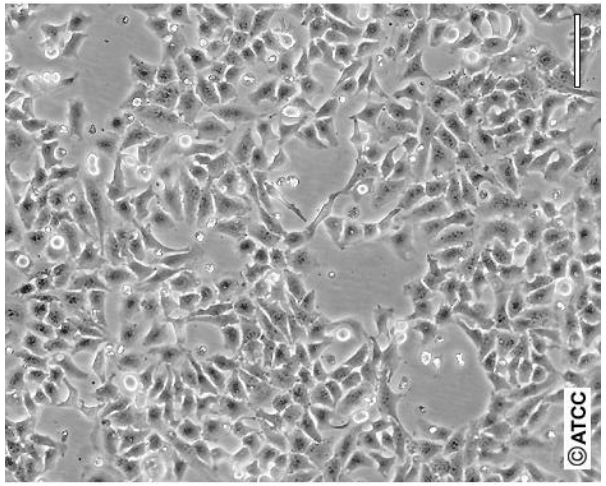


Cell Lines

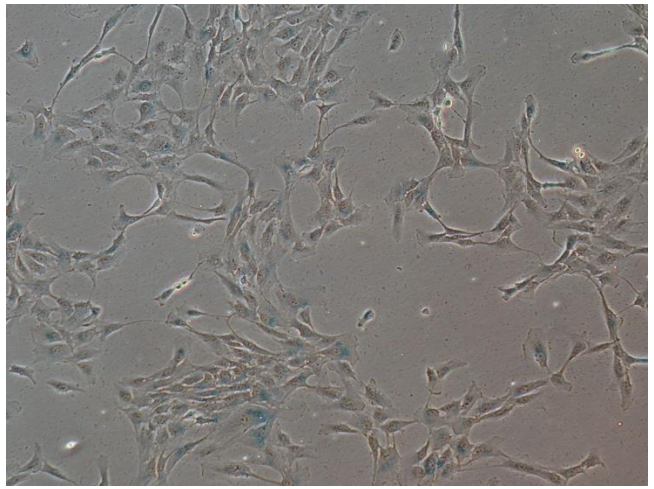
Normal fibroblast



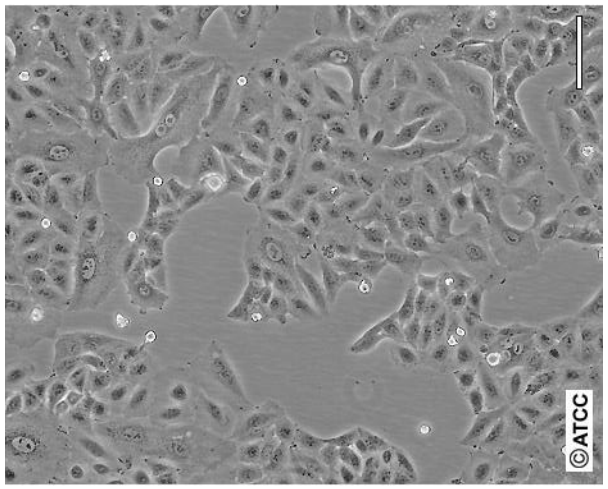
HeLa (Cervical cancer)

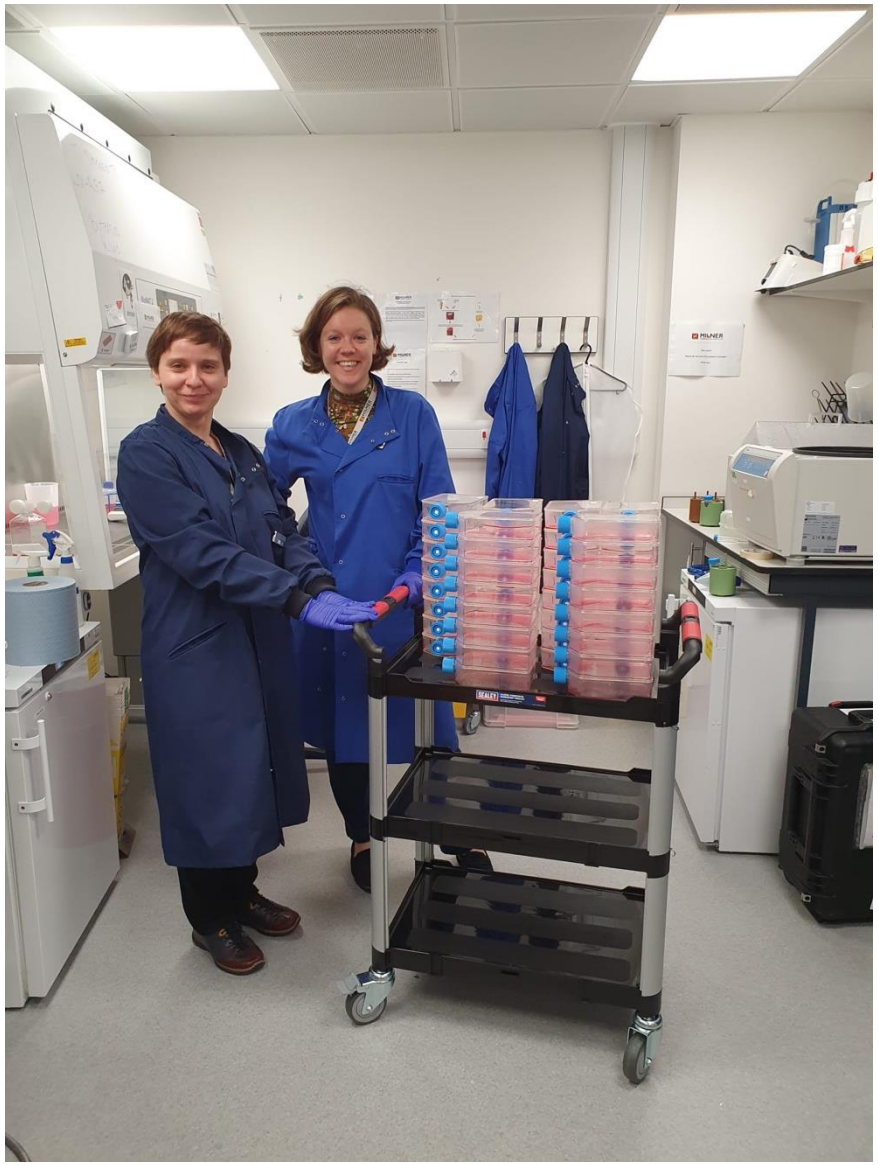


Normal epithelial cell

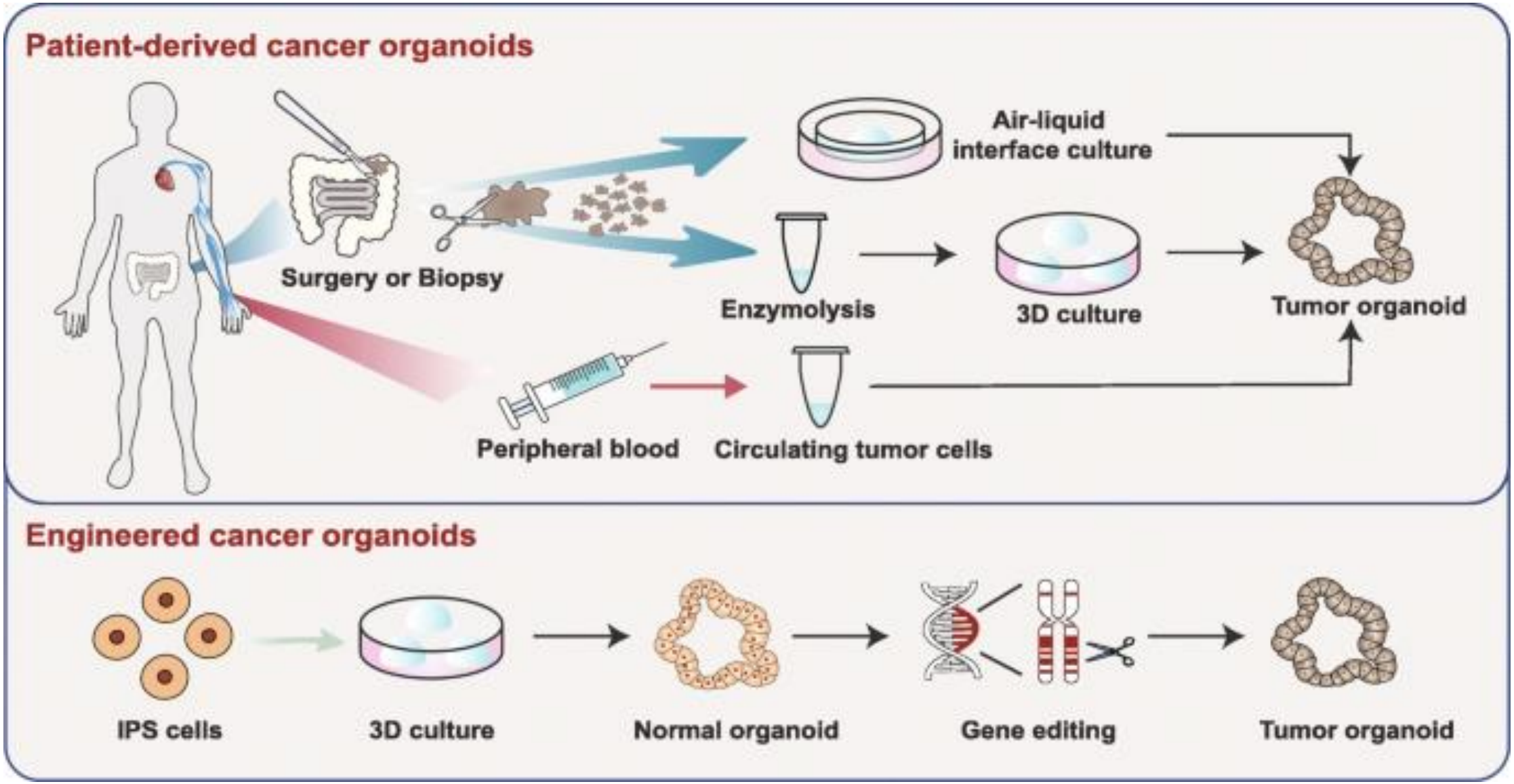


A549 (Lung cancer)

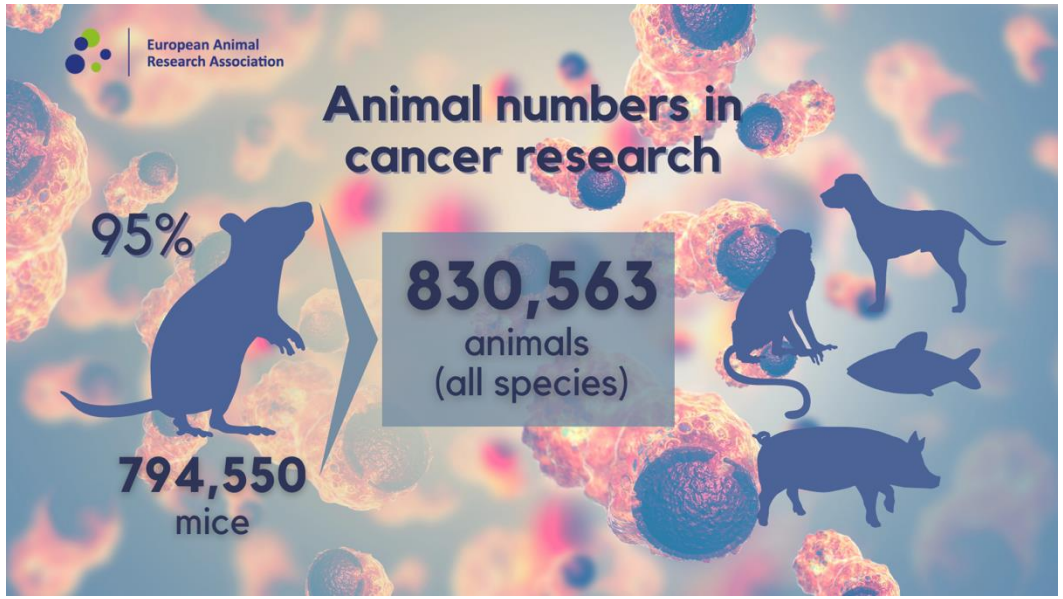


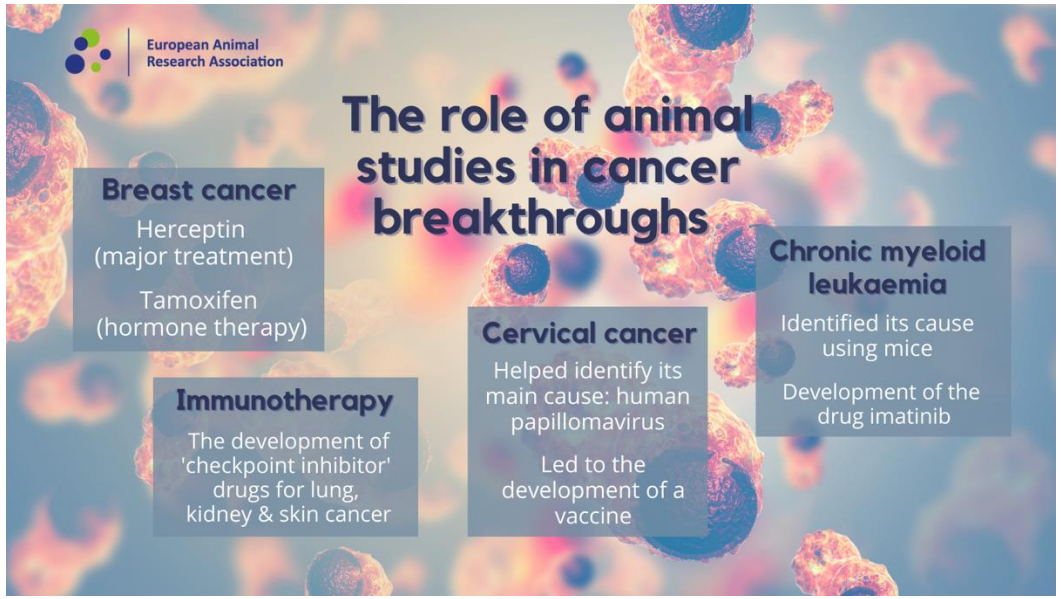


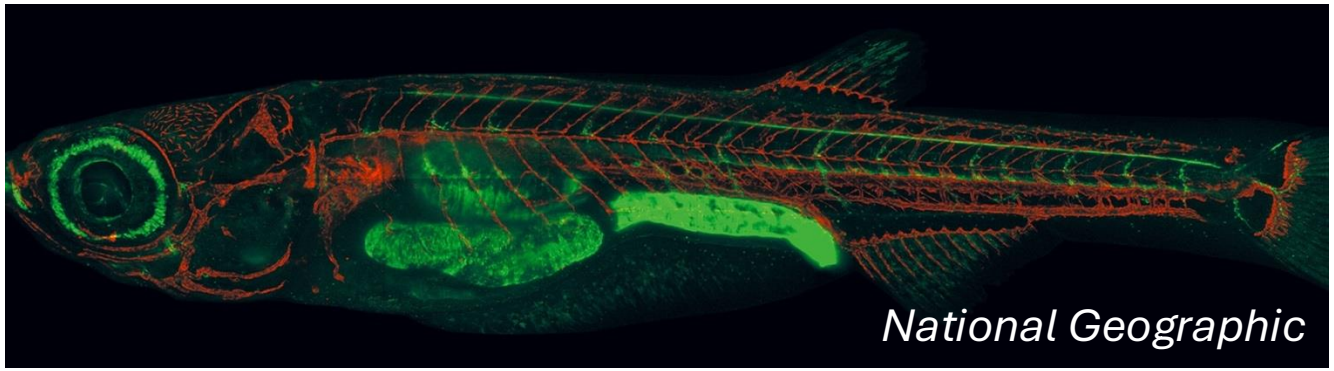
Taking In Vitro Research 3D: Tumour Organoids



Animal Models







"Research involving animals is essential for us to save lives. Most cancer treatments used today wouldn't exist without this type of work."

Cancer Research UK

"We use animal studies alongside many other experimental approaches and they are crucial in building up a complete picture of cancer biology. Our research using animals has helped drive advances in cancer treatment that are benefiting people with cancer all over the world today.."

Institute of Cancer Research, UK

https://www.eara.eu/why-are-animals-used-cancer-research

The Laboratory Mouse

Education

Caltech, Oxford, Stanford, Harvard, MIT, Princeton, Cambridge, Imperial, Berkeley, Chicago, Yale, ETH Zurich, Columbia, UPenn, John Hopkins, UCL, Cornell, Northwestern, UMichigan, Toronto, Carniege Mellon, Duke, UWashington, UTexas at Austin, GA Tech, Tokyo, Melbourne, Singapore, UBC, Wisconsin-Madison, Edinburgh, McGill, Hong Kong, Santa Barbara, Karolinska Institute, UMinnesota, Manchester ... and just about every other major university, medical school & research institution in the world.

Nobel Prizes

1905 - Transmission and treatment of TB
1906 - Structure of Nervous System
1907 - Role of protozoa in disease
1908 - Immunity to infectious diseases
1928 - Investigations on typhus
1929 - Importance of dietary vitamins
1939 - Discovery of antibacterial agent, Prontosil
1945 - Discovery of penicillin
1951 - Yellow fever vaccine
1952 - Discovery of streptomycin
1954 - Culture of the polio virus
1960 - Understanding of immunity
1970 - Understanding of neurotransmitters
1974 - Structural & functional organisation of cells
1975 - Tumour-viruses and genetics of cells
1977 - Hypothalamic hormones
1984 - Techniques of monoclonal antibody formation
1986 - Nerve growth factor and epidermal growth factor
1990 - Organ transplantation techniques
1992 - Regulatory mechanisms in cells
1996 - Immune-system detection of virus-infected cells
1997 - Discovery and characterisations of prions
1999 - Discovery of signal peptides
2000 - Signal transduction in the nervous system
2004 – Odour receptors and organisation of olfactory systems
2008 - Role of HPV and HIV in causing disease
2010 - Development of in vitro fertilization
2011 - Discoveries around innate and adaptive immunity
2012 - Reprogramming mature cells to pluripotent ones

CV of a Lifesaver

Overview

- Involved in around 75% of research
- Short life-span and fast reproductive rate means mice are suitable for studying disease across whole life cycle
- 98% of genes have comparable genes in humans
- Similar reproductive and nervous systems and suffer many of the same diseases as humans including cancer diabetes and anxiety
- Can be genetically modified to include human genes in enhance biological relevance
- Can act as an avatar for a human cancer to allow drug therapies to be trialled safely

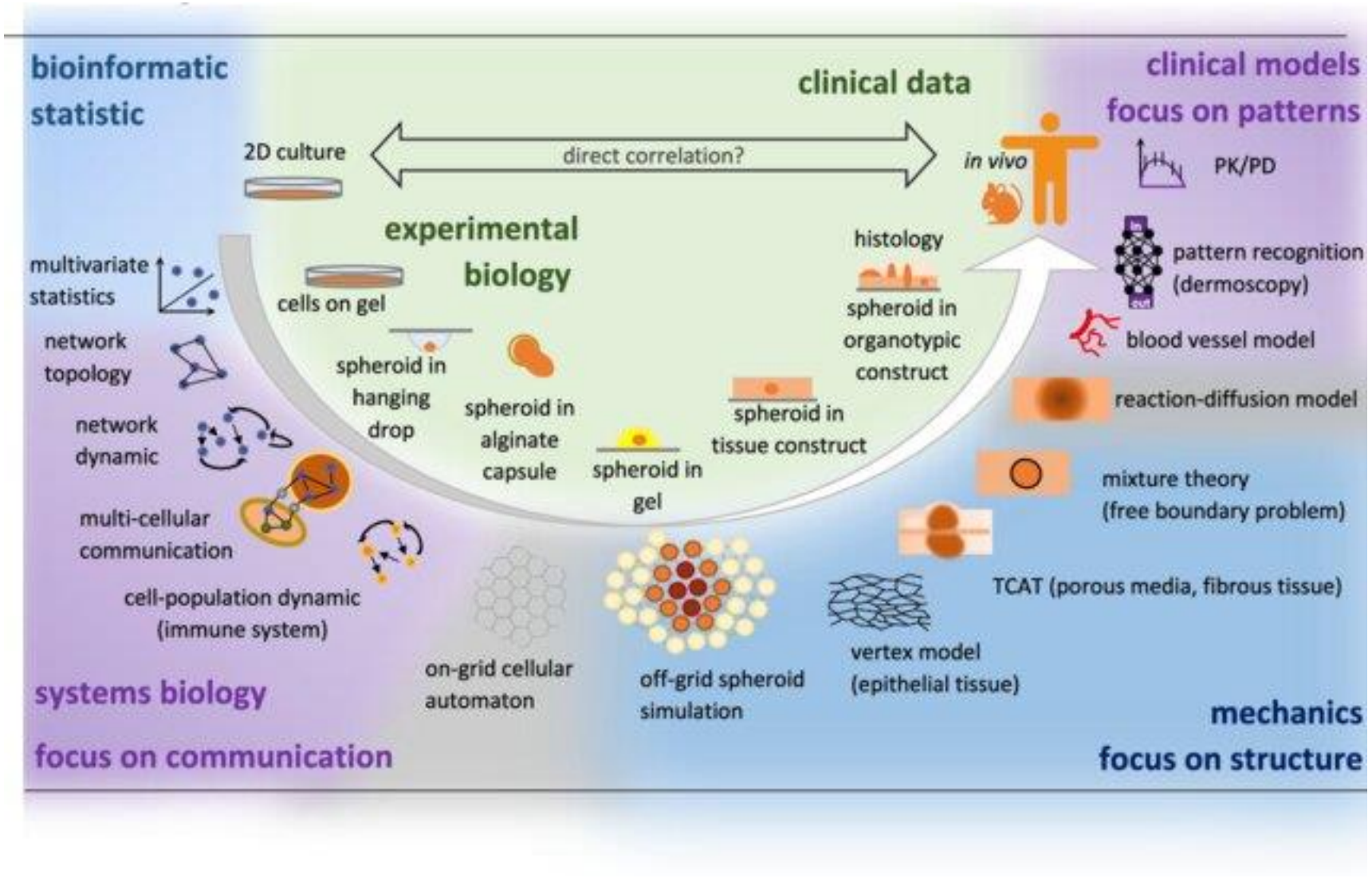
Research Areas

Alzheimer's disease, anaesthetics, AIDS & HIV, anticoagulants, antidepressants, asthma, blindness, bone and joint disease, brain injury, breast cancer, cardiac arrest, cystic fibrosis, deafness/hearing loss, Down's sndrome, drugs for high blood pressure, transplant rejection, Hepatitis B, C & E, Huntington's disease, influenza, leukaemia, malaria, motor neurone disease, multiple sclerosis, muscular dystrophy, Parkinson's disease, prostate cancer, schistomiasis, spinal cord injury, stroke, testicular cancer, tuberculosis,

Contact

www.understandinganimalresearch.org.uk
www.animalresearch.info
www.amprogress.org
www.speakingofresearch.com

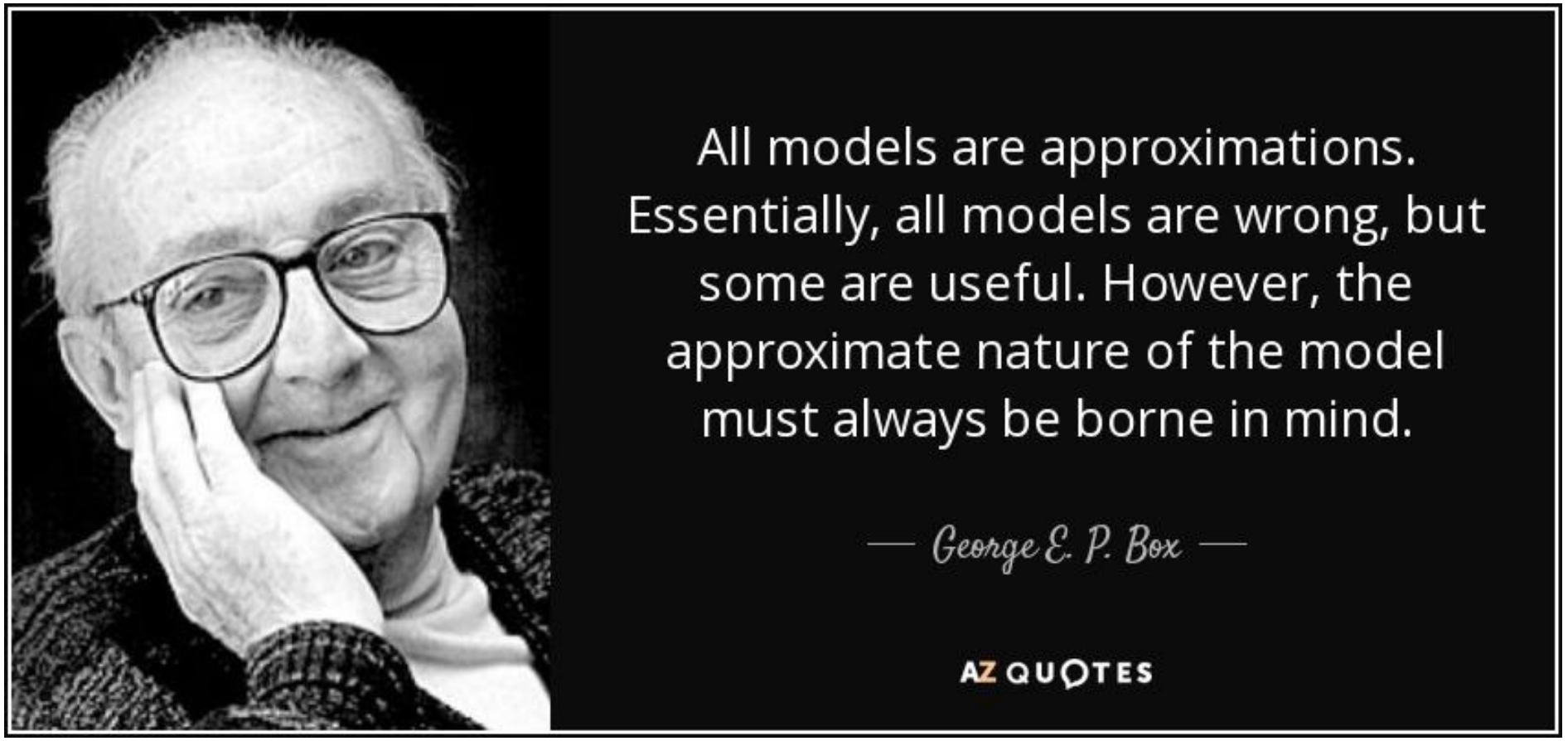
Bioinformatics & Computational Models



Albrecht (2020) Theoretical Biology and Medical Modelling

The Importance of Translation-Focused Research

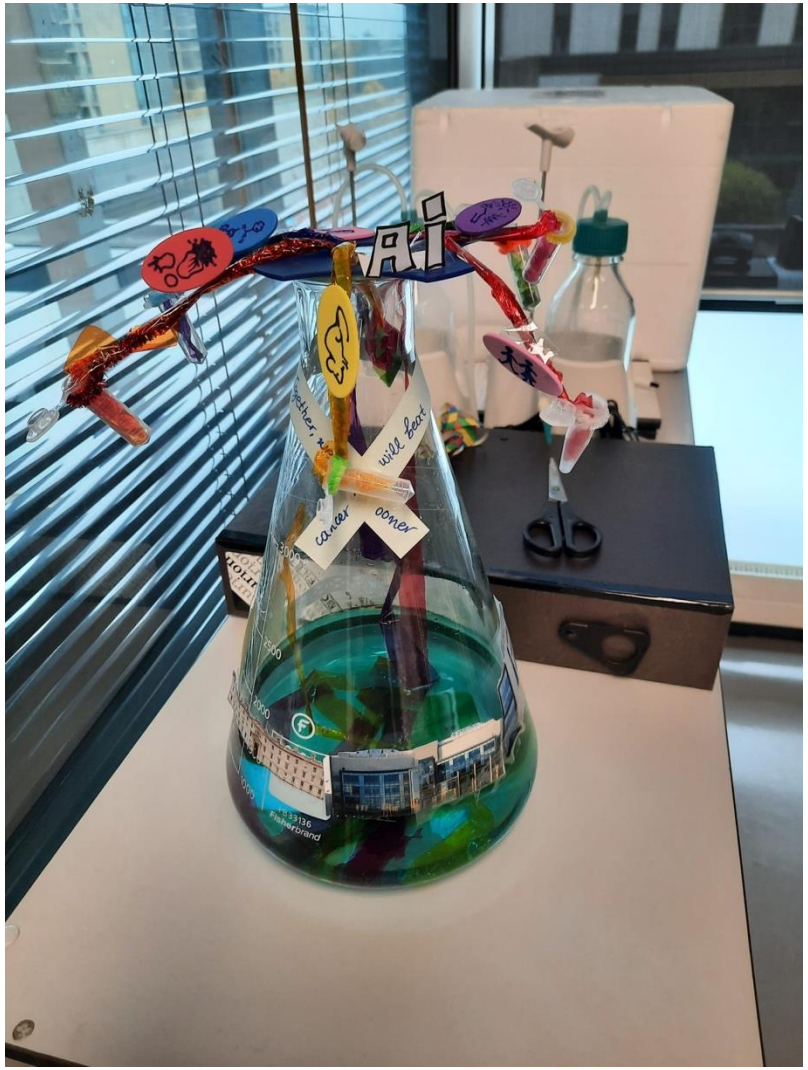
"Show me the phenotype!"
"Analysis for the sake of analysis is a waste of time and money"
Adelyne Chan, when supervising students



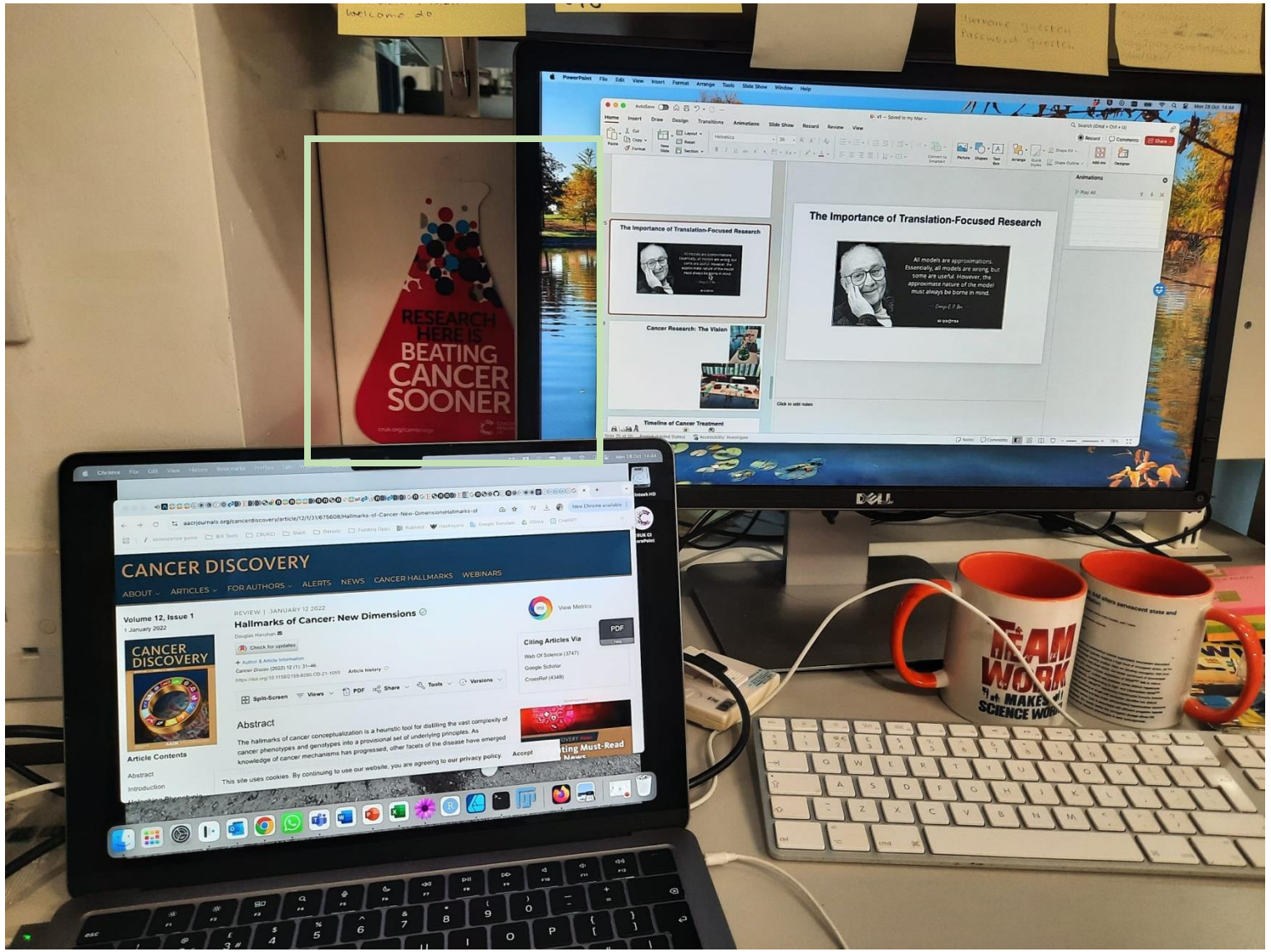
Cancer Research: The Vision & Motivation

Cancer Research: The Vision & Motivation

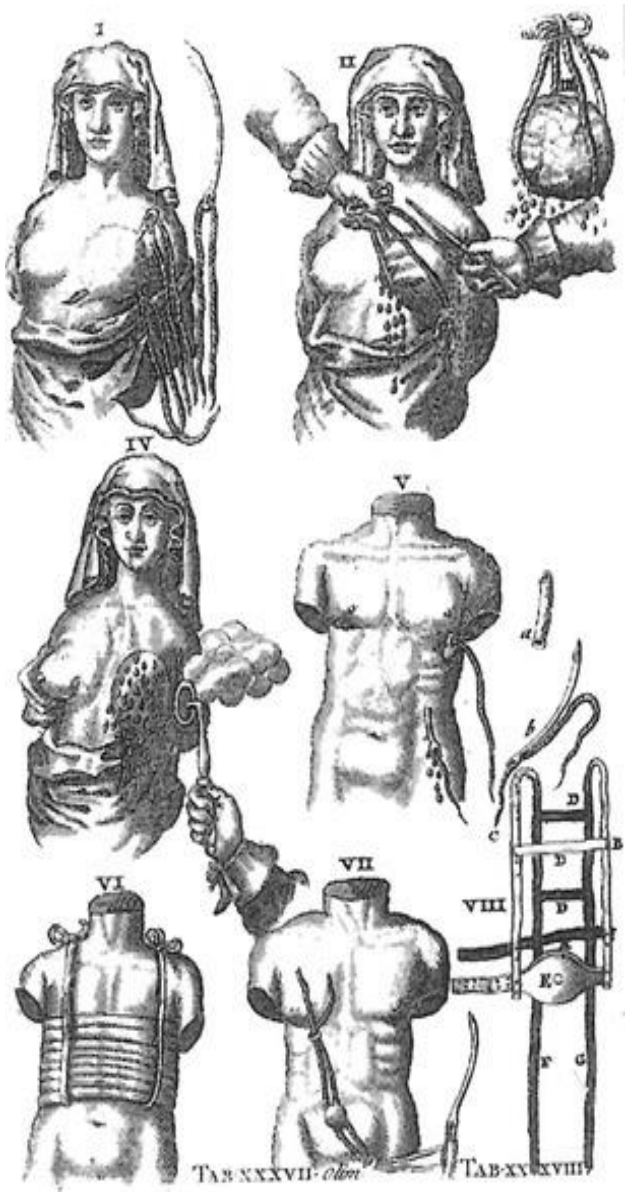
“Create a 3D logo that represents cancer research in Cambridge”

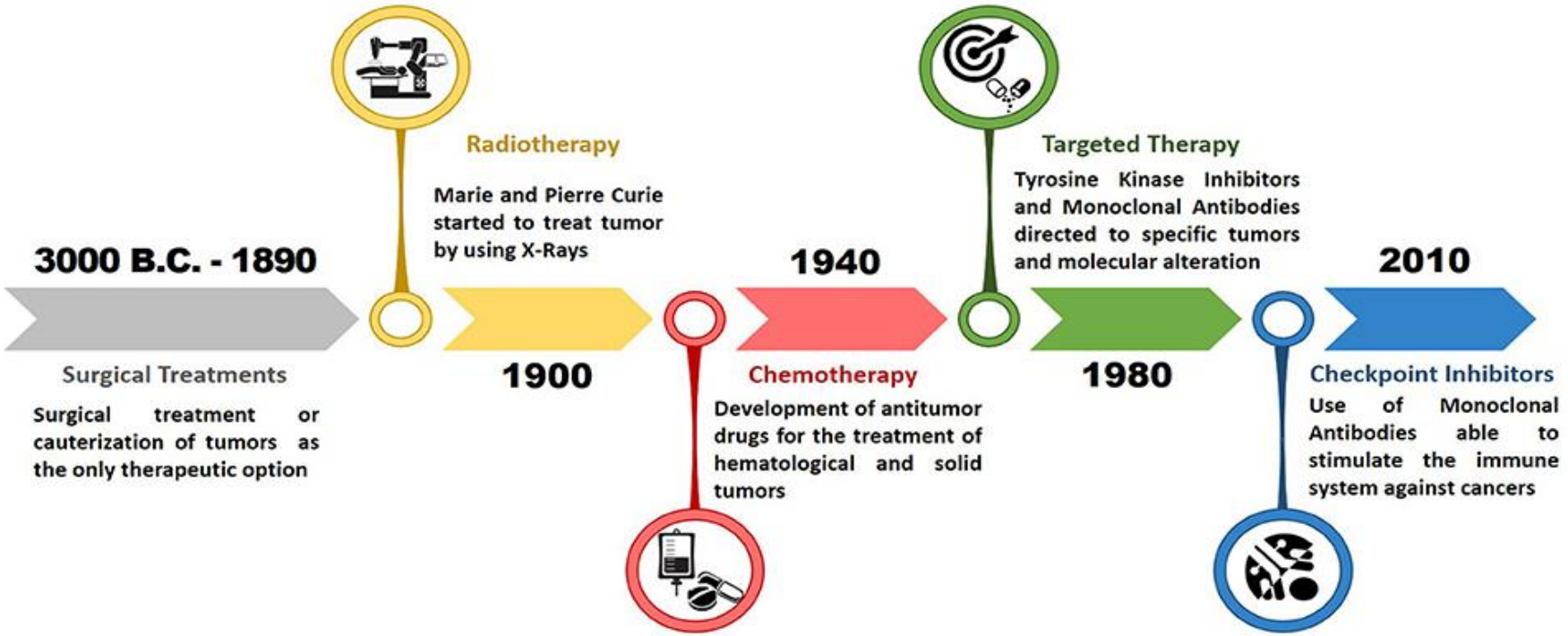


Cancer Research: The Vision & Motivation



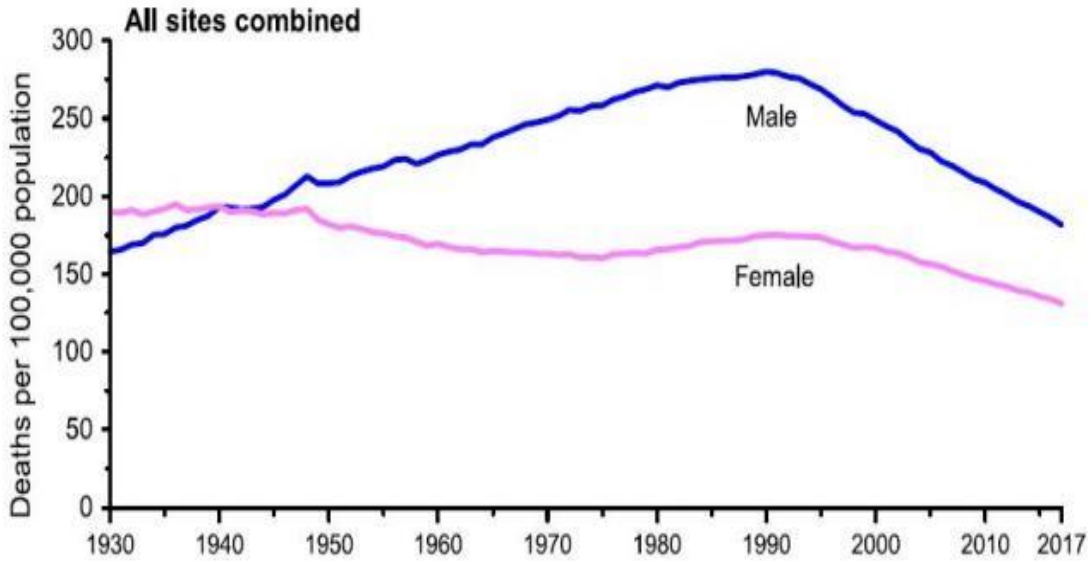
Timeline of Cancer Treatment

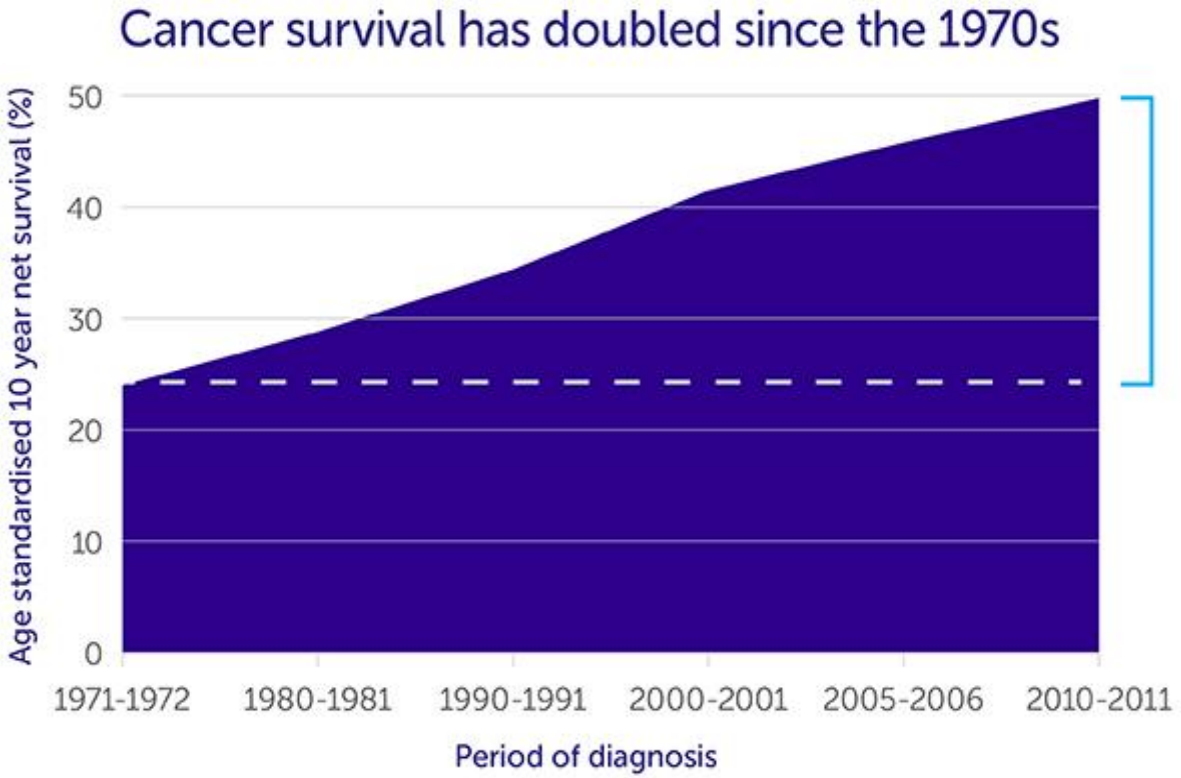




Falzone et al., 2018. Front. Pharmacolol.

Progress in Cancer Survival





Source: cruk.org/cancerstats

Together we will beat cancer

CANCER RESEARCH UK

Progress in Cancer Survival

Reasons for progress:

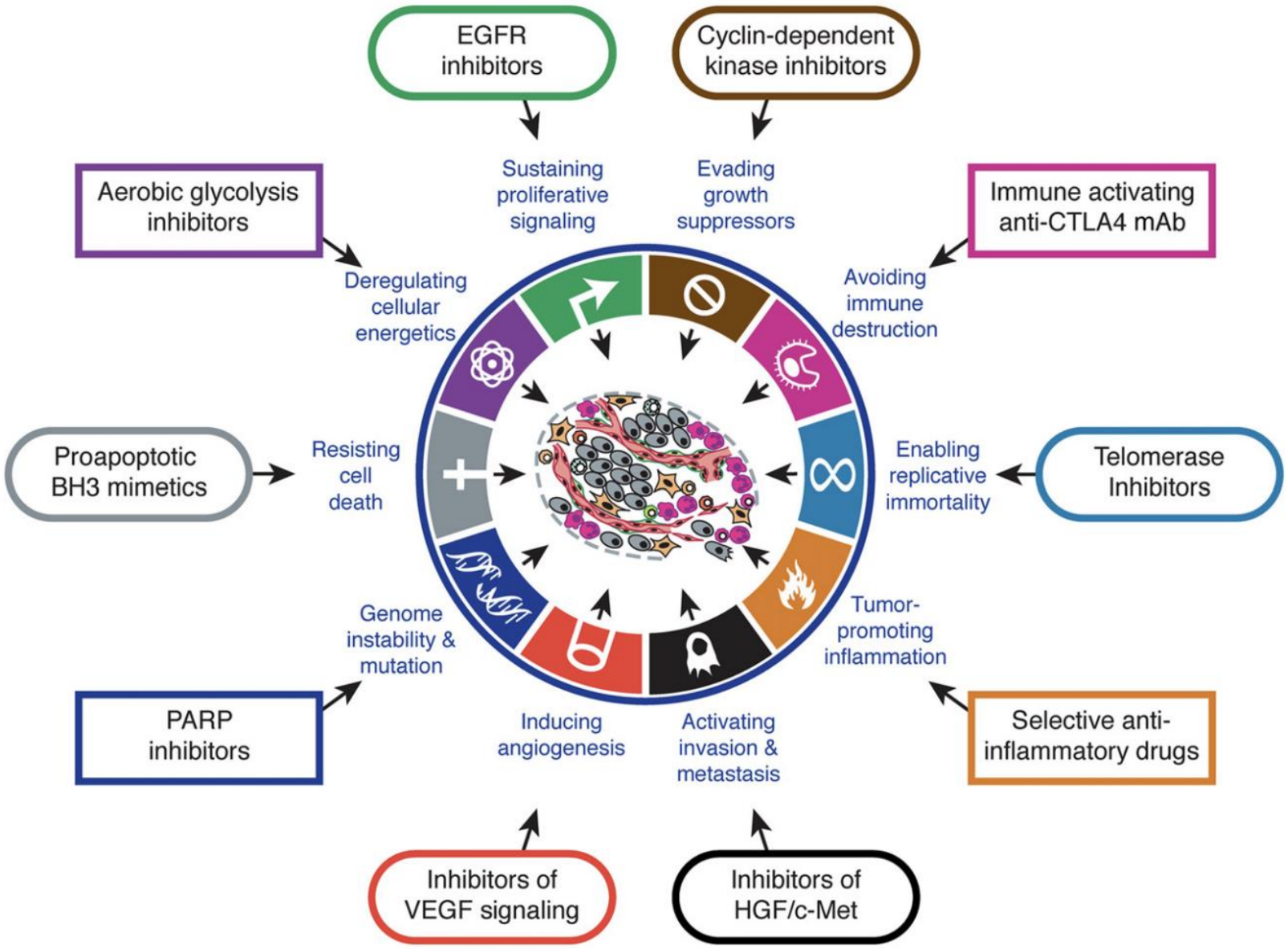
"Good news, Mrs. Bryant—I think we got it all."

Rational Treatment: Targeting the cancer, not everything

Personalised Treatment: Understanding that cancers are different and treating them accordingly

Early Diagnosis: Focus on earlier, more treatable disease

Rational Treatments Based on Hallmarks of Cancer



Personalised Therapies

How is AI Changing the Future of

Precision Medicine?

Identifying Potential Drug Targets

Identifying Causal Genes

Real-Time Monitoring of Patient Health

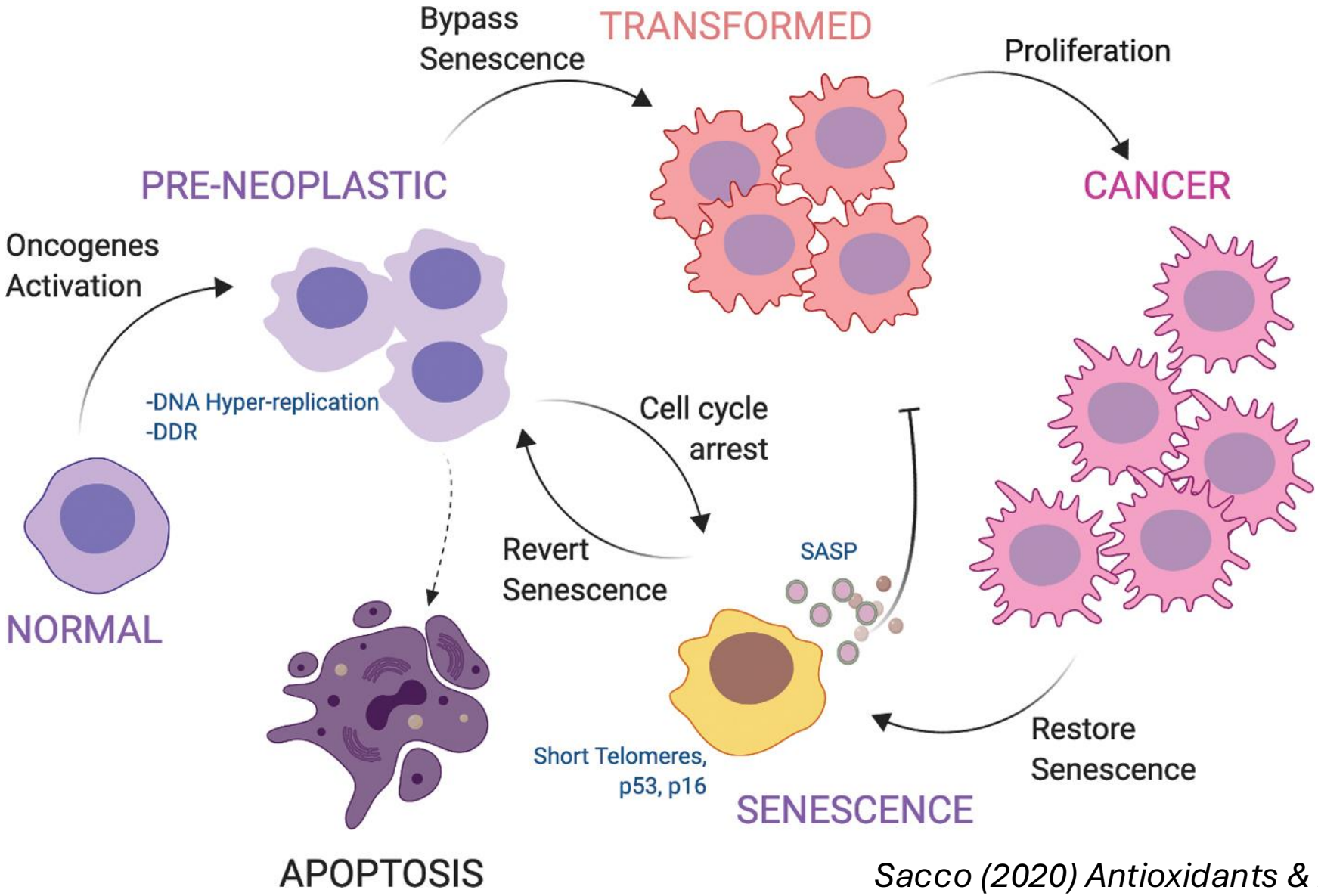
Phenotypic & Genetic Heterogeneity

AI-Powered Early Detection of Diseases

Changing Role of Physicians

nextgeninvent.com

Prevention & Targeting Early Stages of Disease



Sacco (2020) Antioxidants & Redox Signalling

Gentler Therapies

The physician should not treat the disease but the patient who is suffering from it

~ Maimonides

AZ QUOTES

Thank You!!!

Narita Lab, CRUKCI

CANCER RESEARCH UK

UNIVERSITY OF CAMBRIDGE