

Cancer Bio Course 2026

Session 1: Introduction to cancer biology

Gerstner Sloan Kettering PhD program

March 2nd, 2026



Memorial Sloan Kettering
Cancer Center

Pablo Sánchez Vela, MD

Senior Research Scientist

Ross Levine Lab

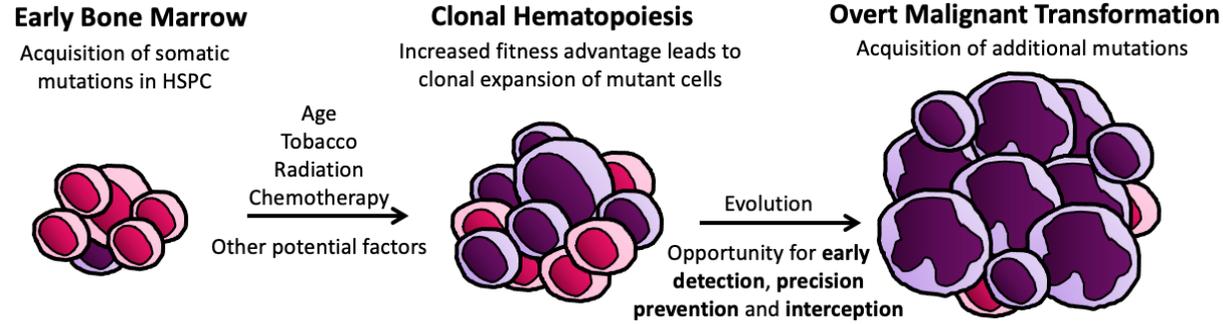
Molecular Cancer Medicine Service

Human Oncology and Pathogenesis Program

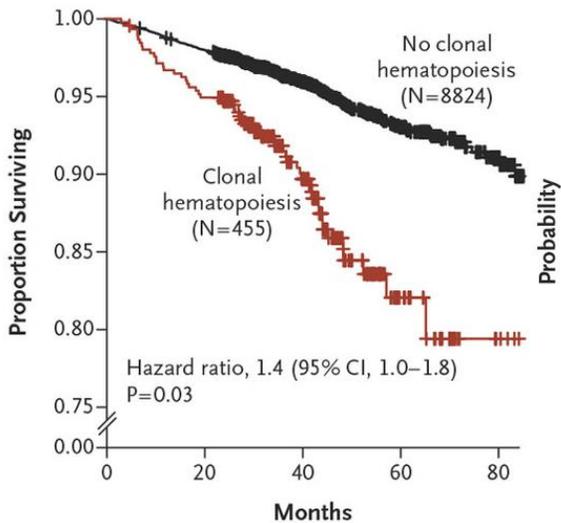
sanchezp@mskcc.org



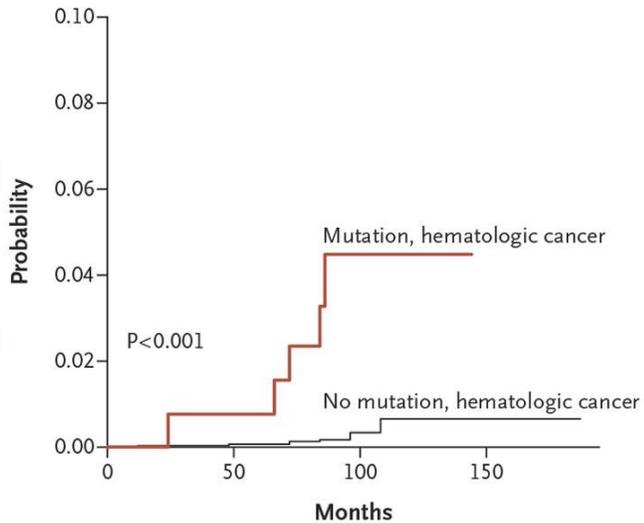
Questions I decided to tackle during my time at MSK



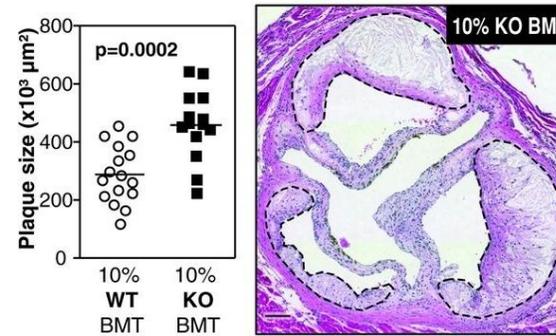
Genovese et al. NEJM 2014
Overall Mortality



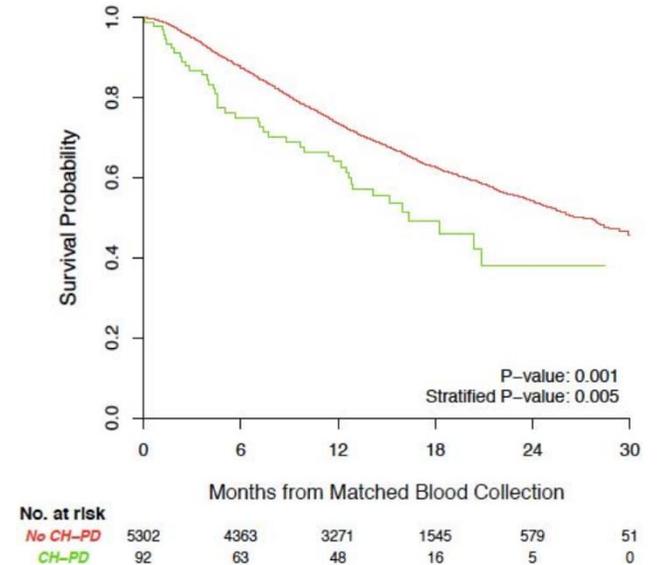
Jaiswal et al. NEJM 2014
Hematologic Malignancies



Fuster et al. Science 2017
Cardiovascular Disease

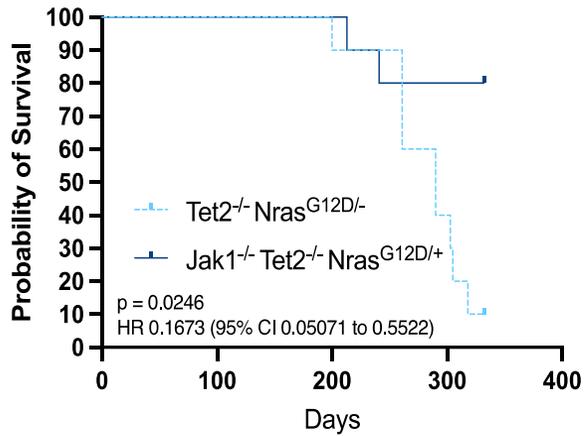


Coombs et al. CellStemCell 2017
Solid Tumors

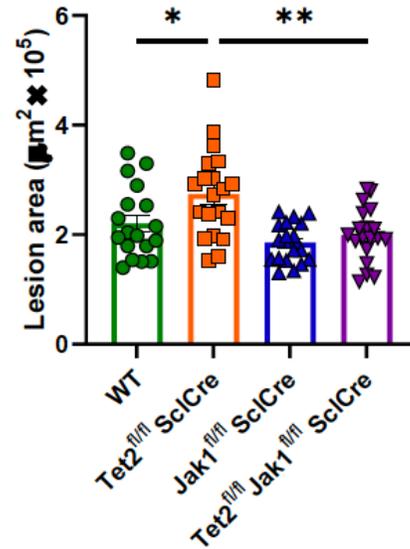


How are we doing so far?

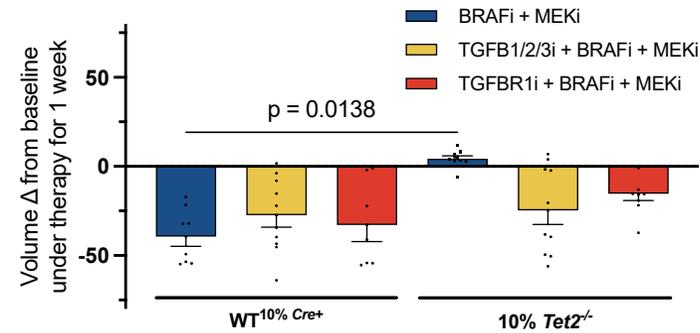
Hematologic Malignancies (Myeloid Leukemia)



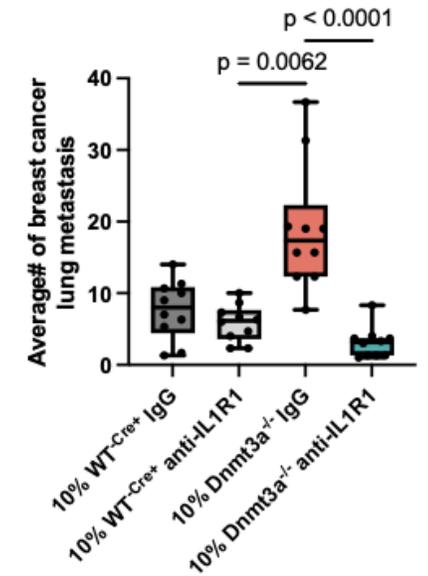
Cardiovascular Disease (Atherosclerosis)



Solid Tumor (Thyroid Cancer) – Treatment Resistance



Solid Tumor (Breast Cancer) – Metastasis



Course structure

Scientific topics covered will include:

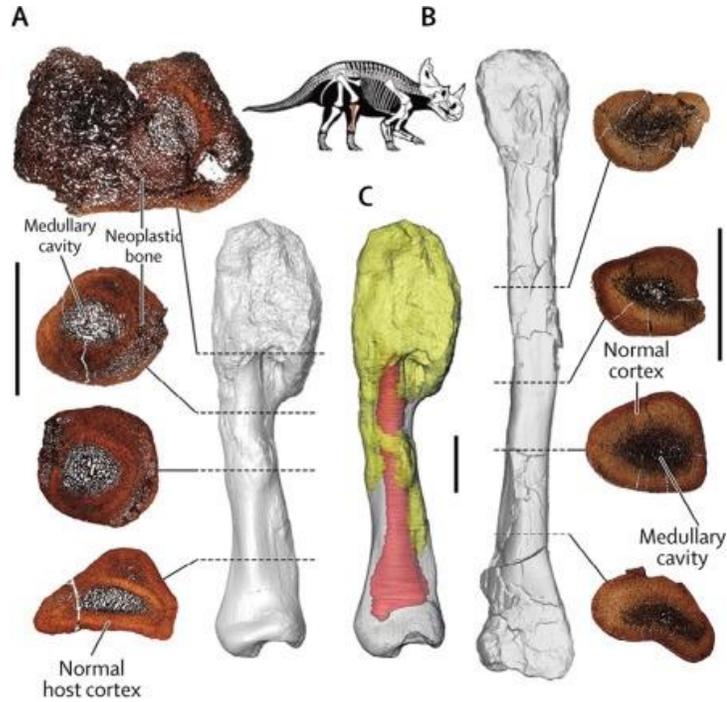
- Historical perspective of cancer treatments.
- Burden of cancer as a disease.
- Evolution of cancer classification
- Understand how tumor cells evolve and adapt.
- Understand the molecular and environmental basis of cancer



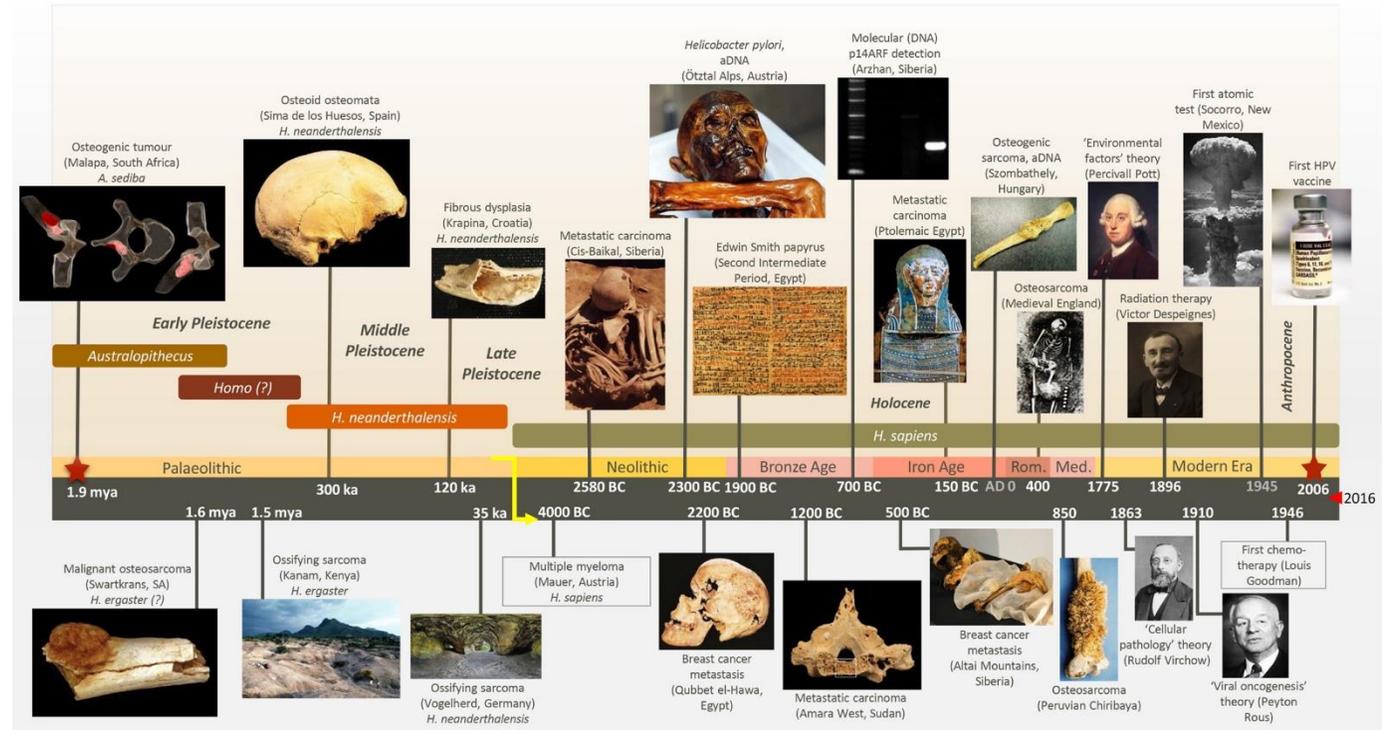
Historical perspective



First records suggestive of cancer as an ancient disease

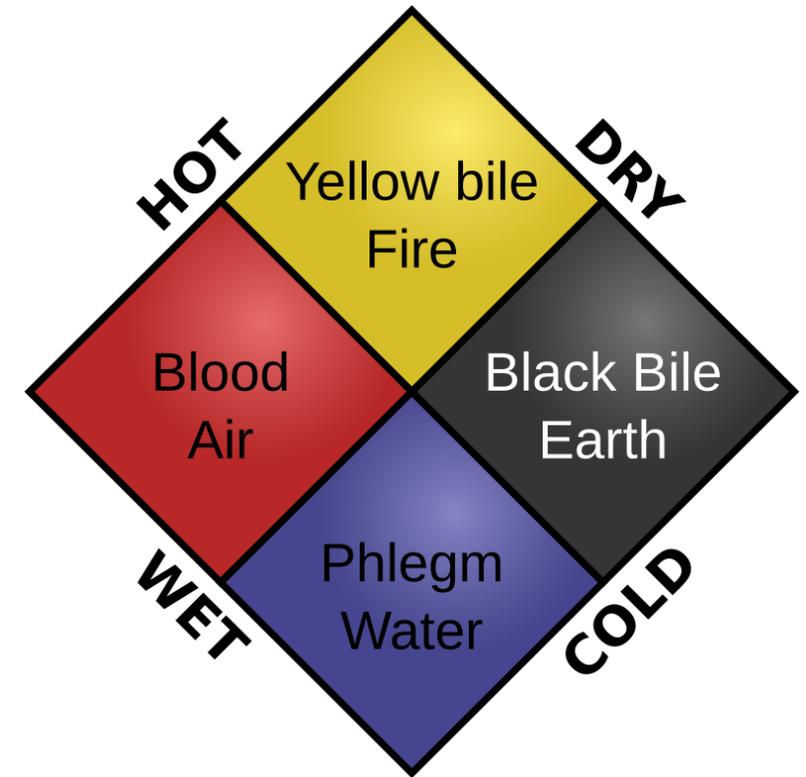
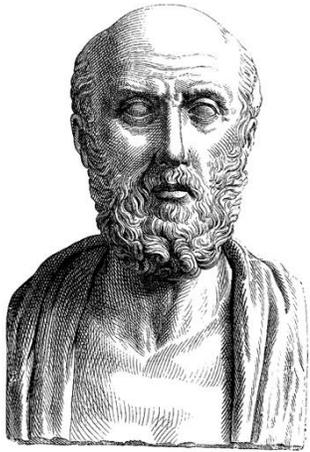


Ekhtiari, Seper et al. First case of osteosarcoma in a dinosaur: a multimodal diagnosis *The Lancet Oncology*, Volume 21, Issue 8, 1021 - 1022



Chronological incidence of prehistoric oncogenic tumours and important milestones concerning cancer aetiology and treatment (Binder et al., 2014; Bona et al., 2014; Monge et al., 2013; Odes et al., 2016; Phelan et al., 2007; Randolph-Quinney et al., 2016) ('Rom.' and 'Med.' refers to Roman and Medieval Periods, respectively)

Early conceptions of health and disease: Humorism



Will one day our scientific hypothesis sound as improbable as these?

Signs of change: Defining diseases



Vienna's General Hospital, founded in 1784.
Copyright © 1998 AKG London/Erich Lessing



Van Gogh's The Ward in the Hospital at Arles (April-October 1889)

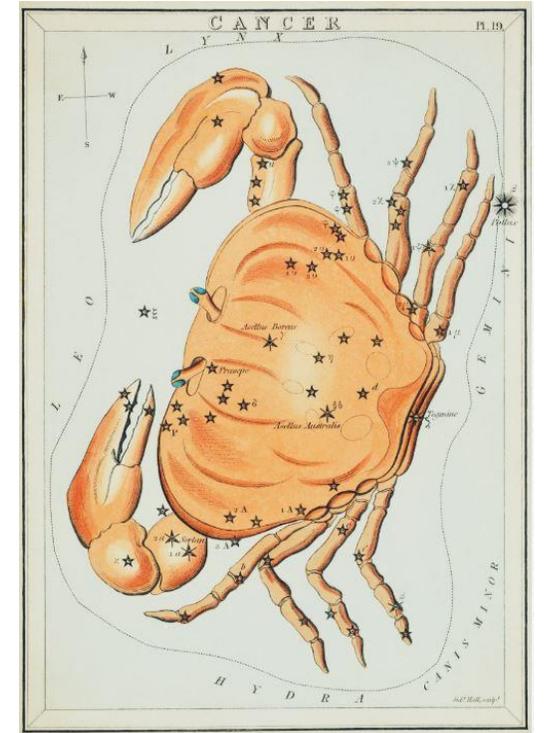
Signs of change: Defining cancer



The Anatomy Lesson of Dr. Nicolaes Tulp is a 1632 oil painting on canvas by Rembrandt

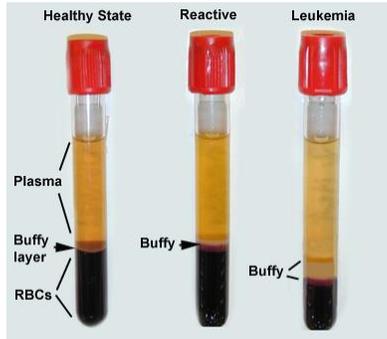


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Onco- tumor or mass

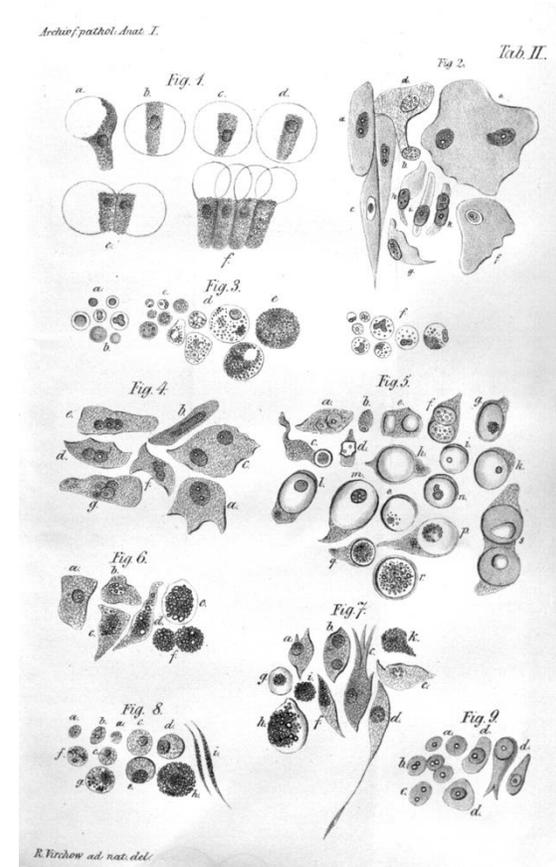
Signs of change: Cellular origins of cancer



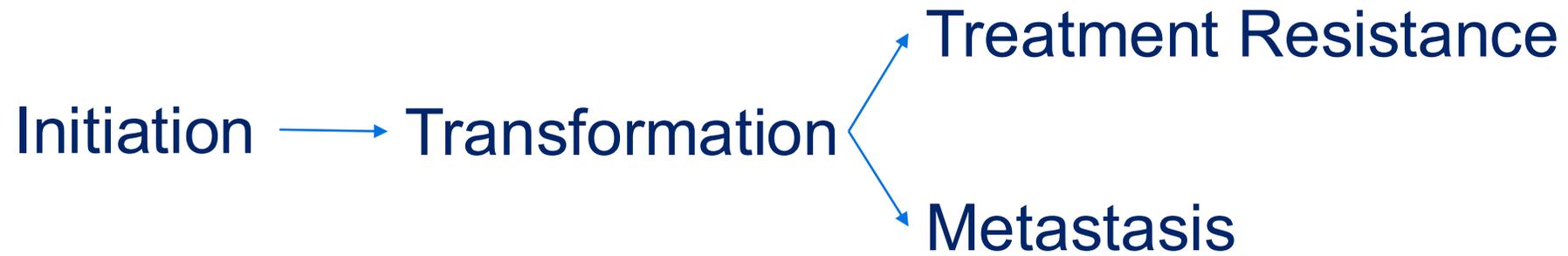
Antonie van Leeuwenhoek microscope



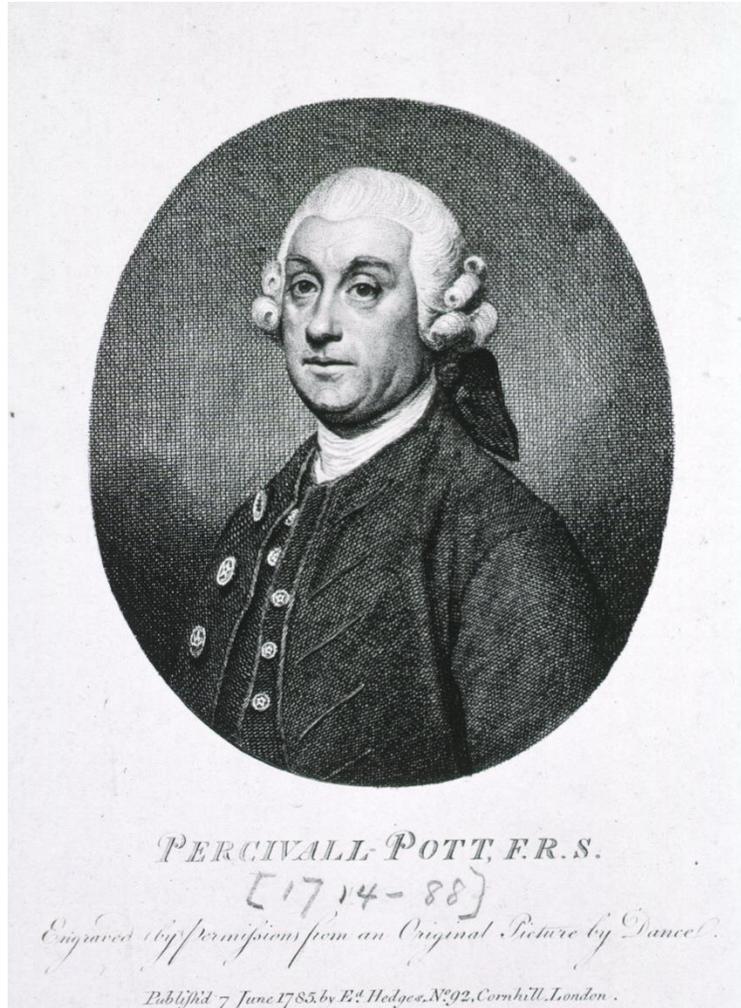
"Omnis cellula e cellula" ("all cells come from cells") Rudolf Virchow



Current problems of cancer research



Interplay between environmental mutagens and tumor promoters in cancer causation



How do carcinogens cause cancer?

Chemical carcinogenesis – What is the nature of initiation?

1983-86

Carcinogen-specific
RAS mutations



RAS Codon 61 = CAA

DMBA ●

Binds to A residues
Causes A-T mutations

CAA
Gln

CTA Leu

CAT His

Dipple, A., et al, 1983

**Mouse skin carcinomas induced *in vivo*
by chemical carcinogens have a
transforming Harvey-*ras* oncogene**

Allan Balmain & Ian B. Pragnell

Beatson Institute for Cancer Research, Garscube Estate,
Switchback Road, Bearsden, Glasgow G61 1BD, UK

Nature, 1983

**Carcinogen-specific mutation and
amplification of Ha-*ras* during
mouse skin carcinogenesis**

Miguel Quintanilla, Ken Brown,
Martin Ramsden* & Allan Balmain

Beatson Institute for Cancer Research, Switchback Road,
Bearsden, Glasgow G61 1BD, UK

Nature, 1986



RAS Codon 12 = GGA

MNU ●

Methylates G residues
Causes G-A transitions

GGA
Gly

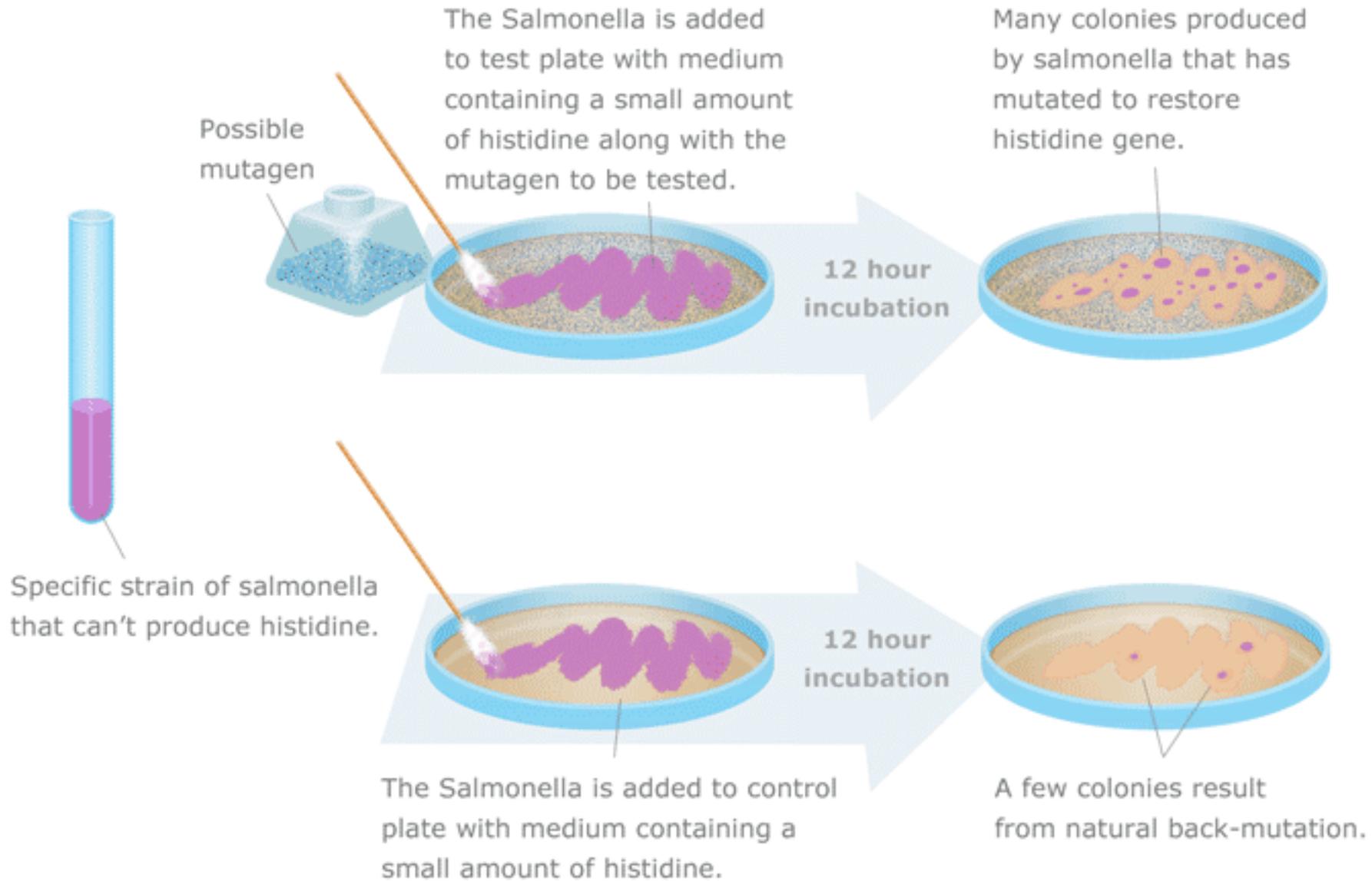
GAA
Asp

98 ARTICLES 102

**Induction of mammary carcinomas in rats by
nitroso-methylurea involves malignant activation
of H-*ras*-1 locus by single point mutations**

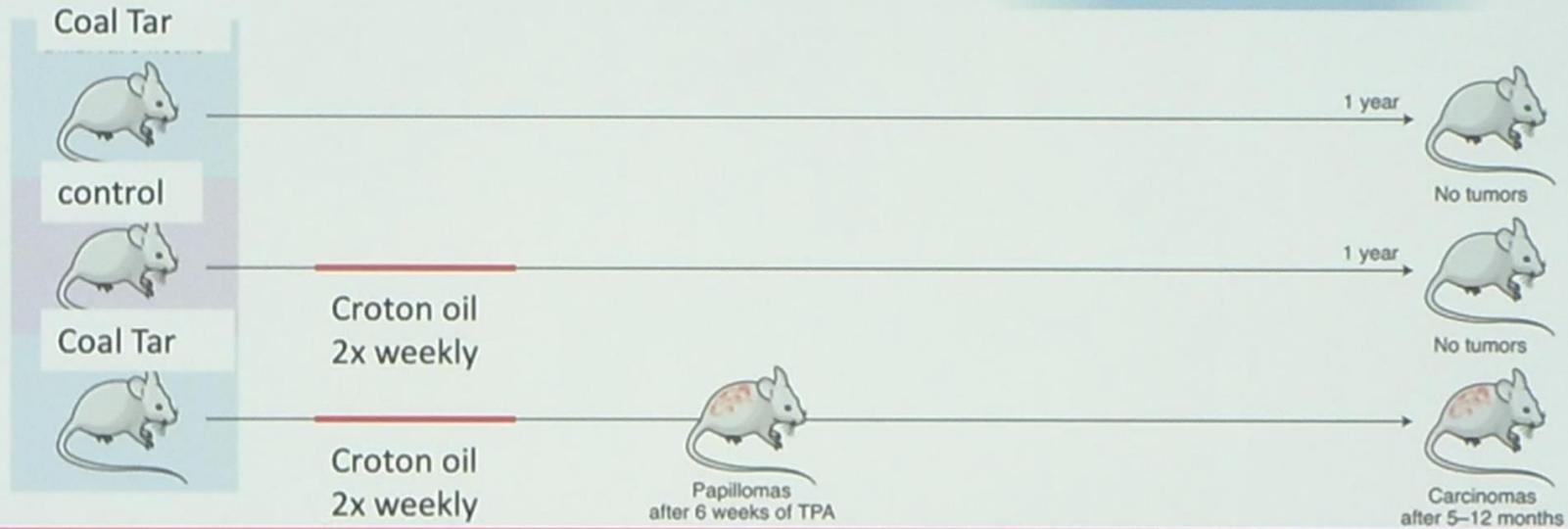
Saraswati Sukumar, Vicente Notario, Dionisio Martín-Zanca & Mariano Barbacid

Ames Test



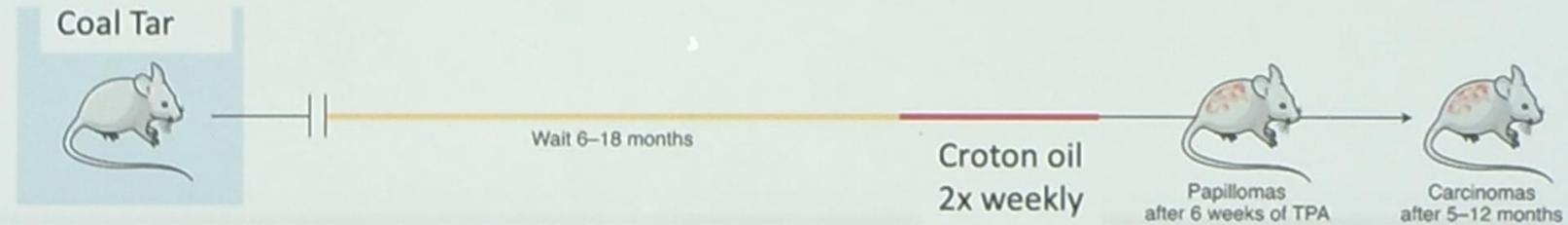
Berenblum and Shubik, 1947

a Standard Initiation-promotion model



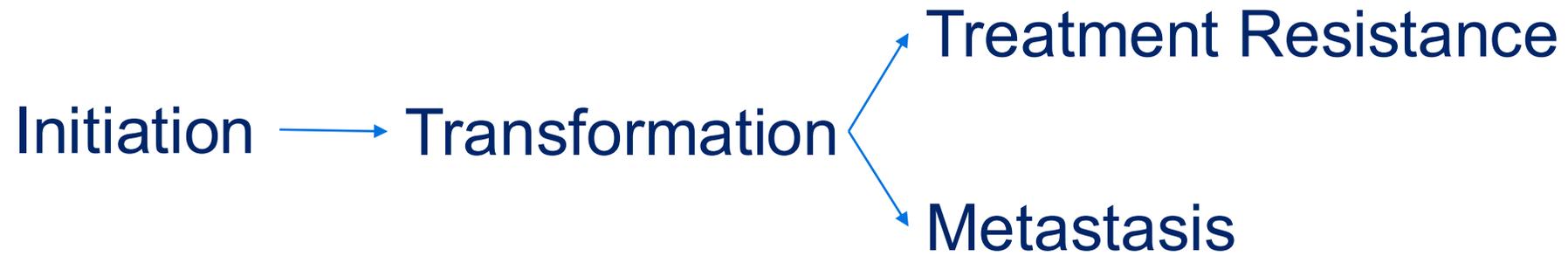
Berenblum and Shubik, 1947

b Delayed-promotion model



The rate-limiting step in carcinogenesis is promotion.

Current problems of cancer research



Surgery, the first cancer treatment

A series of conceptual and technological advances facilitated the development of surgery



Anesthesia



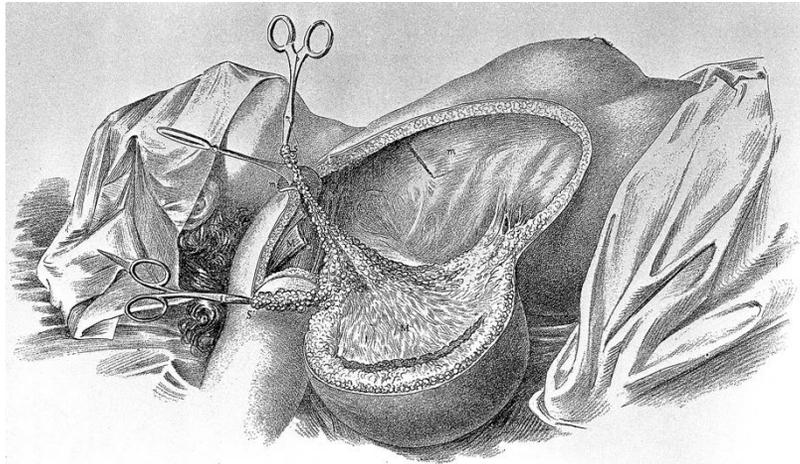
Asepsis



Antisepsis

Surgery: The first cures, yet too little and too much

"In God we trust, all others must have data." Bernard Fisher, M.D.



Radical mastectomy for the treatment of breast cancer.

Radical mastectomy was both too much and too little: too much for small tumors and too little for large tumors that had already metastasized.

DeVita VT Jr, Rosenberg SA. Two hundred years of cancer research. *N Engl J Med.* 2012;366(23):2207-2214. doi:10.1056/NEJMra1204479

> *Science.* 1959 Oct 9;130(3380):918-9. doi: 10.1126/science.130.3380.918.

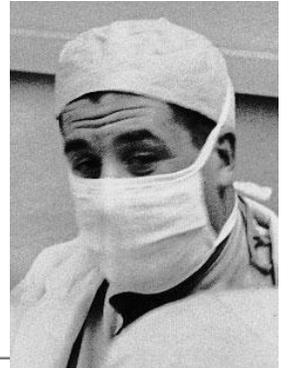
Experimental evidence in support of the dormant tumor cell

B FISHER, E R FISHER

PMID: 13823184 DOI: 10.1126/science.130.3380.918

Abstract

When rats were injected intraperitoneally with as few as 50 Walker-256 carcinosarcoma cells aarcoma cells and then examined 5 months later for hepatic tumor growth, none was evident. If, however, 3 months after injection the rats were subjected to repeated laparotomy and liver examination at 7-day intervals, 100 percent had a tumor within a few weeks.



RADICAL VERSUS TOTAL MASTECTOMY

TWENTY-FIVE-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL COMPARING RADICAL MASTECTOMY, TOTAL MASTECTOMY, AND TOTAL MASTECTOMY FOLLOWED BY IRRADIATION

BERNARD FISHER, M.D., JONG-HYEON JEONG, PH.D., STEWART ANDERSON, PH.D., JOHN BRYANT, PH.D., EDWIN R. FISHER, M.D., AND NORMAN WOLMARK, M.D.

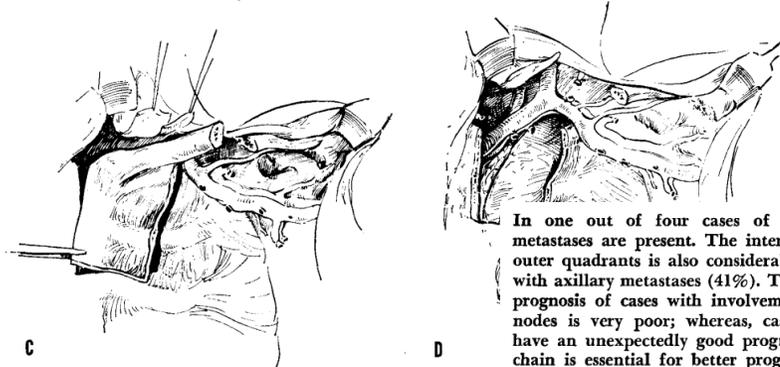
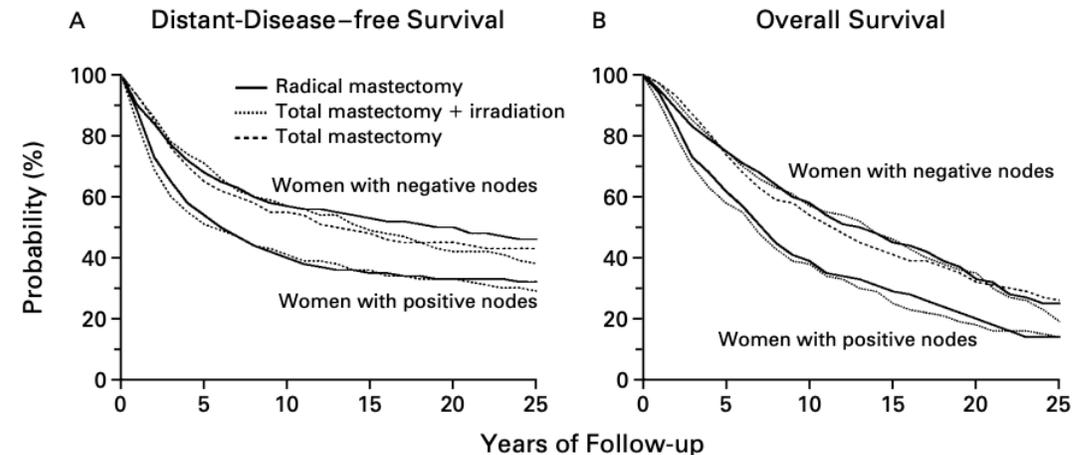


FIG. 2. Technique for superradical ma

Extended radical mastectomy

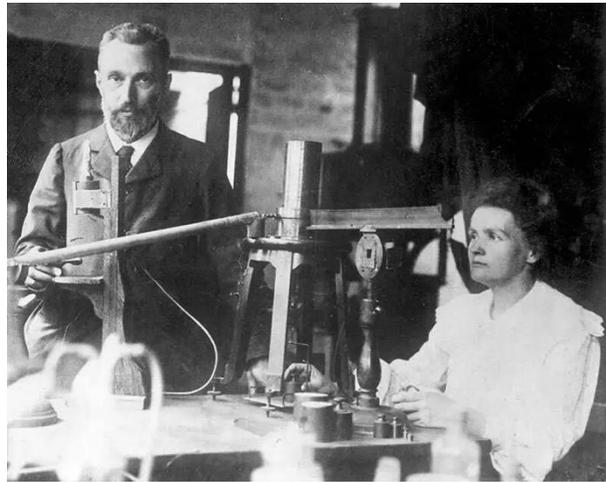
In one out of four cases of operable breast cancer internal mammary metastases are present. The internal mammary involvement of tumors of the outer quadrants is also considerable (18%), being especially frequent in cases with axillary metastases (41%). The 5- and 10-year survival rates show that the prognosis of cases with involvement of both axillary and internal mammary nodes is very poor; whereas, cases with internal mammary metastases only have an unexpectedly good prognosis. The removal of the internal mammary chain is essential for better prognostic evaluation and also seems justified by the radicality additionally given to the Halstead operation. However, only the results of a coordinated clinical trial will give a reliable evaluation of the true value of the procedure. A new technique of super-radical operation is described. The operation is safe, without considerable functional or cosmetic impairment. However, only long-term results will allow evaluation of its effectiveness.



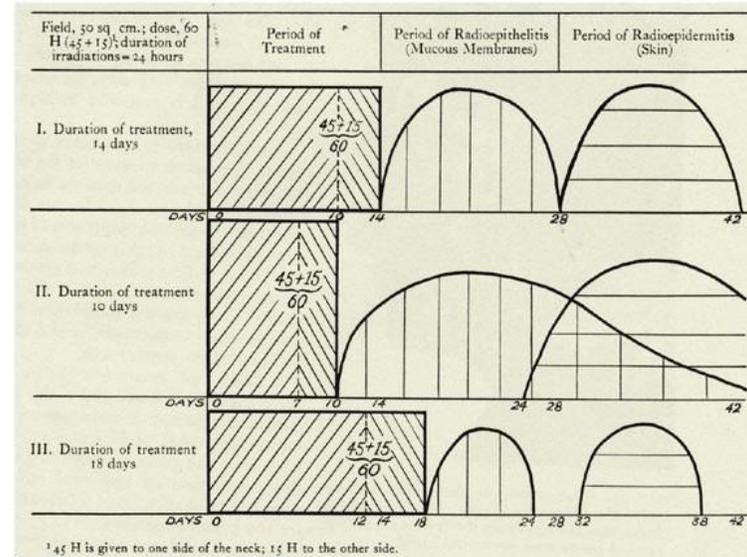
Second generation cancer treatments: Radiation therapy



Josef Albert, München, repr.
Hand des Anatomen Geheimrath von Kölliker.
Im Physikal. Institut der Universität Würzburg
mit X-Strahlen aufgenommen
von Professor Dr. W. C. Röntgen.



Marie and Pierre Curie discover Radium in 1898



In 1928, head and neck cancers could be cured by fractionated radiation treatments

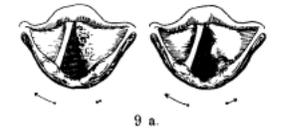
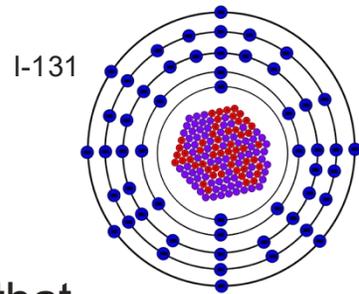
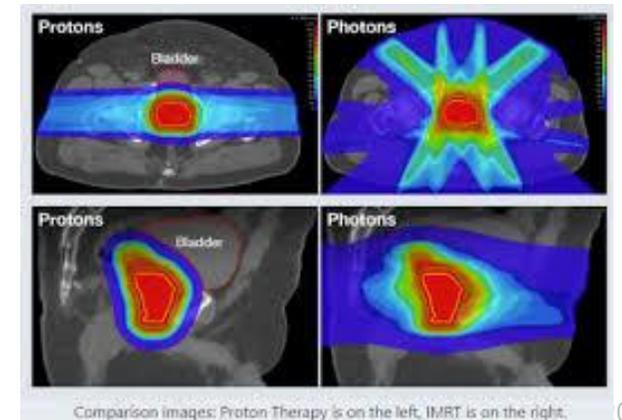
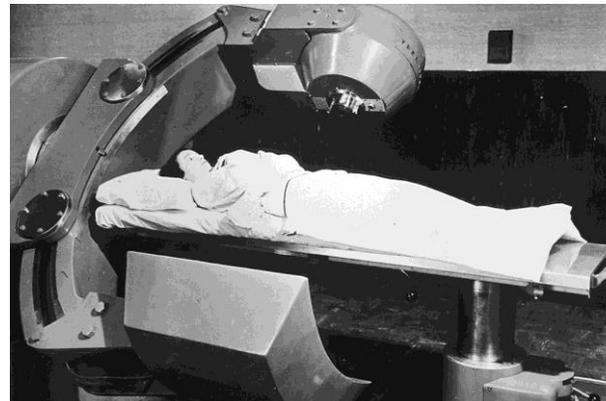


Fig. 9 a. Case 7. Before the treatment and 1 year after.



Cobalt accelerators



Yet, there is only so much that can be controlled using surgery and radiation

Chemical warfare: The origins of chemotherapy

NITROGEN MUSTARD THERAPY

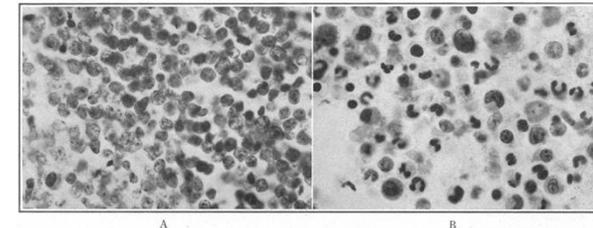
Use of Methyl-Bis(Beta-Chloroethyl)amine Hydrochloride and Tris(Beta-Chloroethyl)amine Hydrochloride for Hodgkin's Disease, Lymphosarcoma, Leukemia and Certain Allied and Miscellaneous Disorders

LOUIS S. GOODMAN, M.D., Salt Lake City
 MAXWELL M. WINTROBE, M.D., Salt Lake City
 WILLIAM DAMESHEK, M.D., Boston
 MORTON J. GOODMAN, M.D., Portland, Ore.
 MAJOR ALFRED GILMAN
 Medical Corps, Army of the United States
 and
 MARGARET T. McLENNAN, M.D., Salt Lake City

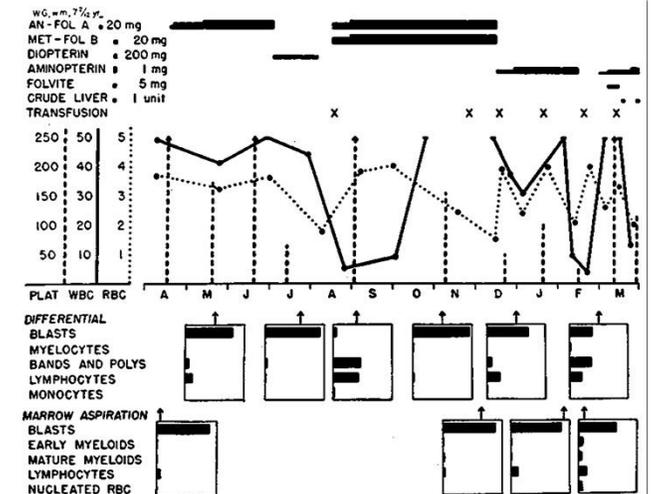


Fig. 1 (case 2).—Appearance in terminal lymphosarcoma in the radiation resistant stage four days after initiation of tris(beta-chloroethyl)amine hydrochloride therapy. Improvement in well-being, strength, appetite and temperature but no visible change in size of tumor masses.

Fig. 2 (case 2).—Eight days later and two days after the last dose. Complete disappearance of tumor masses in axillas, neck, jaw and thorax, with decided improvement in the patient's condition.



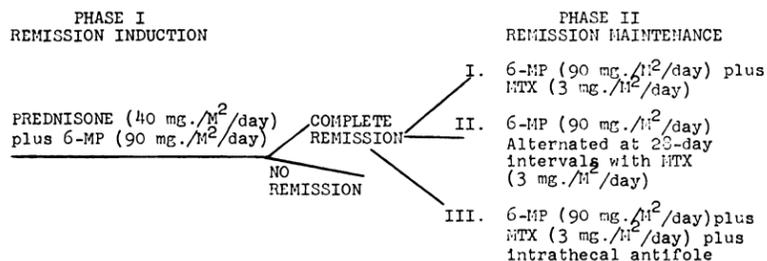
The occurrence of what he interpreted as an "acceleration phenomenon" in the leukemic process as seen in the marrow and viscera of children with acute leukemia treated by the injection of folic acid conjugates¹ — pteroyltriglutamic acid (teropterin) and pteroyldiglutamic acid (diopterin) — and an experience gained from studies on folic acid deficiency suggested to Farber that folic acid antagonists might be of value in the treatment of patients with acute leukemia.² Post-mortem studies of leukemic infiltrates of the bone marrow and viscera in patients treated with folic acid conjugates were regarded by Farber as evidences of an acceleration of the leukemic processes to a degree not encountered in his experience with some 200 post-mortem examinations on children with acute leukemia not so treated. It appeared worth while, therefore, to ascertain if this acceleration phenomenon could be employed to advantage either by radiation or nitrogen mustard therapy after pretreatment with folic acid conjugates or by the administration of antagonists to folic acid.² A series of folic acid antagonists was made available by Dr. Y. Subbarow and his colleagues.³⁻⁵ Farber et al. NEJM 1948



Combination chemotherapy cures pediatric leukemia and Hodgkin's lymphoma

COMBINATIONS OF ANTILEUKEMIC AGENTS

643



MTX Methotrexate
6-MP 6-Mercaptopurine

Fig. 1.—Experimental design.

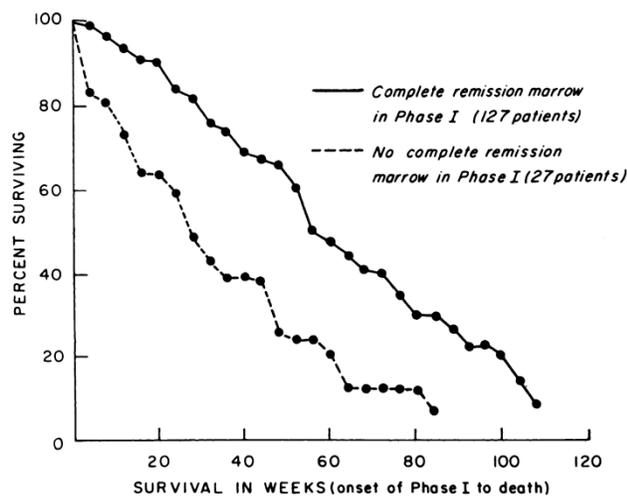


Fig. 5.—Effect of response in Phase I on survival.

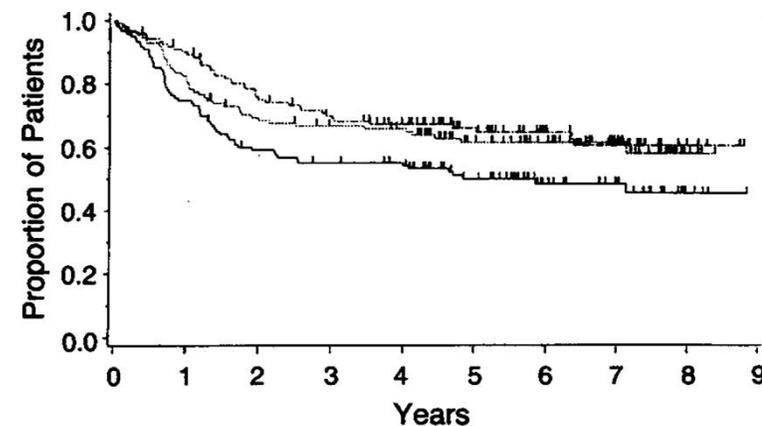
Emil Frei et al. Blood 1965

SCREENING DATA FROM THE CANCER CHEMOTHERAPY NATIONAL SERVICE CENTER SCREENING LABORATORIES. XLIII.

Saul A. Schepartz,¹ Betty J. Abbott,² and Joseph Letter³

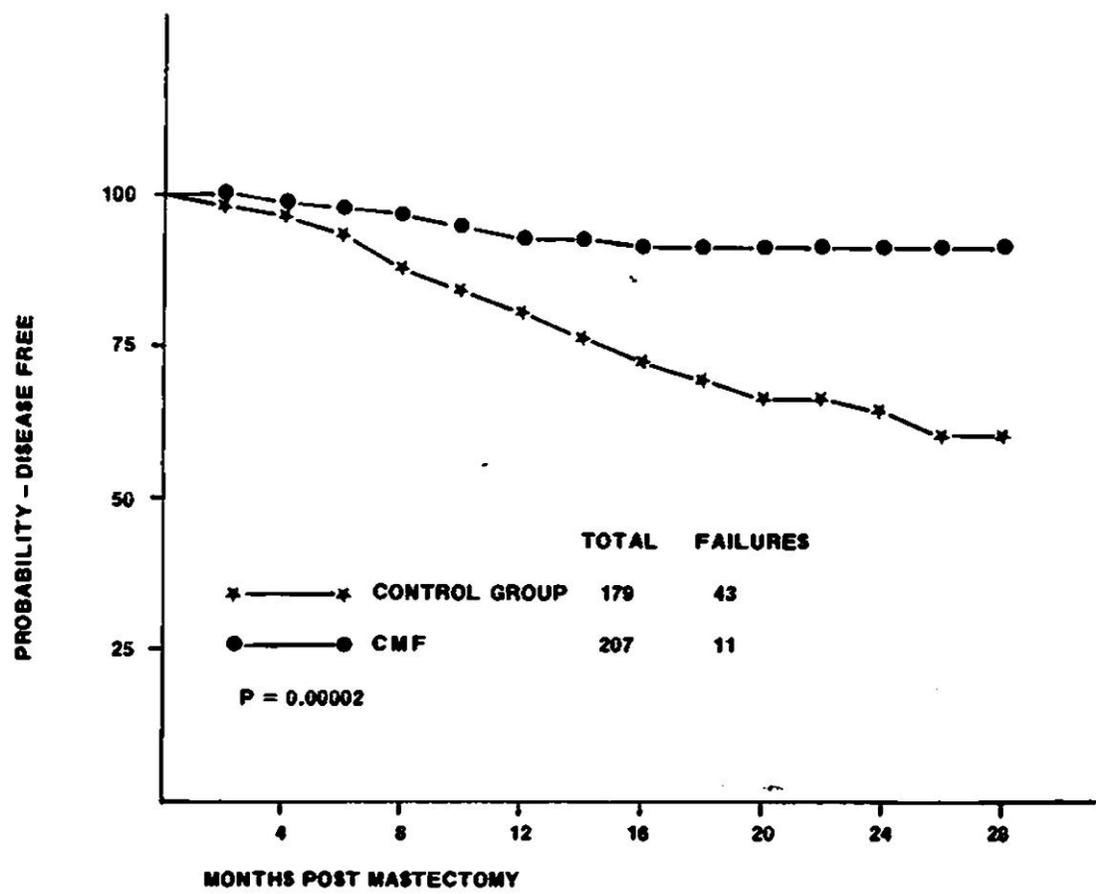
SUMMARY

Data are reported on 1592 synthetic compounds which were tested in the CCNSC primary screens. Almost all of the compounds were tested in Sarcoma 180, Adenocarcinoma 755, Leukemia 1210, and KB cells in culture; some tests were also carried out in Friend virus leukemia, Ehrlich ascites, Human epidermoid carcinoma HEp2, Lewis lung carcinoma, and Walker 256 (intramuscular). Data are reported only on compounds which have not demonstrated sufficient activity in these systems to warrant further investigation. The number of test systems in the screening program has been reduced; the reasons for the reduction are discussed.



Regimen	No. of Patients	No. (%) of Treatment Failures	Median Survival
— MOPP	123	62 (50)	4.84
..... ABVD	115	44 (38)	None
- - - MOPP-ABVD	123	43 (35)	None
All	361	149 (41)	—

Yet, chemotherapy acceptance was hard



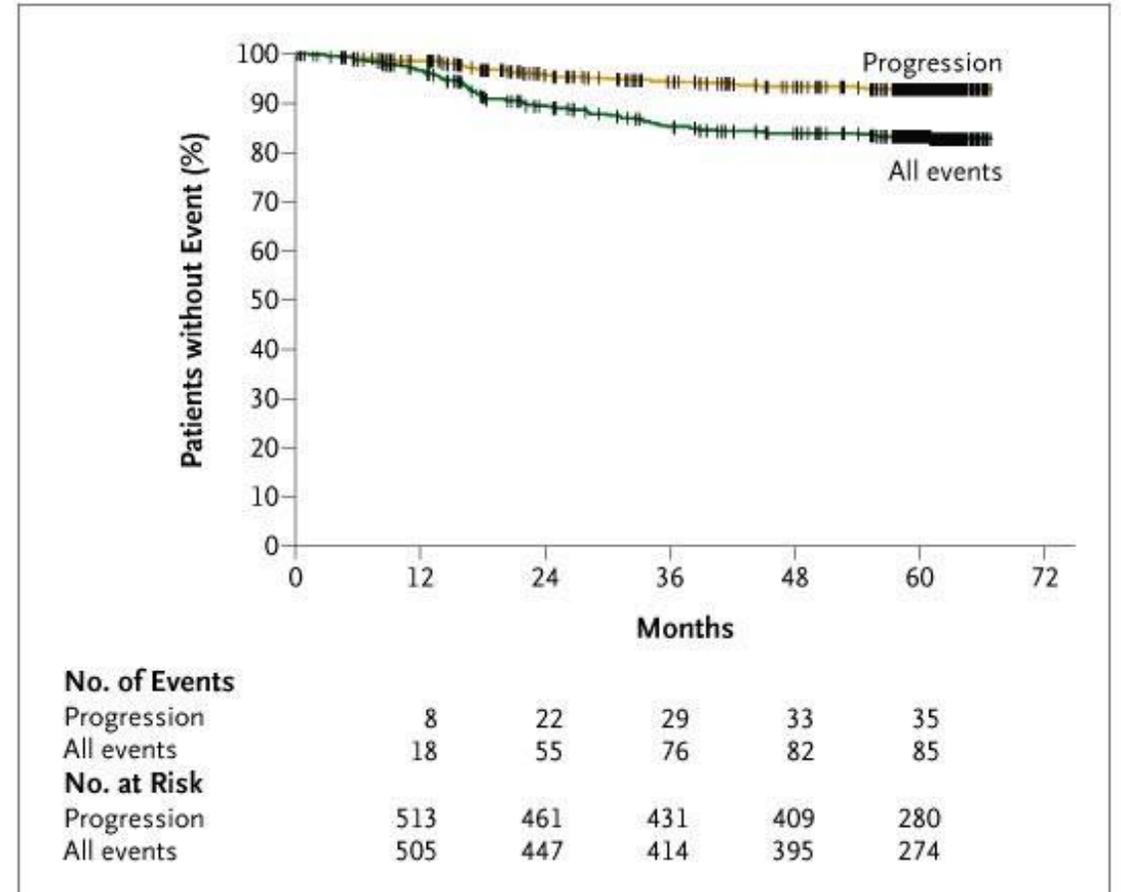
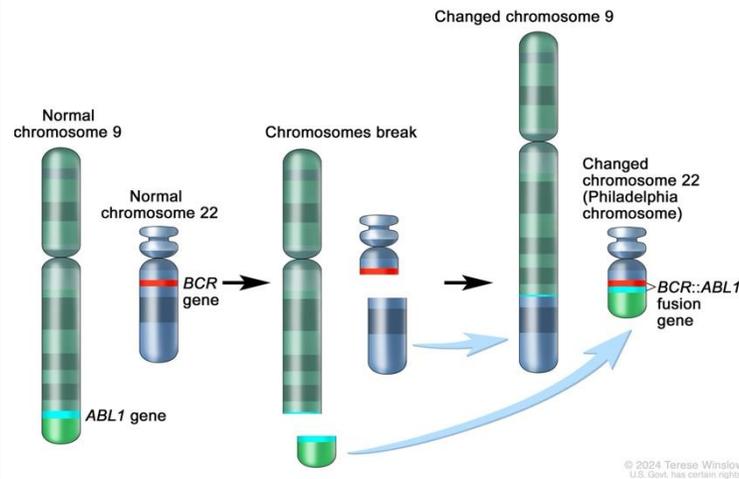
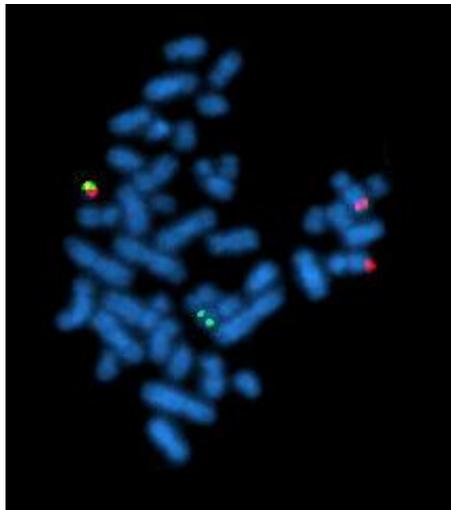
...developed by the NCI but was performed under contract with the Milan Cancer Institute, despite large populations of patients with operable breast cancer in the United States, because **no major U.S. center was willing to test combination chemotherapy as an adjuvant...**

The results of both studies were positive, and the race was on. By 1991, thanks to the **availability of multiple effective chemotherapeutic agents and hormone treatments, improved diagnostic tools for early diagnosis, and intelligently designed clinical trials, the rate of death from breast cancer began to fall, a trend that has continued.**

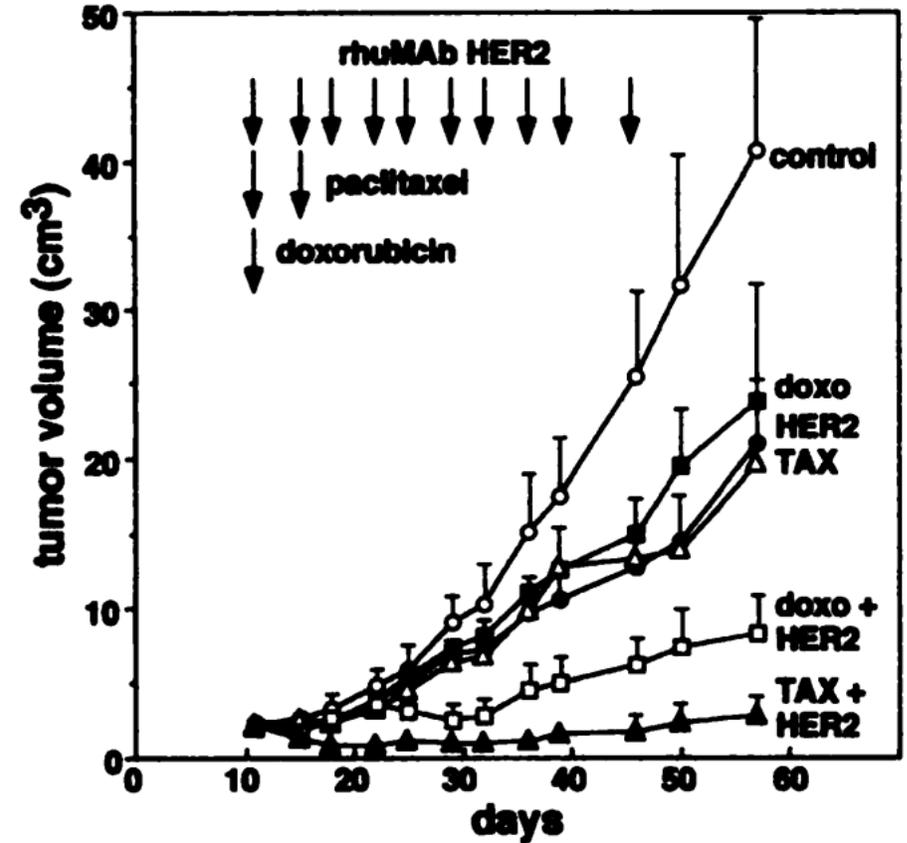
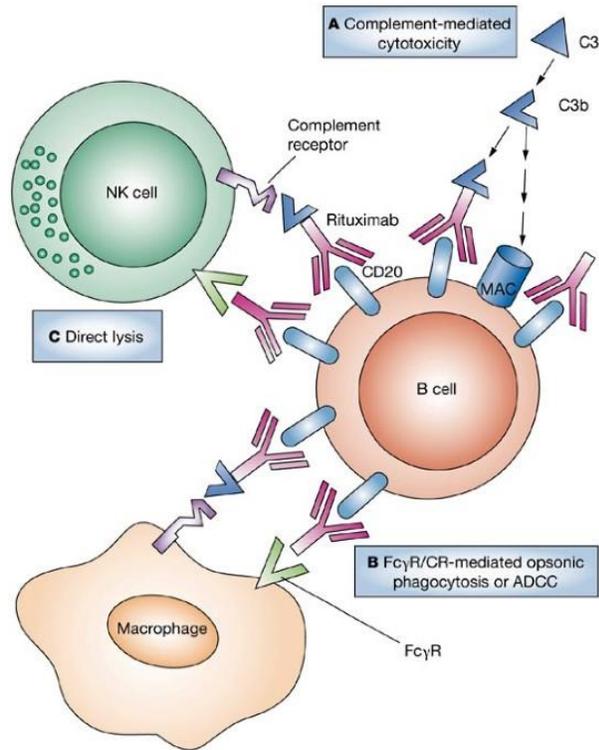
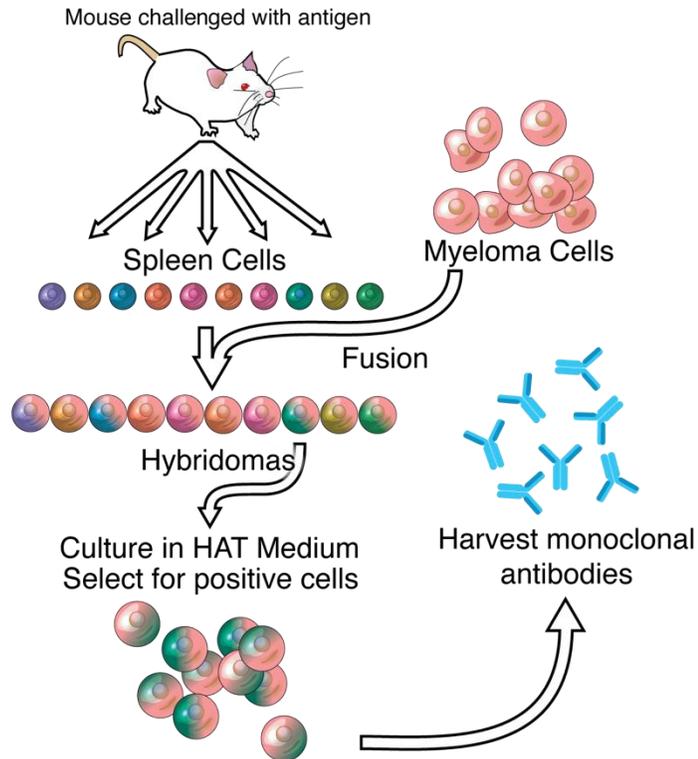
DeVita VT Jr, Rosenberg SA. Two hundred years of cancer research. N Engl J Med. 2012;366(23):2207-2214. doi:10.1056/NEJMra1204479

The new millennium: Molecular-directed targeted therapies

The sequencing of the human genome and the success of Imatinib in CML promised a new era in the personalized treatment of cancer



Hijacking B-cells to fight cancer: Monoclonal Antibodies

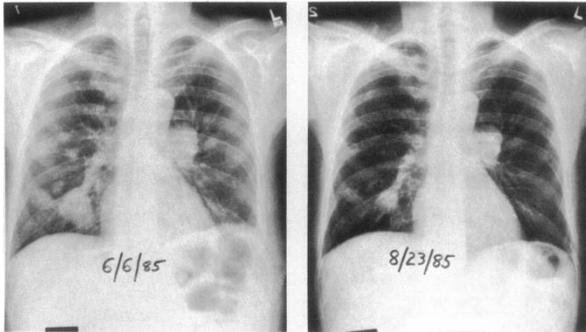


Hybridomas to produce monoclonal antibodies

Baelga et al. Cancer Research 1998

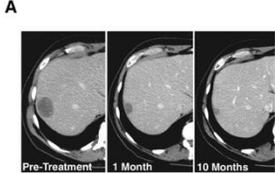
Calling a professional: Boosting the immune system to fight cancer

Recombinant IL2

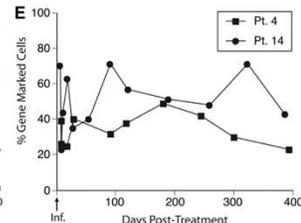
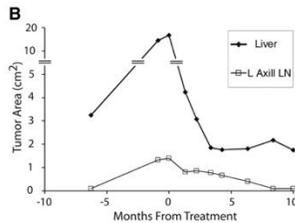


X-ray Films of Multiple Pulmonary Nodules (Metastatic from Renal-Cell Cancer) before (Left) and after (Right) Treatment (Patient 21).
Rosenberg et al. NEJM. 1985

CAR-T

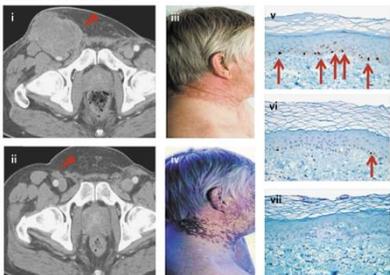


Morgan et al. Science. 2006



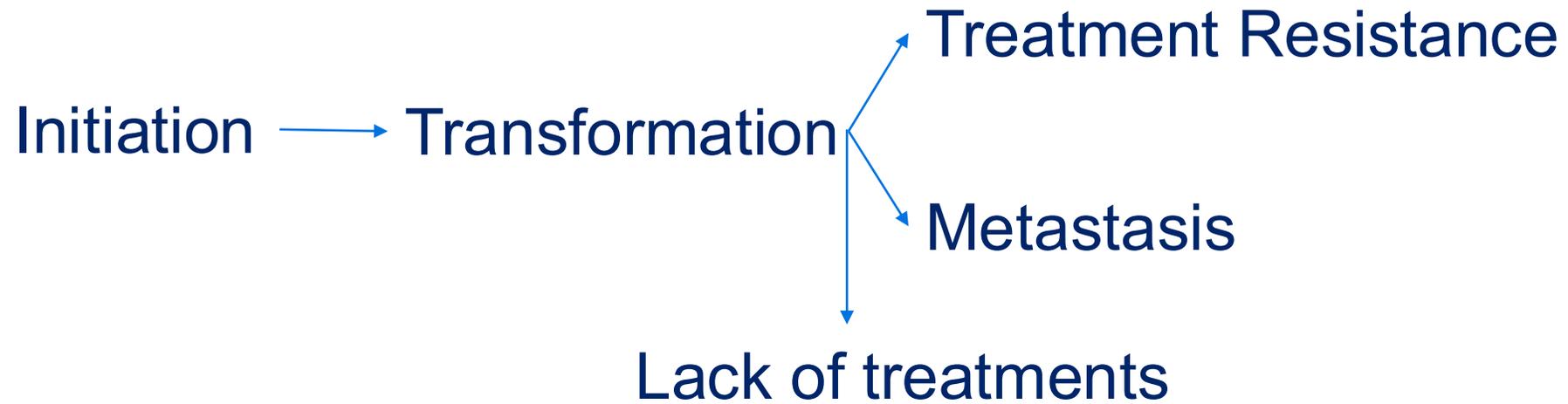
ICB (anti-PD-1 antibodies)

C Patient with Melanoma

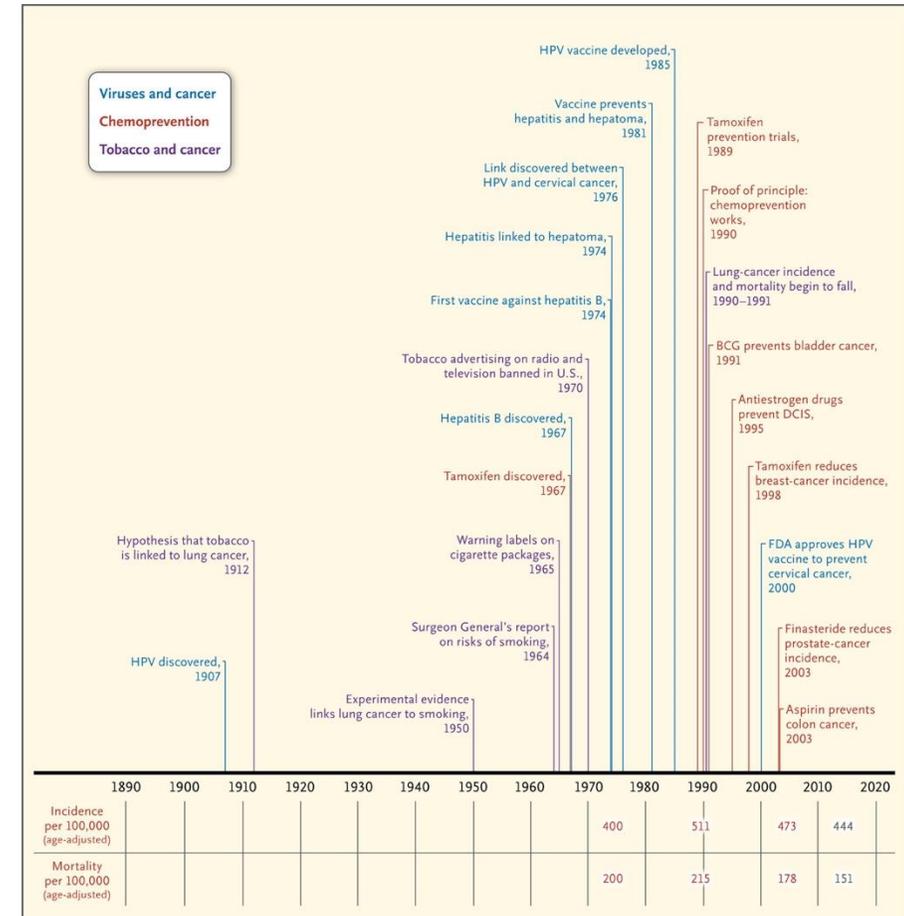
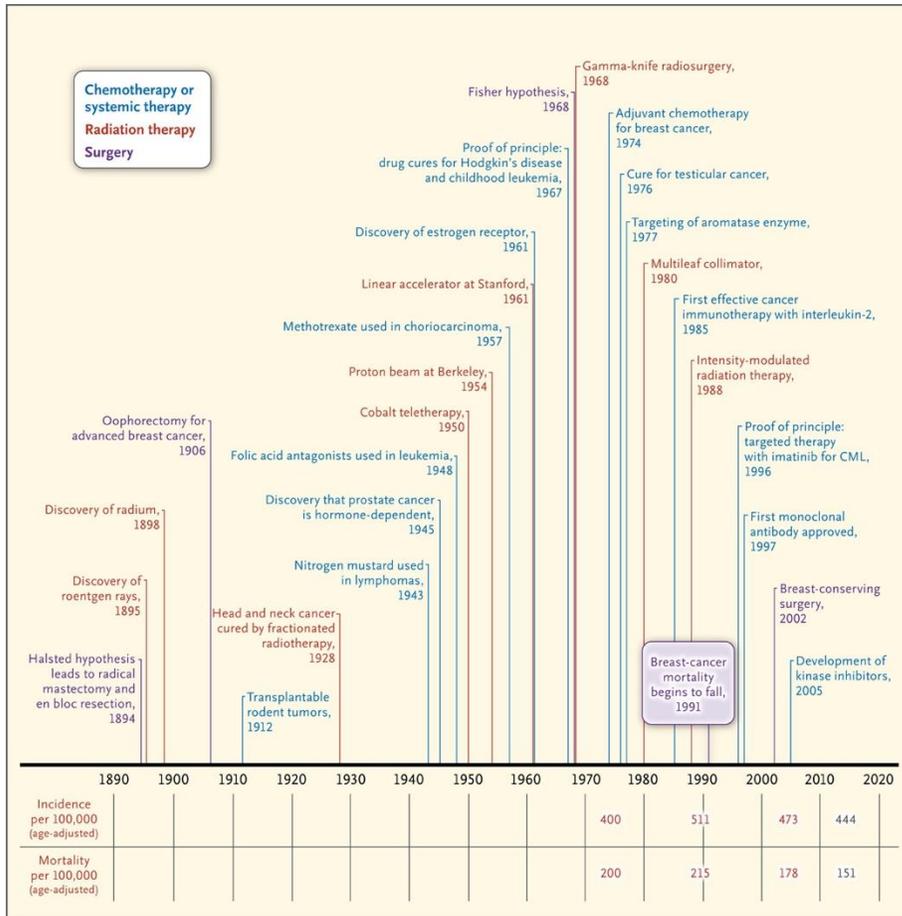


	Class of immunotherapy			
	Oncolytic virus	Anti-CTLA4	Anti-PD1	Adoptive cell therapy
Mechanism of action	Lysed tumour cell → DC	Cytolytic CD8 ⁺ T cell → CTLA4	Progenitor PD1 ^{low} CD8 ⁺ T cell → PD1	CAR T cell
Periphery	Prime new T cells (via tumour lysis)	Enhance T cell priming	Enhance T cell differentiation	<ul style="list-style-type: none"> Bypass priming Augment immunity
Metabolic barriers	Glucose → Glycolysis	CD80/CD86 → CTLA4 → Glycolysis	PDL1 → PD1 → FAO → Glycolysis	<ul style="list-style-type: none"> Hyperglycaemic media Reduced tumour control
Mechanism of action	Lyse tumour cells and inflame the TME	Inhibit T _{reg} cells	Induce differentiation	Infiltrate and lyse tumour cells
TME	<ul style="list-style-type: none"> Low O₂ level vs Sufficient O₂ Hypoxia inhibits (some) viral replication and spread Hypoxia prevents infiltration 	<ul style="list-style-type: none"> Lactate → T_{reg} cell Glycolytic tumour High lactic acid levels can support T_{reg} cell function Suppress glycolysis Upregulation of OXPHOS 	<ul style="list-style-type: none"> Low O₂ and αKG levels O₂, αKG needed for epigenetic remodelling 	<ul style="list-style-type: none"> Glucose Competition for glucose within the TME Hypoxia prevents infiltration

Current problems of cancer research



Prevention can be as effective or more than treatment to improve cancer-related outcomes

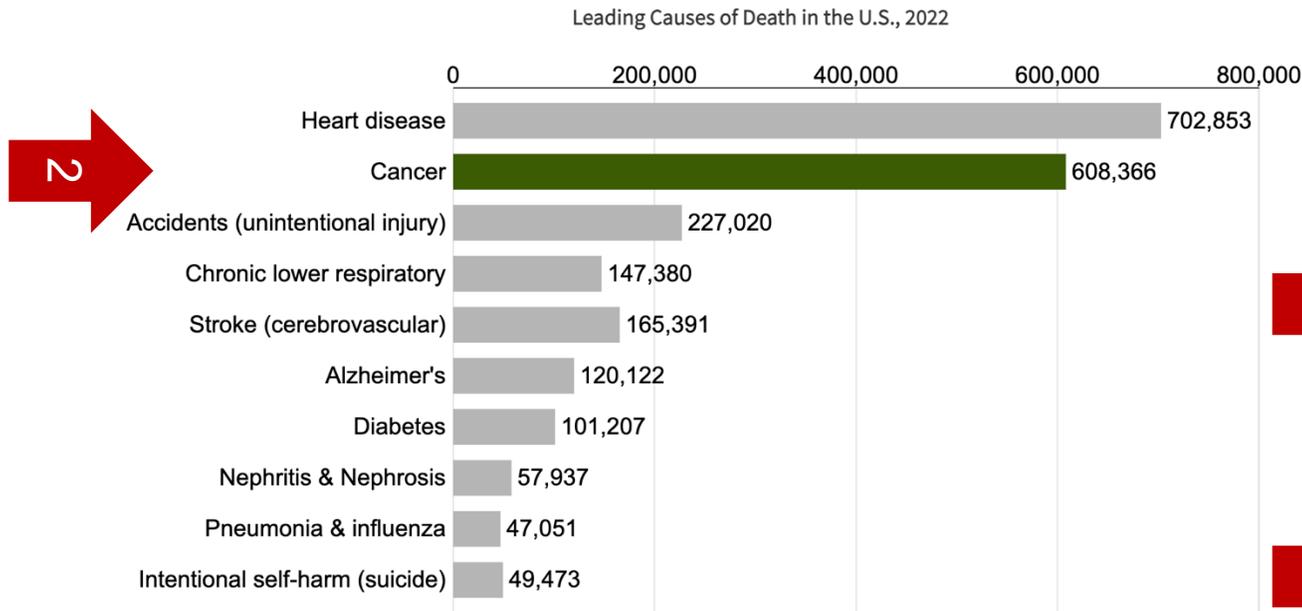


DeVita VT Jr, Rosenberg SA. Two hundred years of cancer research. N Engl J Med. 2012;366(23):2207-2214. doi:10.1056/NEJMrat1204479

The burden of cancer



Cancer 101: Why do we study cancer?

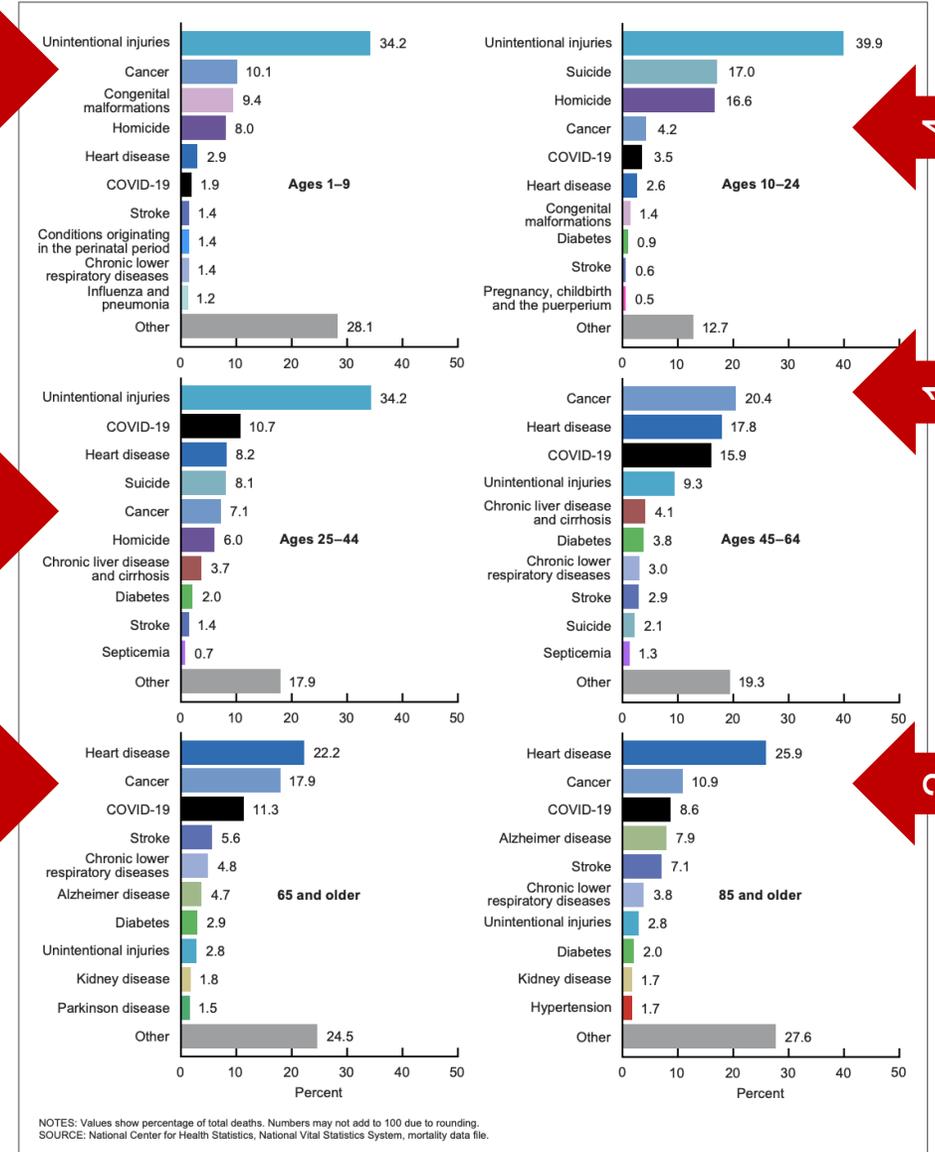


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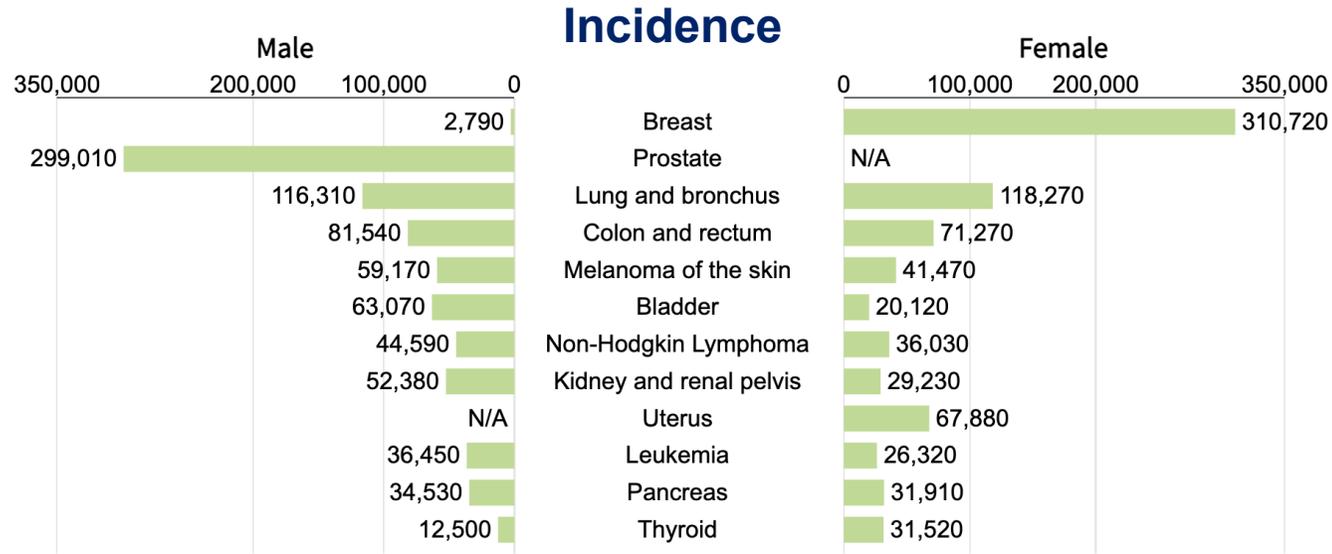


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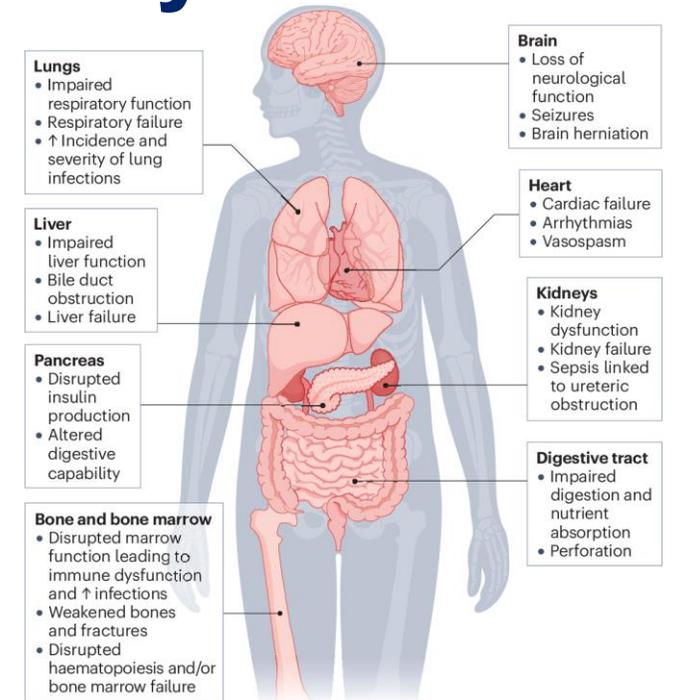
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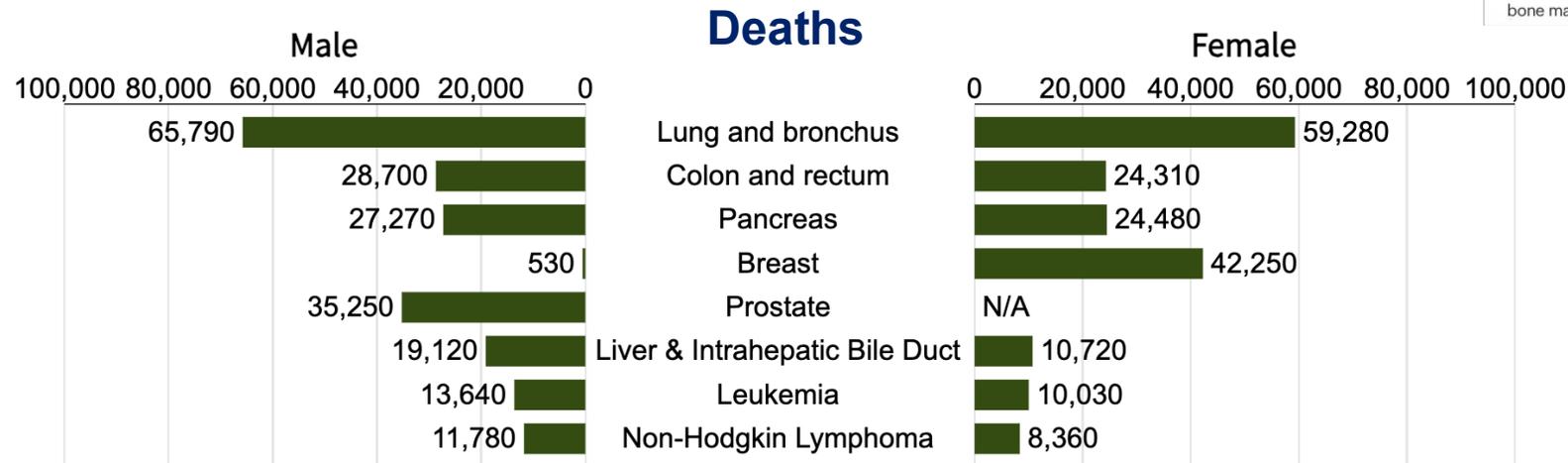
Cancer 101: Cancer diagnosis and mortality



Source: Cancer Facts & Figures 2024, American Cancer Society (ACS), Atlanta, Georgia, 2024.



Boire, A., Burke, K., Cox, T.R. *et al.* Why do patients with cancer die?. *Nat Rev Cancer* 24, 578–589 (2024).



Source: Cancer Facts & Figures 2024, American Cancer Society (ACS), Atlanta, Georgia, 2024.

2 types of treatment:

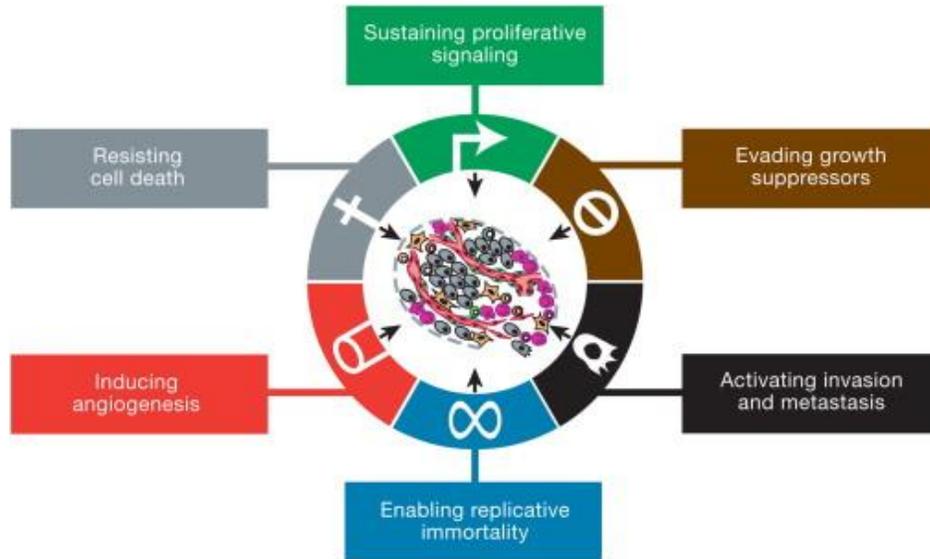
- Local
- Systemic

The burden of cancer

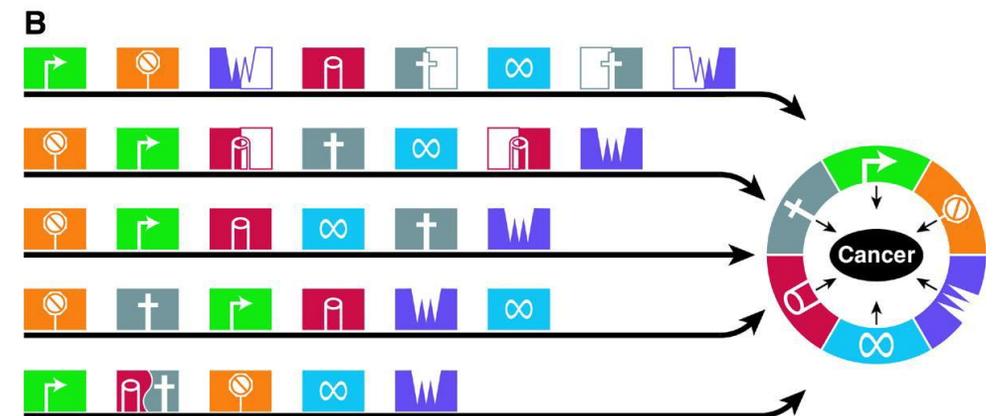


Cancer 101: What is a cancer cell?

“Cells”: Basic unit of life

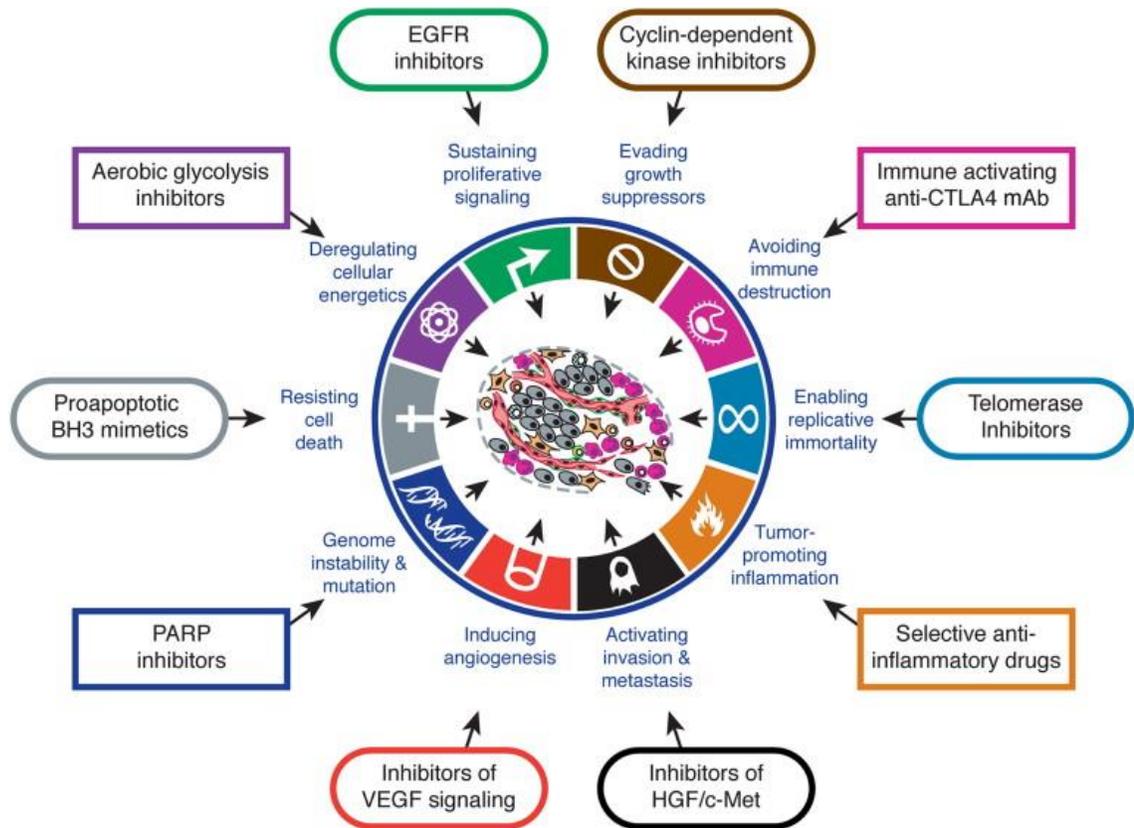


A	Component	Acquired Capability	Example of Mechanism
		Self-sufficiency in growth signals	Activate H-Ras oncogene
		Insensitivity to anti-growth signals	Lose retinoblastoma suppressor
		Evading apoptosis	Produce IGF survival factors
		Limitless replicative potential	Turn on telomerase
		Sustained angiogenesis	Produce VEGF inducer
		Tissue invasion & metastasis	Inactivate E-cadherin

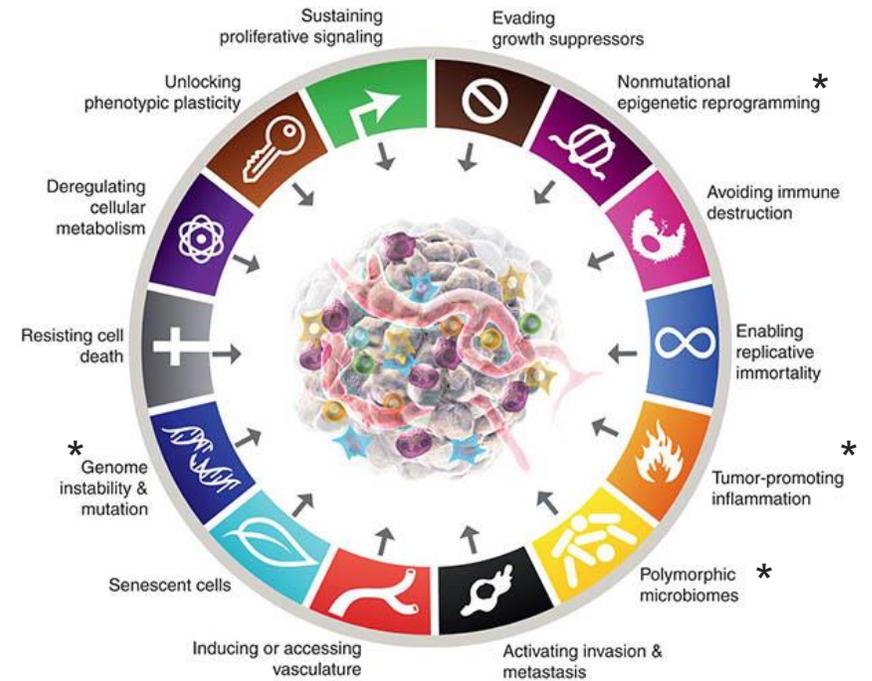


Cancer 101: What is a cancer cell?

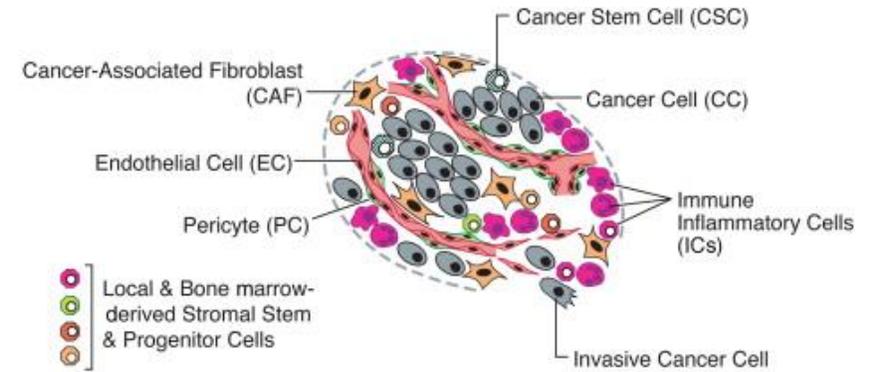
“Cells”: Basic unit of life



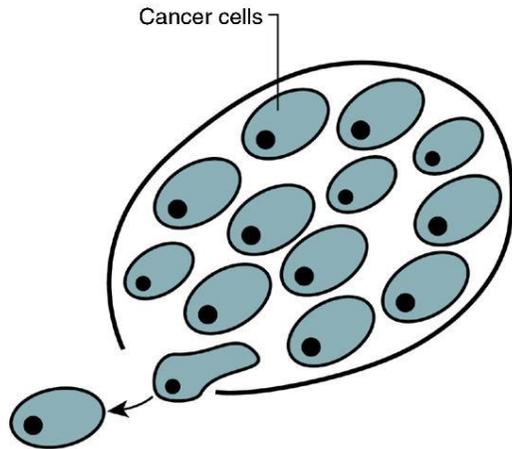
Cancer Hallmarks and Enabling Characteristics*



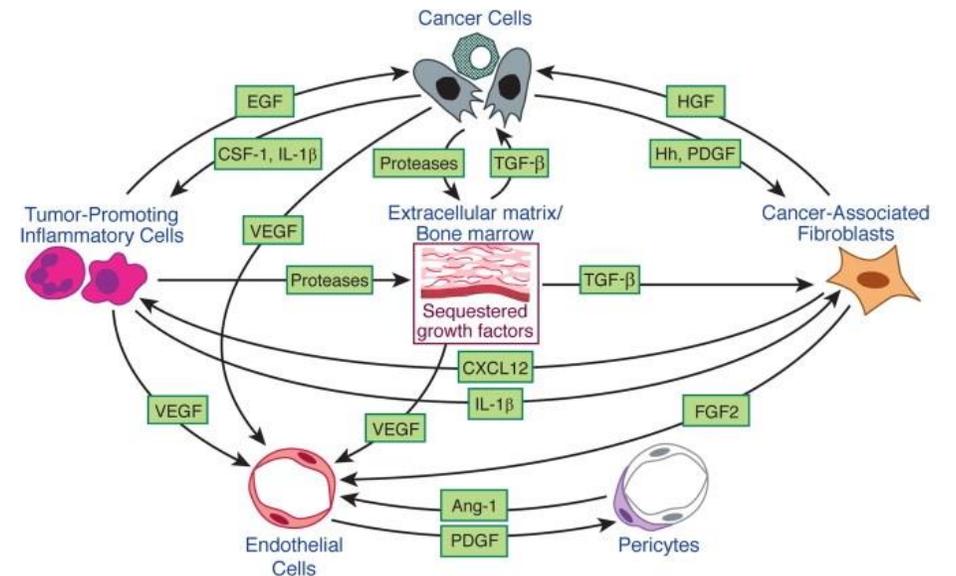
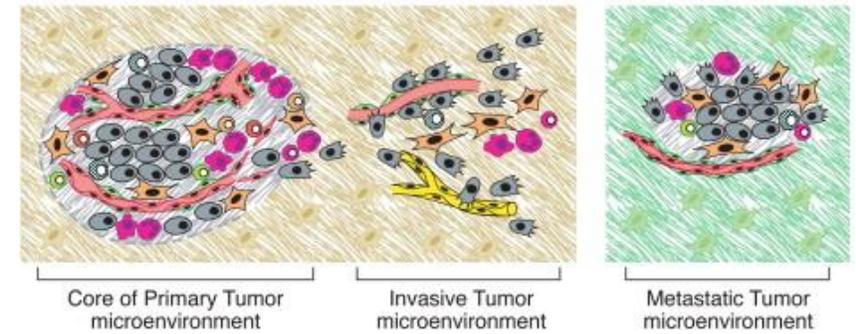
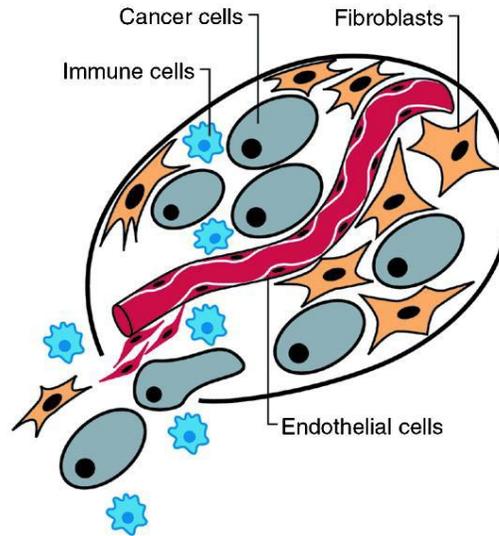
The importance of context



The Reductionist View

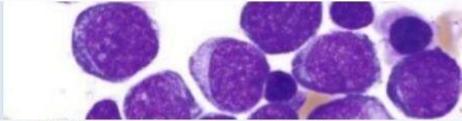
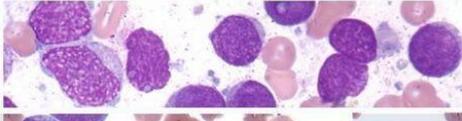
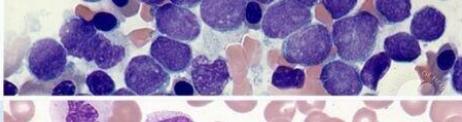
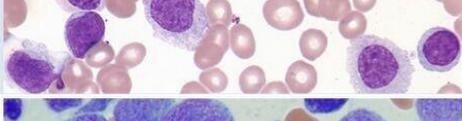
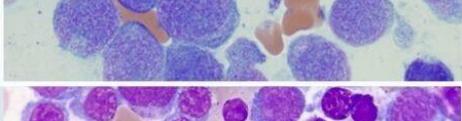
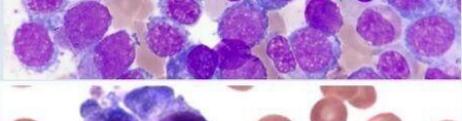


A Heterotypic Cell Biology



Historical classification of blood cancer

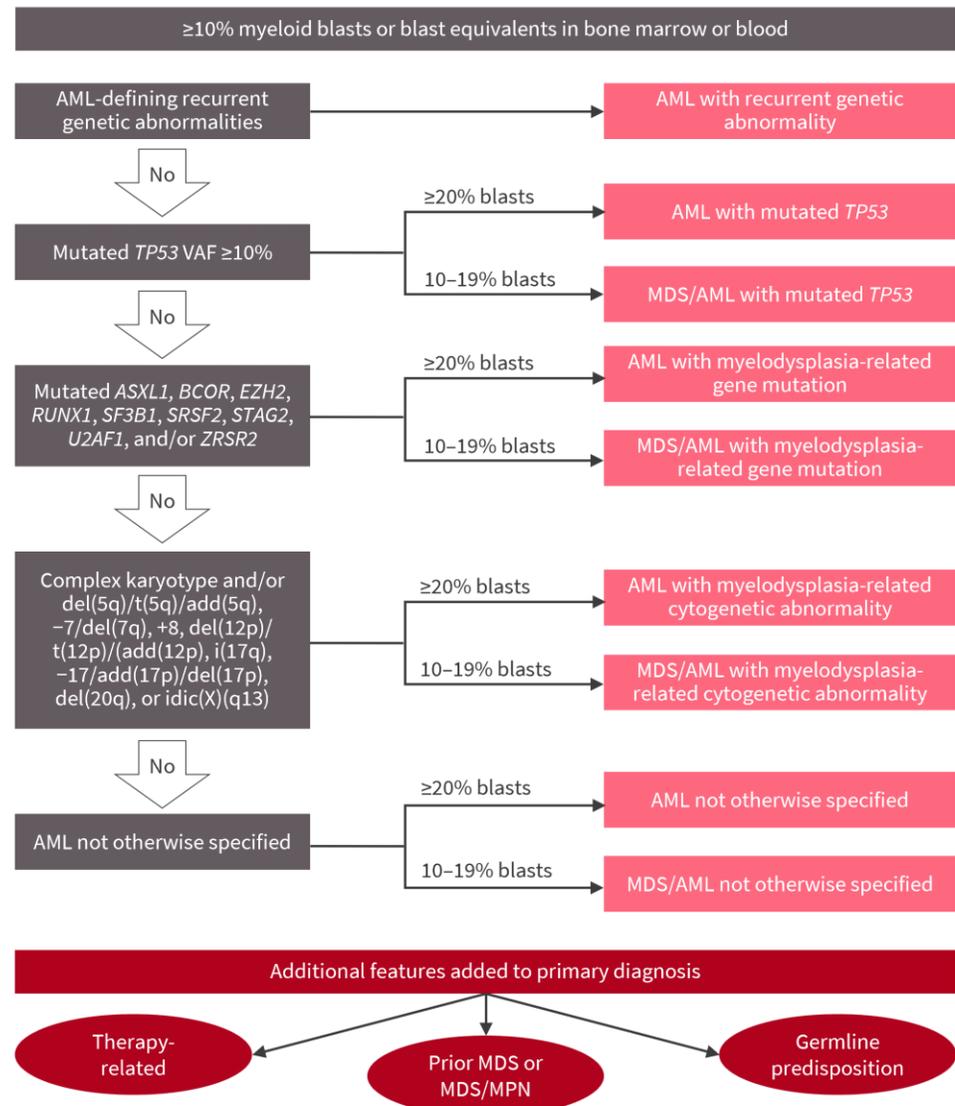
MORPHOLOGY-based: How things look?

FAB CLASSIFICATION SYSTEM OF ACUTE MYELOID LEUKAEMIA		
M0	AML with minimal differentiation	
M1	AML without maturation	
M2	AML with maturation	
M3	Acute promyelocytic leukaemia	
M4	Acute myelomonocytic leukaemia	
M5	Acute monoblastic and monocytic leukaemia	
M6	Pure erythroid leukaemia	
M7	Acute megakaryoblastic leukemia	

WWW.BLOOD-ACADEMY.COM

Current classification of blood cancer

MOLECULAR-based: What genetic abnormalities do you carry?



Thanks for your attention!

Any questions?



Memorial Sloan Kettering
Cancer Center