Cancer Bio Course 2025

Session 2: Introduction to cancer biology

Bridge and Engage Scholars

August 13th, 2025

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

Course structure

In-person activities:

- Session 1 – Introduction to course and basic techniques applied in basic cancer research
  - **Explanation of the question under research** - *why on earth did they decide to do this?*
  - **Discussion figure by figure –** *is this paper not as good as authors think?:*
    - What is the point of each figure/panel?
    - Are there any missing experimental conditions?
    - Are results interpretable?
    - Do the results support the conclusions by the authors?
    - Would you have done anything differently?
    - Are there any missing experiments?
    - What are the limitations of the work?
    - What experiments could be done as a follow-up to the paper?
- Session 2 – Paper discussion
- Session 3 – Paper discussion
- Session 4 – Paper discussion

+ Presentations!!

- Session 5 – Guided live research activity


Cancer Cell
Article

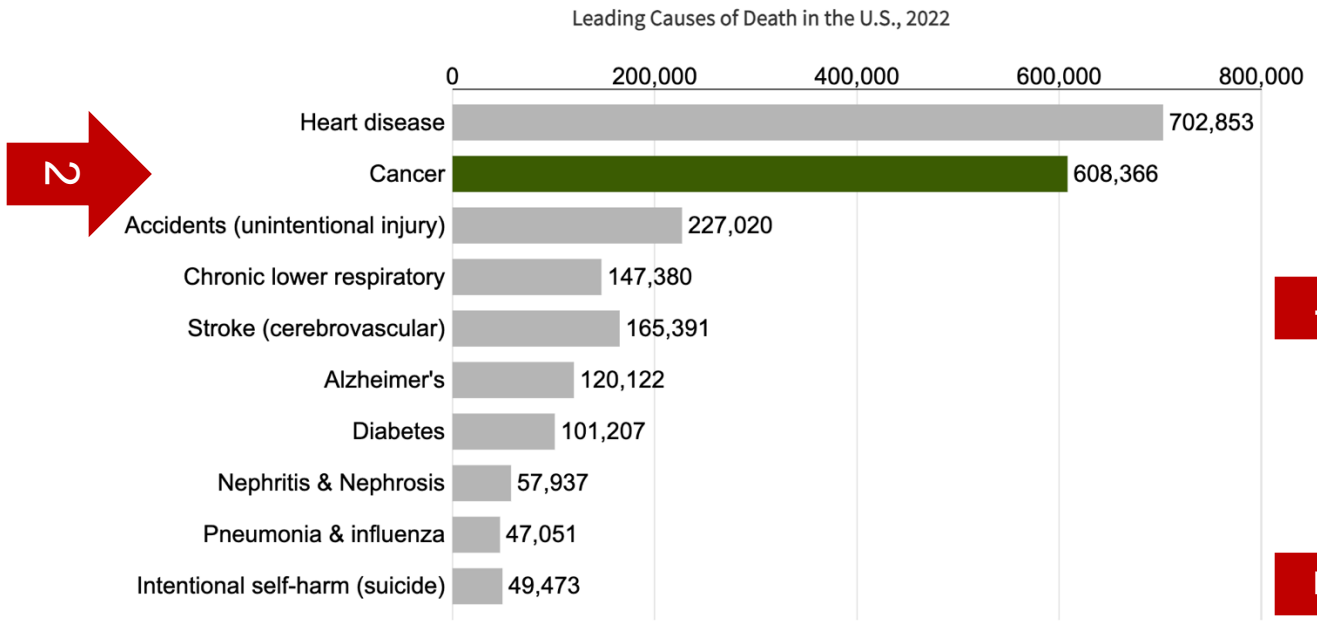
The Genomic Landscape of Endocrine-Resistant Advanced Breast Cancers


Article

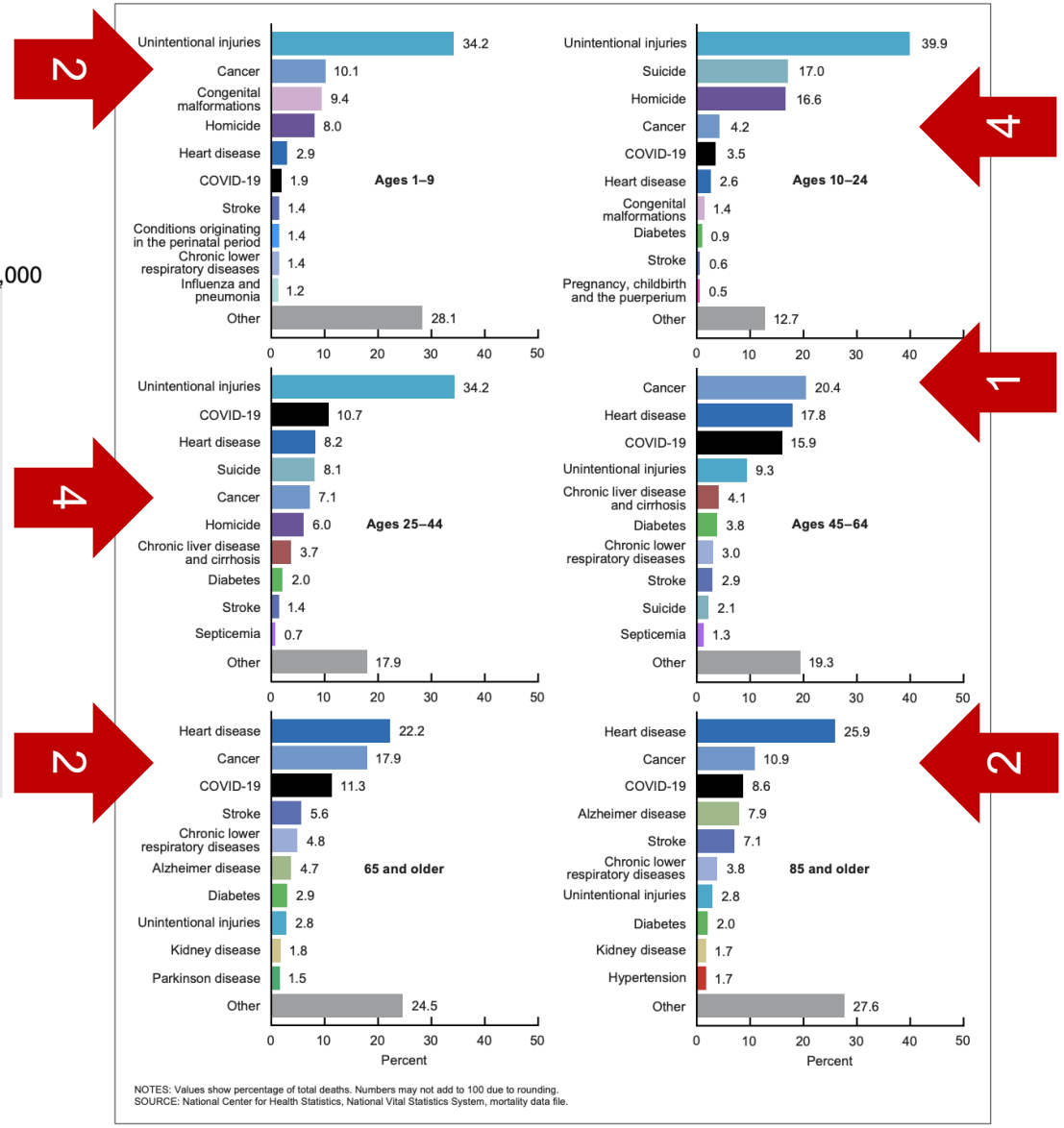
Lung adenocarcinoma promotion by air pollutants

Dealing with cancer

Cancer 101: Why do we study cancer?



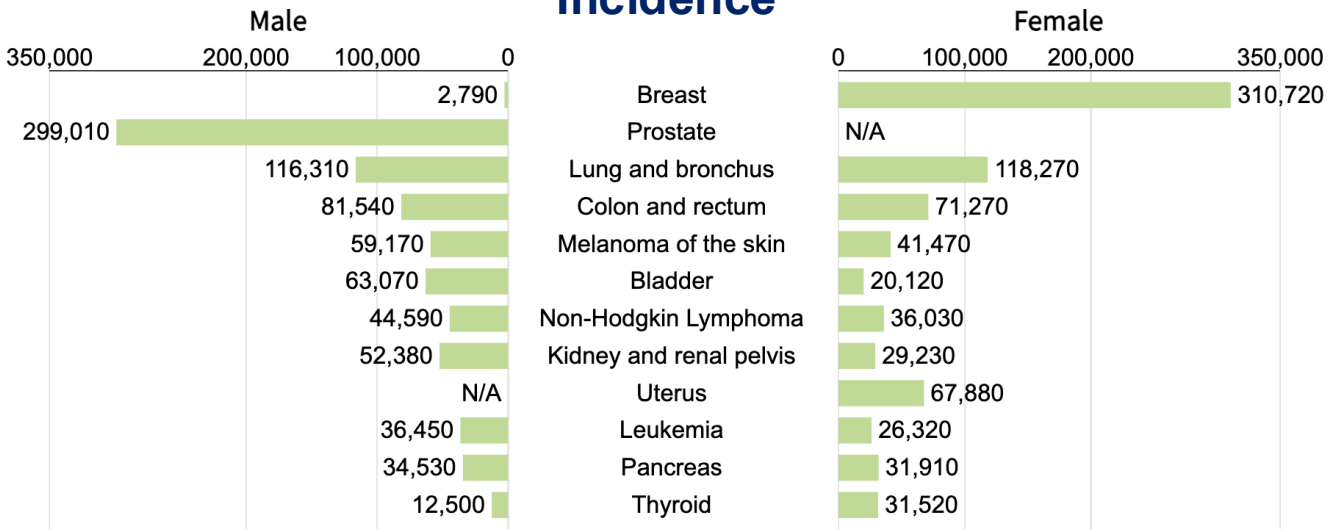
NCHS Data Brief, Number 492, December 2023



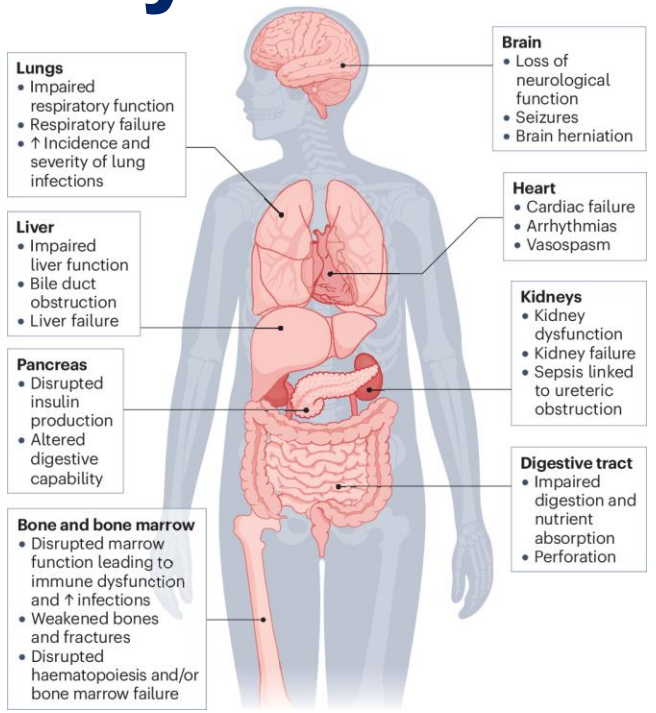
National Vital Statistics Reports Volume 73, Number 4 April 8, 2024 Death Leading Causes for 2021

Cancer 101: Cancer diagnosis and mortality

Incidence

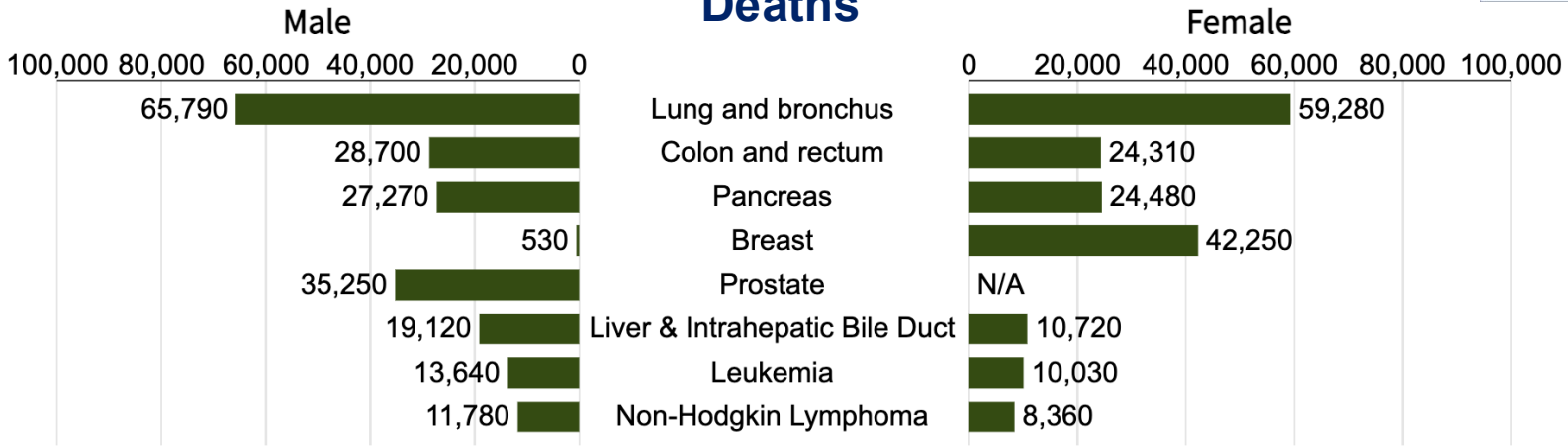


Source: Cancer Facts & Figures 2024, American Cancer Society (ACS), Atlanta, Georgia, 2024.



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

Deaths



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

2 types of treatment:
- Local
- Systemic

Surgery, the first cancer treatment

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

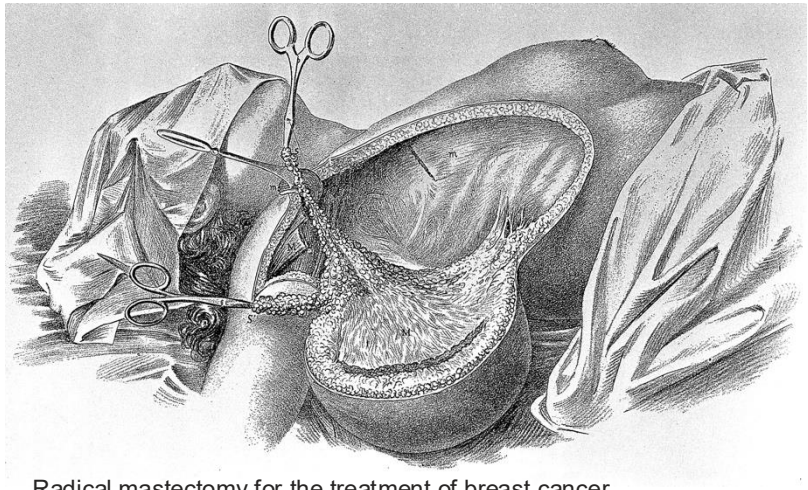
Asepsis

Antisepsis

Anesthesia

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

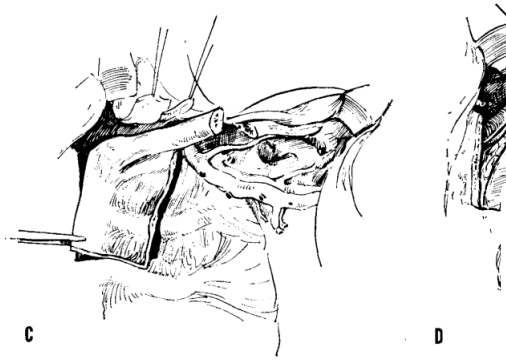
"In God we trust, all others must have data." Bernard Fisher, M.D.



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



C 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.

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

Experimental evidence in support of the dormant tumor cell

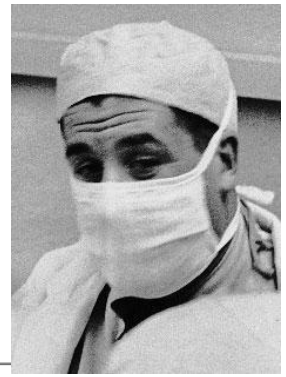
B FISHER, E R FISHER

PMID: 13823184 DOI: 10.1126/science.130.3380.918

Abstract

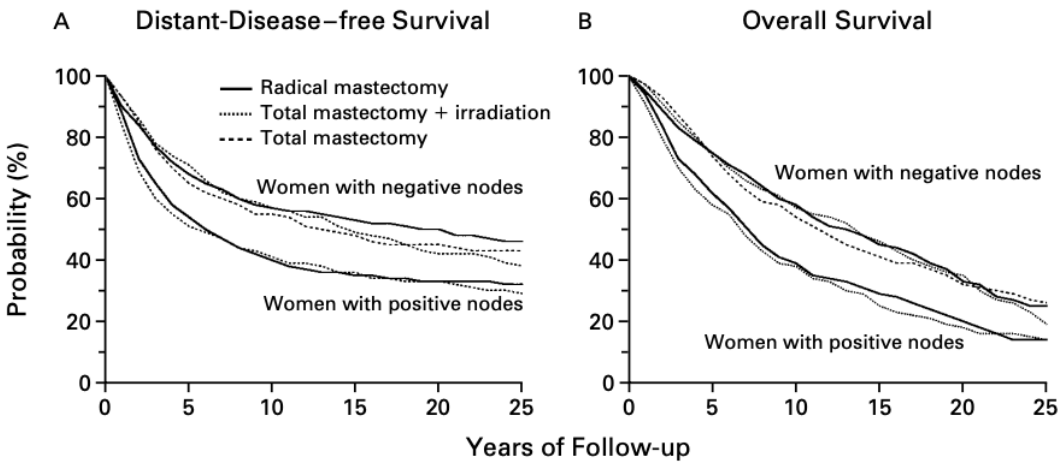
When rats were injected intraportally with as few as 50 Walker-256 carcinosarcoma cells aarcoma cells and then examined 5 months later for hepatic tumor growth, none was evident. If, however, 3 months after injection the rats were subjected to repeated laparotomy and liver examination at 7-day intervals,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

RADICAL VERSUS TOTAL MASTECTOMY

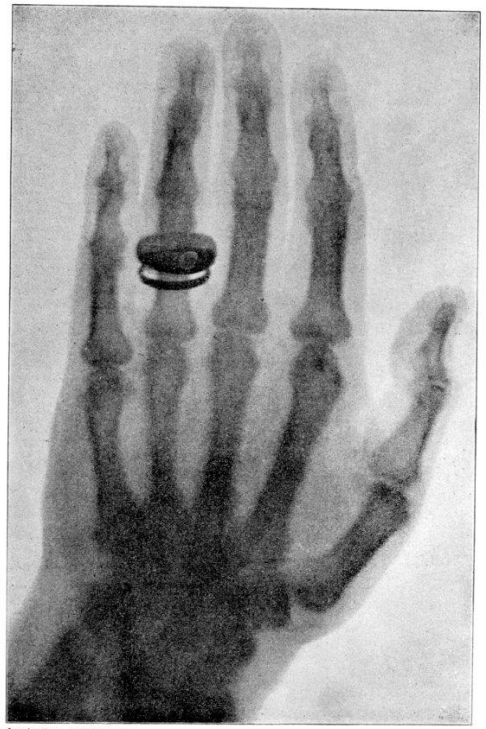


TWENTY-FIVE-YEAR FOLLOW-UP OF A RANDOMIZED TRIAL COMPARING RADICAL MASTECTOMY, TOTAL MASTECTOMY, AND TOTAL MASTECTOMY FOLLOWED BY IRRADIATION

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.

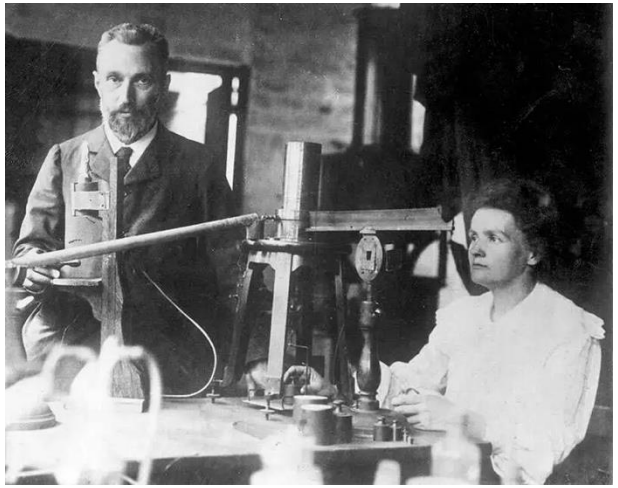


Second generation cancer treatments: Radiation therapy

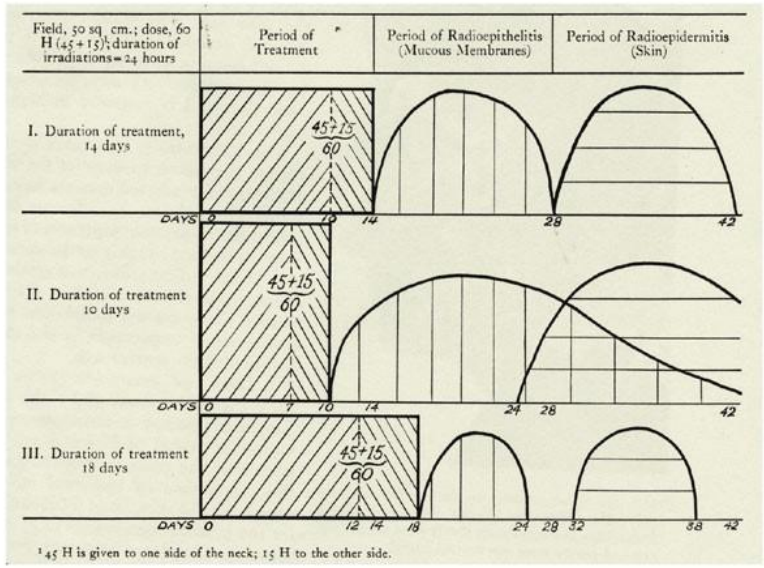


Josef Albert, München, repr.

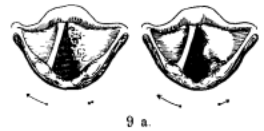
Hand des Anatomen Geheimrath von Kölliker.
Im Physikal. Institut der Universität Würzburg
mit X-Strahlen aufgenommen
von Professor Dr. W. C. Röntgen.



Marie and Pierre Curie discover Radium in 1898



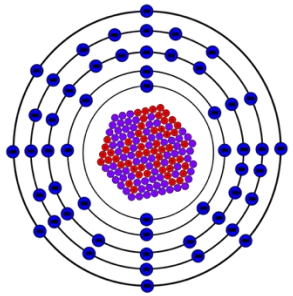
In 1928, head and neck cancers could be cured by fractionated radiation treatments

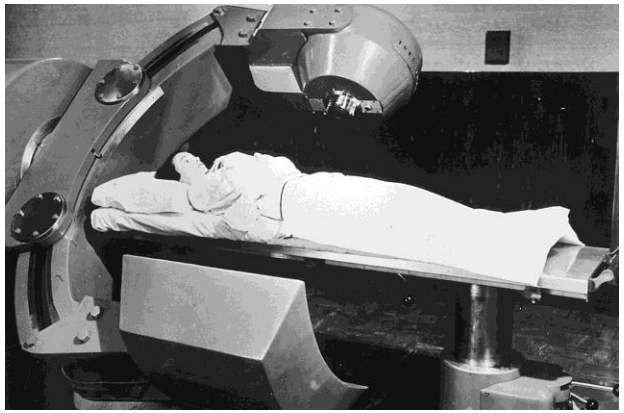


9 a.

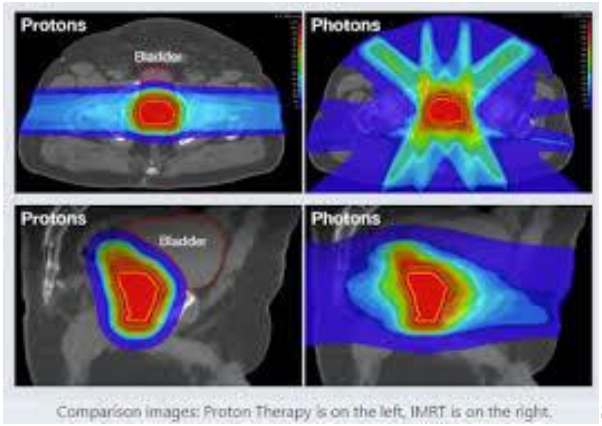
Fig. 9 a. Case 7. Before the treatment and 1 year after.

I-131



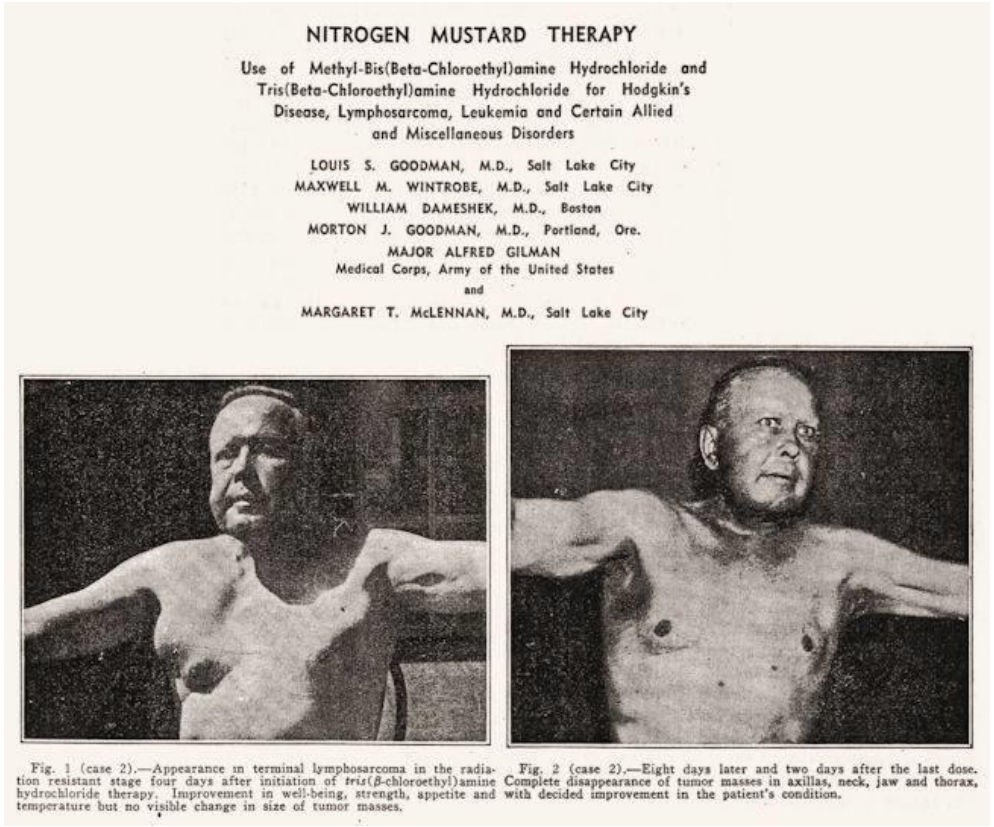


Cobalt accelerators



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

Chemical warfare: The origins of chemotherapy



NITROGEN MUSTARD THERAPY

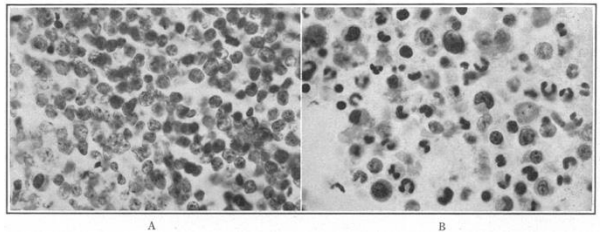
Use of Methyl-Bis(Beta-Chloroethyl)amine Hydrochloride and Tris(Beta-Chloroethyl)amine Hydrochloride for Hodgkin's Disease, Lymphosarcoma, Leukemia and Certain Allied and Miscellaneous Disorders

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

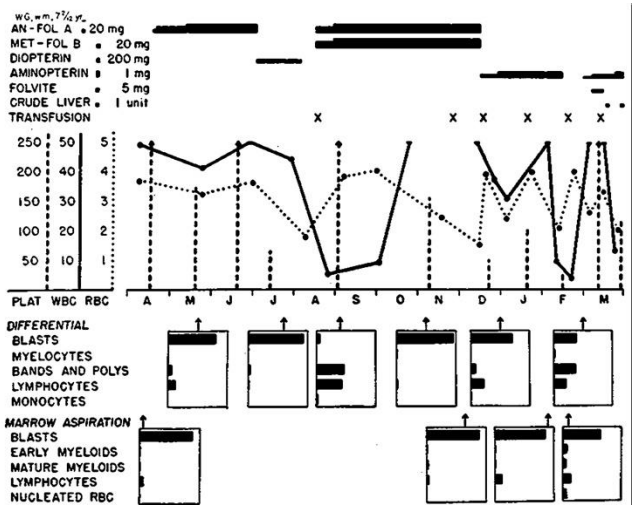
Fig. 1 (case 2).—Appearance in terminal lymphosarcoma in the radiation resistant stage four days after initiation of *tris*(β-chloroethyl)amine hydrochloride therapy. Improvement in well-being, strength, appetite and temperature but no visible change in size of tumor masses.

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 conjugates**[1] — 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**



A B



Combination chemotherapy cures pediatric leukemia and Hodgkin's lymphoma

COMBINATIONS OF ANTILEUKEMIC AGENTS 643

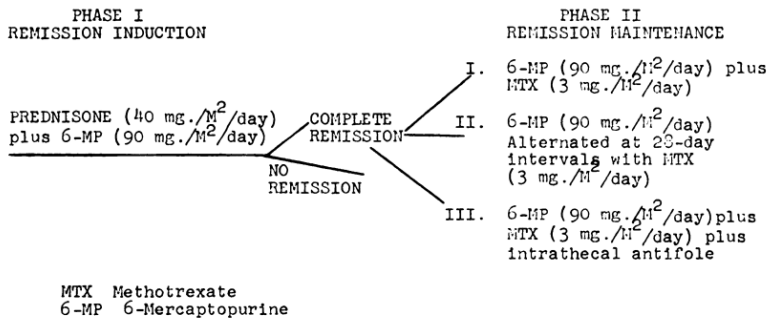


Fig. 1.—Experimental design.

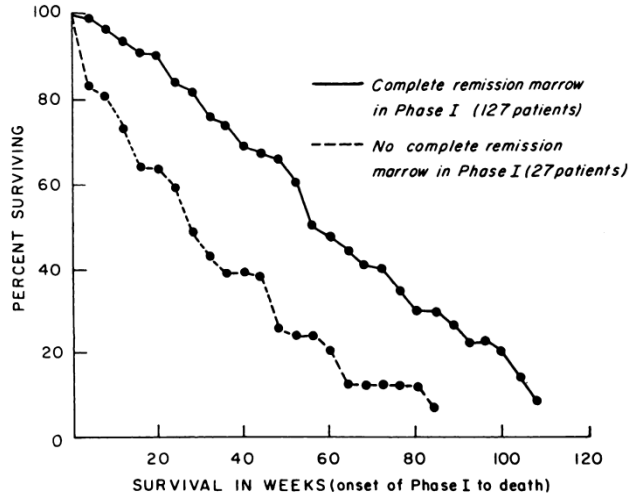


Fig. 5.—Effect of response in Phase I on survival.

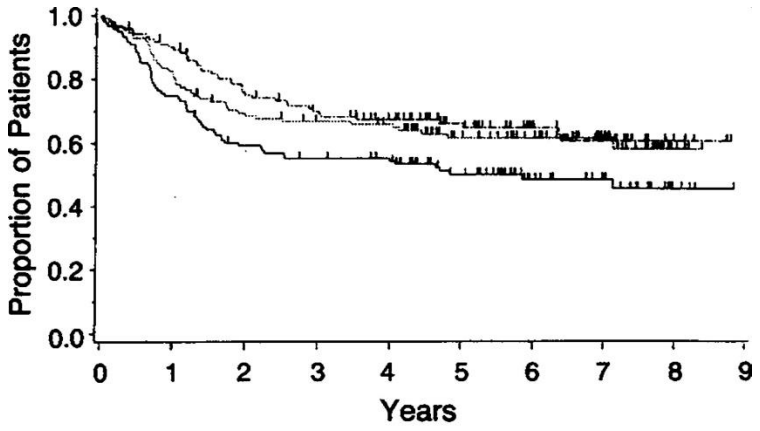
Emil Frei et al. Blood 1965

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

Saul A. Schepartz,[1] Betty J. Abbott,[2] and Joseph Leiter[3]

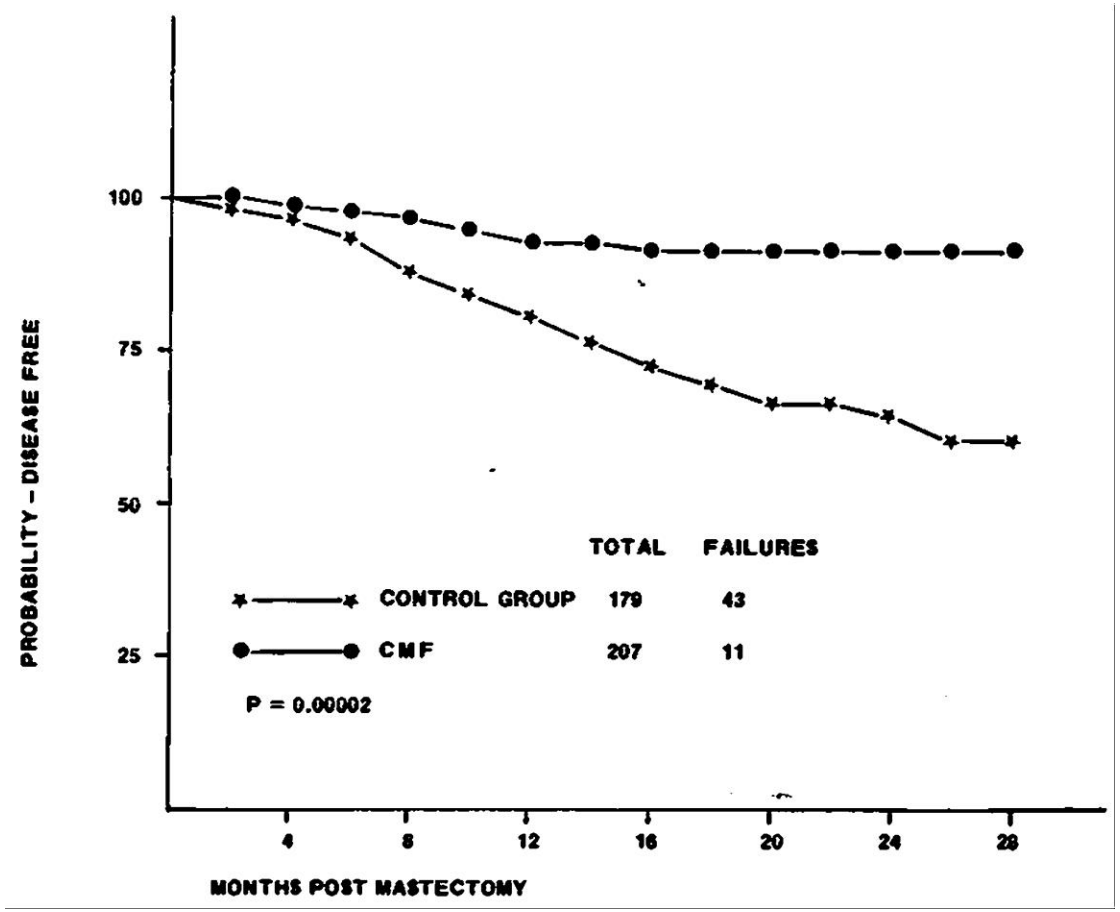
SUMMARY

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



Bonadonna et al. 1976 NEJM

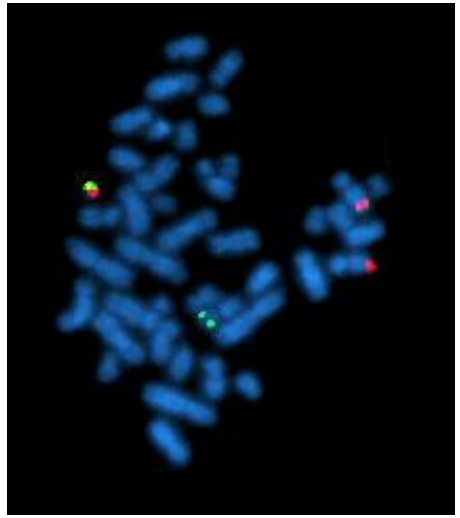
…developed by the NCI but was performed under contract with the Milan Cancer Institute, despite large populations of patients with operable breast cancer in the United States, because **no major U.S. center was willing to test combination chemotherapy as an adjuvant**…

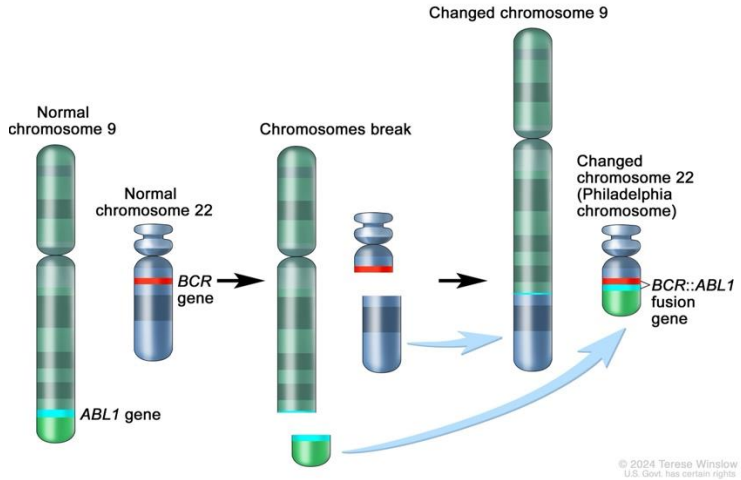
The results of both studies were positive, and the race was on. By 1991, thanks to the **availability of multiple effective chemotherapeutic agents and hormone treatments, improved diagnostic tools for early diagnosis, and intelligently designed clinical trials**, the **rate of death from breast cancer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

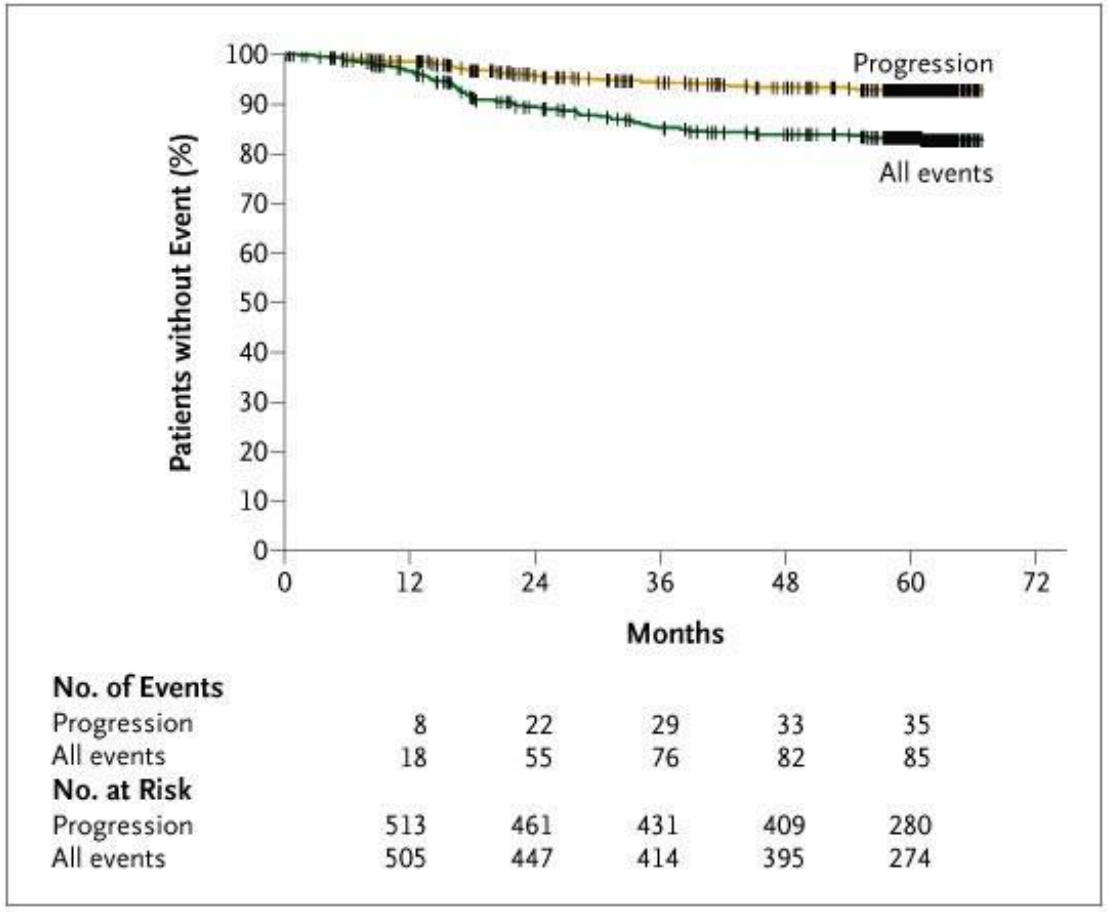
DeVita VT Jr, Rosenberg SA. Two hundred years of cancer research. N Engl J Med. 2012;366(23):2207-2214. doi:10.1056/NEJMra1204479

The new millennium: Molecular-directed targeted therapies

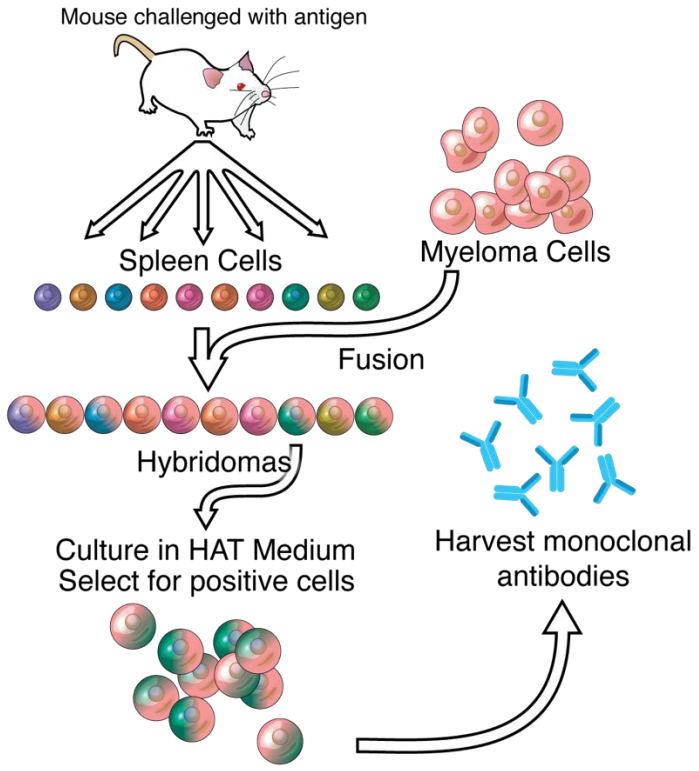
The sequencing of the human genome and the success of Imatinib in CML promised a new era in the personalized treatment of cancer

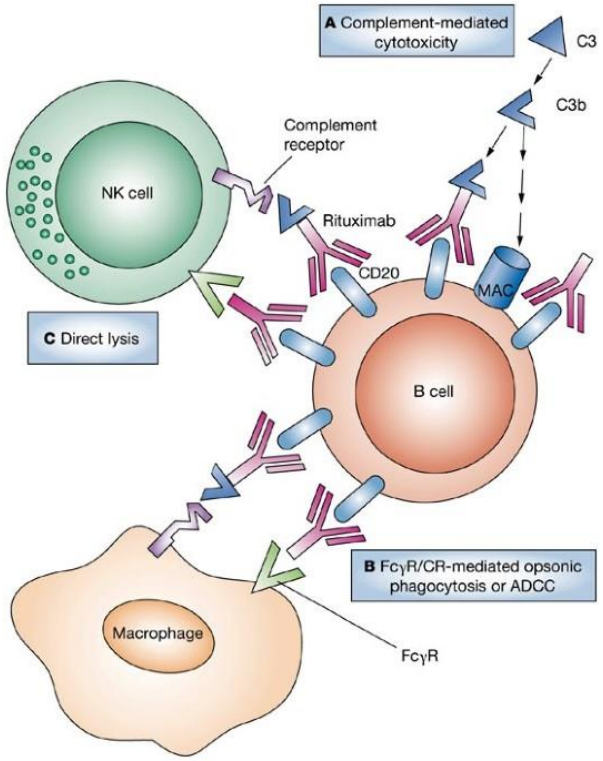


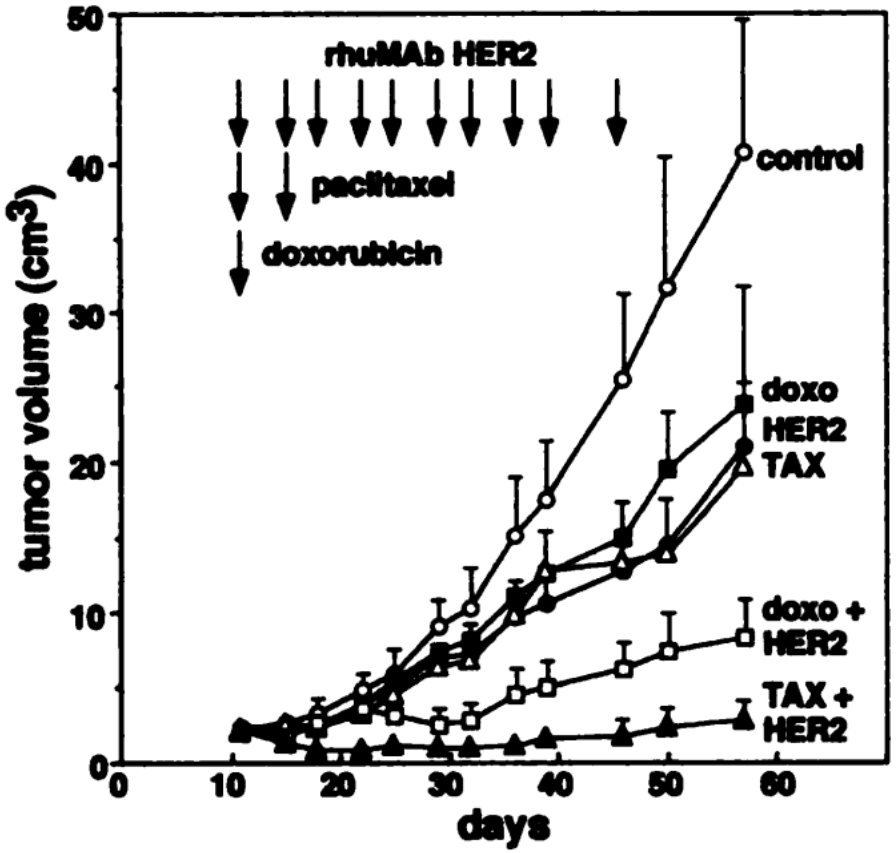




Hijacking B-cells to fight cancer: Monoclonal Antibodies





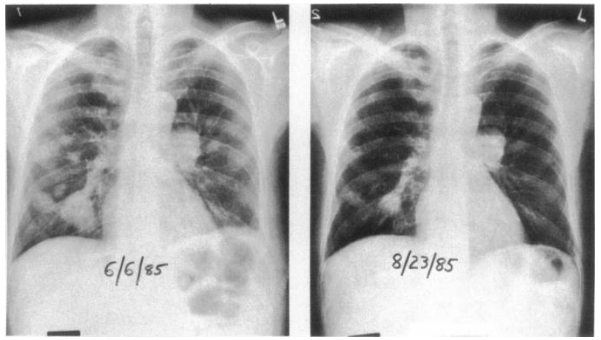


Hybridomas to produce monoclonal antibodies

Baelga et al. Cancer Research 1998

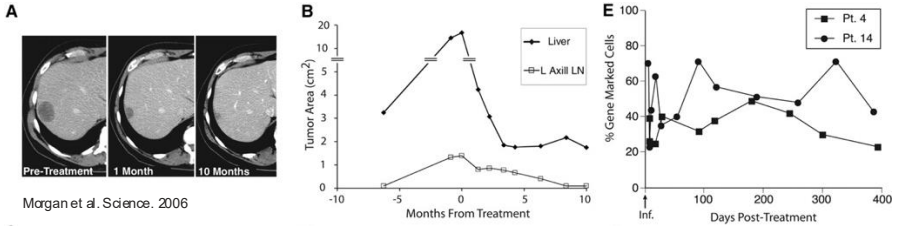
Calling a professional: Boosting the immune system to fight cancer

Recombinant IL2



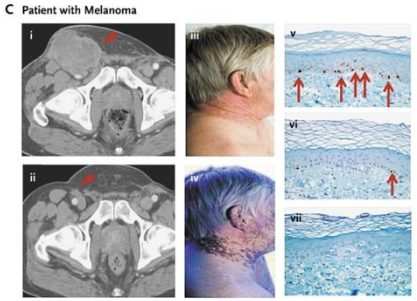
X-ray Films of Multiple Pulmonary Nodules (Metastatic from Renal-Cell Cancer) before (Left) and after (Right) Treatment (Patient 21).
Rosenberg et al. NEJM. 1985

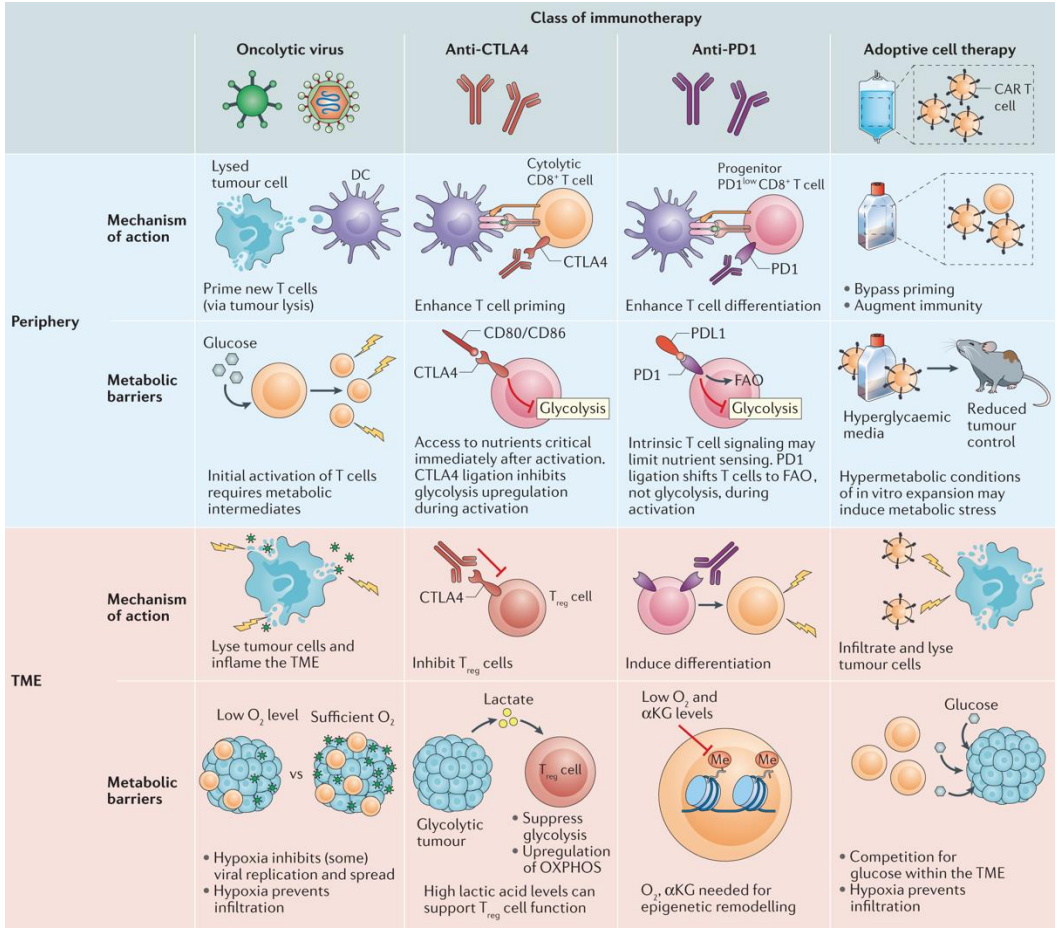
CAR-T



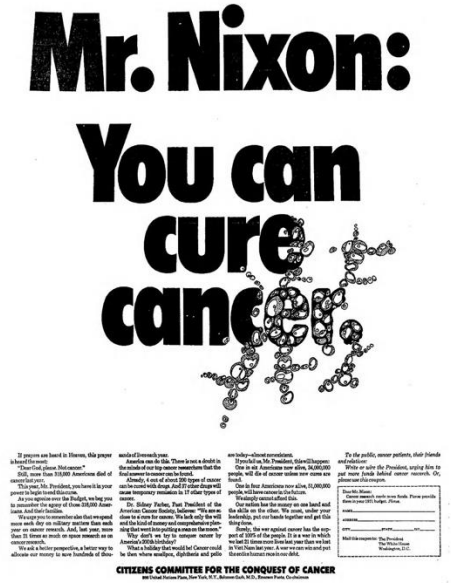
Morgan et al. Science. 2006

ICB (anti-PD-1 antibodies)



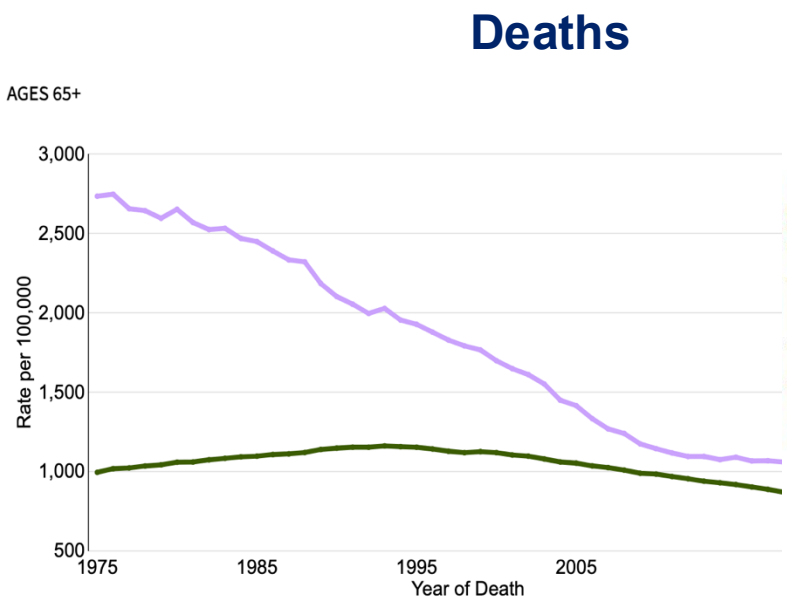


Cancer 101: How are we doing so far?

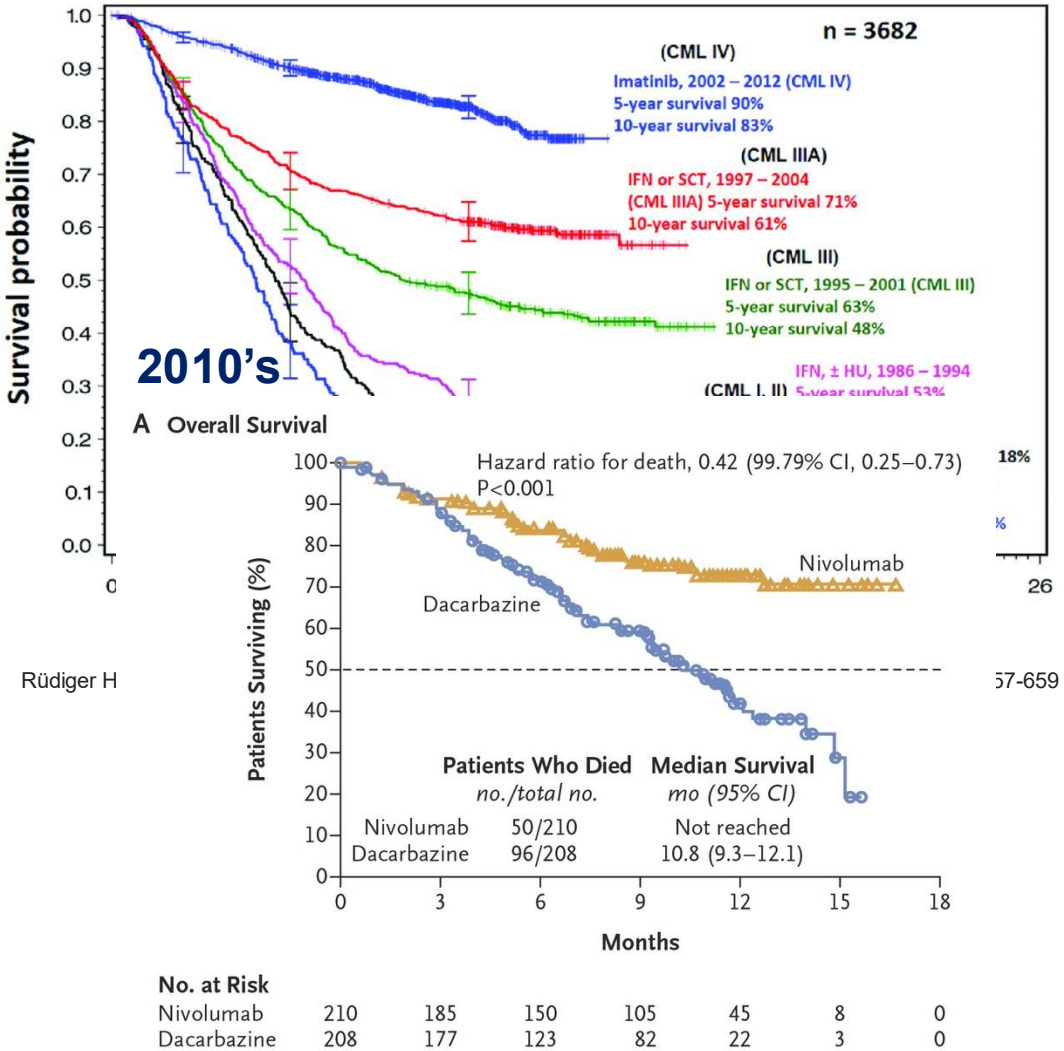


Mary Lasker. Washington Post 1969

Richard Nixon. Rockefeller Research Laboratories, 1971



Source: U.S. Mortality Files, National Center for Health Statistics, Centers for Disease Control
Rates are age-adjusted.

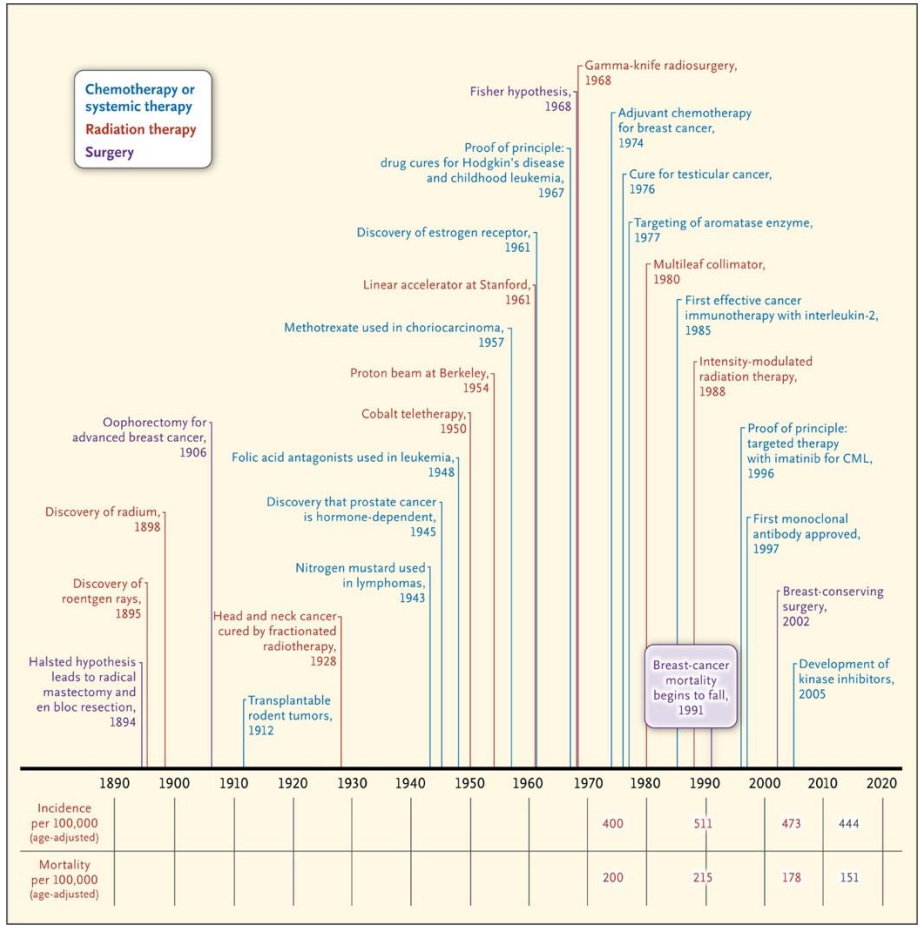


Rüdiger H

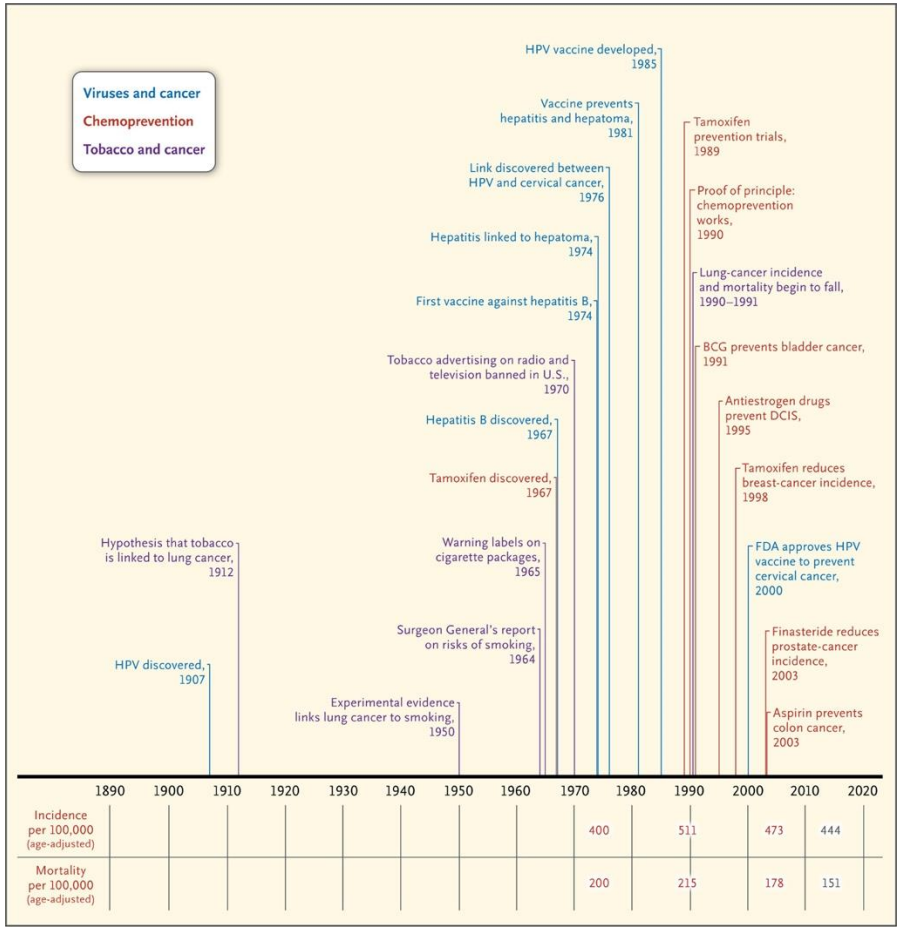
Robert C et al. N Engl J Med 2015;372:320-330

"Whether it was Cancer or Alzheimer's or another condition […] We clearly needed fundamental basic research to understand those diseases before we could hope to cure them." — Benno Schmidt 1995

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/NEJMra1204479



Paper discussion

nature genetics

ARTICLES

https://doi.org/10.1038/s41588-020-00710-0

Check for updates

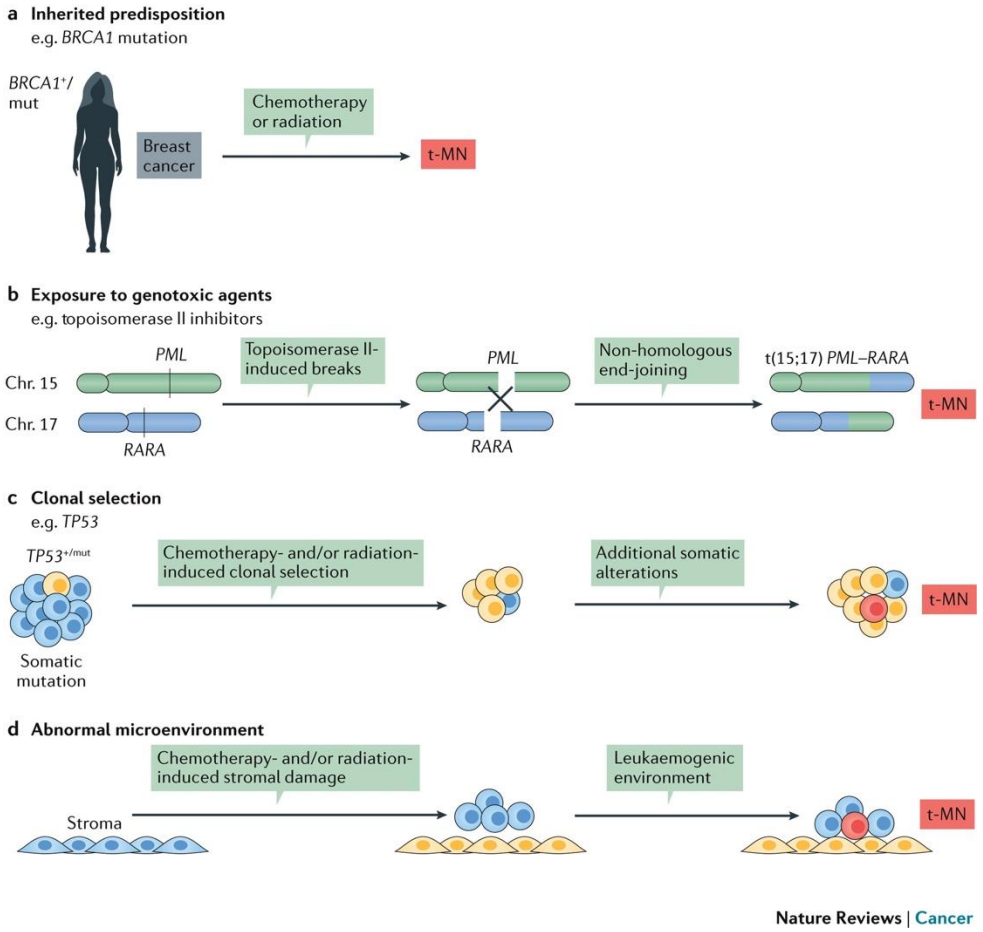
Cancer therapy shapes the fitness landscape of clonal hematopoiesis

Kelly L. Bolton[1], Ryan N. Ptashkin[2,34], Teng Gao[3,34], Lior Braunstein[4], Sean M. Devlin[5], Daniel Kelly[6],

Paper discussion

- **Explanation of the question under research** - *why did they decide to do this?*
- **Discussion figure by figure –** *is this paper not as good as authors think?:*
  - What is the point of each figure/panel?
  - Are there any missing experimental conditions?
  - Are results interpretable?
  - Do the results support the conclusions by the authors?
  - Would you have done anything differently?
  - Are there any missing experiments?
  - What are the limitations of the work?
  - What experiments could be done as a follow-up to the paper?

Both intrinsic and extrinsic factors contribute to the development of therapy-related myeloid neoplasms.



Research Question

- **Explanation of the question under research** - *why did they decide to do this?*

“understanding of the processes that drive transformation of certain clones to cancer is limited. Here we study this phenomenon in the context of clonal hematopoiesis (CH) and the development of therapy-related myeloid neoplasms (tMNs).”

What is the impact of the study?

“A detailed characterization of the genomic landscape of breast cancer metastasis could provide important insights including identifying:

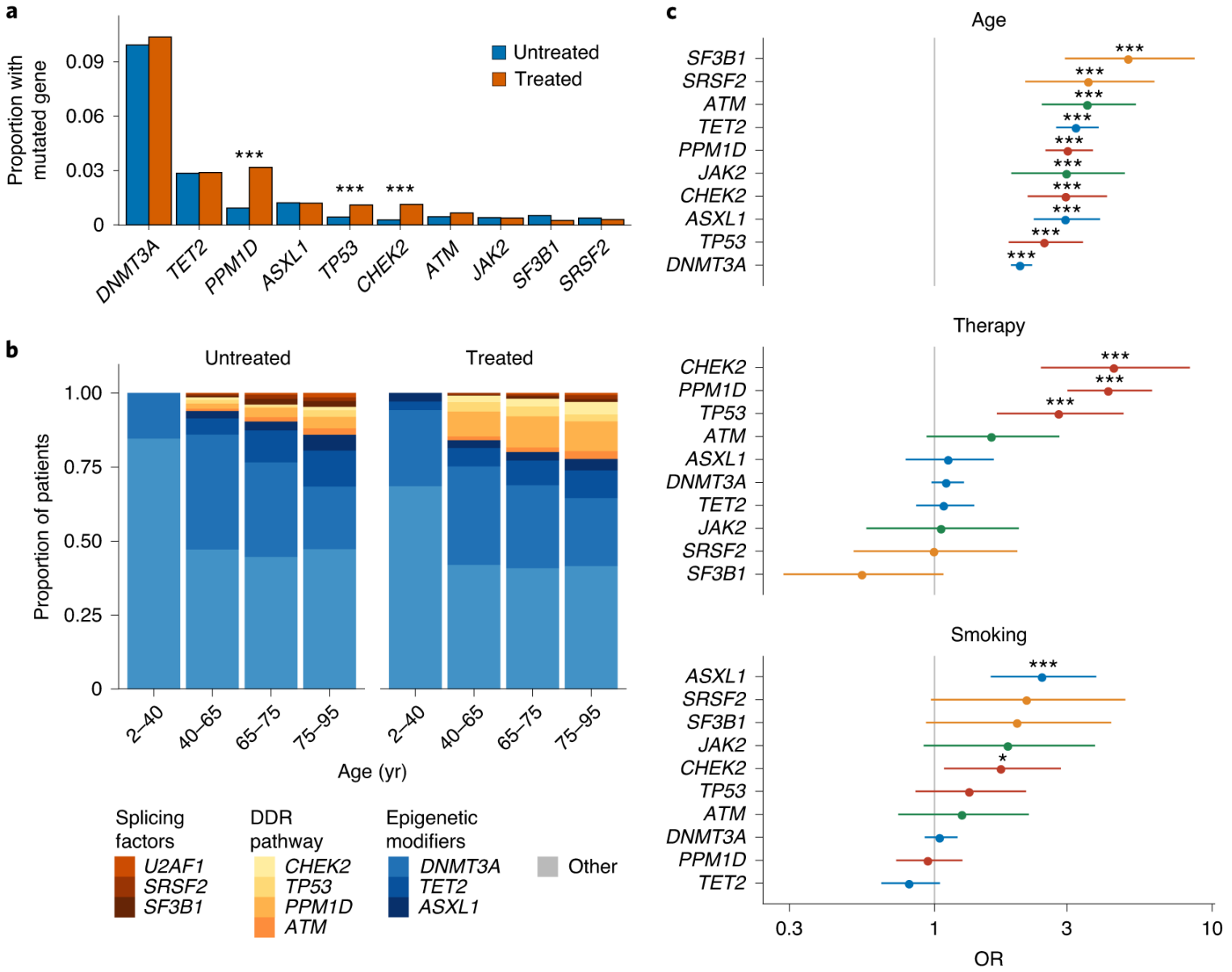
(1) genomic drivers of metastatic disease progression,

(2) the extent and clinical impact of tumoral heterogeneity,

(3) the biologic determinants of variable response of individual patients to different therapies, and

(4) additional potential therapeutic targets.”

Figure 1


a
Proportion with mutated gene
0.09
0.06
0.03
0
Untreated
Treated
***
***
***
DNMT3A
TET2
PPM1D
ASXL1
TP53
CHEK2
ATM
JAK2
SF3B1
SRSF2
b
Untreated
Treated
Proportion of patients
1.00
0.75
0.50
0.25
0
2–40
40–65
65–75
75–95
Age (yr)
Splicing factors
U2AF1
SRSF2
SF3B1
DDR pathway
CHEK2
TP53
PPM1D
ATM
Epigenetic modifiers
DNMT3A
TET2
ASXL1
Other
c
Age
SF3B1
SRSF2
ATM
TET2
PPM1D
JAK2
CHEK2
ASXL1
TP53
DNMT3A
Therapy
CHEK2
PPM1D
TP53
ATM
ASXL1
DNMT3A
TET2
JAK2
SRSF2
SF3B1
Smoking
ASXL1
SRSF2
SF3B1
JAK2
CHEK2
TP53
ATM
DNMT3A
PPM1D
TET2
*
0.3
1
3
10
OR

OR

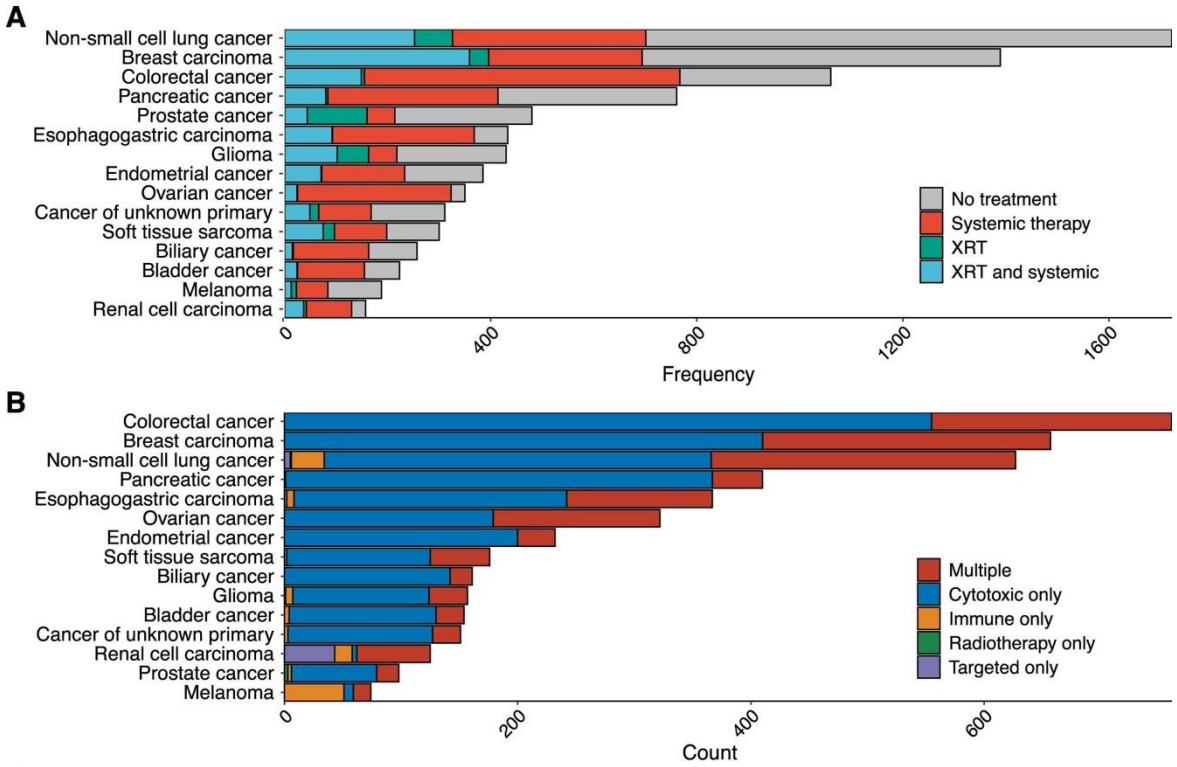
		OUTCOME	
		Disease (Case)	No Disease (Controls)
EXPOSURE	Exposed	a	b
	Unexposed	c	d

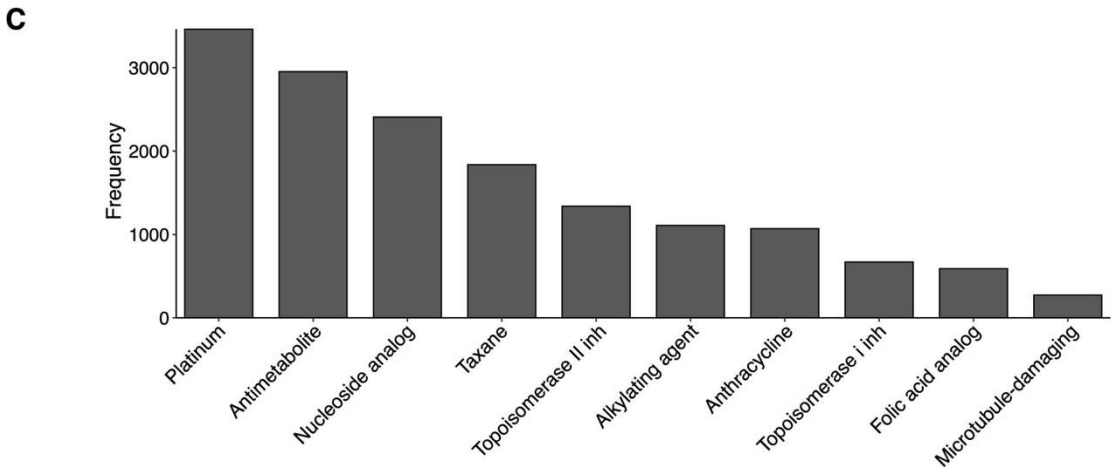
$$Odds\ of\ Exposure\ in\ Cases = \frac{Number\ of\ Cases\ with\ Exposure}{Number\ of\ Cases\ without\ Exposure} = \frac{a}{c}$$

$$Odds\ of\ Exposure\ in\ Controls = \frac{Number\ of\ Controls\ with\ Exposure}{Number\ of\ Controls\ without\ Exposure} = \frac{b}{d}$$

$$Odds\ Ratio = \frac{Odds\ of\ Exposure\ in\ Cases}{Odds\ of\ Exposure\ in\ Controls} = \frac{a/c}{b/d} = \frac{a * d}{b * c}$$

Extended Data Figure 1





Extended Data Figure 2

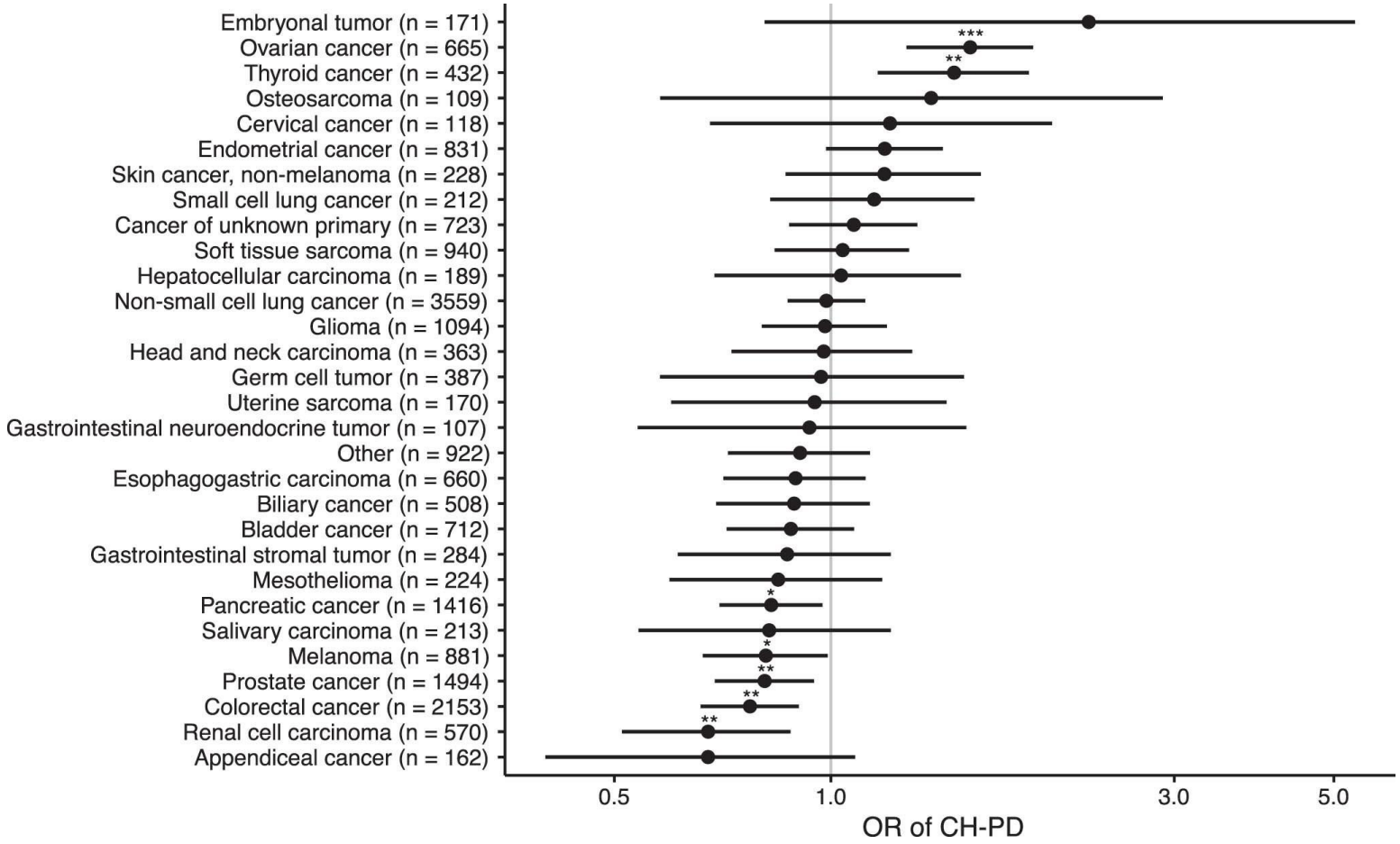


Figure 2

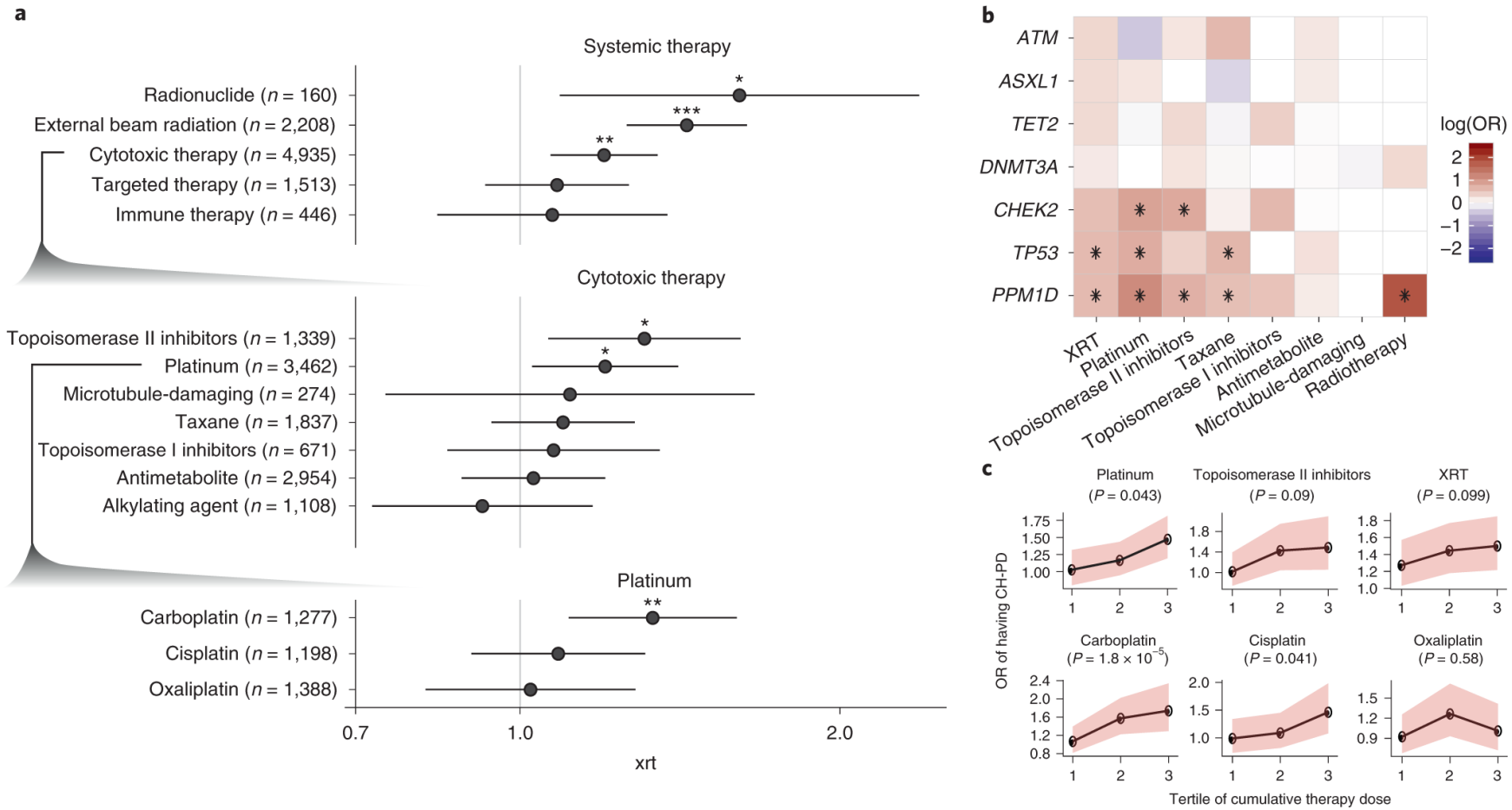
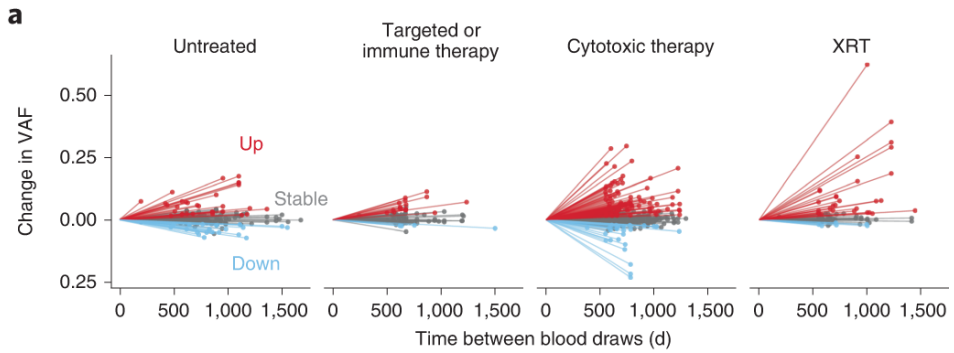
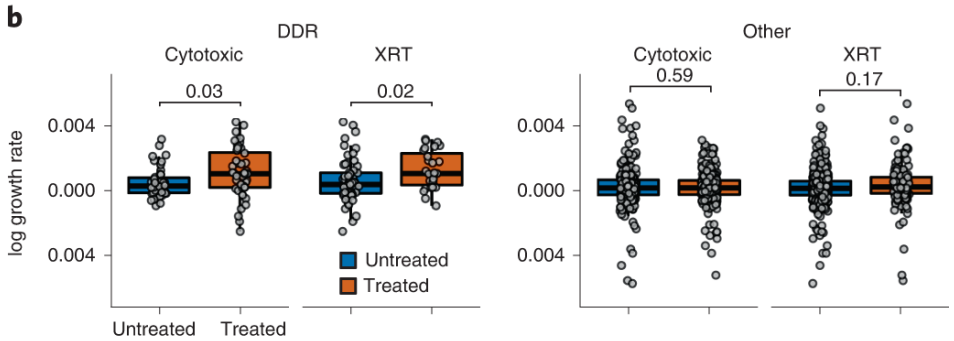
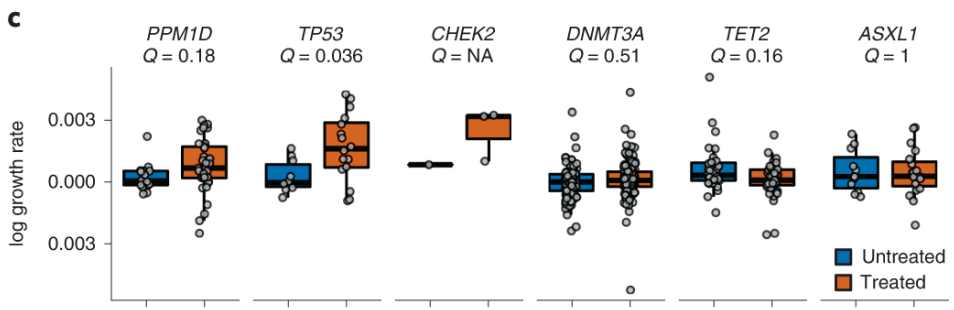
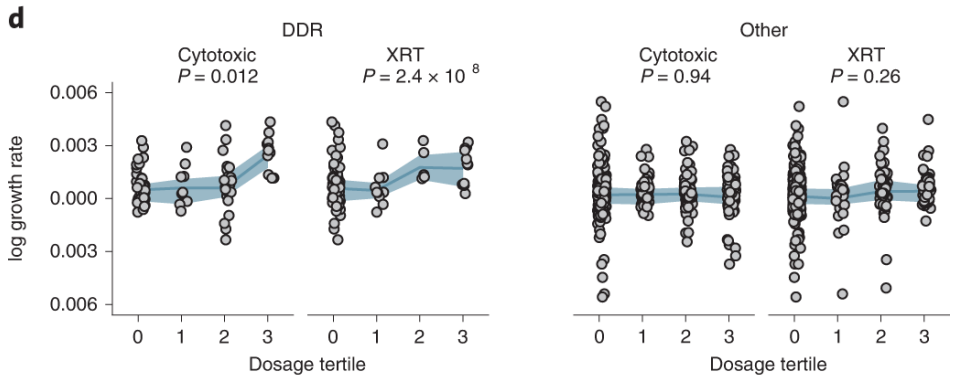

a
Systemic therapy
Radionuclide (n = 160)
External beam radiation (n = 2,208)
Cytotoxic therapy (n = 4,935)
Targeted therapy (n = 1,513)
Immune therapy (n = 446)
Cytotoxic therapy
Topoisomerase II inhibitors (n = 1,339)
Platinum (n = 3,462)
Microtubule-damaging (n = 274)
Taxane (n = 1,837)
Topoisomerase I inhibitors (n = 671)
Antimetabolite (n = 2,954)
Alkylating agent (n = 1,108)
Platinum
Carboplatin (n = 1,277)
Cisplatin (n = 1,198)
Oxaliplatin (n = 1,388)
0.7
1.0
2.0
xrt
b
ATM
ASXL1
TET2
DNMT3A
CHEK2
TP53
PPM1D
log(OR)
2
1
0
−1
−2
XRT
Platinum
Topoisomerase II inhibitors
Taxane
Topoisomerase I inhibitors
Antimetabolite
Microtubule-damaging
Radiotherapy
c
Platinum (P = 0.043)
Topoisomerase II inhibitors (P = 0.09)
XRT (P = 0.099)
Carboplatin (P = 1.8 × 10−5)
Cisplatin (P = 0.041)
Oxaliplatin (P = 0.58)
OR of having CH-PD
Tertile of cumulative therapy dose

Figure 3


a
Untreated
Targeted or immune therapy
Cytotoxic therapy
XRT
Change in VAF
Up
Stable
Down
Time between blood draws (d)


b
DDR
Other
Cytotoxic
XRT
0.03
0.02
0.59
0.17
log growth rate
Untreated
Treated


c
PPM1D Q = 0.18
TP53 Q = 0.036
CHEK2 Q = NA
DNMT3A Q = 0.51
TET2 Q = 0.16
ASXL1 Q = 1
log growth rate
Untreated
Treated


d
DDR
Other
Cytotoxic
P = 0.012
XRT
P = 2.4 × 10 8
Cytotoxic
P = 0.94
XRT
P = 0.26
log growth rate
Dosage tertile

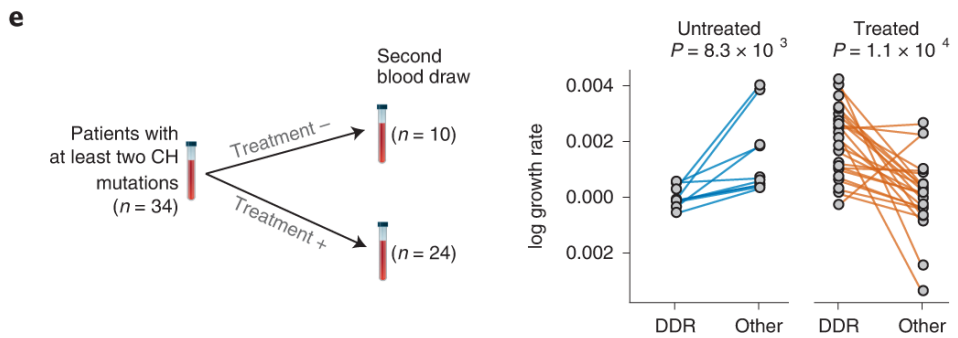
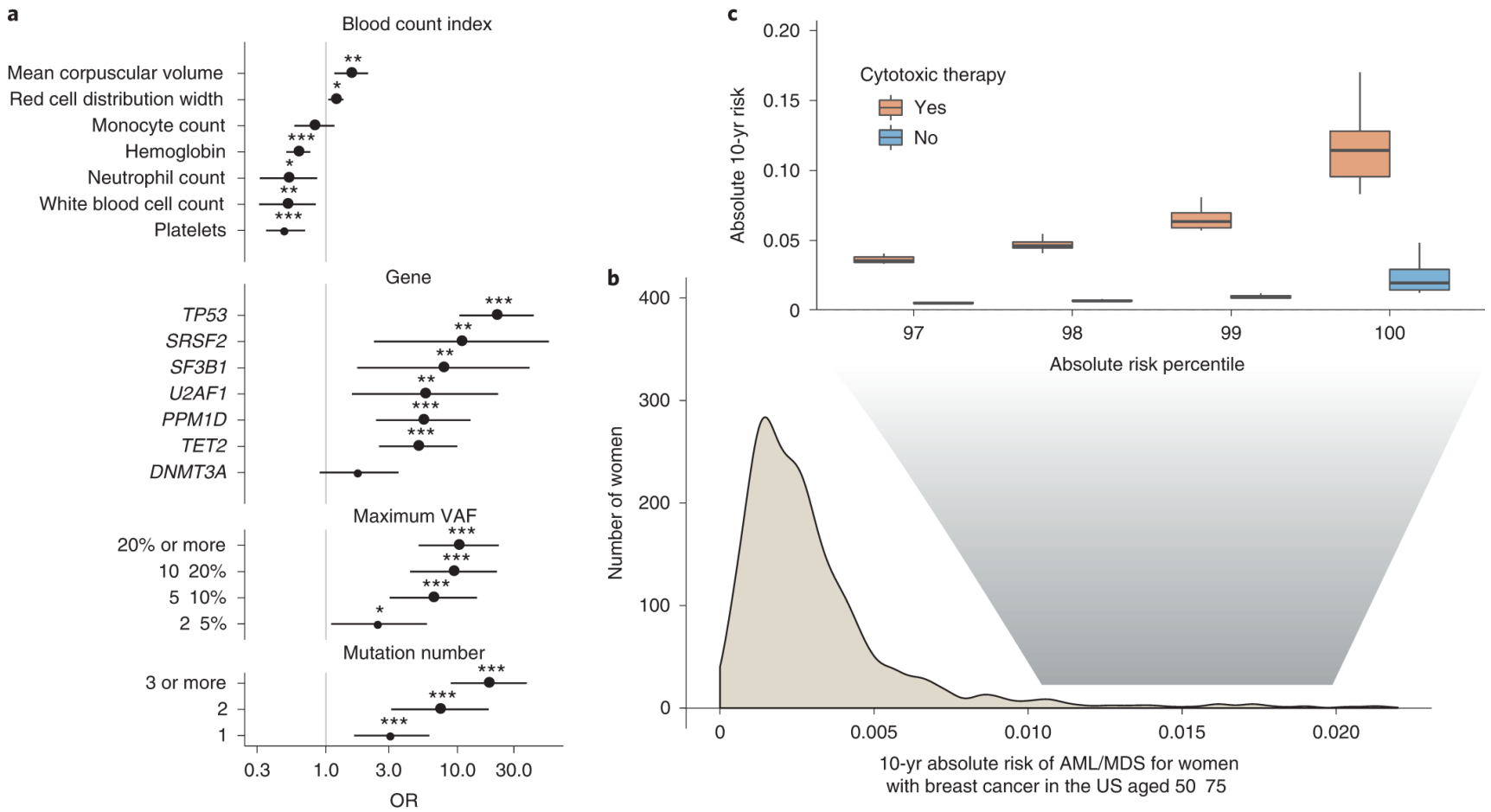
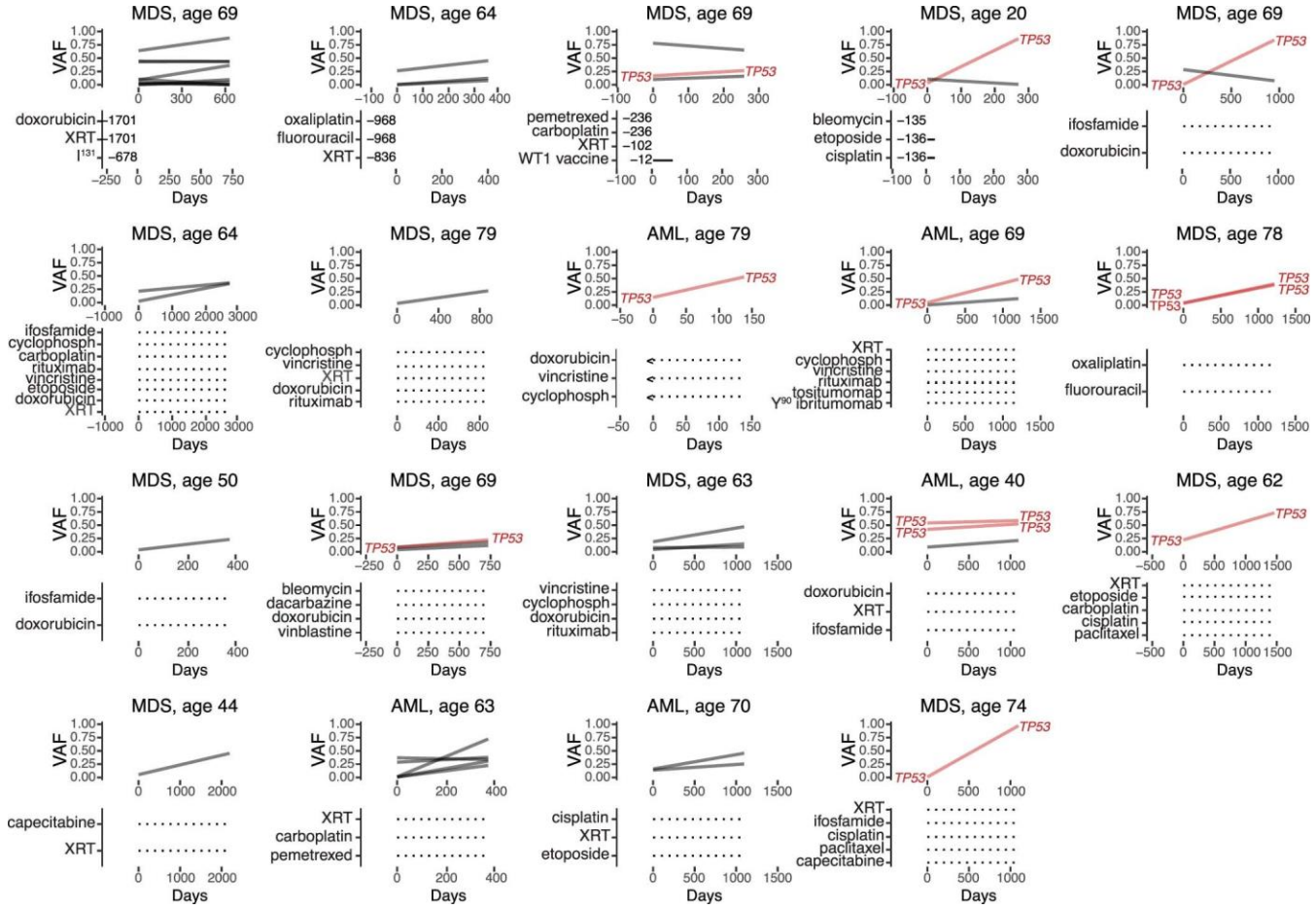

e
Patients with at least two CH mutations (n = 34)
Treatment −
Treatment +
Second blood draw
(n = 10)
(n = 24)
Untreated
P = 8.3 × 10 3
Treated
P = 1.1 × 10 4
log growth rate
DDR
Other

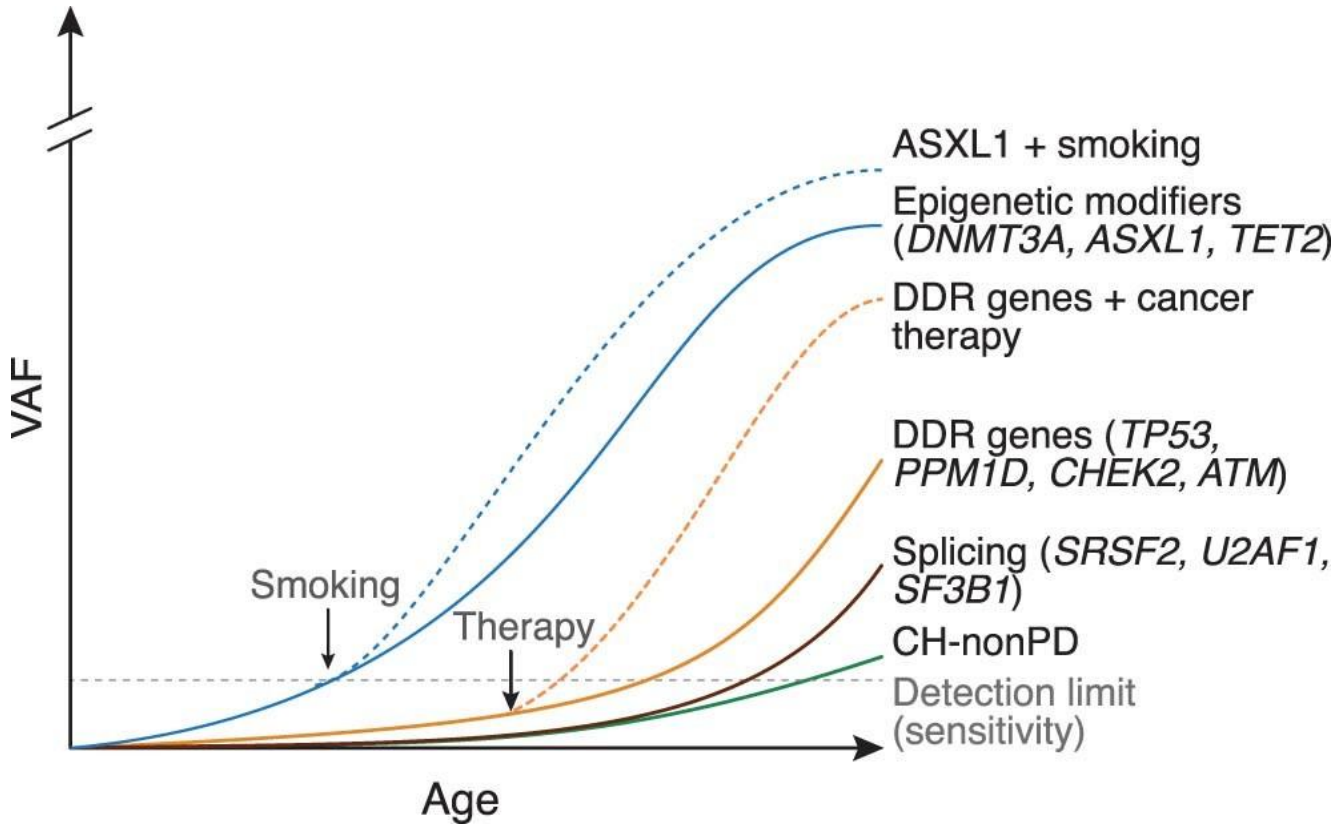
Figure 4


a
Blood count index
Mean corpuscular volume
Red cell distribution width
Monocyte count
Hemoglobin
Neutrophil count
White blood cell count
Platelets
Gene
TP53
SRSF2
SF3B1
U2AF1
PPM1D
TET2
DNMT3A
Maximum VAF
20% or more
10 20%
5 10%
2 5%
Mutation number
3 or more
2
1
0.3
1.0
3.0
10.0
30.0
OR
b
Number of women
400
300
200
100
0
0
0.005
0.010
0.015
0.020
10-yr absolute risk of AML/MDS for women
with breast cancer in the US aged 50 75
c
Absolute 10-yr risk
0.20
0.15
0.10
0.05
0
Cytotoxic therapy
Yes
No
97
98
99
100
Absolute risk percentile

Extended Data Figure 4



Conclusion/Model



Thanks for your attention!

Any questions?


Memorial Sloan Kettering
Cancer Center