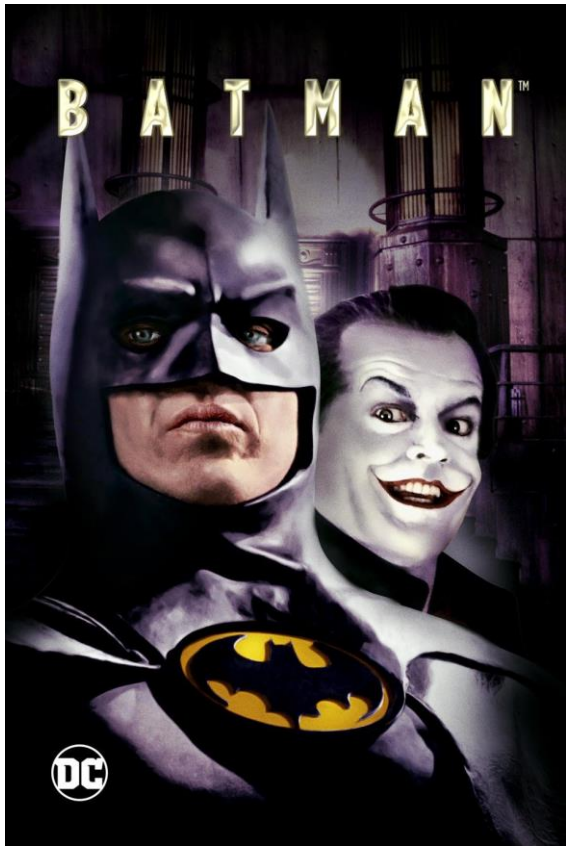
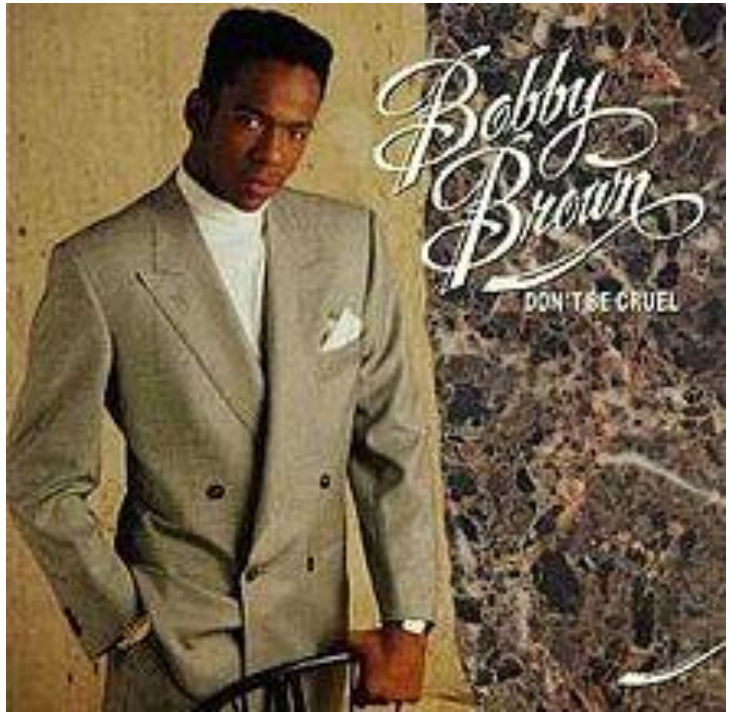
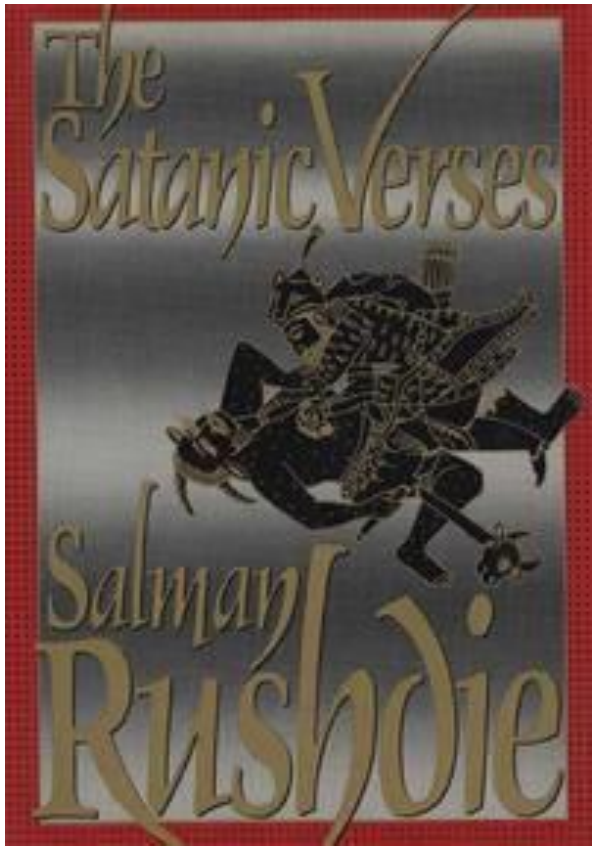
Opening Address to Cancer Progress 30th Anniversary Event

Jeffrey M. Bockman, PhD, EVP
Oncology Practice Head,
Cello Health BioConsulting, previously Defined Health







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The Nobel Prize in Physiology or Medicine 1989

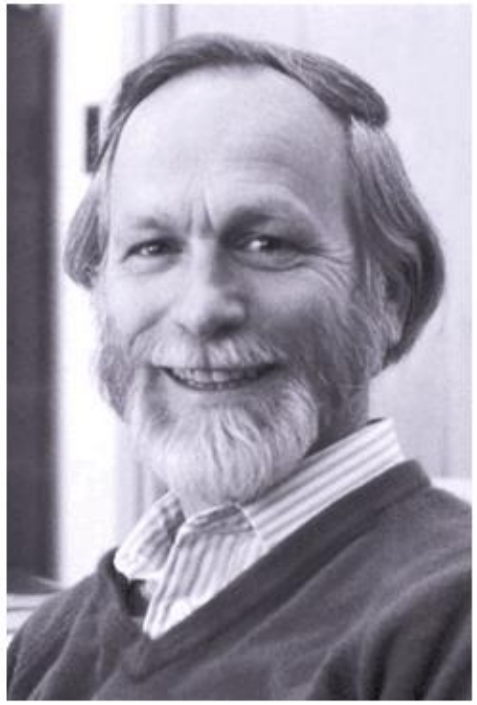


Photo from the Nobel Foundation archive.

J. Michael Bishop

Prize share: 1/2

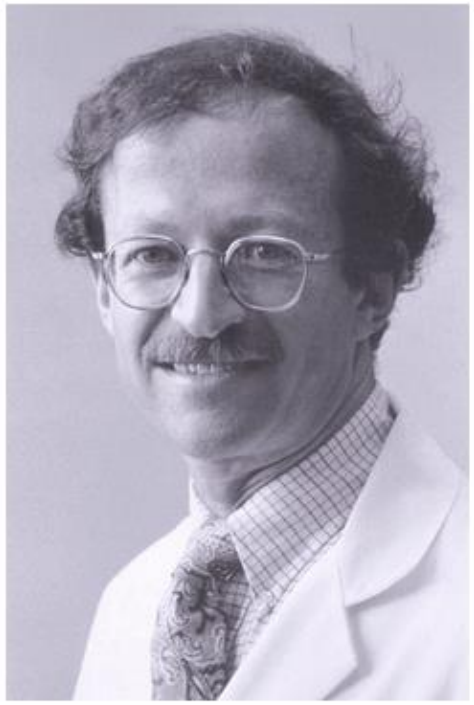


Photo from the Nobel Foundation archive.

Harold E. Varmus

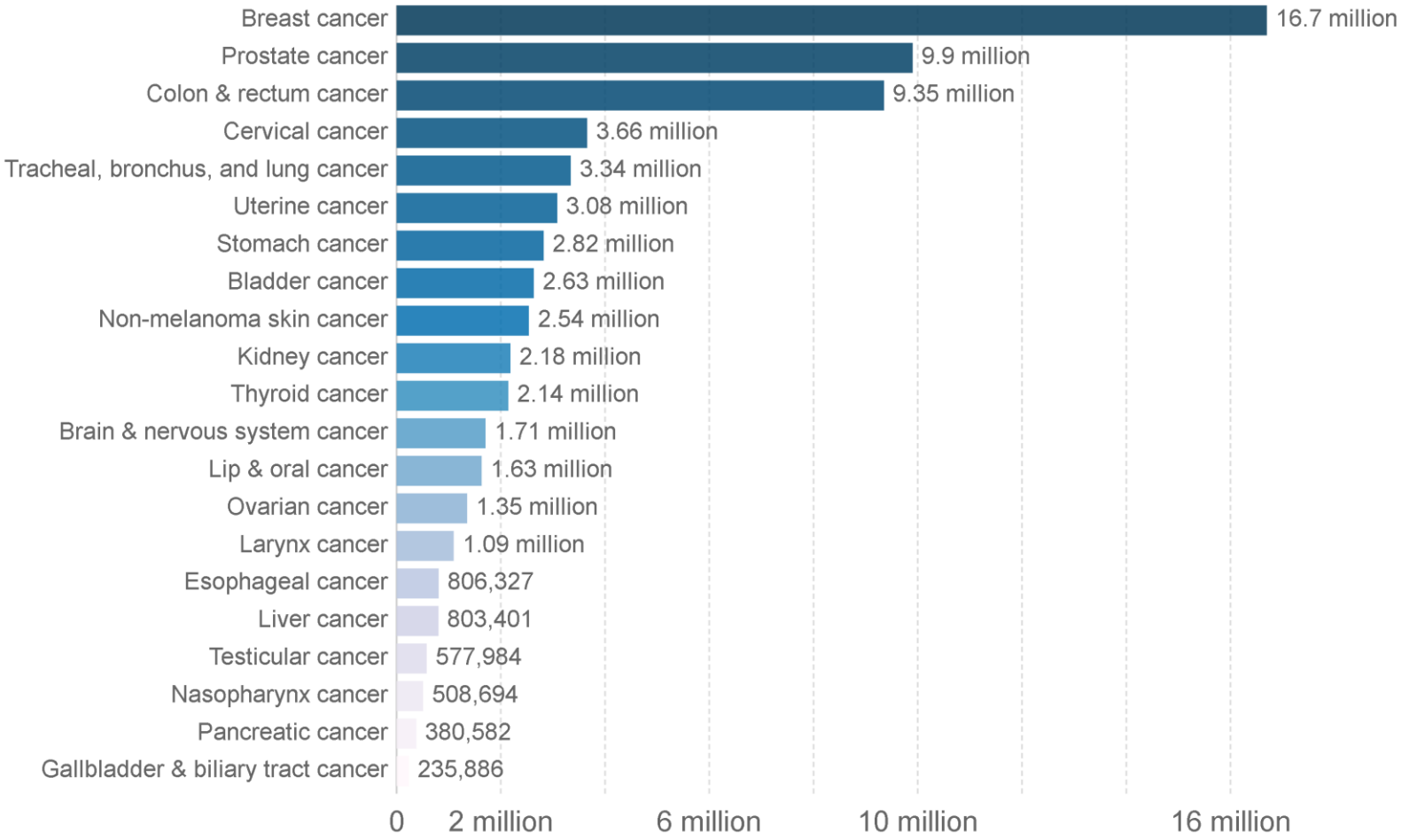
Prize share: 1/2

The Nobel Prize in Physiology or Medicine 1989 was awarded jointly to J. Michael Bishop and Harold E. Varmus "for their discovery of the cellular origin of retroviral oncogenes."

Number of people with cancer by type, World, 2017

Total number of people suffering from cancer at any given time, differentiated by cancer type. This is measured across both sexes and all ages.

Our World in Data

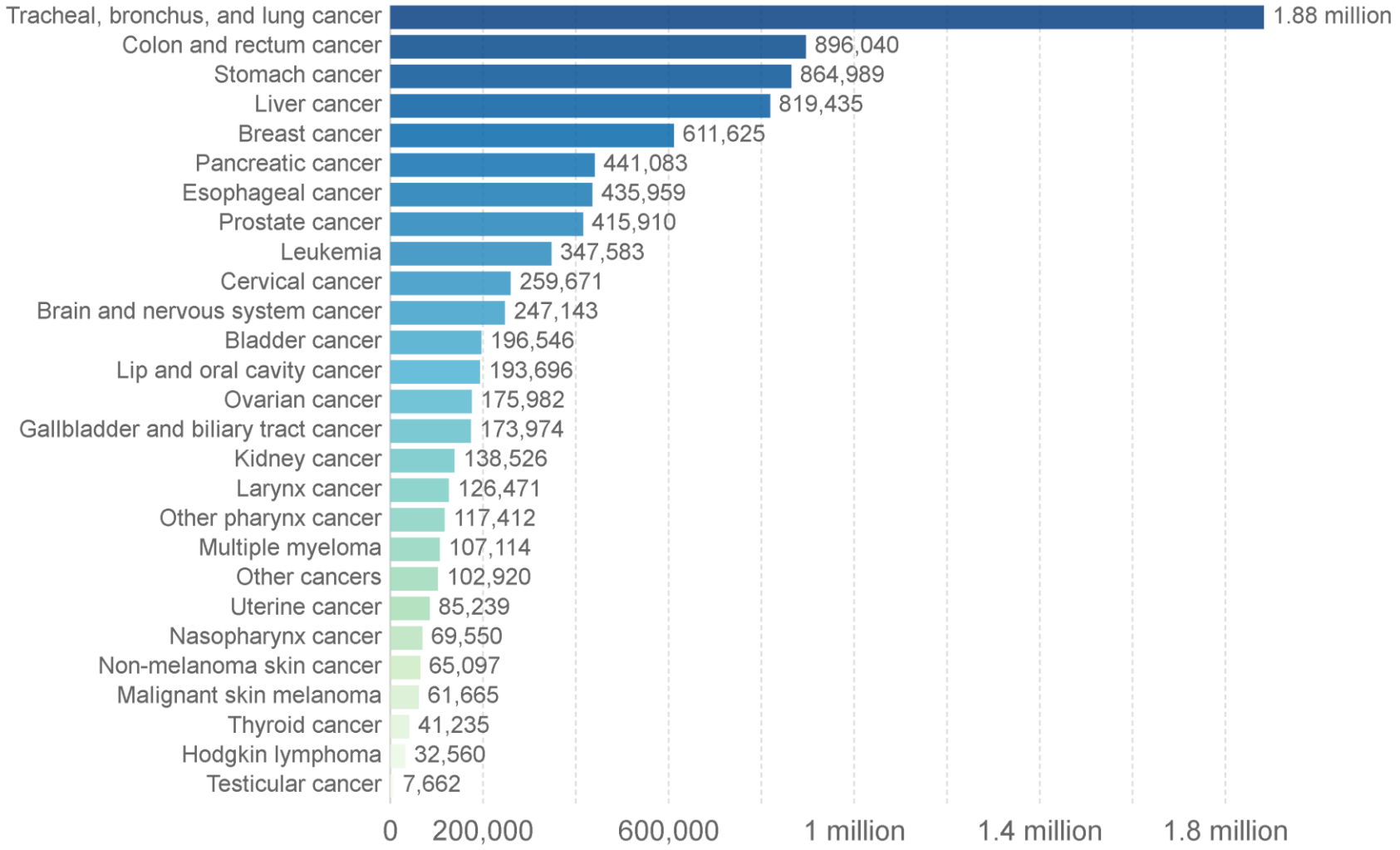


Source: IHME, Global Burden of Disease

Cancer deaths by type, World, 2017

Total annual number of deaths from cancers across all ages and both sexes, broken down by cancer type.

Our World in Data



Source: IHME, Global Burden of Disease (GBD)

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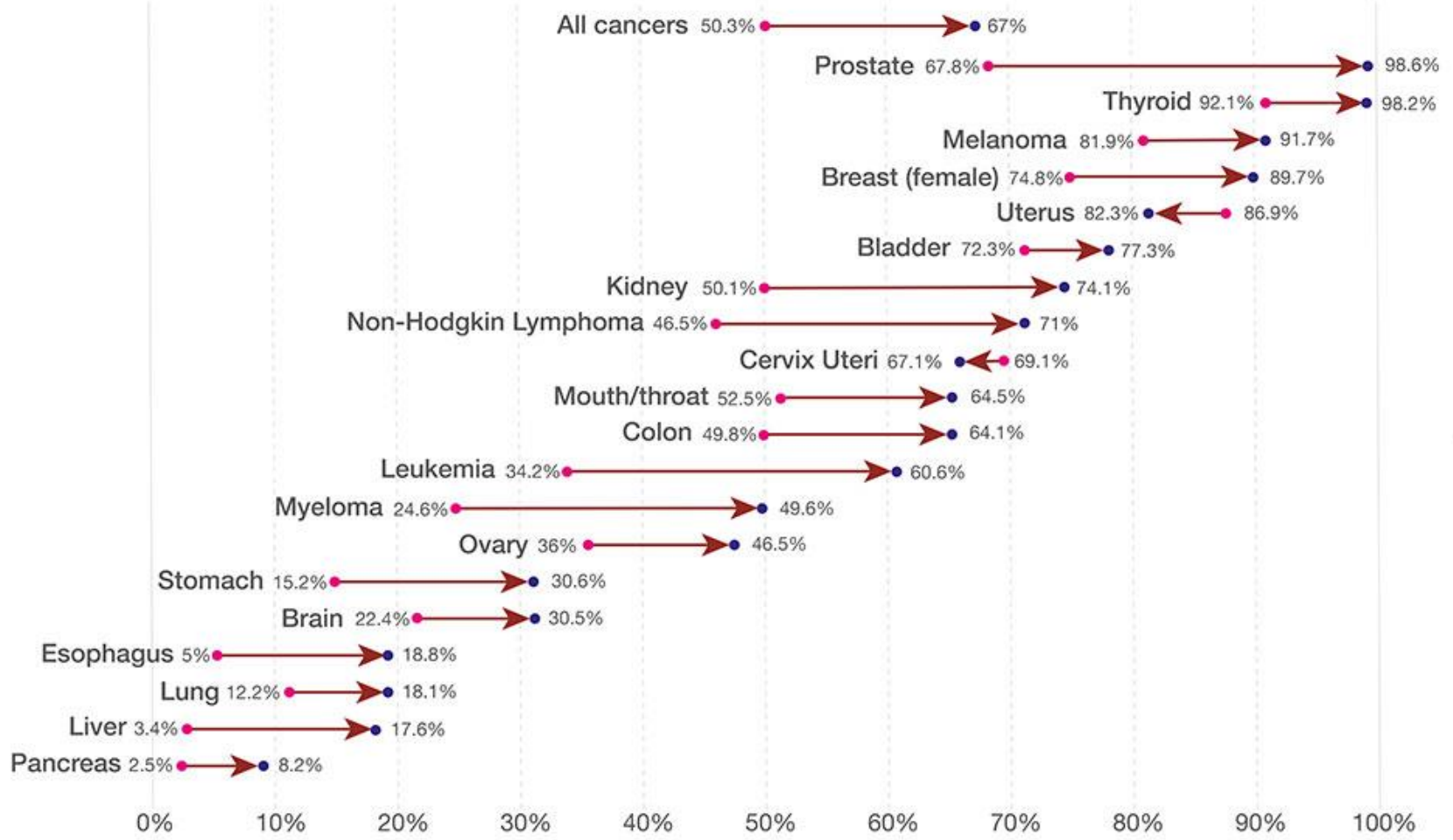
Five-year cancer survival rates in the USA

Average five-year survival rates from common cancer types in the United States, shown as the rate over the period 1970-77 [●] and over the period 2007-2013 [●]: 1970-77 ● → ● 2007-2013

This five-year interval indicates the percentage of people who live longer than five years following diagnosis.

Our World in Data



Based on data by Journal of the National Cancer Institute; Surveillance, Epidemiology and End Results Program.
The data visualization is available at OurWorldinData.org. There you find research and more visualizations on this topic.

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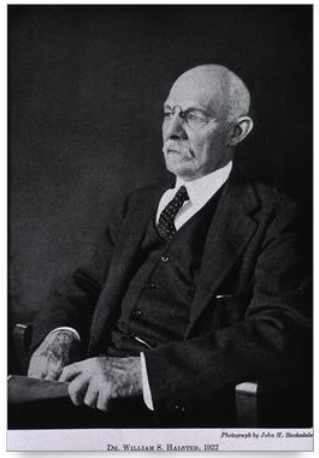


William Halsted (U.S. National Library of Medicine)

1882

The First Radical Mastectomy to Treat Breast Cancer

William Halsted performs the first radical mastectomy to treat breast cancer. This surgical procedure remains the standard operation for breast cancer until the latter half of the 20th century.

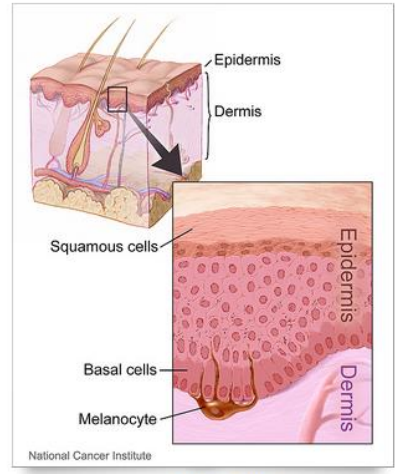
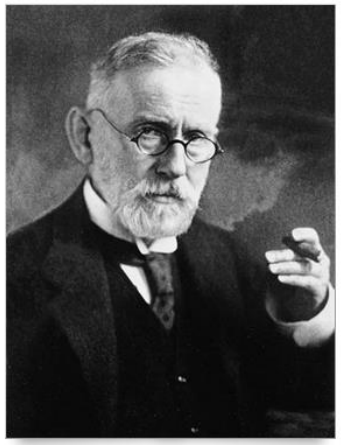


Illustration of the layers of skin (NCIVisuals Online)

1903

The First Use of Radiation Therapy to Cure Cancer

S.W. Goldberg and Efim London describe the use of radium to treat two patients with basal cell carcinoma of the skin. The disease was eradicated in both patients. Learn more about radiation therapy.

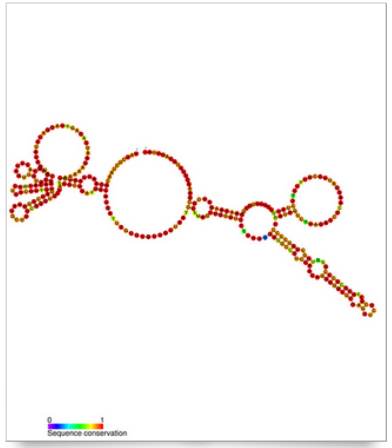


Paul Ehrlich

1909

Immune Surveillance

Paul Ehrlich proposes that the immune system usually suppresses tumor formation, a concept that becomes known as the "immune surveillance" hypothesis. This proposal prompts research, which continues today, to harness the power of the immune system to fight cancer. Learn about biological therapies for cancer.



Part of the Rous sarcoma virus (Wikimedia Commons)

Theodor Boveri

1902

Cancer Tumors & Single Cells with Chromosome Damage

Theodor Boveri proposes that cancerous tumors arise from single cells that have experienced chromosome damage and suggests that chromosome alterations cause the cells to divide uncontrollably.

1911

Cancer in Chickens

Peyton Rous discovers a virus that causes cancer in chickens (Rous sarcoma virus), establishing that some cancers are caused by infectious agents.

https://www.cancer.gov/research/progress/250-years-milestones

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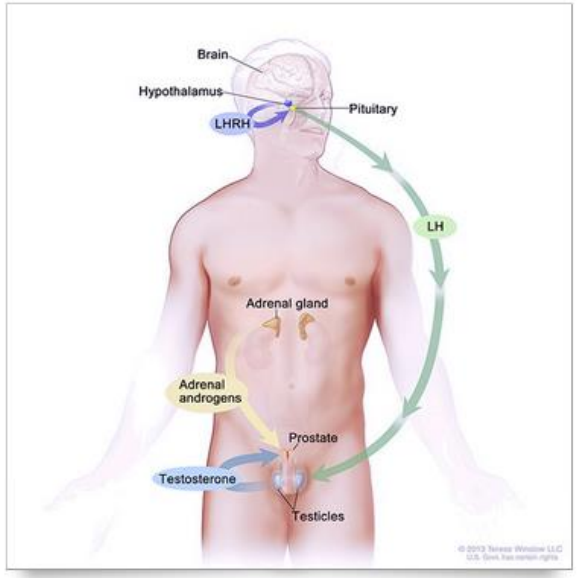


Illustration of the regulation of testosterone production in males

1941

Hormonal Therapy

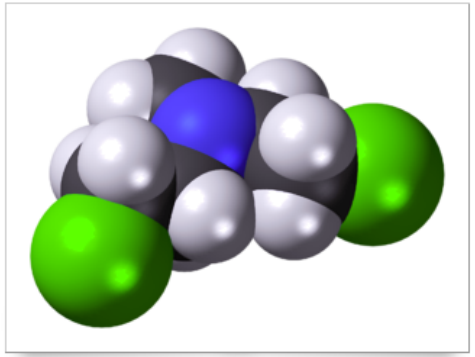
Charles Huggins discovers that removing the testicles to lower testosterone production or administering estrogens causes prostate tumors to regress. Such hormonal manipulation—more commonly known as hormonal therapy—continues to be a mainstay of prostate cancer treatment. Find out more about hormonal therapy.

Dr. Farber with a young patient in 1960 (NCI Visuals Online)

1947

Antimetabolites

Sidney Farber shows that treatment with the antimetabolite drug aminopterin, a derivative of folic acid, induces temporary remissions in children with acute leukemia. Antimetabolite drugs are structurally similar to chemicals needed for important cellular processes, such as DNA synthesis, and cause cell death by blocking those processes.

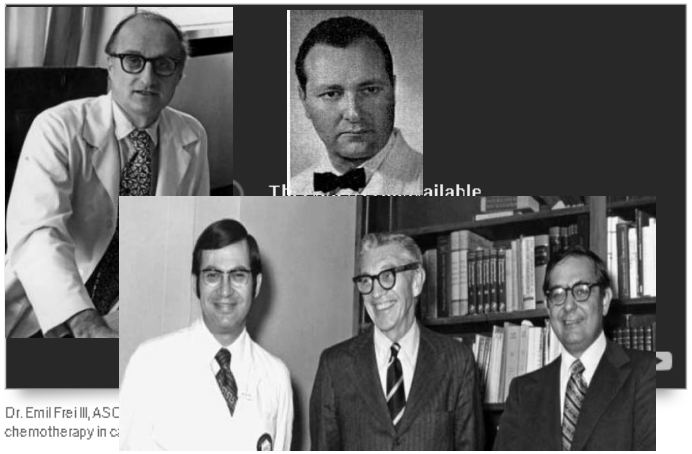


Space-filling model of the mechlorethamine molecule by Jynto (Black: Carbon, C/ White: Hydrogen, H/ Blue: Nitrogen, N/ Green: Chlorine, Cl by) (Wikimedia Commons)

1949

Nitrogen Mustard

The Food and Drug Administration (FDA) approves nitrogen mustard (mechlorethamine) for the treatment of cancer. Nitrogen mustard belongs to a class of drugs called alkylating agents, which kill cells by chemically modifying their DNA



Dr. Emil Frei III, ASC
chemotherapy in c

1958

Combination Chemotherapy

NCI researchers Emil Frei, Emil Freireich, and James Holland and their colleagues demonstrate that combination chemotherapy with the drugs 6-mercaptopurine and methotrexate can induce partial and complete remissions and prolong survival in children and adults with acute leukemia.

https://www.cancer.gov/research/progress/250-years-milestones

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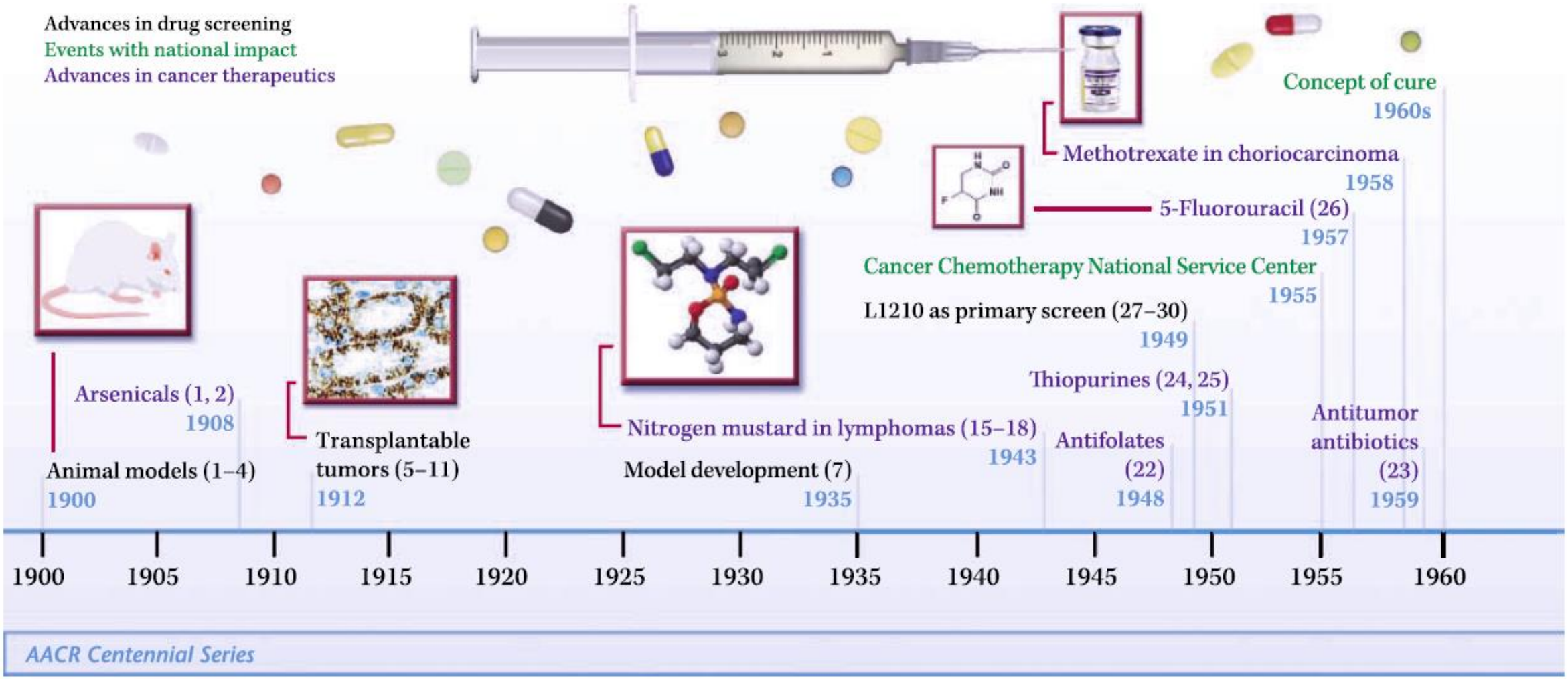
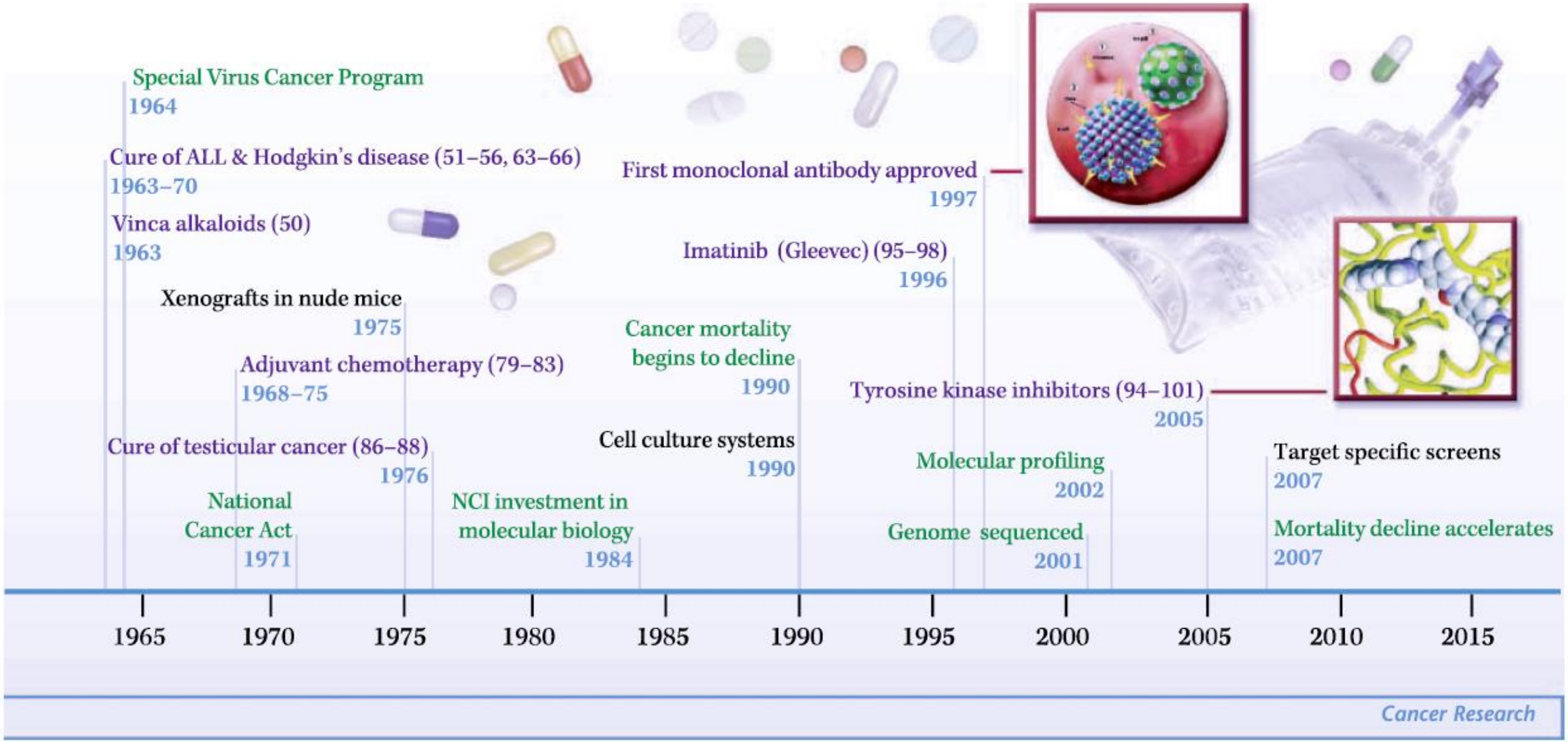
CELLO HEALTH BioConsulting
Previously Defined Health
www.cellohealthbioconsulting.com

THERAPEUTIC INSIGHT
www.therapeuticinsight.com

CANCER PROGRESS
www.cancerprogressbyDH.com



Cancer Res 2008;68(21):8643–53



Cancer Res 2008;68(21):8643–53

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1989

1989

Drugs to boost blood cells help patients finish cancer treatment, reduce infections

The FDA approves the drug epoetin alpha (Procrit, Epogen) to stimulate production of red blood cells in patients with severe anemia, one of the most common and serious side effects of chemotherapy. These drugs are soon joined by white blood cell-boosting drugs such as filgrastim (Neupogen) and pegfilgrastim (Neulasta). The new treatments help reduce the need for blood transfusions and make chemotherapy safer by reducing the risk of infections and related hospitalizations.

Carboplatin–Paraplatin (Bristol-Myers-Squibb)

- **Regulatory history:**
  - 1st approved in 1989 for advanced ovarian carcinoma
  - WR issued: 4/11/2001; amended 11/13/2002 extension of due date for submission of reports/data
  - Exclusivity Granted: 4/30/2004
- **Population of Interest:** Refractory or relapsed pediatric malignancies
- **Types of Studies:**

  Phase I study to establish the MTD and recommended dose of carboplatin when given with irinotecan [carboplatin q 3 weeks with irinotecan daily (x5) x 2 q 3 weeks]
  Number of centers - 8

  Phase II randomized, 2-arm, non-comparative, open-label study to evaluate the response rate of carboplatin (AUC 4 mg/ml/min) administered in combination with irinotecan (12 mg/m^2/day x 10 days) and of irinotecan administered as a single agent (20 mg/m^2/day x 10 days)
  Number of centers - 56
- **Age groups:** 1-<21 yrs
- **Total # patients:** Phase I = 28; Phase II = 151

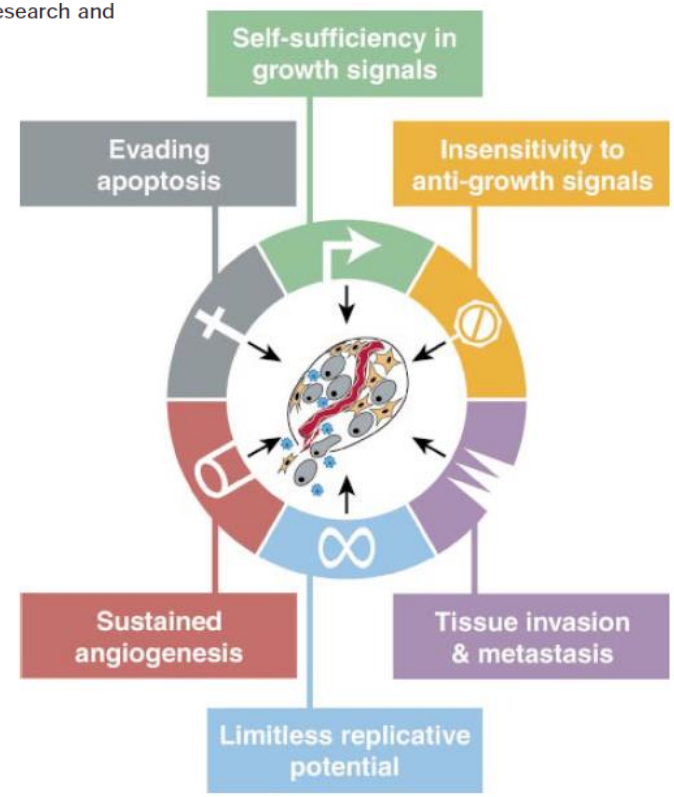
ANTITUMOR ACTIVITY

The impressive antitumor activity which has been observed with paclitaxel in a broad range of cancers has been the subject of numerous reviews and monographs and will not be reviewed in detail here. Paclitaxel was initially approved by the FDA in 1992 for the treatment of women with refractory ovarian cancer on the basis of five phase II trials of paclitaxel as a single agent given over 24 h. These data were

Cell, Vol. 100, 57–70, January 7, 2000, Copyright ©2000 by Cell Press

The Hallmarks of Cancer

Douglas Hanahan* and Robert A. Weinberg†
*Department of Biochemistry and Biophysics and Hormone Research Institute
University of California at San Francisco
San Francisco, California 94143
†Whitehead Institute for Biomedical Research and Department of Biology
Massachusetts Institute of Technology
Cambridge, Massachusetts 02142



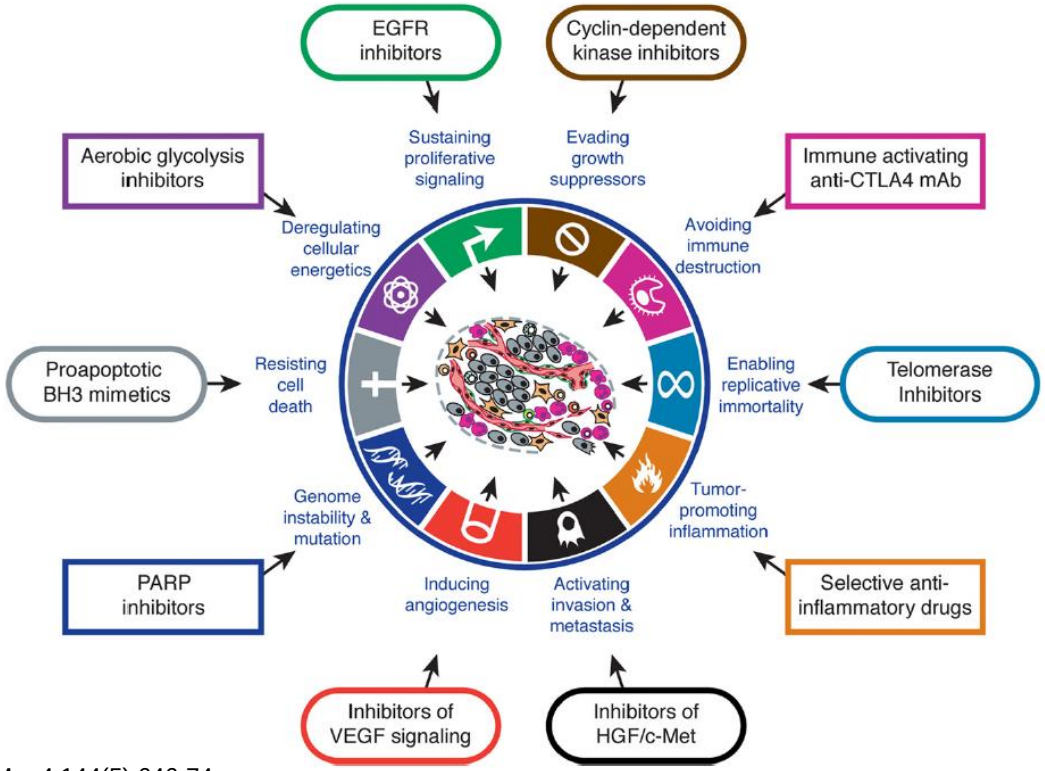
Cell, Vol. 100, 57–70, January 7, 2000

Cell

Leading Edge
Review

Hallmarks of Cancer: The Next Generation

Douglas Hanahan[1,2,*] and Robert A. Weinberg[3,*]
[1]The Swiss Institute for Experimental Cancer Research (ISREC), School of Life Sciences, EPFL, Lausanne CH-1015, Switzerland
[2]The Department of Biochemistry & Biophysics, UCSF, San Francisco, CA 94158, USA
[3]Whitehead Institute for Biomedical Research, Ludwig/MIT Center for Molecular Oncology, and MIT Department of Biology, Cambridge, MA 02142, USA
*Correspondence: dh@epfl.ch (D.H.), weinberg@wi.mit.edu (R.A.W.)
DOI 10.1016/j.cell.2011.02.013



Cell. 2011 Mar 4;144(5):646-74

Drugs Approved in 2019

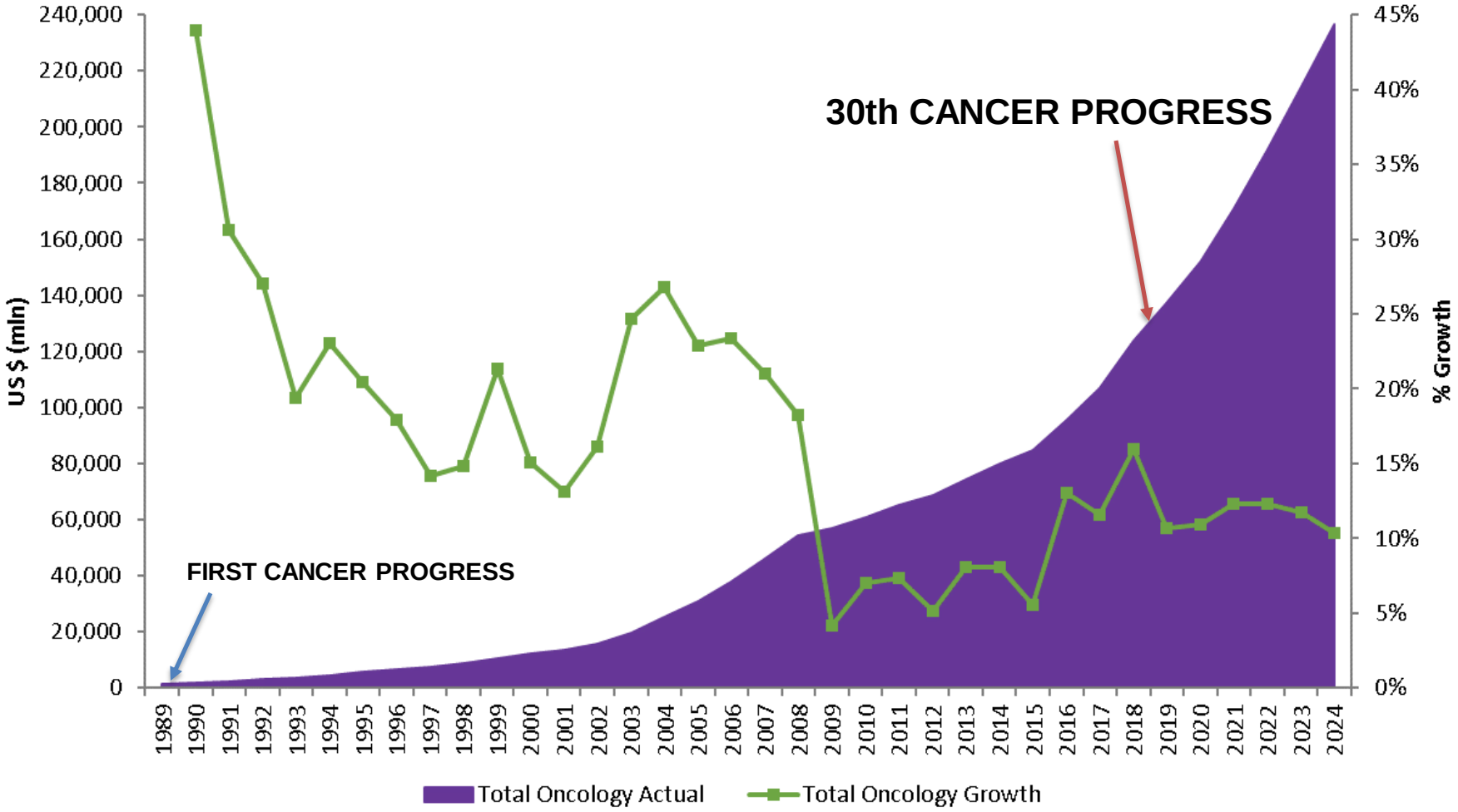
Balversa (erdafitinib); Janssen Oncology; For the treatment of locally advanced or metastatic urothelial carcinoma , Approved April 2019
Herceptin Hylecta (trastuzumab and hyaluronidase-oysk); Halozyme; For the treatment of HER2-overexpressing breast cancer, Approved February 2019
Keytruda (pembrolizumab); Merck; For the treatment of stage III non-small cell lung cancer, Approved April 2019
Keytruda (pembrolizumab); Merck; For the treatment of advanced renal cell carcinoma, Approved April 2019
Tecentriq (atezolizumab); Genentech/Roche; For the treatment of extensive-stage small cell lung cancer , Approved March 2019
Tecentriq (atezolizumab); Genentech/Roche; For the treatment of triple negative breast cancer, Approved March 2019

Drugs Approved in 2018

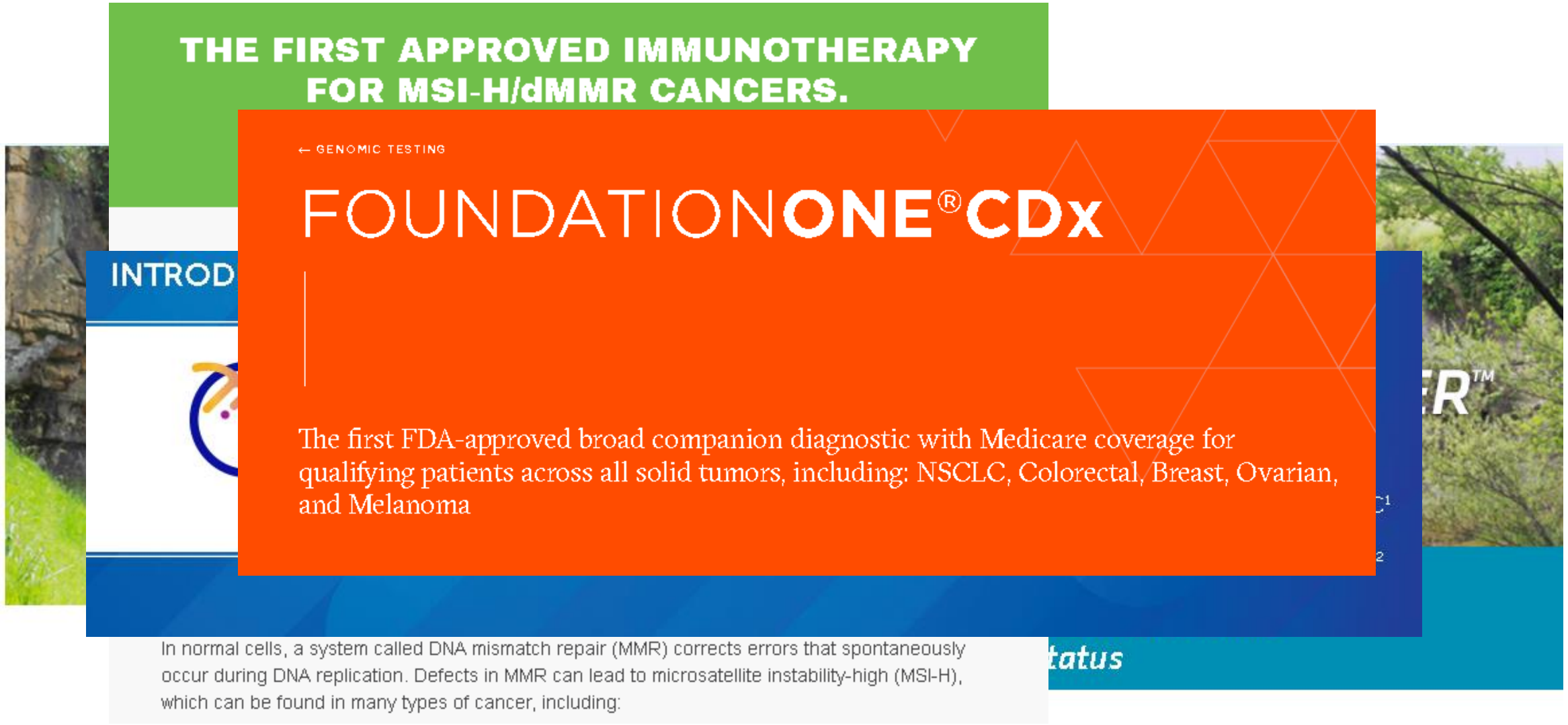
Asparlas (calaspargase pegol-mknl); Servier; For the treatment of acute lymphoblastic leukemia in pediatrics and young adults, Approved December 2018
Braftovi (encorafenib) + Mektovi (binimetinib); Array BioPharma; For the treatment of unresectable or metastatic melanoma with a BRAFV600E or BRAFV600K mutation, Approved June 2018
Copiktra (duvelisib); Verastem; For the treatment of chronic lymphocytic leukemia, small lymphocytic lymphoma or follicular lymphoma, Approved September 2018
Daurismo (glasdegib); Pfizer; For the treatment of newly-diagnosed acute myeloid leukemia in adults 75 years of age or older , Approved November 2018
Elzonris (tagraxofusp-erzs); Stemline Therapeutics; For the treatment of blastic plasmacytoid dendritic cell neoplasm in adults and pediatrics, Approved December 2018
Erleada (apalutamide); Janssen Oncology; For the treatment of prostate cancer, Approved February 2018
Keytruda (pembrolizumab); Merck; For the treatment of recurrent or metastatic cervical cancer , Approved June 2018
Keytruda (pembrolizumab); Merck; For the treatment of primary mediastinal B-cell lymphoma, Approved June 2018
Keytruda (pembrolizumab); Merck; For the treatment of Merkel cell carcinoma, Approved December 2018
Keytruda (pembrolizumab); Merck; For the treatment of hepatocellular carcinoma, Approved November 2018
Lenvima (lenvatinib); Eisai; For the treatment of unresectable hepatocellular carcinoma, Approved August 2018
Libtayo (cemiplimab-rwlc); Regeneron Pharmaceuticals; For the treatment of cutaneous squamous cell carcinoma, Approved September 2018
Lorbrena (lorlatinib); Pfizer; For the treatment of ALK-positive metastatic non-small cell lung cancer , Approved November 2018
Lumoxiti (moxetumomab pasudotox-tdf); AstraZeneca; For the treatment of relapsed or refractory hairy cell leukemia, Approved September 2018
Lutathera (lutetium Lu 177 dotatate); Advanced Accelerator Applications; For the treatment of gastroenteropancreatic neuroendocrine tumors, Approved January 2018
Opdivo (nivolumab); Bristol-Myers Squibb; For the treatment of advanced small cell lung cancer, Approved August 2018
Opdivo (nivolumab); Bristol-Myers Squibb; For the treatment of MSI-H or dMMR metastatic colorectal cancer , Approved August 2018
Poteligeo (mogamulizumab-kpkc); Kyowa Kirin; For the treatment of mycosis fungoides or Sézary syndrome , Approved August 2018
Talzenna (talazoparib); Pfizer; For the treatment of deleterious germline BRCA-mutated HER2-negative locally advanced or metastatic breast cancer, Approved October 2018
Tibsovo (ivosidenib); Agios Pharmaceuticals; For the treatment of acute myeloid leukemia with a susceptible IDH1 mutation, Approved July 2018
Vitrakvi (larotrectinib); Loxo Oncology; For the treatment of solid tumors that have a neurotrophic receptor tyrosine kinase (NTRK) gene fusion, Approved November 2018
Vizimpro (dacomitinib); Pfizer; For the treatment of metastatic non-small cell lung cancer , Approved September 2018
Xospata (gilteritinib) ; Astellas; For the treatment of acute myeloid leukemia with a FLT3 mutation, Approved November 2018

Total WW Oncology Sales & Growth: Actual & Growth

Source: Evaluate Ltd



EvaluatePharma, May 2019



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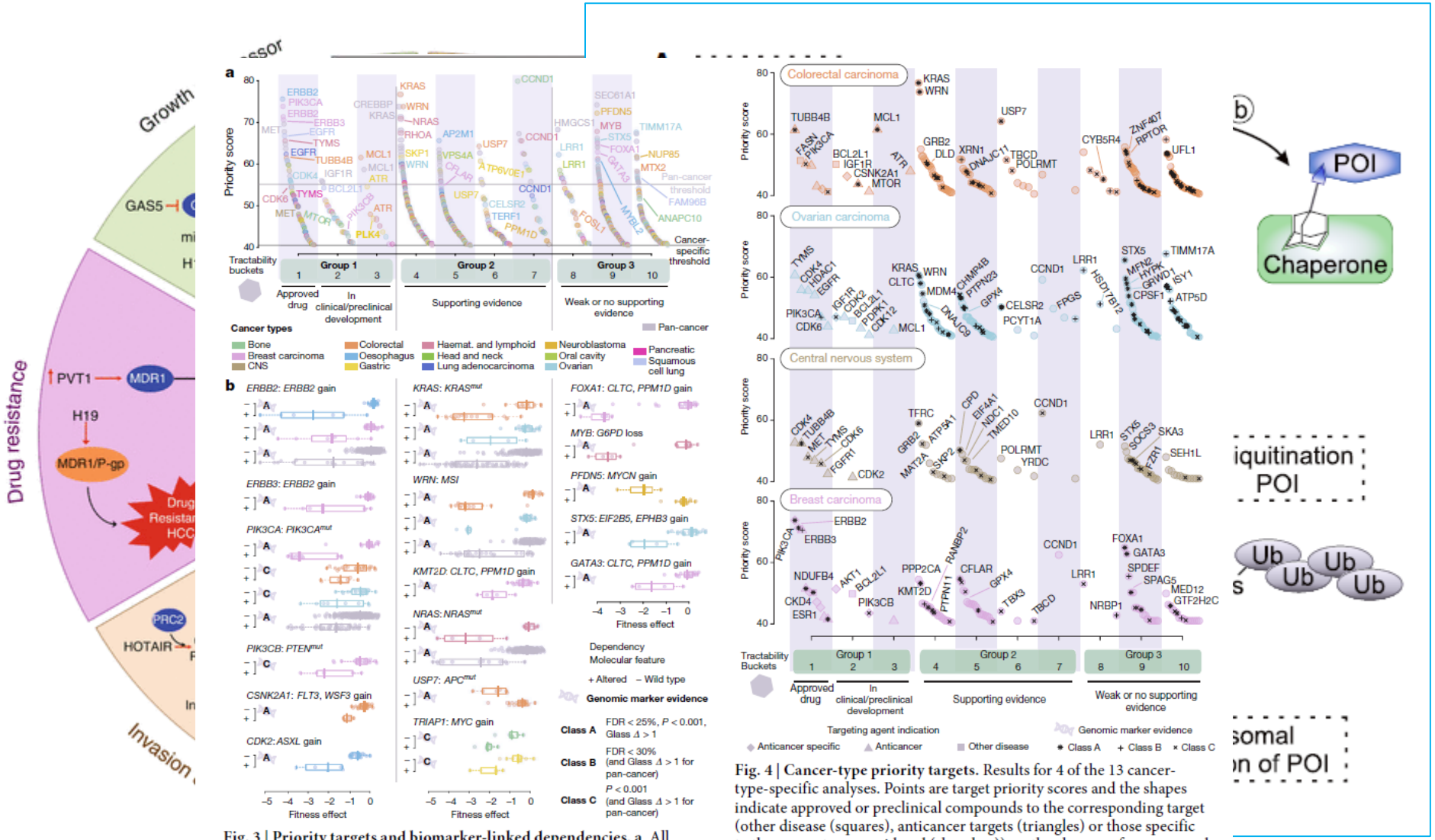
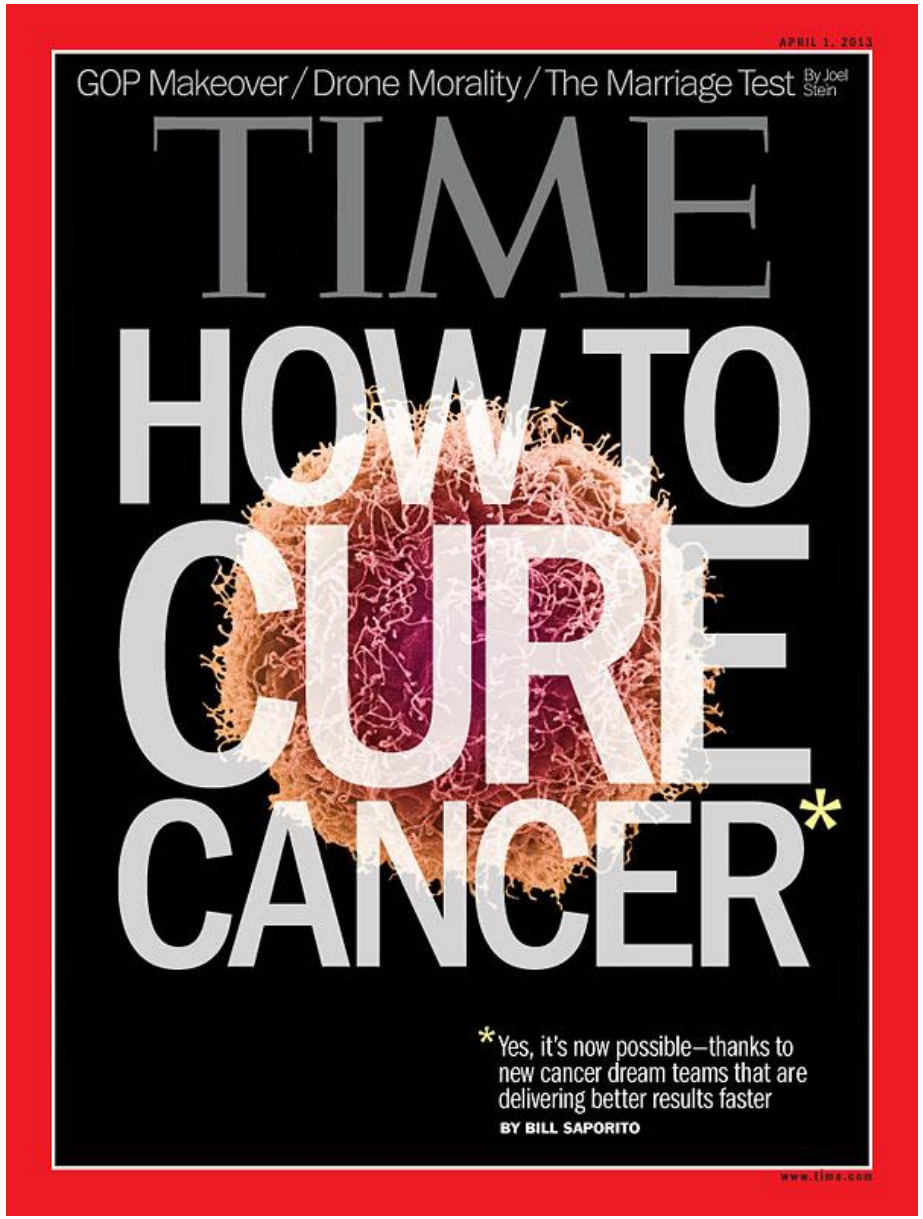


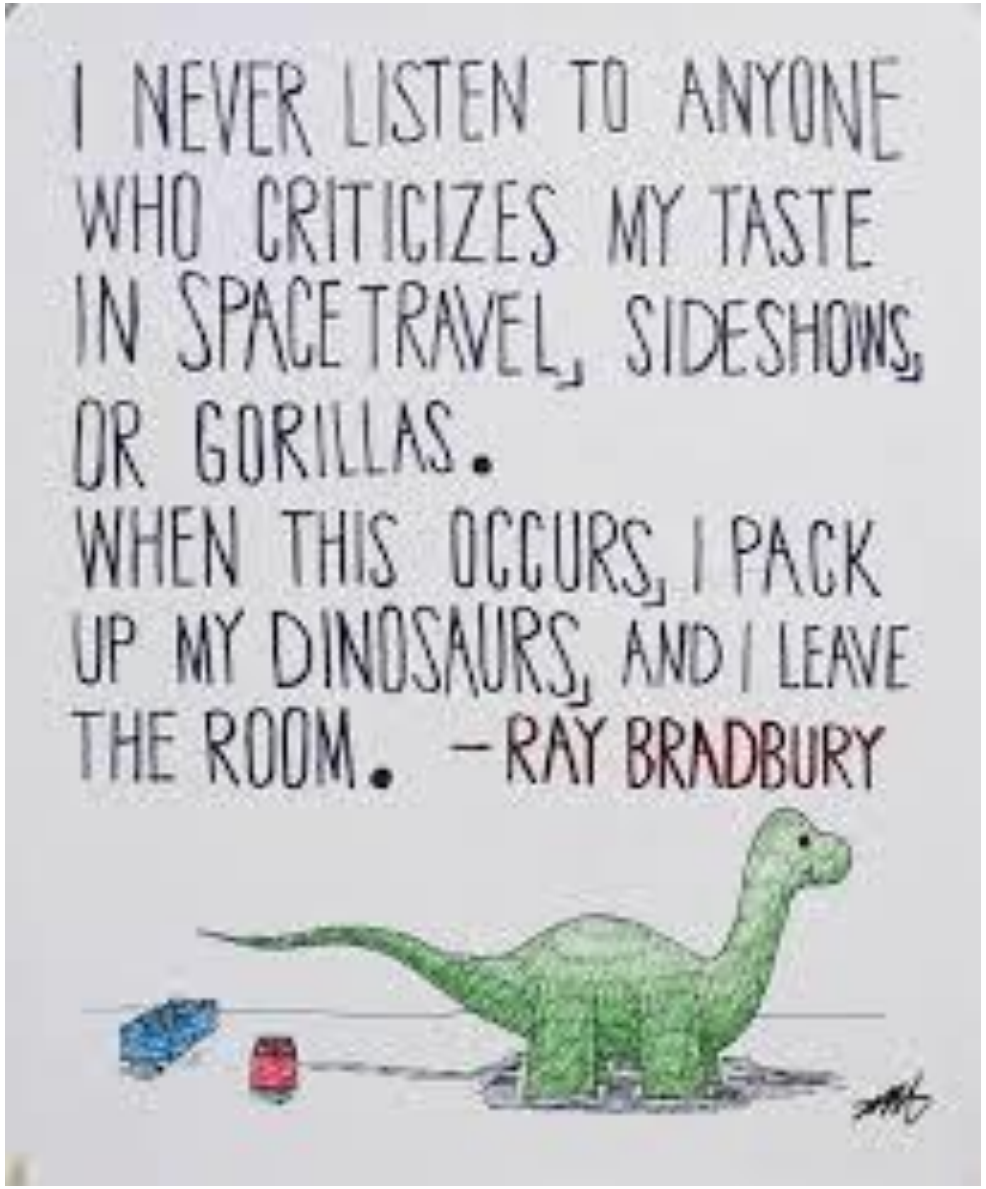
Fig. 3 | Priority targets and biomarker-linked dependencies. a, All priority targets from cancer-type and pan-cancer analyses and their tractability. Priority score thresholds are indicated and selected examples

Fig. 4 | Cancer-type priority targets. Results for 4 of the 13 cancer-type-specific analyses. Points are target priority scores and the shapes indicate approved or preclinical compounds to the corresponding target (other disease (squares), anticancer targets (triangles) or those specific to the cancer type considered (rhombus)), or the absence of a compound (circles). Symbols indicate the strength of a genomic biomarker. Selected priority targets are labelled.

Biotechnology

Renganathan A., Felley-Bosco E. (2017) Long Noncoding RNAs in Cancer and Therapeutic Potential. In: Rao M. (eds) Long Non Coding RNA Biology. Advances in Experimental Medicine and Biology, vol 1008. Springer, Singapore; Trends Biotechnol. 2017 Jul;35(7):665-676; Cell Chem Biol. 2017 Sep 21;24(9):1181-1190; Nature Vol 568, pp 511–516 (2019)





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