MINI **Medical School**

A 20/20 VIEW OF CANCER

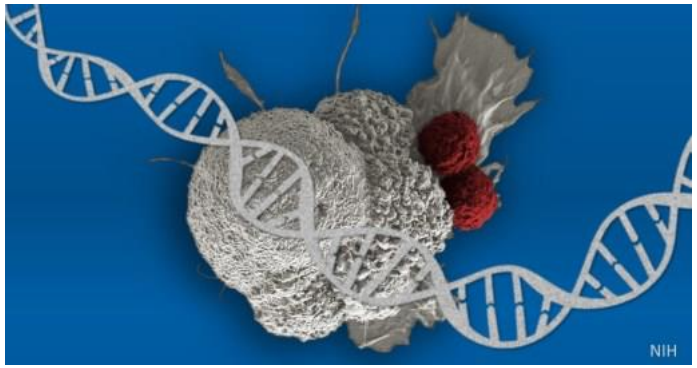
Cancer Genetics: Cracking Cancer's Code

David Largaespada, Ph.D.

Professor

Department of Pediatrics

Associate Director for Basic Sciences, Masonic Cancer Center



NIH Directors Blog

Masonic Cancer Center
University of Minnesota
Comprehensive Cancer Center designated by the National Cancer Institute

Office of Academic Clinical Affairs
University of Minnesota
Driven to Discover®

Disclosures

- I have no actual or potential conflict of interest in relation to this program/presentation.
- I am a co-founder, consultant, and co-owner of NeoClone Biotechnologies, Inc., Discovery Genomics, Inc., (recently acquired by Immusoft, Inc.), B-MoGen Biotechnologies, Inc. (recently acquired by Biotechne, Inc.), and Luminary Therapeutics, Inc. This presentation is not directly related to the business of these companies and I obtain no funds for my laboratory research from these companies.
- Some of my laboratory's work is funded by Genentech, Inc. That work will not be discussed today.
- I hold equity in and serve as the Chief Scientific Officer of Surrogen, a subsidiary of Recombinetics, a genome-editing company. That work will not be discussed today.

Learning Objectives

- All cancer has a genetic cause – but that doesn't (usually) mean the genes you're born with cause cancer, instead cancer is primarily caused by mutations occurring in rare cells in your body.

Learning Objectives

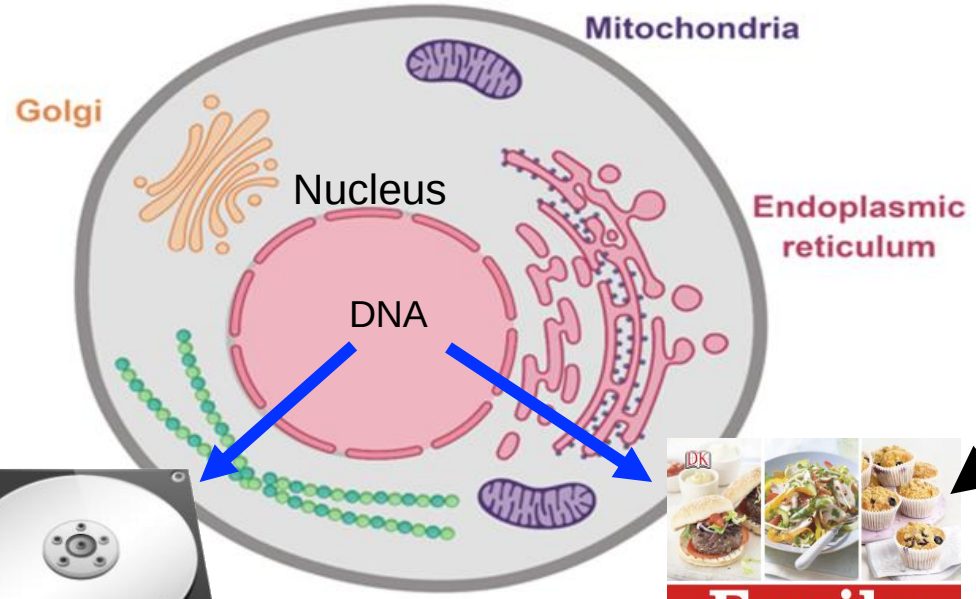
- All cancer has a genetic cause – but that doesn't (usually) mean the genes you're born with cause cancer, instead cancer is primarily caused by mutations occurring in rare cells in your body.
- For most people, their cancer risk is more determined by lifestyle choices than who their parents are. But some families do pass along high risk cancer-causing gene mutations from parent to child.
- Cancer cells typically have many, many gene mutations and about 6 or more of these "drive" the abnormal behavior of the cancer cells, while the rest are merely "passengers".
- It is thought that the genes mutated in a cancer can produce abnormal proteins allowing the immune system to kill off the cancer cells. This is how "immunotherapies" like Keytruda can work for some cases of cancer.
- The specific genes that are mutated in a tumor or leukemia may determine the prognosis of the patient and dictate the best therapy for the physician to choose.

All Cancer is "Genetic" Because:

- ALL cancer cells have altered genomes compared to a normal cell
- Those DNA alterations are called mutations

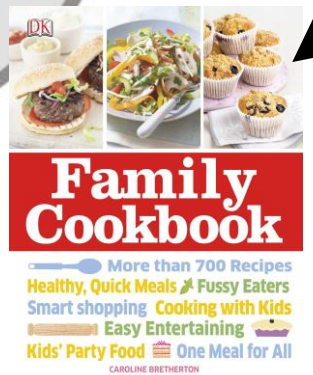
GENOME

GENOME



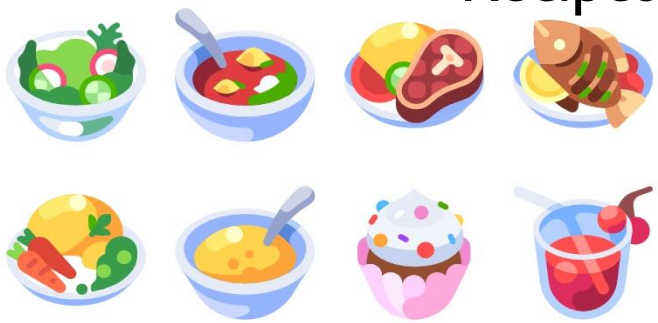
Files

Hard Drive



Cookbook

Recipes



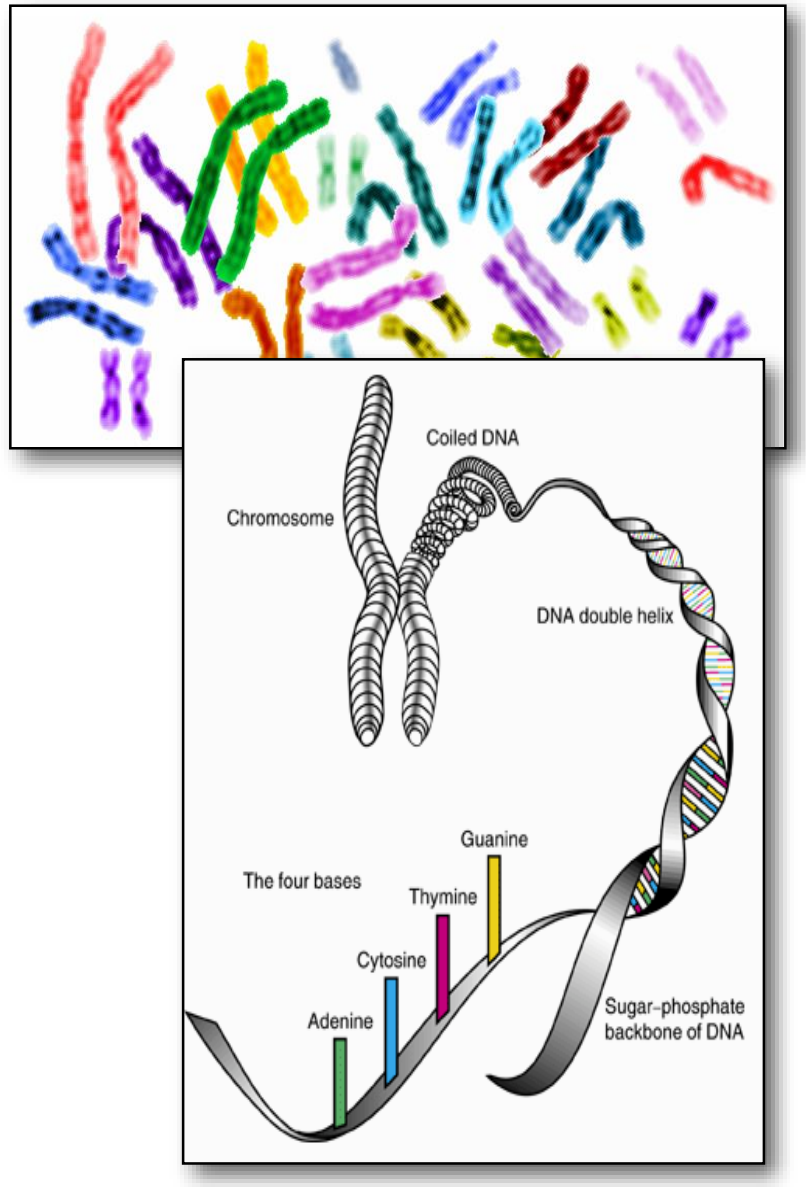
Genes

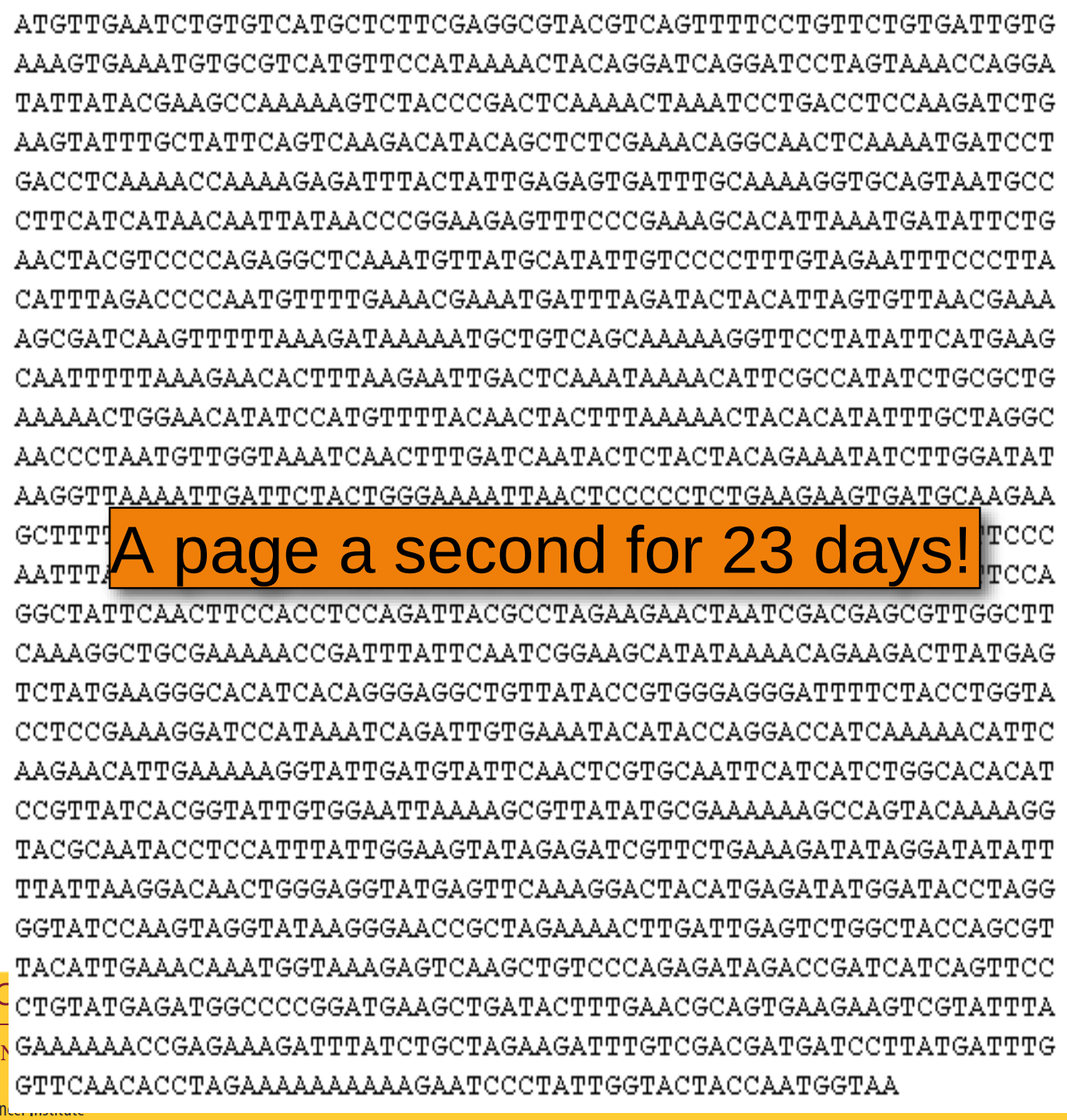
Cancers Are Genetic Diseases that Result from Alterations in DNA Sequence &/or Expression

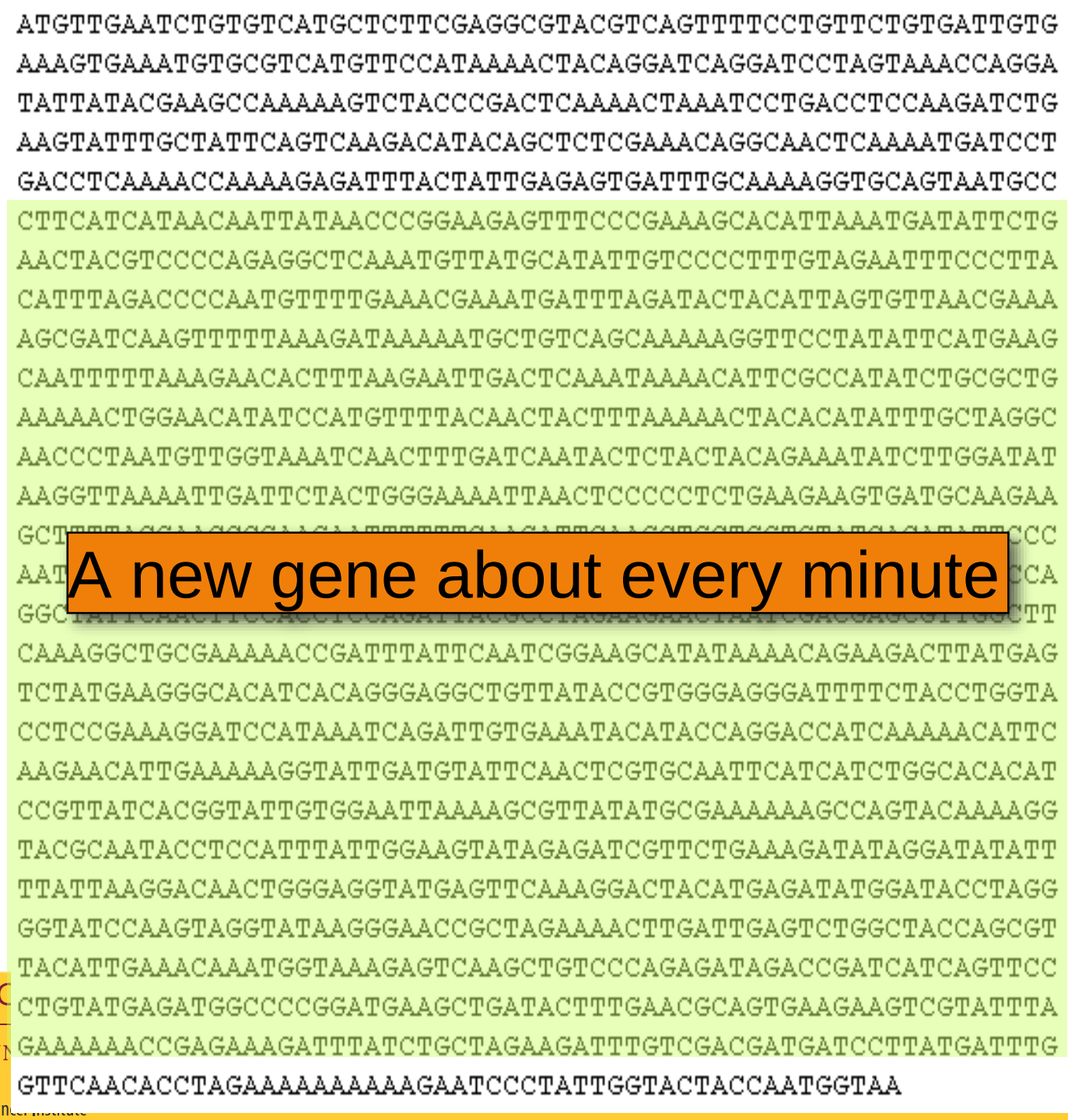
- Cancers result from the corruption or misuse of DNA.
  - Corruption results from changes in DNA that can be small (single nucleotide changes/mutations) or large (chromosomal abnormalities).
  - Misuse results from changes in when and what genetic information is accessed (epigenetics).
- Cancers are often genetically unstable.
  - DNA copying/repair machinery is compromised leading to greater accumulations of DNA mistakes during cell division.

Consider How Much Information is Stored in Every Human Cell

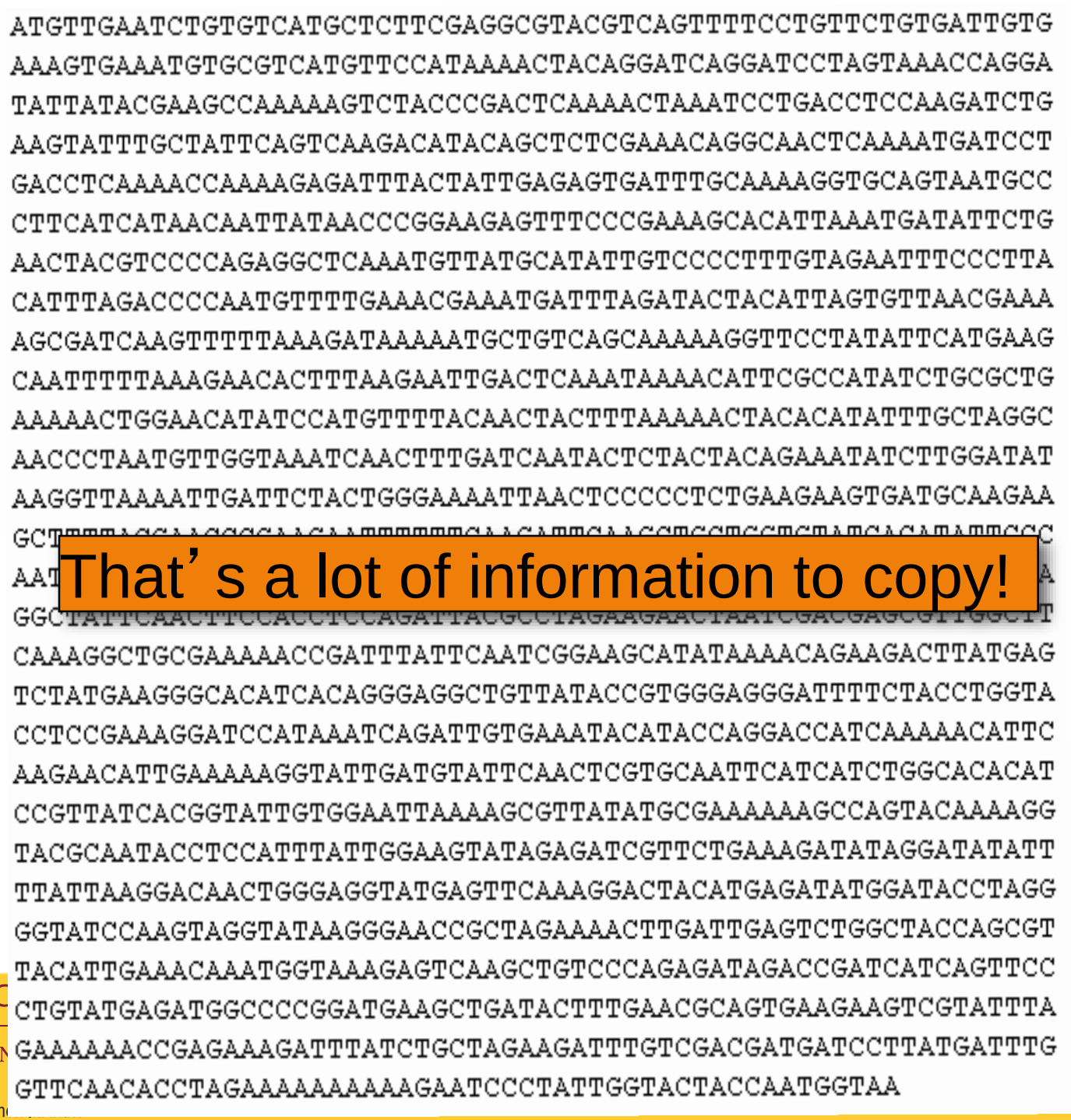
- All the DNA in one cell, if stretched out, would be over 2 meters long!
- The human genome would take 6,000,000 pages of 500 words each just to print out



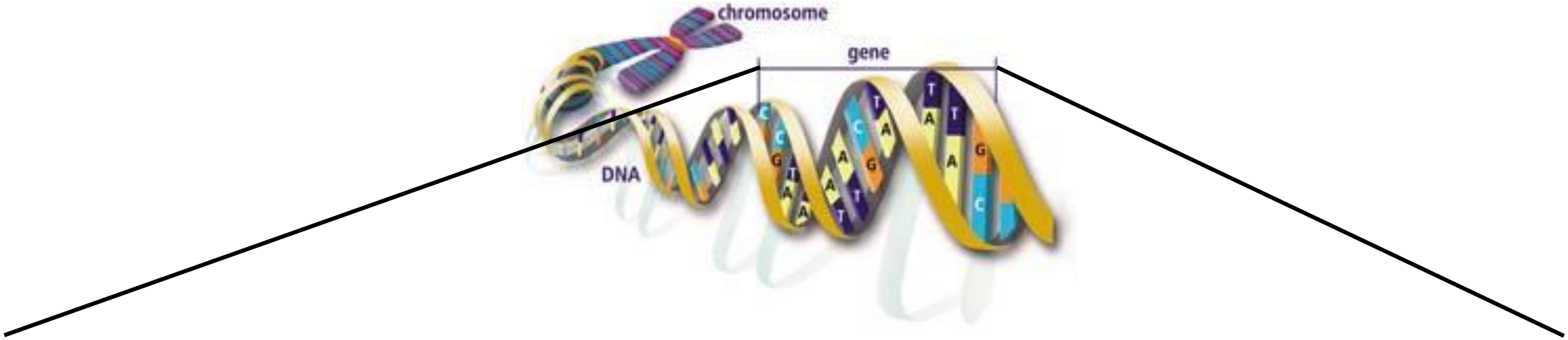

ATGTTGAATCTGTGTCATGCTCTTCGAGGCGTACGTCAGTTTTCCTGTTCTGTGATTGTG
AAAGTGAAATGTGCGTCATGTTCCATAAAACTACAGGATCAGGATCCTAGTAAACCAGGA
TATTATACGAAGCCAAAAAGTCTACCCGACTCAAAACTAAATCCTGACCTCCAAGATCTG
AAGTATTTGCTATTCAGTCAAGACATACAGCTCTCGAAACAGGCAACTCAAAATGATCCT
GACCTCAAAACCAAAAGAGATTTACTATTGAGAGTGATTTGCAAAAGGTGCAGTAATGCC
CTTCATCATAACAATTATAACCCGGAAGAGTTTCCCGAAAGCACATTAAATGATATTCTG
AACTACGTCCCCAGAGGCTCAAATGTTATGCATATTGTCCCCTTTGTAGAATTTCCCTTA
CATTTAGACCCCAATGTTTTGAAACGAAATGATTTAGATACTACATTAGTGTTAACGAAA
AGCGATCAAGTTTTTAAAGATAAAAATGCTGTCAGCAAAAAGGTTCCTATATTCATGAAG
CAATTTTTAAAGAACACTTTAAGAATTGACTCAAATAAAACATTCGCCATATCTGCGCTG
AAAAACTGGAACATATCCATGTTTTACAACTACTTTAAAAACTACACATATTTGCTAGGC
AACCCTAATGTTGGTAAATCAACTTTGATCAATACTCTACTACAGAAATATCTTGGATAT
AAGGTTAAAATTGATTCTACTGGGAAAATTAACTCCCCCTCTGAAGAAGTGATGCAAGAA
GCTTTT[A page a second for 23 days!]TCCC
AATTTA[illegible]TCCA
GGCTATTCAACTTCCACCTCCAGATTACGCCTAGAAGAACTAATCGACGAGCGTTGGCTT
CAAAGGCTGCGAAAAACCGATTTATTCAATCGGAAGCATATAAAACAGAAGACTTATGAG
TCTATGAAGGGCACATCACAGGGAGGCTGTTATACCGTGGGAGGGATTTTCTACCTGGTA
CCTCCGAAAGGATCCATAAATCAGATTGTGAAATACATACCAGGACCATCAAAAACATTC
AAGAACATTGAAAAAGGTATTGATGTATTCAACTCGTGCAATTCATCATCTGGCACACAT
CCGTTATCACGGTATTGTGGAATTAAAAGCGTTATATGCGAAAAAAGCCAGTACAAAAGG
TACGCAATACCTCCATTTATTGGAAGTATAGAGATCGTTCTGAAAGATATAGGATATATT
TTATTAAGGACAACTGGGAGGTATGAGTTCAAAGGACTACATGAGATATGGATACCTAGG
GGTATCCAAGTAGGTATAAGGGAACCGCTAGAAAACTTGATTGAGTCTGGCTACCAGCGT
TACATTGAAACAAATGGTAAAGAGTCAAGCTGTCCCAGAGATAGACCGATCATCAGTTCC
CTGTATGAGATGGCCCCGGATGAAGCTGATACTTTGAACGCAGTGAAGAAGTCGTATTTA
GAAAAAACCGAGAAAGATTTATCTGCTAGAAGATTTGTCGACGATGATCCTTATGATTTG
GTTCAACACCTAGAAAAAAAAAAGAATCCCTATTGGTACTACCAATGGTAA



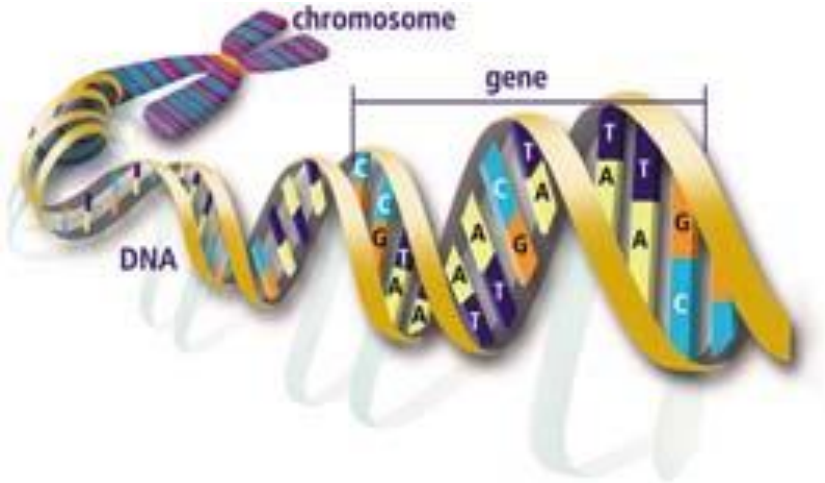
A new gene about every minute



Each DNA Strand is Copied During Replication



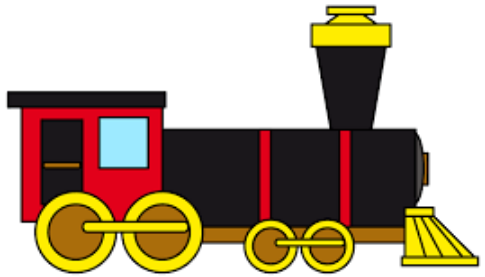
Each DNA Strand is Copied During Replication



G G A A T T G A A A C C C A G A A C T

C C T T A A C T T T G G G T C T T G A T T G A T

Radiation Can Break DNA

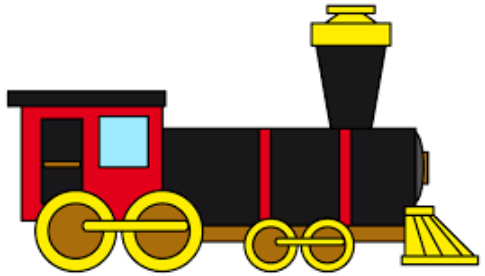


T G A A AC C C

C C T T A A C T T T G G G

G A T T G A T

Errors in DNA Repair Cause Mutations



AGAAACCCAGTACTAA

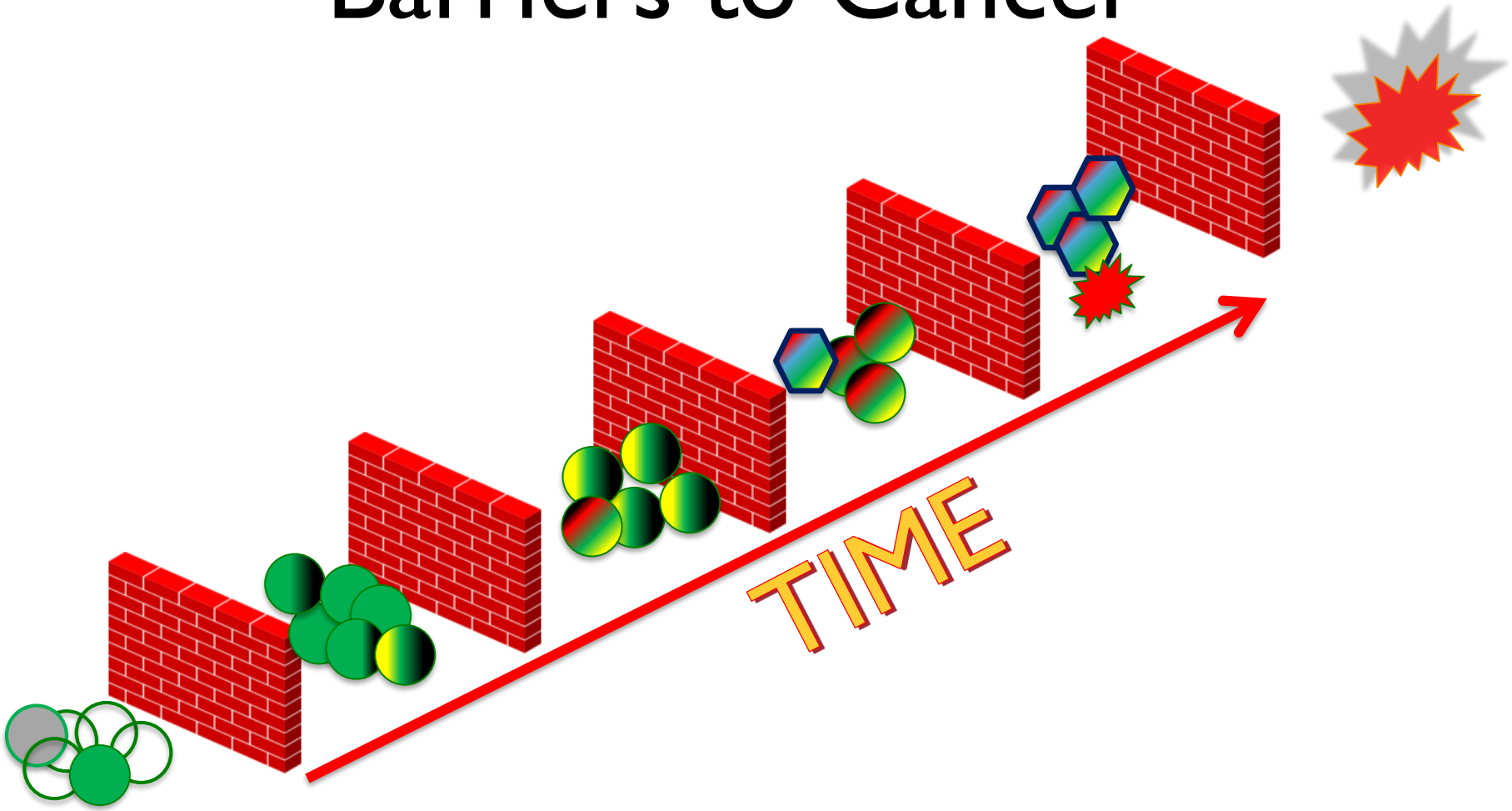
CCTTAACTTTGGG GATTGAT

Carcinogens Can Alter DNA

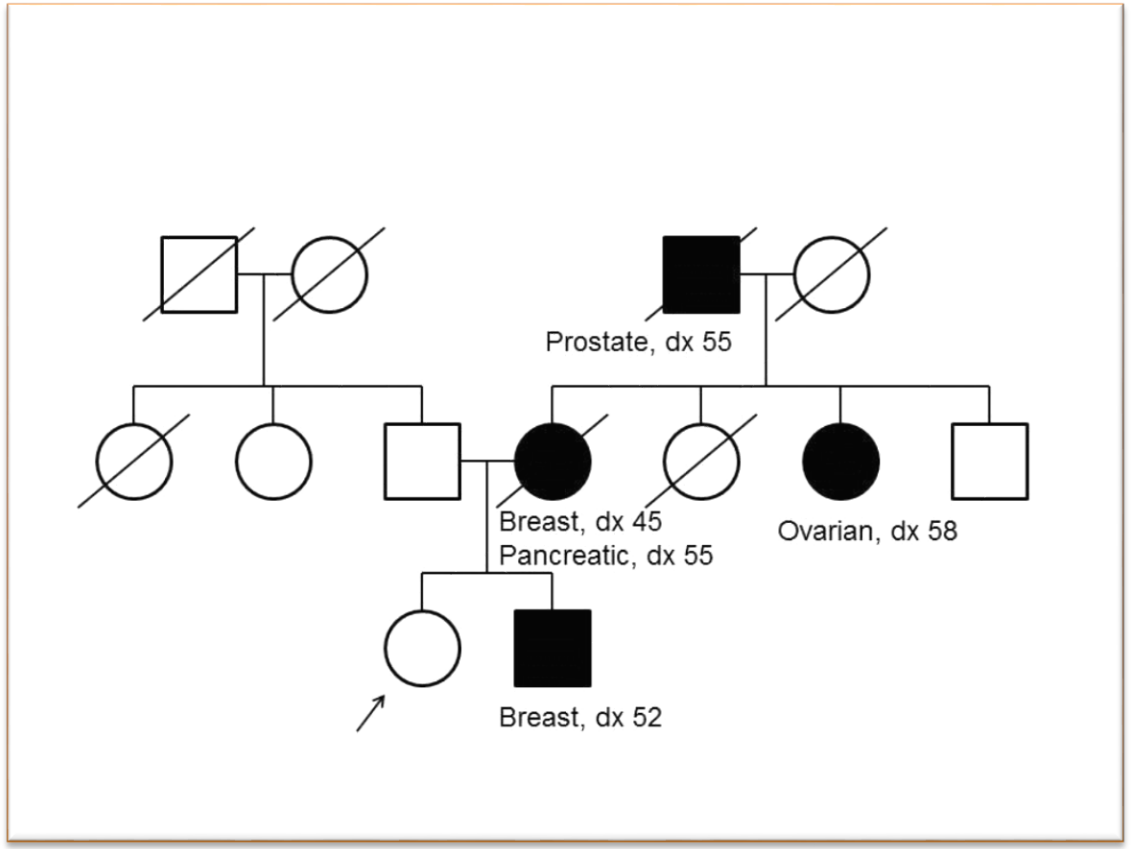
Carcinogens Can Alter DNA

ADDUCT
(add a duck)

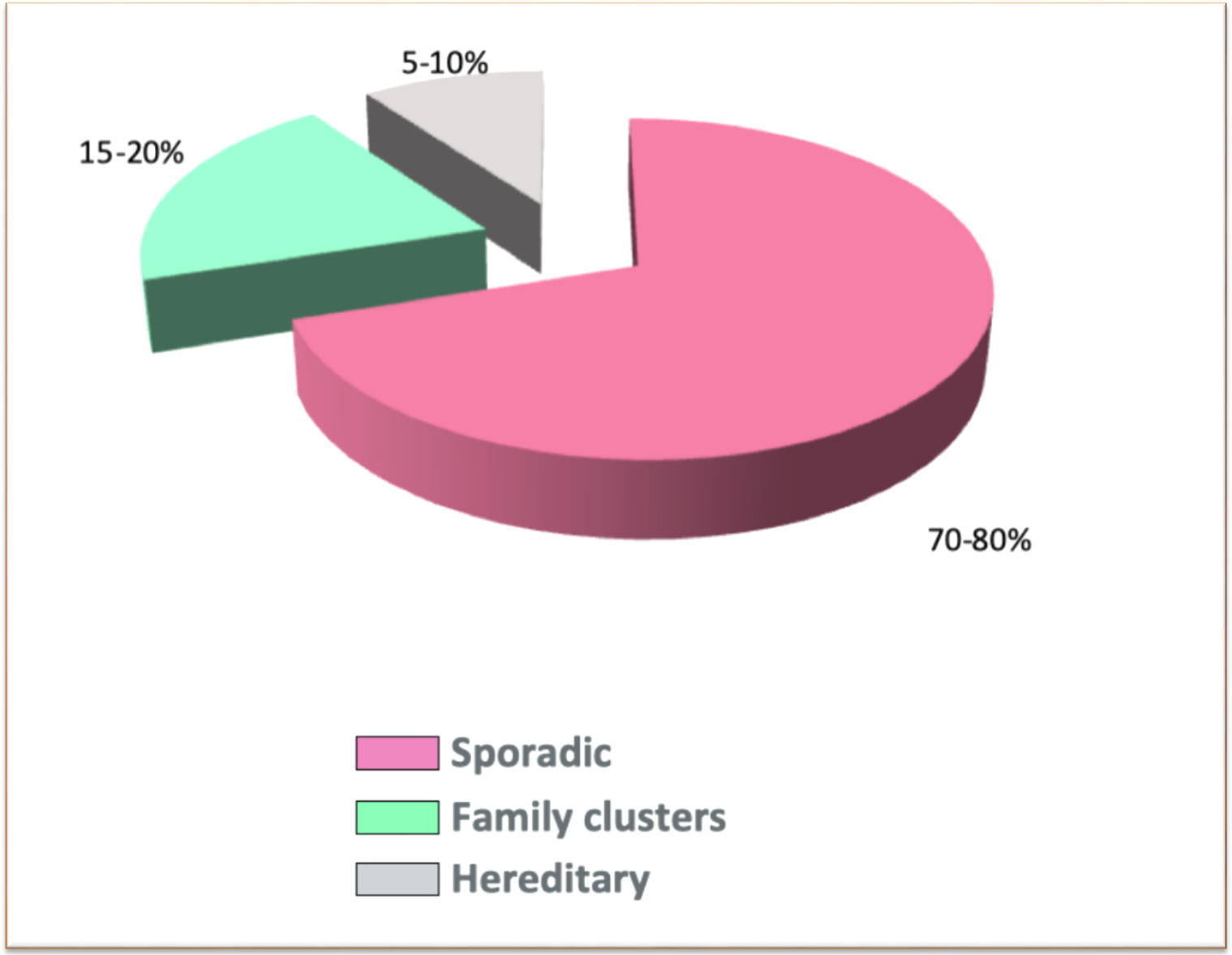
Mutations Allow Cells to Overcome Barriers to Cancer



If Cancer is Caused by DNA Damage During our Lifetimes, Then Why Does Cancer "Run in the Family" Sometimes?

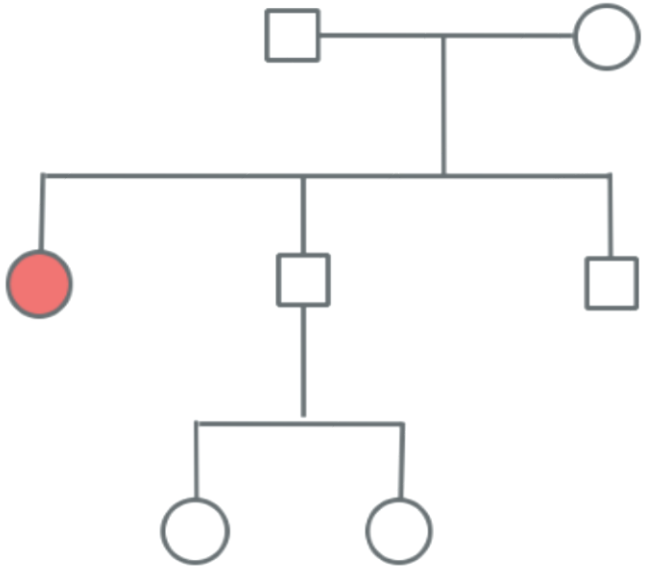


How Much of Cancer is Hereditary?



Sporadic

70-80% of cancer in families



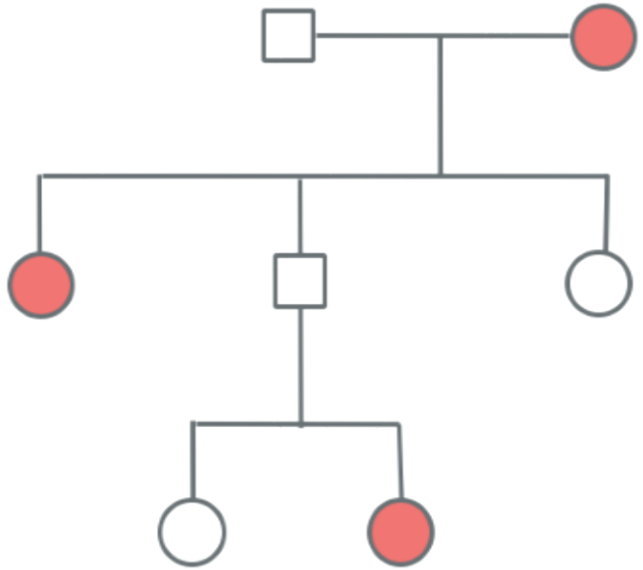
Acquired mutations in the tumor

Single or Unilateral Tumor

Later age of onsets

Familial

15-20% of cancer in families



Germline Mutation??

Single or Unilateral Tumors

Early/late age of onset

"Red Flags" for Hereditary Breast and Ovarian Cancer?

- Breast cancer before age 50
- Ovarian cancer at any age
- Male breast cancer at any age
- Multiple primary cancers
- Ashkenazi Jewish ancestry
- Relatives of a mutation carrier

Cancer Risk Spectrum

HIGH

- Multiple generations affected (AD inheritance)
- Early onset
- Multiple primary tumors

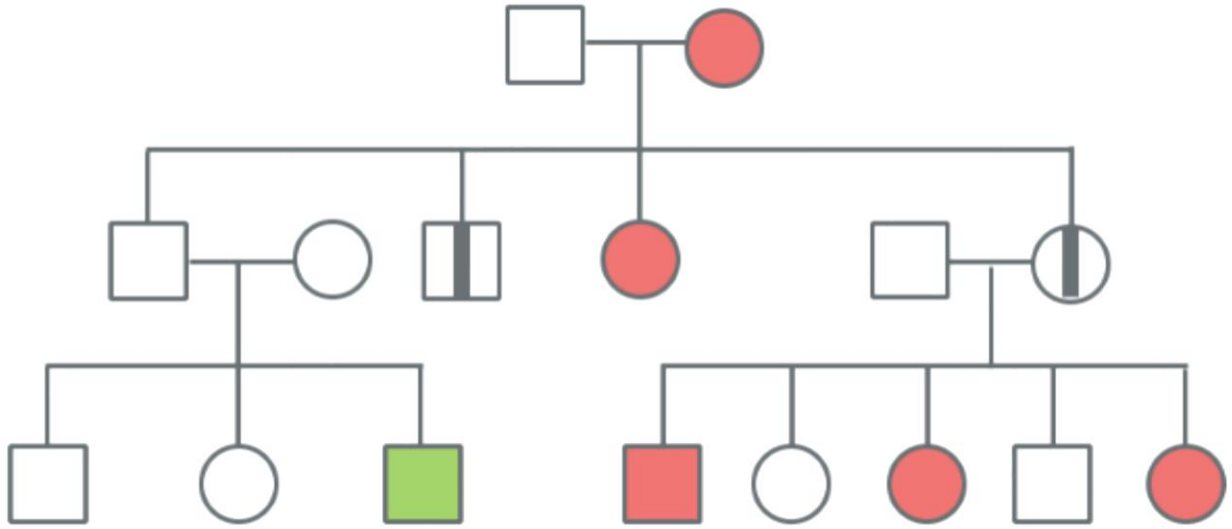
MODERATE

- Several family members affected
- No single gene pattern
- Variable onset

LOW

- No family history
- Late onset

Hereditary Cancer is Usually Inherited as Dominant Trait



Normal

Susceptible Carrier

Carrier, affected with cancer

Sporadic cancer

- Penetrance is often incomplete
- May appear to "skip" generations
- Individuals inherit altered cancer susceptibility gene, not cancer

What if You're Concerned your Family is Affected?

- Cancer management clinic contact information thru M Health: https://www.mhealth.org/care/services/cancer-risk-management-program

- There are hereditary cancer clinics in all the major health systems

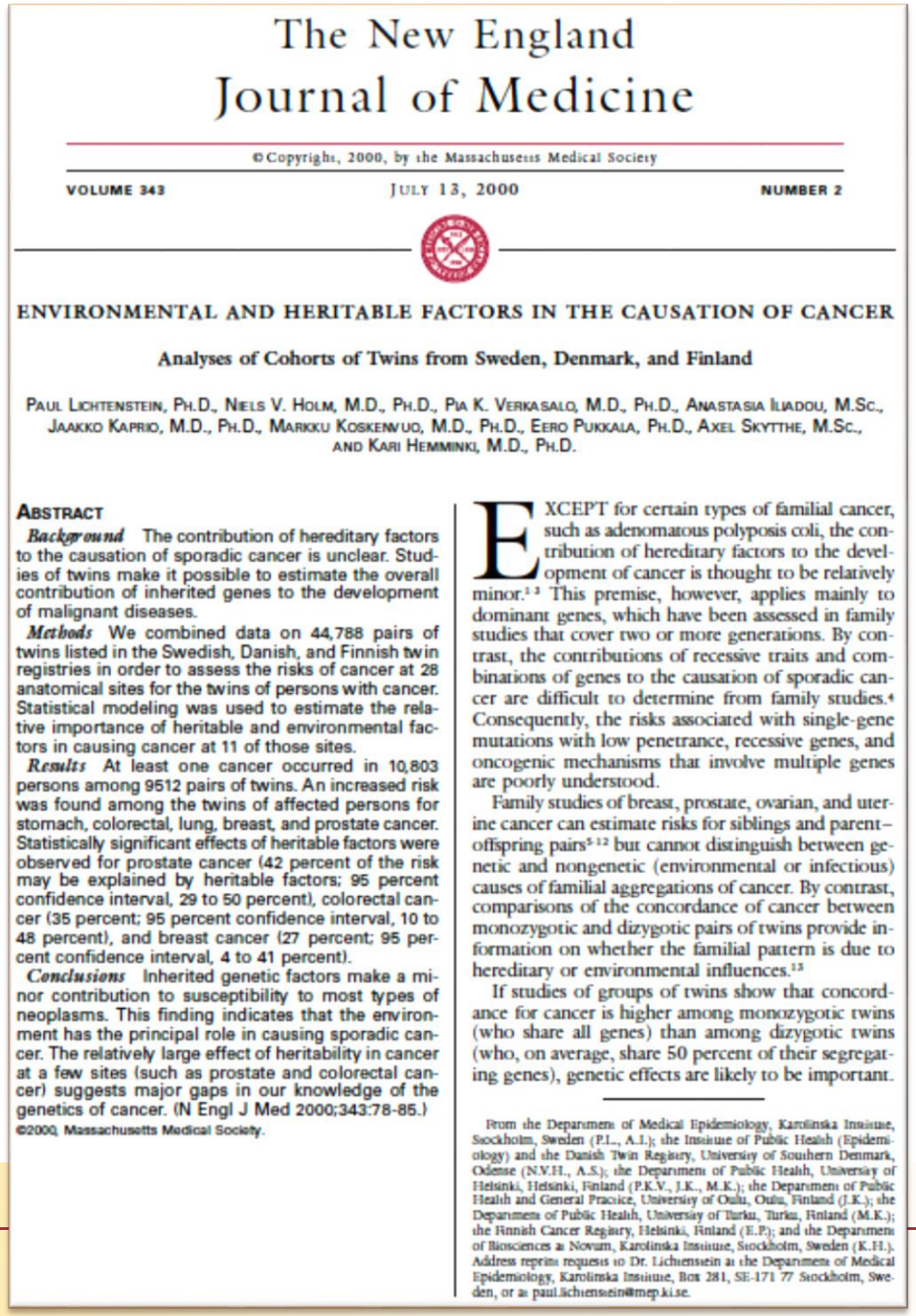
- There are online telehealth genetic counseling options like GeneMatters or Genome Medical that consumers can use as a resource.

Learning Objectives

- All cancer has a genetic cause – but that doesn't (usually) mean the genes you're born with cause cancer, instead cancer is primarily caused by mutations occurring in rare cells in your body.
- For most people, their cancer risk is more determined by lifestyle choices than who their parents are. But some families do pass along high risk cancer-causing gene mutations from parent to child.
- Cancer cells typically have many, many gene mutations and about 6 or more of these "drive" the abnormal behavior of the cancer cells, while the rest are merely "passengers".
- It is thought that the genes mutated in a cancer can produce abnormal proteins allowing the immune system to kill off the cancer cells. This is how "immunotherapies" like Keytruda can work for some cases of cancer.
- The specific genes that are mutated in a tumor or leukemia may determine the prognosis of the patient and dictate the best therapy for the physician to choose.

Large Study of Twins Suggests Lifestyle Choices have a Strong Role in Determining Cancer Risk

FOR MOST PEOPLE!



The New England Journal of Medicine

©Copyright, 2000, by the Massachusetts Medical Society

VOLUME 343 JULY 13, 2000 NUMBER 2

ENVIRONMENTAL AND HERITABLE FACTORS IN THE CAUSATION OF CANCER

Analyses of Cohorts of Twins from Sweden, Denmark, and Finland

PAUL LICHTENSTEIN, PH.D., NIELS V. HOLM, M.D., PH.D., PIA K. VERKASALO, M.D., PH.D., ANASTASIA ILIADOU, M.SC., JAAKKO KAPRIO, M.D., PH.D., MARKKU KOSKENVUO, M.D., PH.D., EERO PUKKALA, PH.D., AXEL SKYTTHE, M.SC., AND KARI HEMMINKI, M.D., PH.D.

ABSTRACT

Background The contribution of hereditary factors to the causation of sporadic cancer is unclear. Studies of twins make it possible to estimate the overall contribution of inherited genes to the development of malignant diseases.

Methods We combined data on 44,788 pairs of twins listed in the Swedish, Danish, and Finnish twin registries in order to assess the risks of cancer at 28 anatomical sites for the twins of persons with cancer. Statistical modeling was used to estimate the relative importance of heritable and environmental factors in causing cancer at 11 of those sites.

Results At least one cancer occurred in 10,803 persons among 9512 pairs of twins. An increased risk was found among the twins of affected persons for stomach, colorectal, lung, breast, and prostate cancer. Statistically significant effects of heritable factors were observed for prostate cancer (42 percent of the risk may be explained by heritable factors; 95 percent confidence interval, 29 to 50 percent), colorectal cancer (35 percent; 95 percent confidence interval, 10 to 48 percent), and breast cancer (27 percent; 95 percent confidence interval, 4 to 41 percent).

Conclusions Inherited genetic factors make a minor contribution to susceptibility to most types of neoplasms. This finding indicates that the environment has the principal role in causing sporadic cancer. The relatively large effect of heritability in cancer at a few sites (such as prostate and colorectal cancer) suggests major gaps in our knowledge of the genetics of cancer. (N Engl J Med 2000;343:78-85.)

EXCEPT for certain types of familial cancer, such as adenomatous polyposis coli, the contribution of hereditary factors to the development of cancer is thought to be relatively minor.[1,2] This premise, however, applies mainly to dominant genes, which have been assessed in family studies that cover two or more generations. By contrast, the contributions of recessive traits and combinations of genes to the causation of sporadic cancer are difficult to determine from family studies.[4] Consequently, the risks associated with single-gene mutations with low penetrance, recessive genes, and oncogenic mechanisms that involve multiple genes are poorly understood.

Family studies of breast, prostate, ovarian, and uterine cancer can estimate risks for siblings and parent–offspring pairs[5-12] but cannot distinguish between genetic and nongenetic (environmental or infectious) causes of familial aggregations of cancer. By contrast, comparisons of the concordance of cancer between monozygotic and dizygotic pairs of twins provide information on whether the familial pattern is due to hereditary or environmental influences.[13]

If studies of groups of twins show that concordance for cancer is higher among monozygotic twins (who share all genes) than among dizygotic twins (who, on average, share 50 percent of their segregating genes), genetic effects are likely to be important.

From the Department of Medical Epidemiology, Karolinska Institute, Stockholm, Sweden (P.L., A.I.); the Institute of Public Health (Epidemiology) and the Danish Twin Registry, University of Southern Denmark, Odense (N.V.H., A.S.); the Department of Public Health, University of Helsinki, Helsinki, Finland (P.K.V., J.K., M.K.); the Department of Public Health and General Practice, University of Oulu, Oulu, Finland (J.K.); the Department of Public Health, University of Turku, Turku, Finland (M.K.); the Finnish Cancer Registry, Helsinki, Finland (E.P.); and the Department of Biosciences at Novum, Karolinska Institute, Stockholm, Sweden (K.H.). Address reprint requests to Dr. Lichtenstein at the Department of Medical Epidemiology, Karolinska Institute, Box 281, SE-171 77 Stockholm, Sweden, or at paul.lichtenstein@mep.ki.se.

Determined Concordance Rate for Cancer in Identical Twins Versus Fraternal Twins

How often did both get cancer?
How often did just one of the two get cancer?

How often did both get cancer?
How often did just one of the two get cancer?

- Allows estimate of heritability
- If fraternal twins are concordant as often as identical twins, then it suggests shared environmental effects important in cancer risk
- If identical twins are concordant more often than fraternal twins, then it suggests shared heritable effects important in cancer risk

For Most Cancers, for Most People, Environment has Principal Role in Determining Cancer Risk

Conclusions Inherited genetic factors make a minor contribution to susceptibility to most types of neoplasms. This finding indicates that the environment has the principal role in causing sporadic cancer. The relatively large effect of heritability in cancer at a few sites (such as prostate and colorectal cancer) suggests major gaps in our knowledge of the genetics of cancer. (N Engl J Med 2000;343:78-85.)

Learning Objectives

- All cancer has a genetic cause – but that doesn't (usually) mean the genes you're born with cause cancer, instead cancer is primarily caused by mutations occurring in rare cells in your body.
- For most people, their cancer risk is more determined by lifestyle choices than who their parents are. But some families do pass along high risk cancer-causing gene mutations from parent to child.
- Cancer cells typically have many, many gene mutations and about 6 or more of these "drive" the abnormal behavior of the cancer cells, while the rest are merely "passengers".
- It is thought that the genes mutated in a cancer can produce abnormal proteins allowing the immune system to kill off the cancer cells. This is how "immunotherapies" like Keytruda can work for some cases of cancer.
- The specific genes that are mutated in a tumor or leukemia may determine the prognosis of the patient and dictate the best therapy for the physician to choose.

Epidemiologic Studies Have Shown that *Age* is a Surprisingly *Large Factor in the Incidence of Cancer*

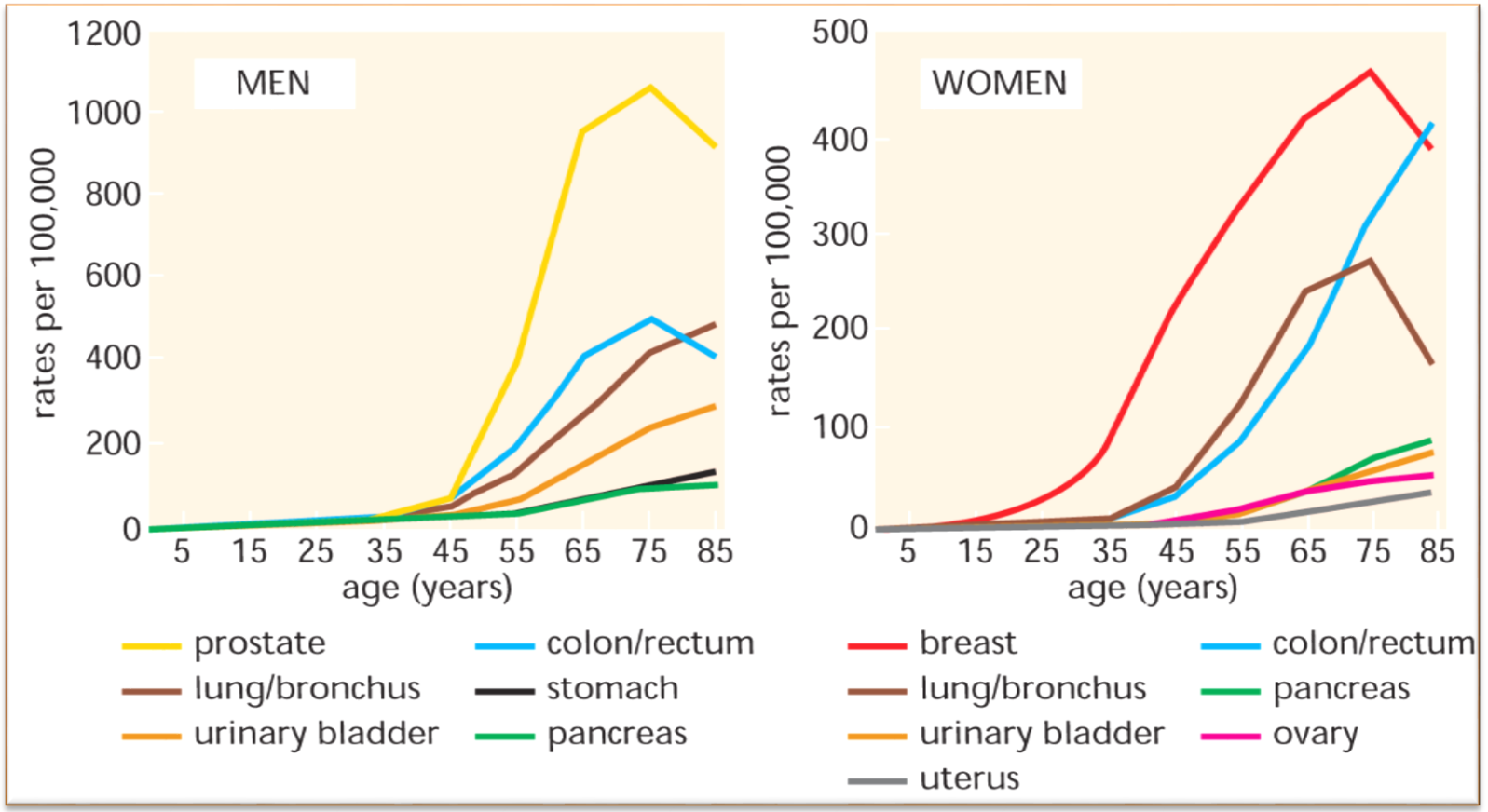
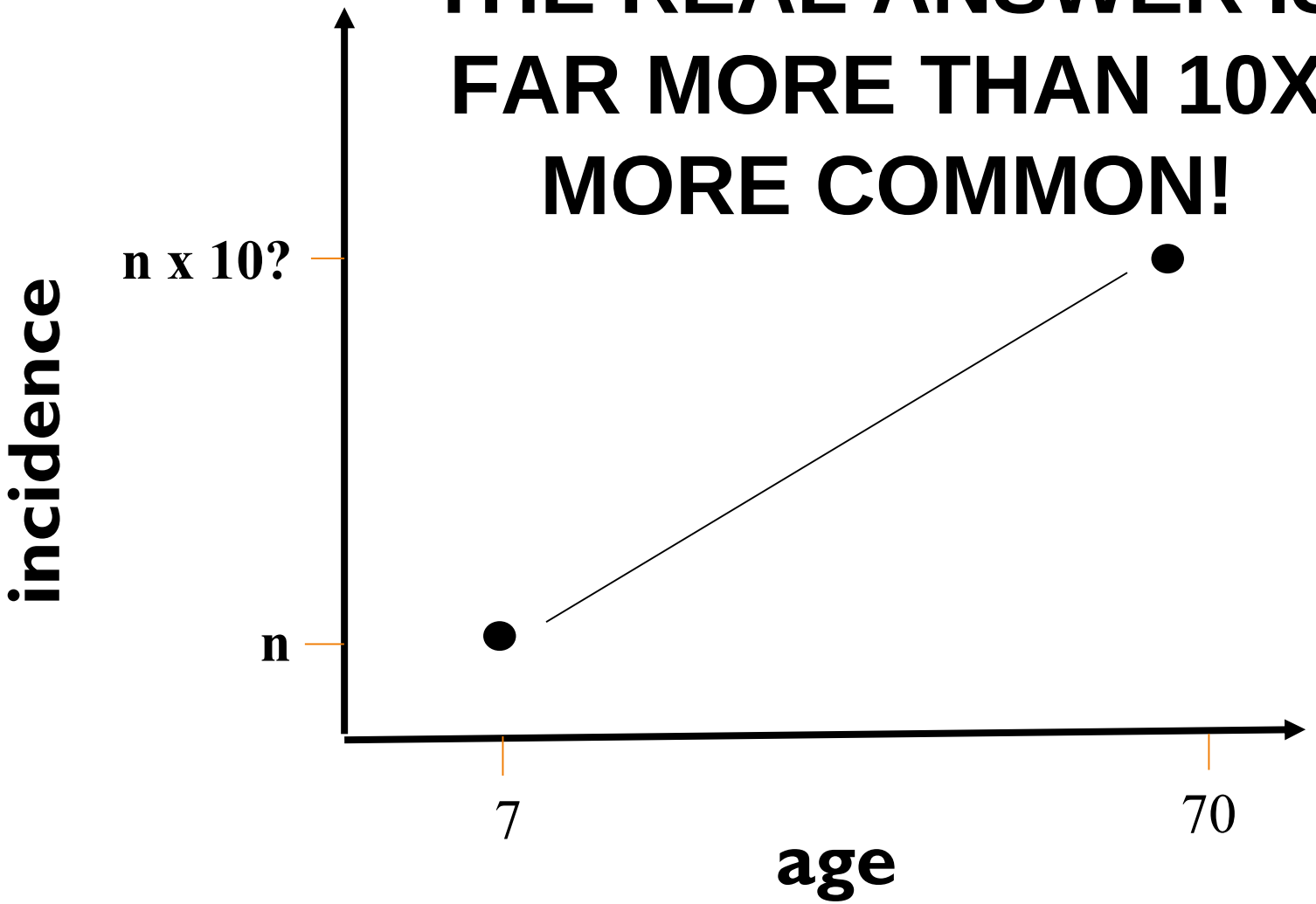


Figure 11.1 *The Biology of Cancer* (© Garland Science 2007)

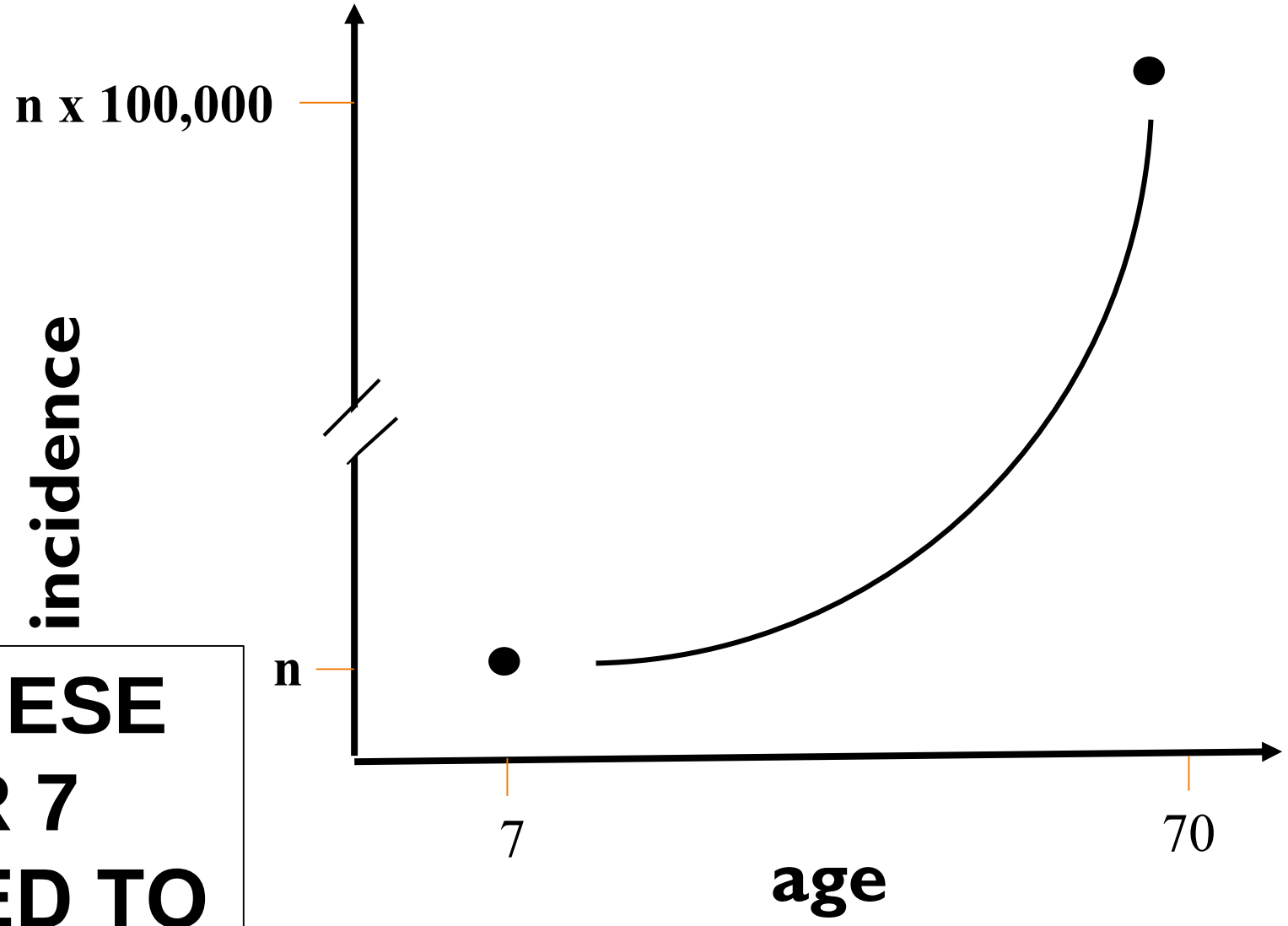
- **Late age of onset indicates that the development of most cancers requires an extended period of time**

How Much More Likely is Cancer in Aged Versus Young People?

THE REAL ANSWER IS FAR MORE THAN 10X MORE COMMON!



How Much More Likely is Cancer in Aged Versus Young People?



STUDIES LIKE THESE SUGGEST 6 OR 7 "STEPS" REQUIRED TO GET CLINICALLY EVIDENT CANCER

Histopathology Provides Evidence of Multi-Step Tumor Formation

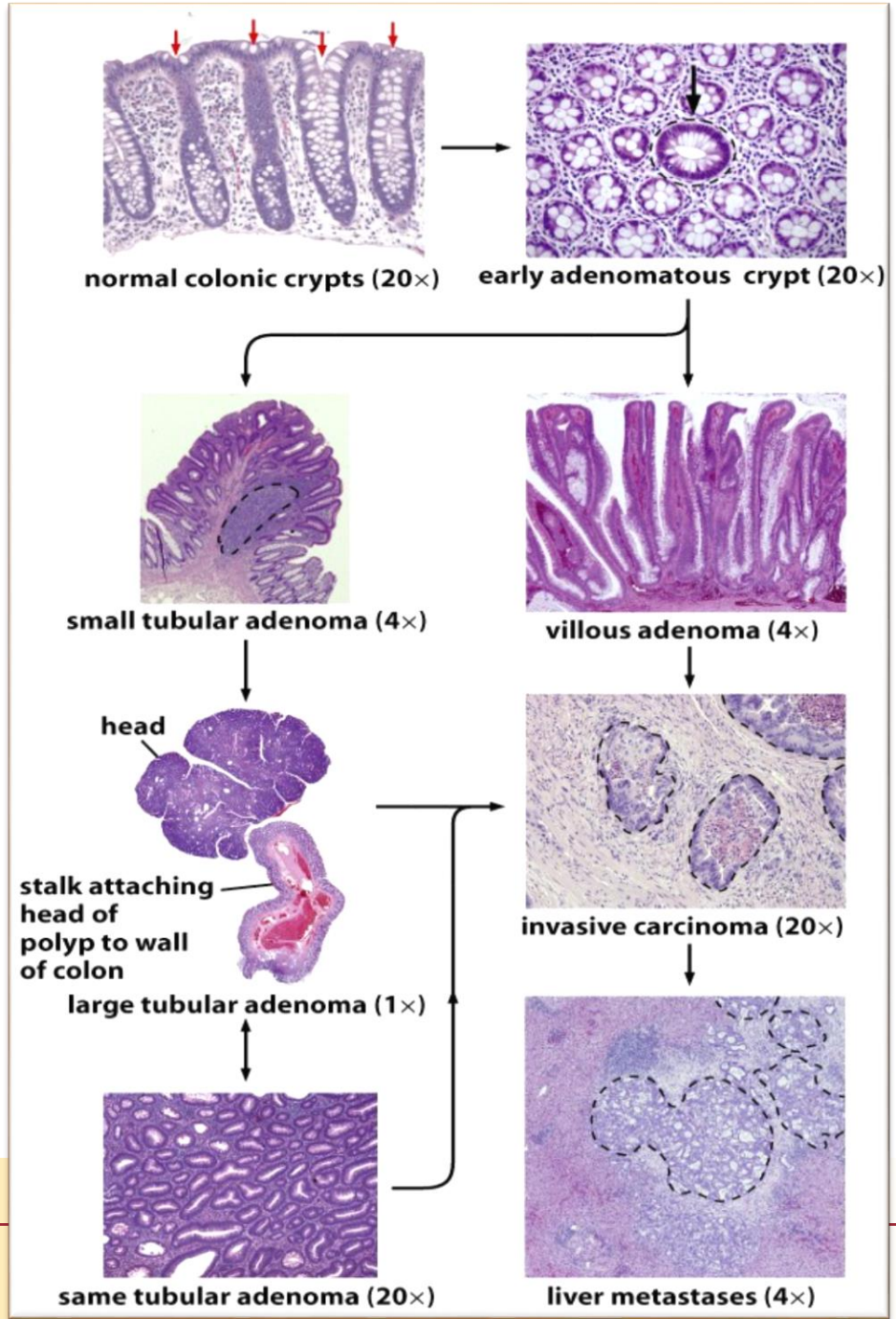


Figure 11.6 *The Biology of Cancer* (© Garland Science 2007)

Genetic Alterations Cause These Multiple Steps

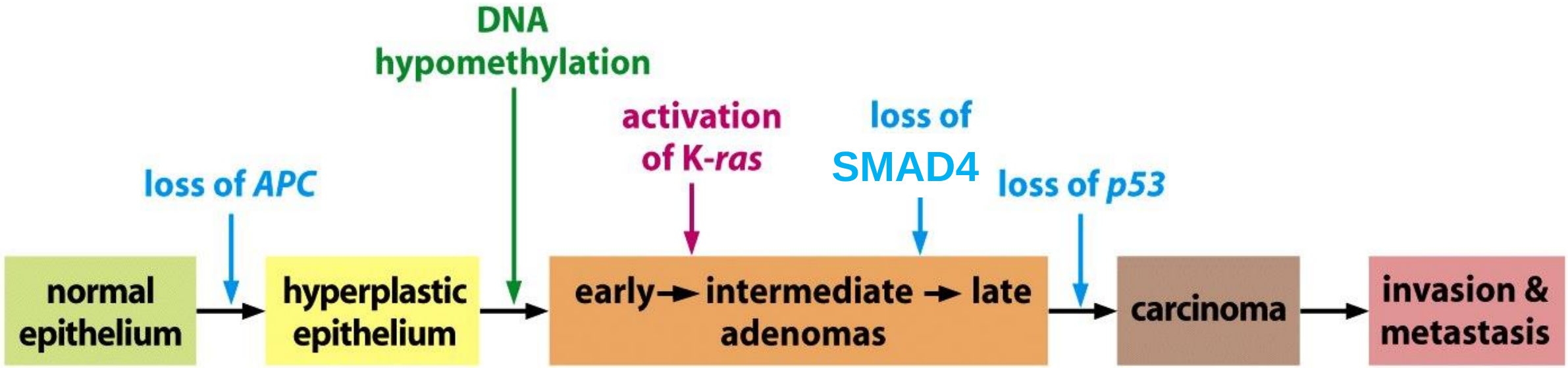
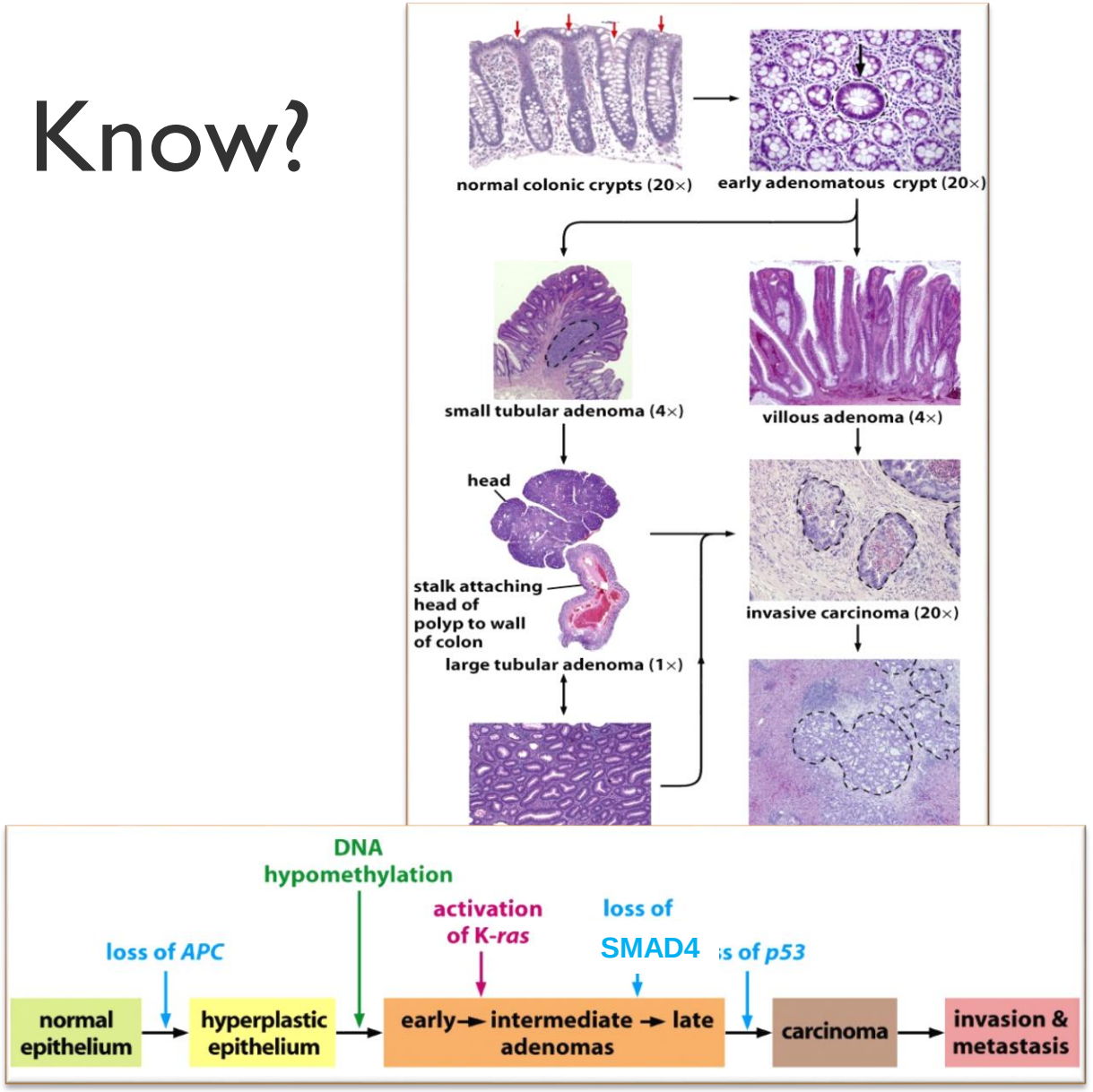


Figure 11.9 *The Biology of Cancer* (© Garland Science 2007)

Why is this Important to Know?

- We can detect cancer at early stages!
- We can intervene in the process!
  - Remove it
  - Prevent progression
- Knowing the specific mutations that are present informs therapy

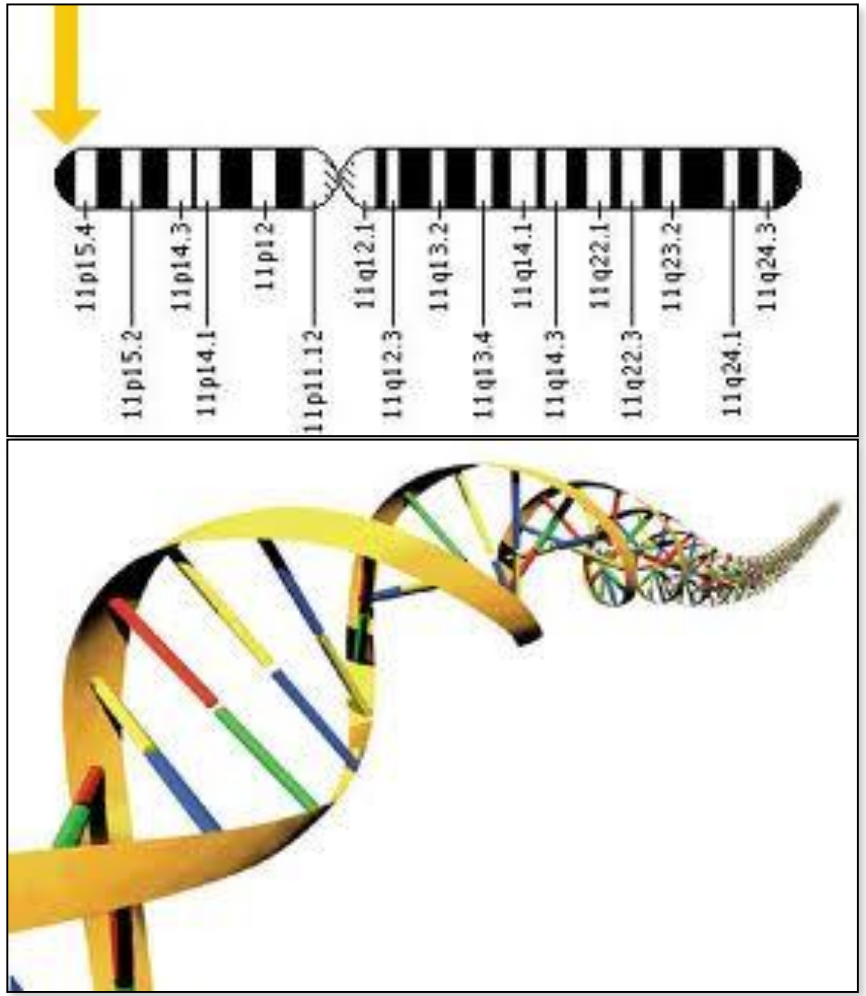


Remember All Mutations Are Not Created Equal

- Many mutations discovered in cancer cells are neutral passengers that merely accompany functionally important drivers that have been subject to selective pressure.
- These mixtures of passenger and driver mutations together comprise the mutated gene sets of the tumors in question.

Basic Research Has Revealed Many of These Cancer Drivers

- In 1970's we didn't know that cancer was caused by mutated genes
- The first cancer gene discovered in 1982 – *HRAS*
- The first hereditary cancer gene identified in 1986 – *RB1*
- Now hundreds of cancer genes known
- The first cancer genome sequenced completely in 2008

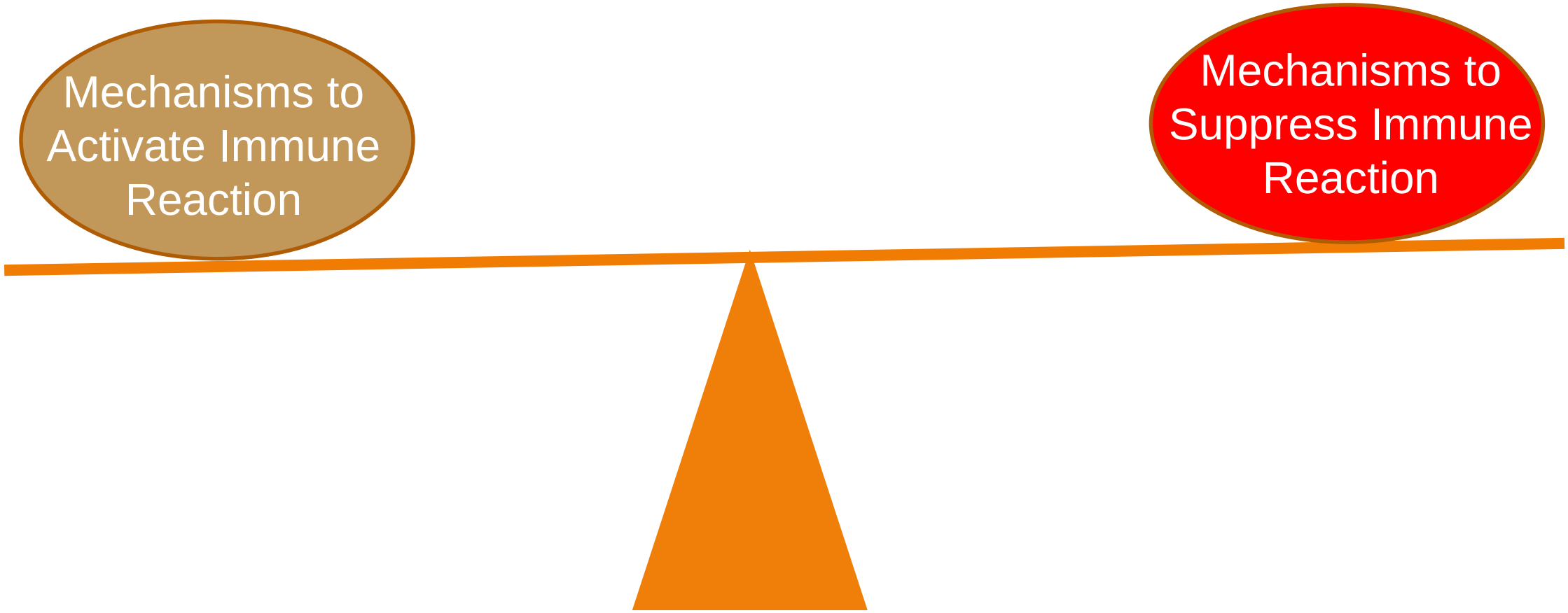


Learning Objectives

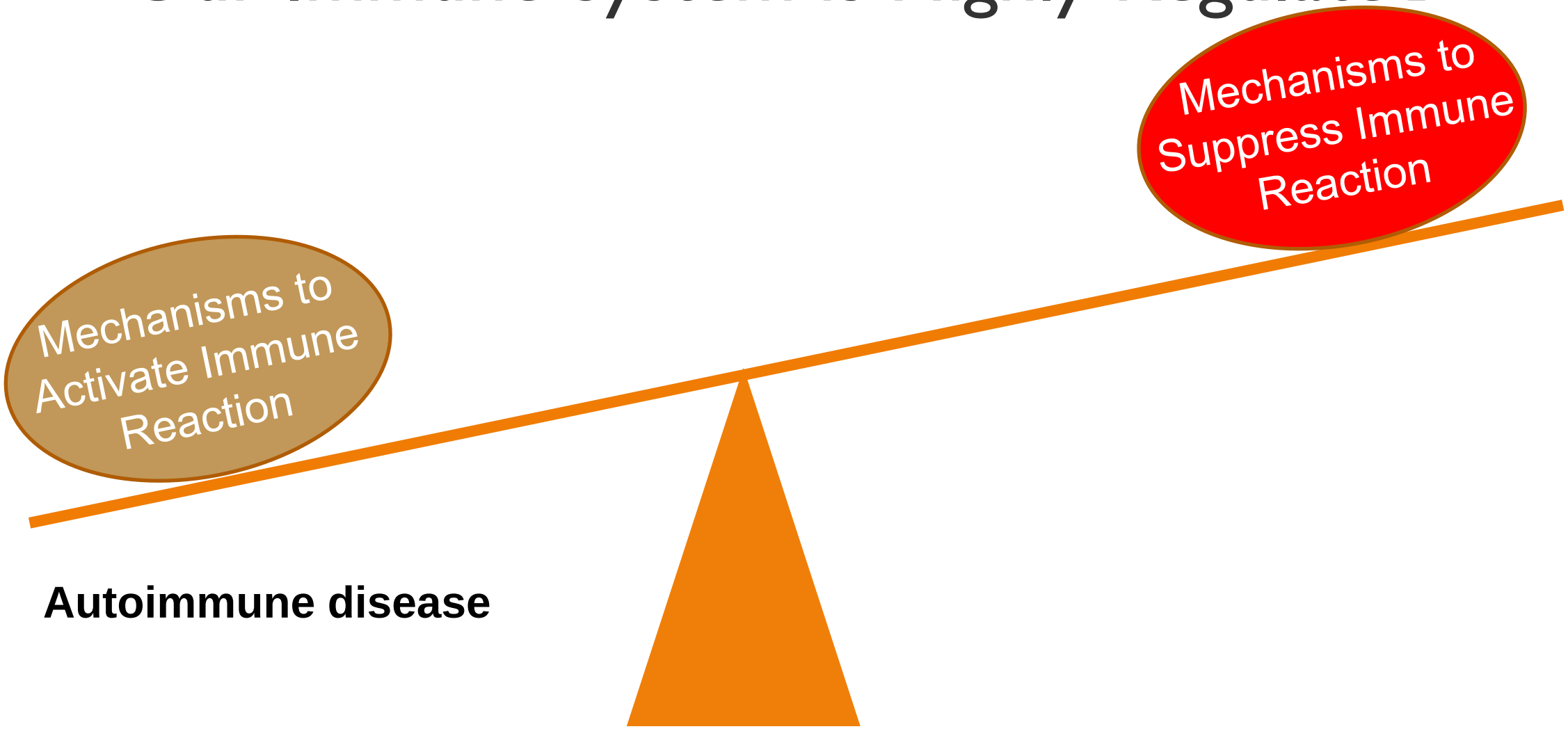
- All cancer has a genetic cause – but that doesn't (usually) mean the genes you're born with cause cancer, instead cancer is primarily caused by mutations occurring in rare cells in your body.
- For most people, their cancer risk is more determined by lifestyle choices than who their parents are. But some families do pass along high risk cancer-causing gene mutations from parent to child.
- Cancer cells typically have many, many gene mutations and about 6 or more of these "drive" the abnormal behavior of the cancer cells, while the rest are merely "passengers".
- It is thought that the genes mutated in a cancer can produce abnormal proteins allowing the immune system to kill off the cancer cells. This is how "immunotherapies" like Keytruda can work for some cases of cancer.
- The specific genes that are mutated in a tumor or leukemia may determine the prognosis of the patient and dictate the best therapy for the physician to choose.

KEYTRUDA will not work for everyone. Results may vary.

Our Immune System is Highly Regulated

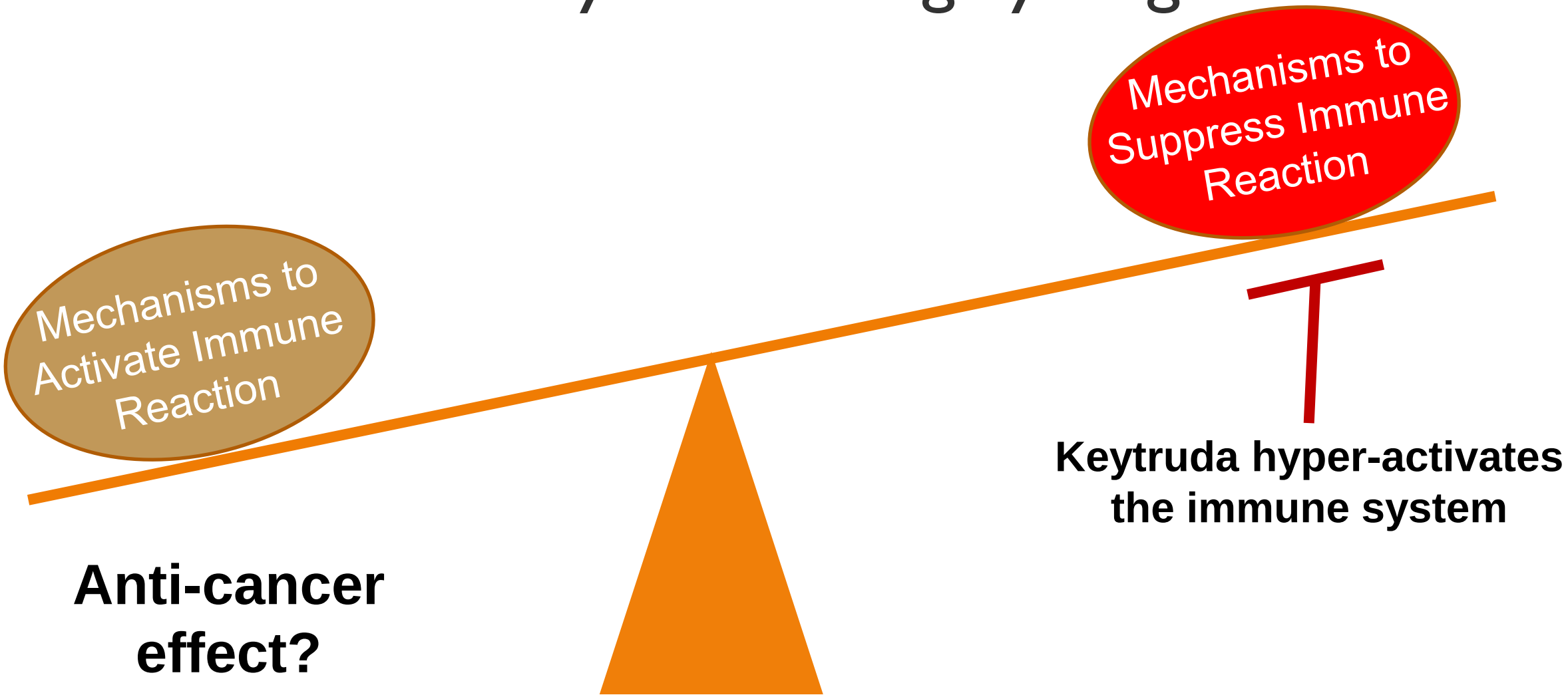


Our Immune System is Highly Regulated

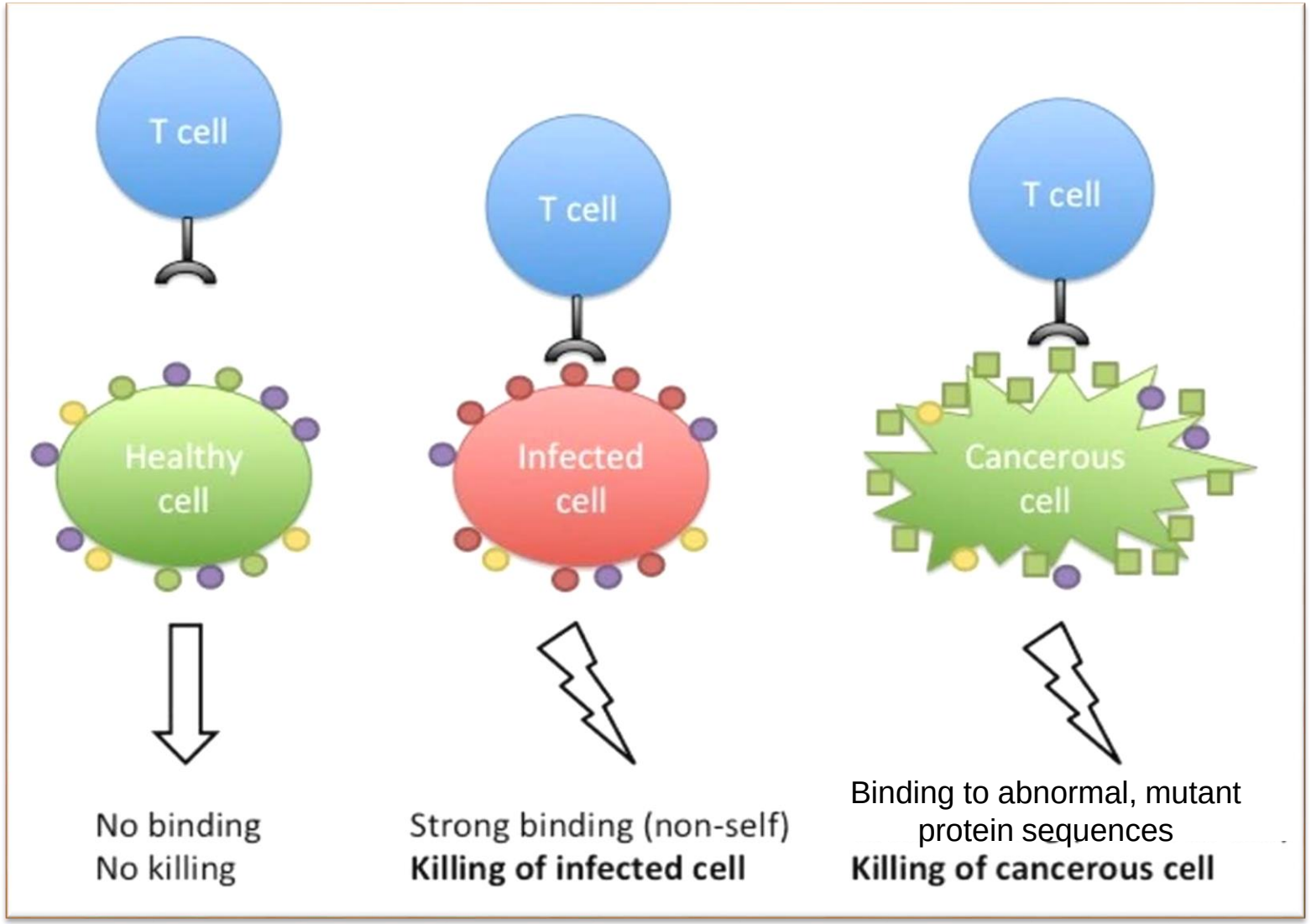


Autoimmune disease

Our Immune System is Highly Regulated



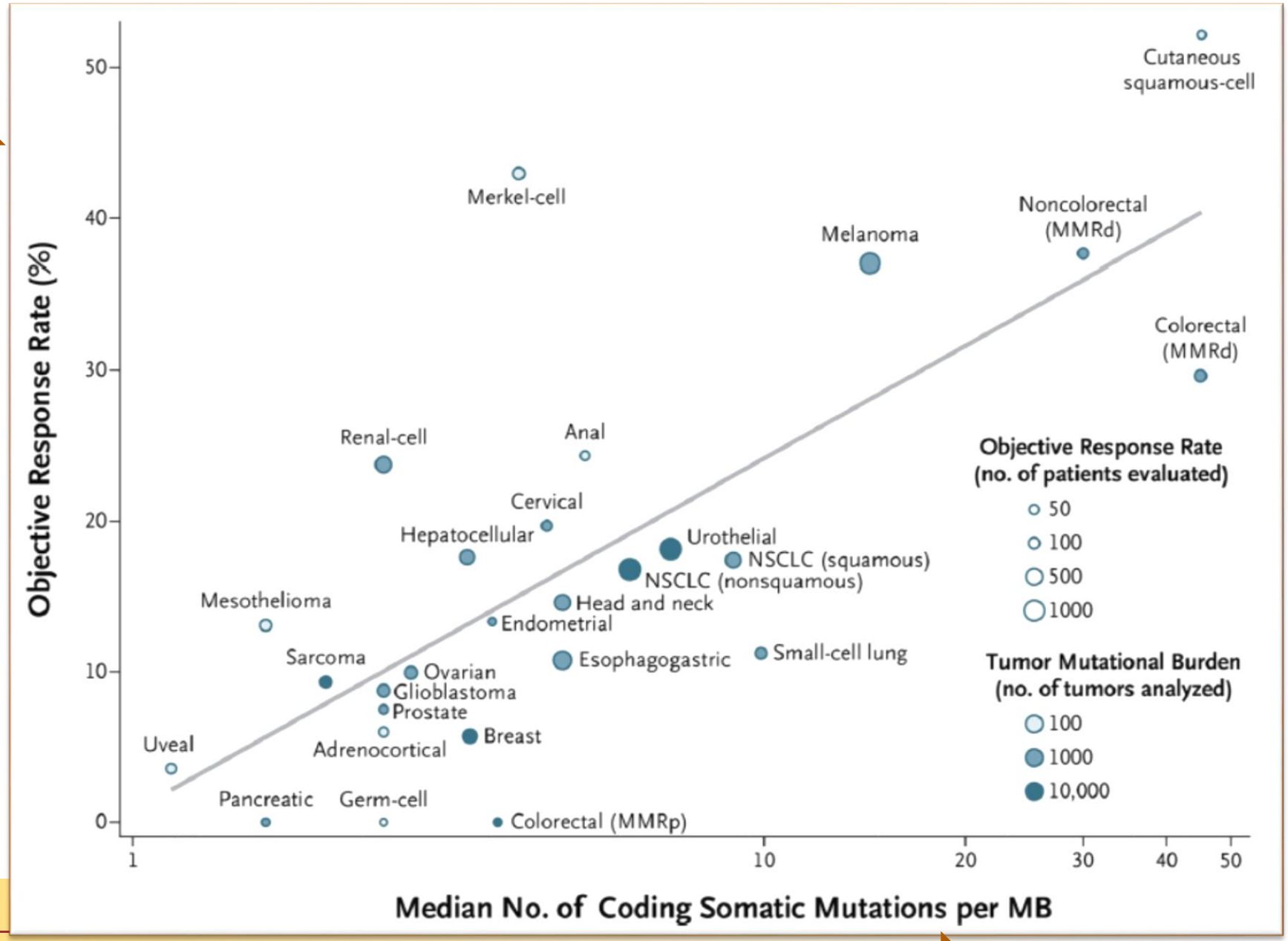
If Tumors Express Many Non-normal Proteins, Due to Mutations, They May Respond to this Kind of Immunotherapy



The Conversation , May 26, 2015

The More Mutations Present the Better the Chance to Respond to Immunotherapies like Keytruda

Chance the therapy worked



Aurora et al., Adv. Ther., 2019

Number of abnormal proteins

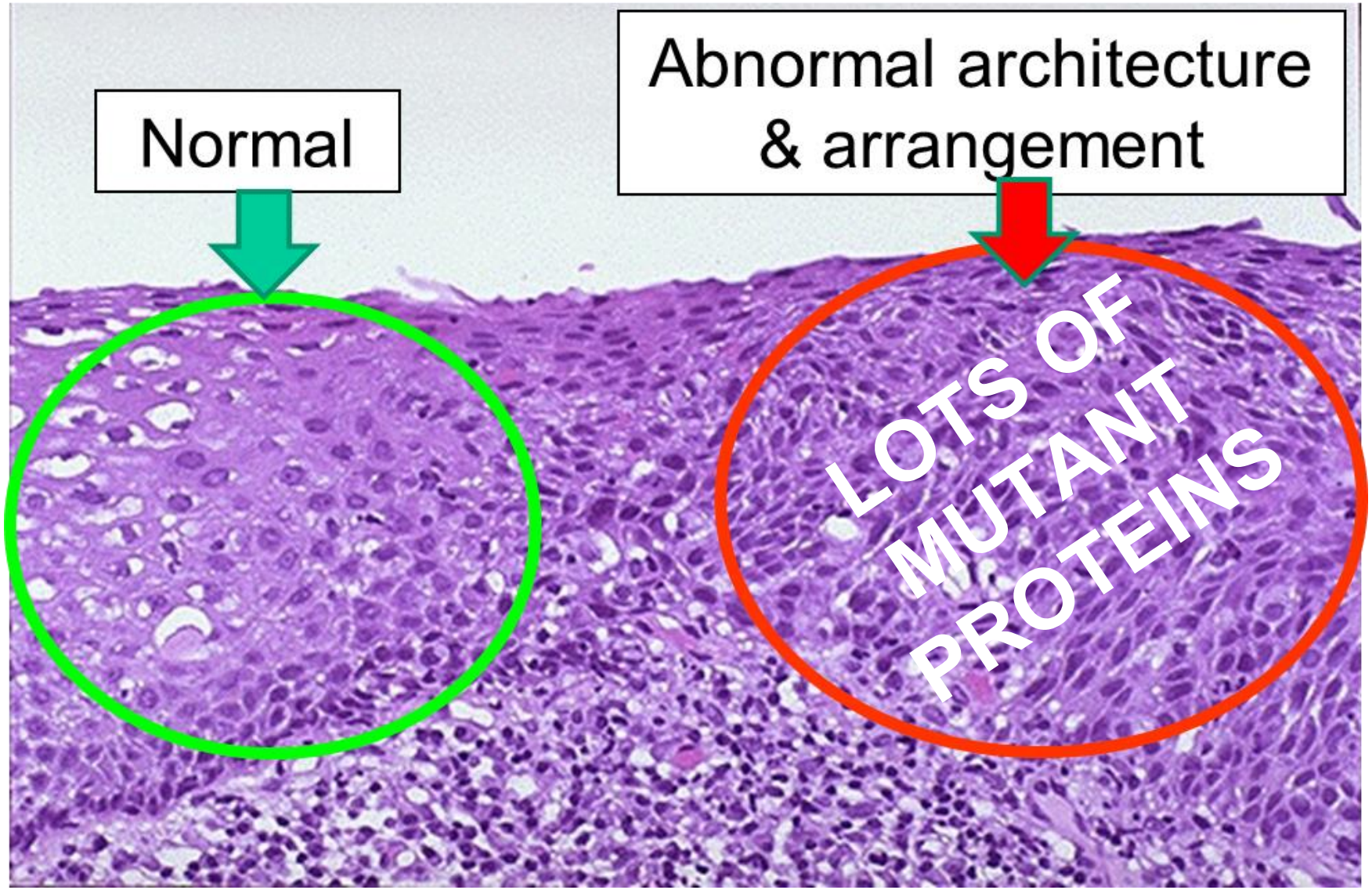
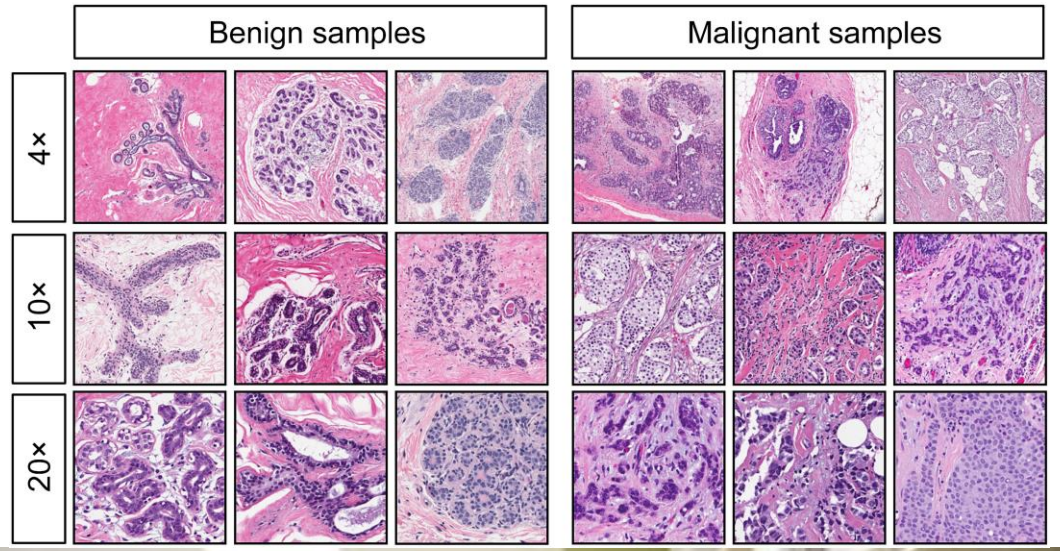


Image source: http://library.med.utah.edu/WebPath/FEMHTML/FEM008.html

Learning Objectives

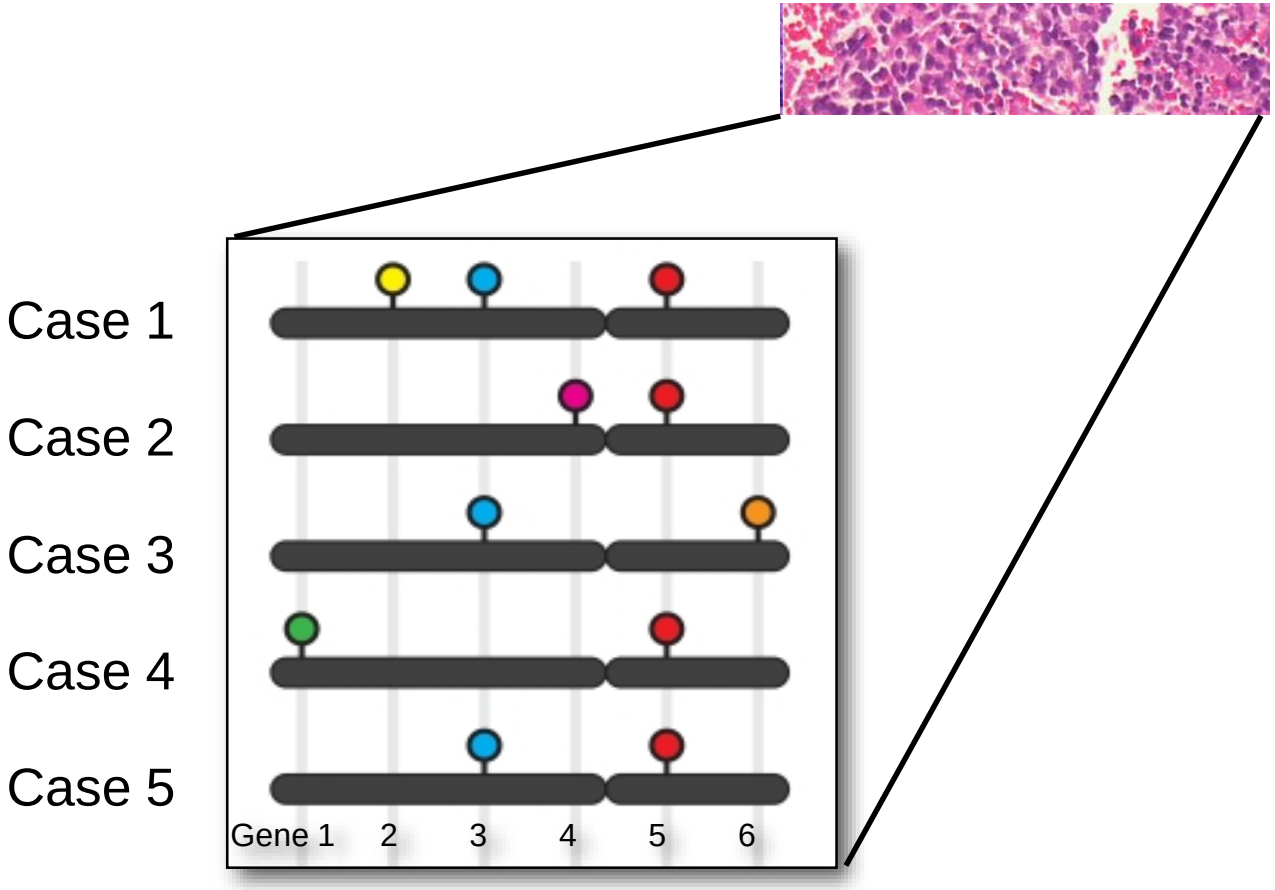
- All cancer has a genetic cause – but that doesn't (usually) mean the genes you're born with cause cancer, instead cancer is primarily caused by mutations occurring in rare cells in your body.
- For most people, their cancer risk is more determined by lifestyle choices than who their parents are. But some families do pass along high risk cancer-causing gene mutations from parent to child.
- Cancer cells typically have many, many gene mutations and about 6 or more of these "drive" the abnormal behavior of the cancer cells, while the rest are merely "passengers".
- It is thought that the genes mutated in a cancer can produce abnormal proteins allowing the immune system to kill off the cancer cells. This is how "immunotherapies" like Keytruda can work for some cases of cancer.
- The specific genes that are mutated in a tumor or leukemia may determine the prognosis of the patient and dictate the best therapy for the physician to choose.


Benign samples
Malignant samples
4×
10×
20×


DCIS
DCIS
Invasive
breast cancer

A picture is worth a thousand words…true

But…you can't judge a book by it's cover either



Altered Genes = Altered Proteins

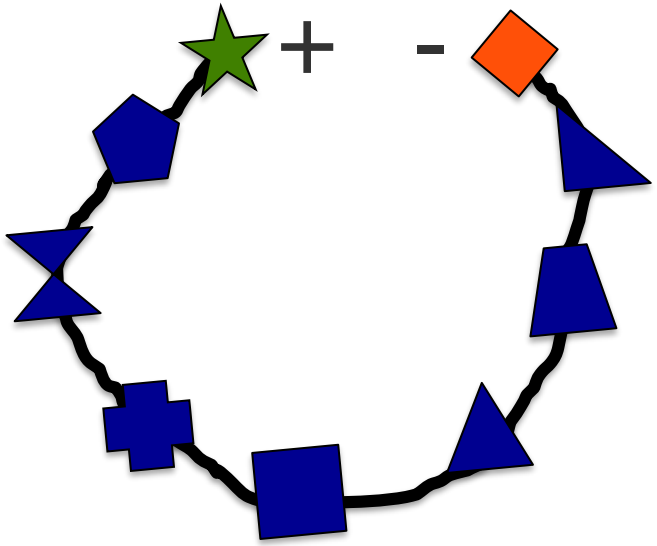
- Despite cancers being genetic diseases, aberrant and dysregulated genes **indirectly** cause pathology.
  - *That is, genes underlie the pathology but are not themselves the causative agents.*

- Altered gene products **–altered proteins -** are the direct causes of pathology.

Form = Function

…AAA GGG ACT GCC TGG CAT TGC GTT GAC…

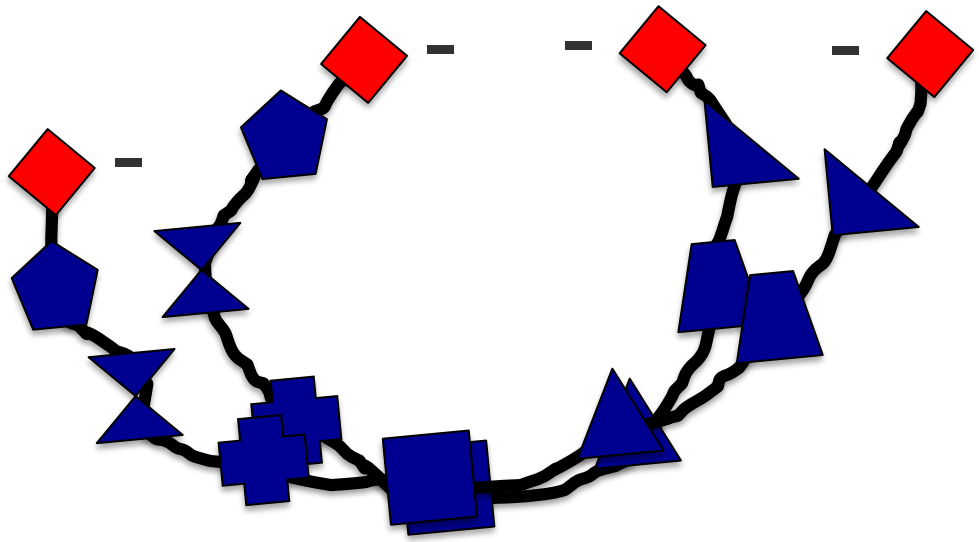
…Lys Gly Thr Ala Trp His Cys Val Asp…



Mutations Disrupt Form/Function

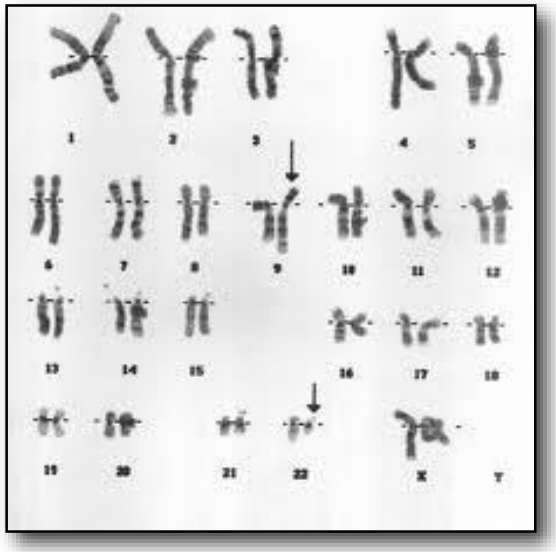
…GAA GGG ACT GCC TGG CAT TGC GTT GAC…

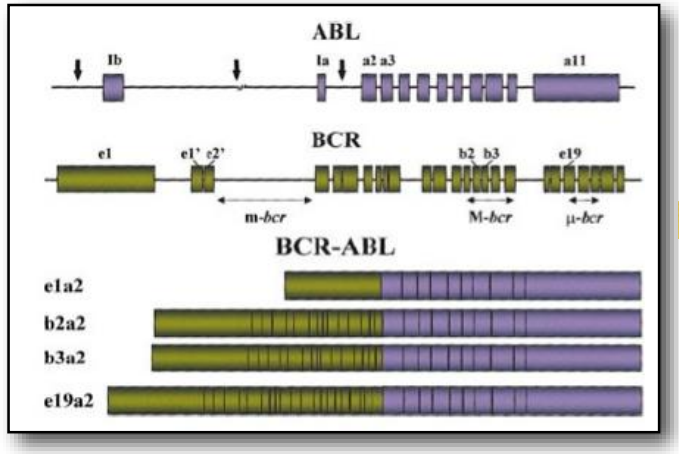
…Asp Gly Thr Ala Trp His Cys Val Asp…

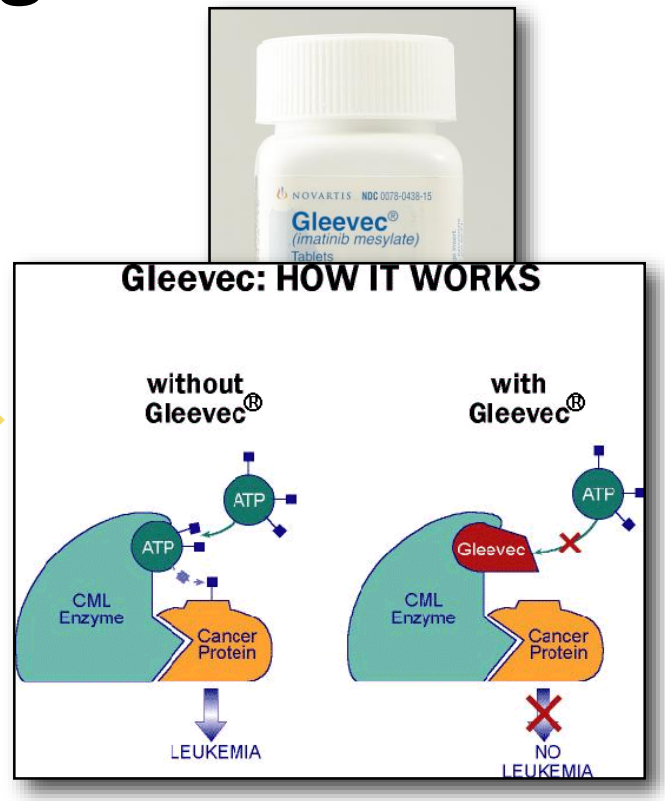


Identifying cancer drivers has had profound implications for therapy

Chronic myelogenous leukemia

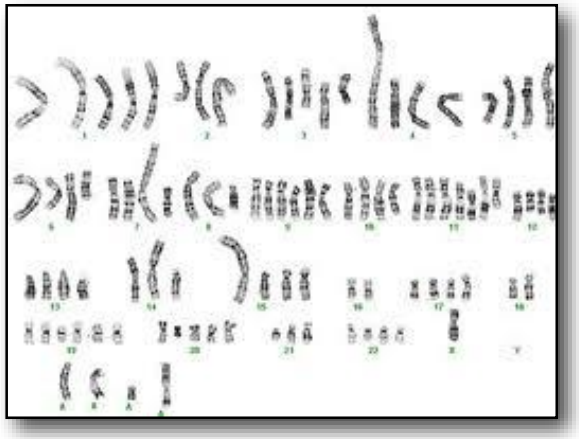


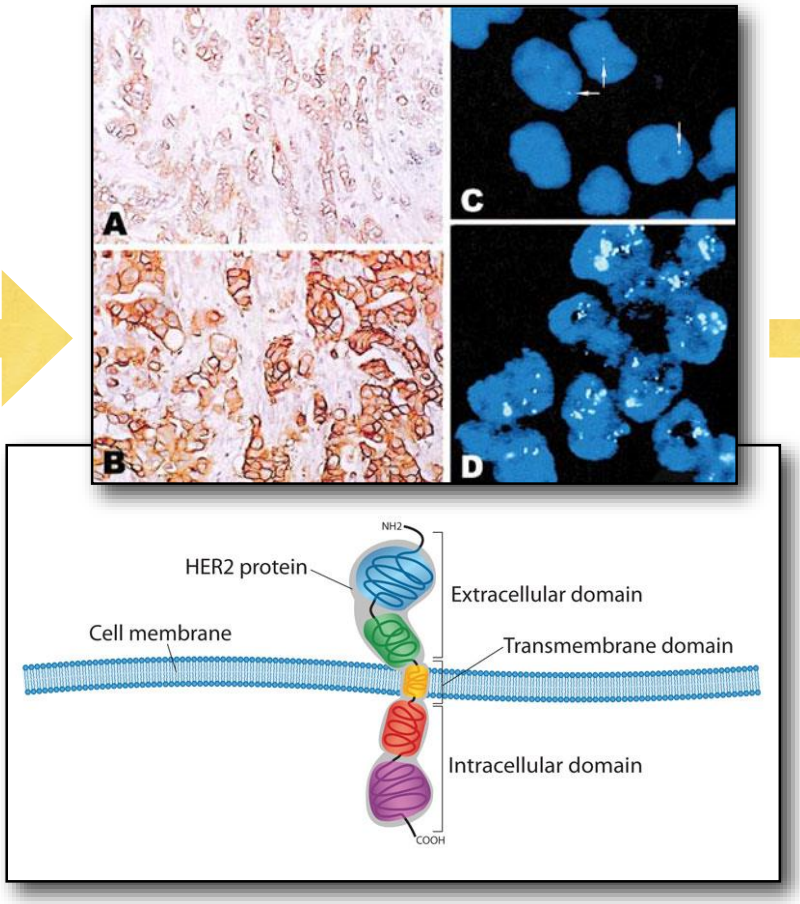


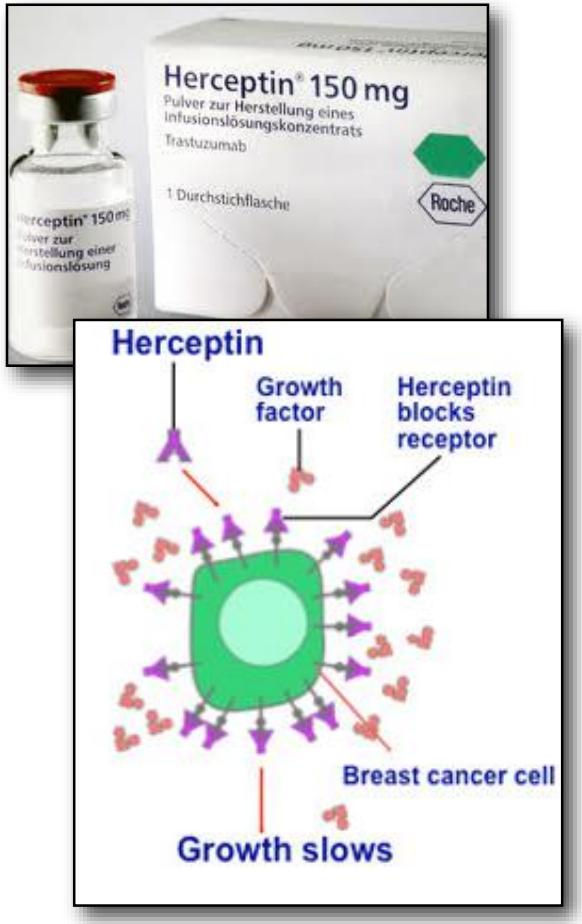


Identifying cancer drivers has had profound implications for therapy

Breast cancer







Precision Medicine

Masonic Cancer Center
University of Minnesota

Comprehensive Cancer Center designated by the National Cancer Institute

Office of Academic Clinical Affairs
University of Minnesota
Driven to Discover℠

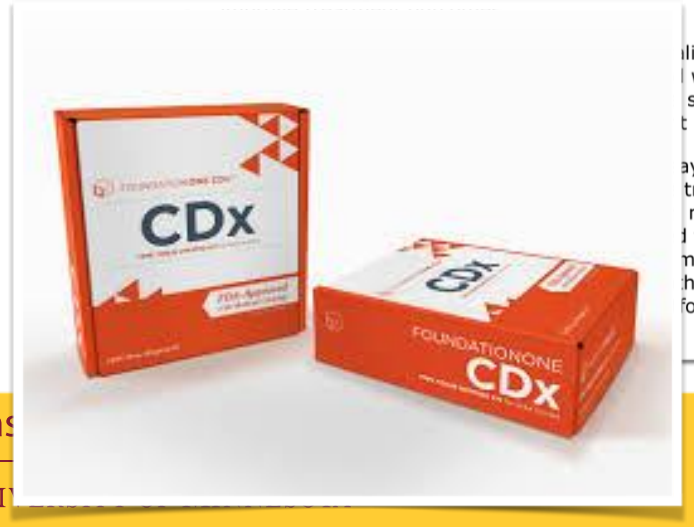
Cancer Driver Gene Identification is an FDA Approved Concept for Precision Medicine

FoundationOne CDx™, the First FDA-Approved Comprehensive Genomic Profiling Assay for All Solid Tumors Incorporating Multiple Companion Diagnostics

-- FoundationOne CDx is the First Next Generation Sequencing Test for All Solid Tumors to Complete the FDA/CMS Parallel Review Process and Launch with National Medicare Coverage --

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Foundation Medicine, Inc. (NASDAQ:FMI) today announced that FoundationOne CDx™, the first U.S. Food and Drug Administration (FDA) approved comprehensive genomic profiling (CGP) assay for all solid tumors incorporating multiple companion diagnostics, is now available in the United States. FoundationOne CDx is a first-of-its-kind test for individuals with advanced cancer that is offered as a nationally covered benefit across all solid tumors for Medicare and Medicare Advantage beneficiaries who meet eligibility requirements.

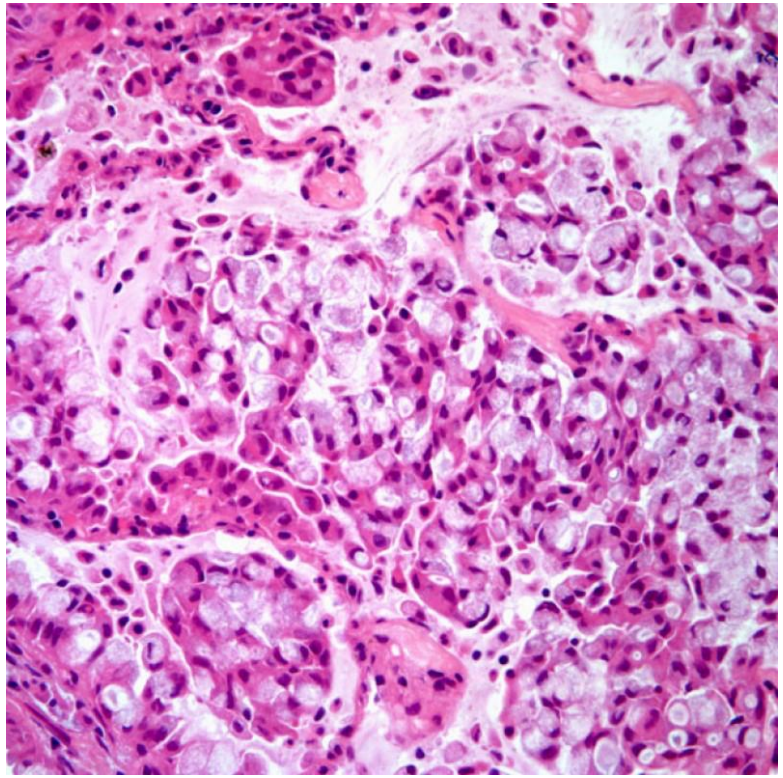
"Now that FoundationOne CDx is widely available in the U.S., oncologists can begin using this valuable test to help guide and simplify personalized treatment decisions for their patients," Vincent Miller, M.D., chief medical officer at Foundation Medicine. "By integrating FoundationOne CDx early into routine clinical care, oncologists can create treatment efficiencies and expand access to biomarker-driven medicines for patients, with the potential to



lidated genomic profiling may establish a path toward improved patient outcomes. Personalized, biomarker-
with clinical benefit across tumor types and biomarkers,[1] making therapy selection ever more complex.
single, FDA-approved comprehensive platform for all solid tumors to detect specific genomic alterations
t decisions, while reducing the time and tissue needed when testing for biomarkers one at a time.

ay for all solid tumors, assesses genomic alterations in 324 genes known to drive cancer growth, providing
treatment options. FoundationOne CDx is also FDA-approved as a broad companion diagnostic for patients
melanoma, colorectal cancer, ovarian cancer or breast cancer to identify those patients who may benefit
l therapies, 12 of which are approved as first line therapy for their respective indications. FoundationOne
microsatellite instability (MSI) and tumor mutational burden (TMB), that can help inform the use of other
herapies and relevant clinical trial information. In all of these ways, FoundationOne CDx is available to
form for clinical research and as a CGP platform for biopharma companies seeking to develop companion

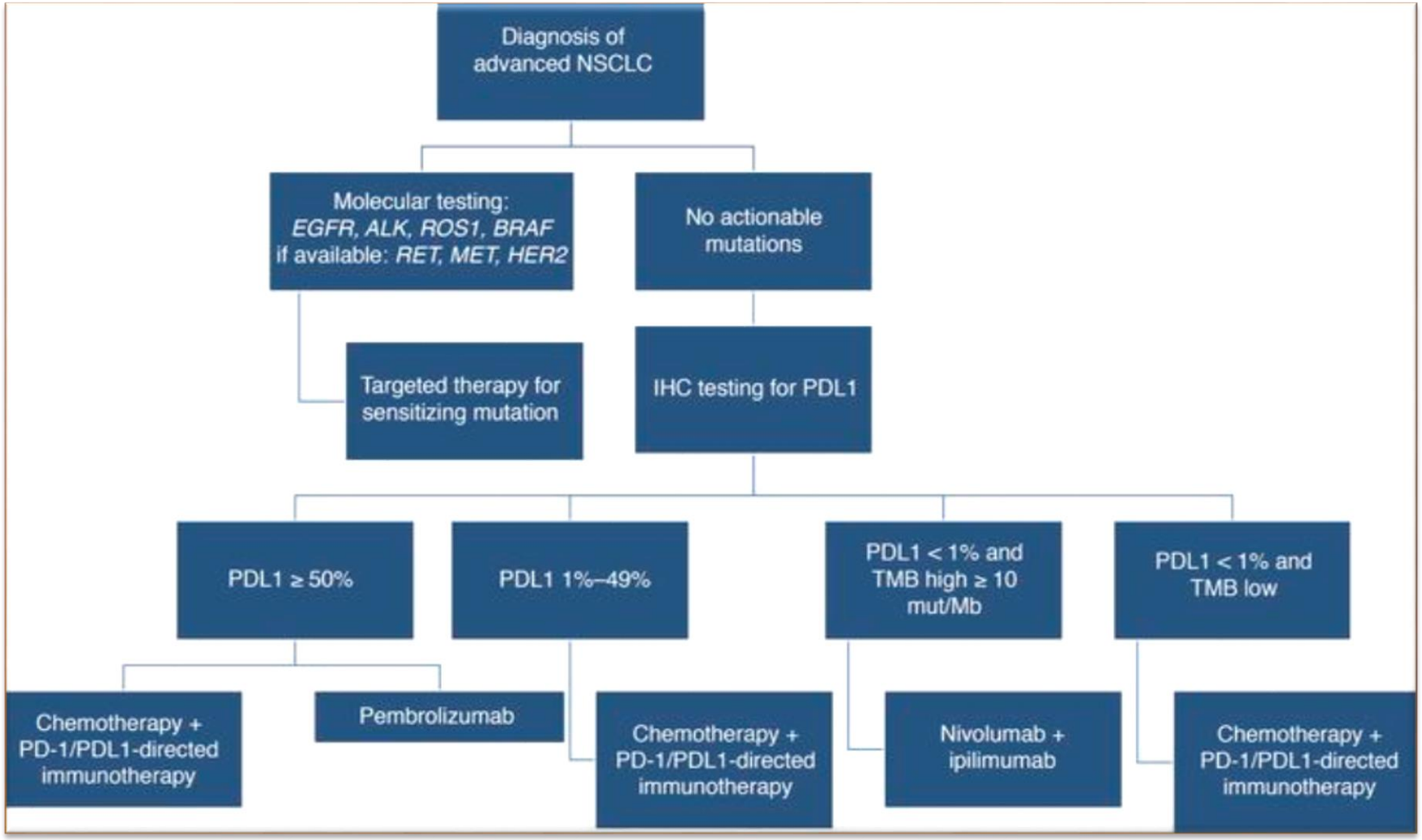
Old Situation for Lung Cancer



Everyone gets the same therapy

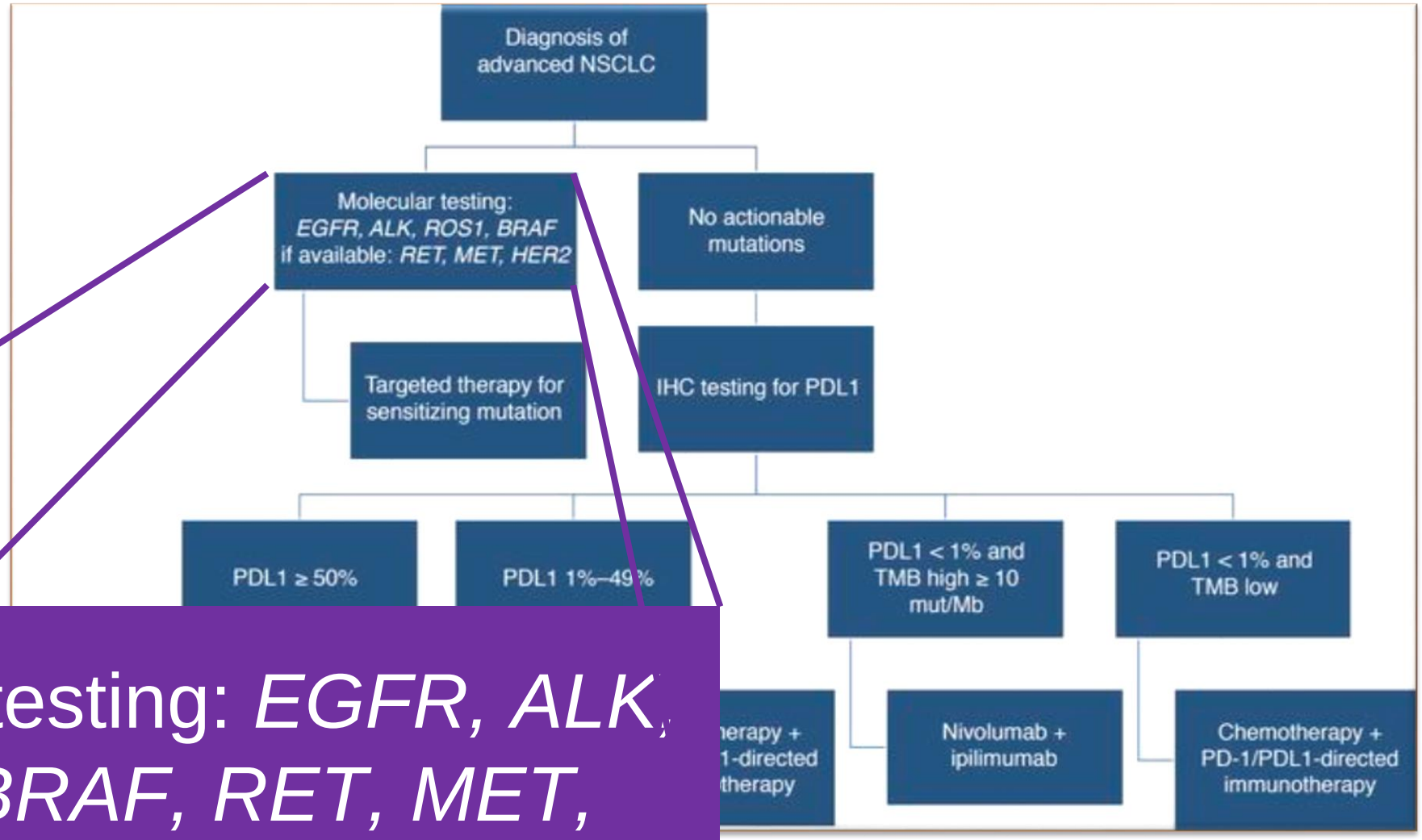
Surgery, radiation, Chemotherapy (anti-folates, platinum drugs, gemcitabine)

Personalized Therapy for Lung Cancer



Pakala and Ramalingam, JCI Insight, 2018

Personalized Therapy for Lung Cancer

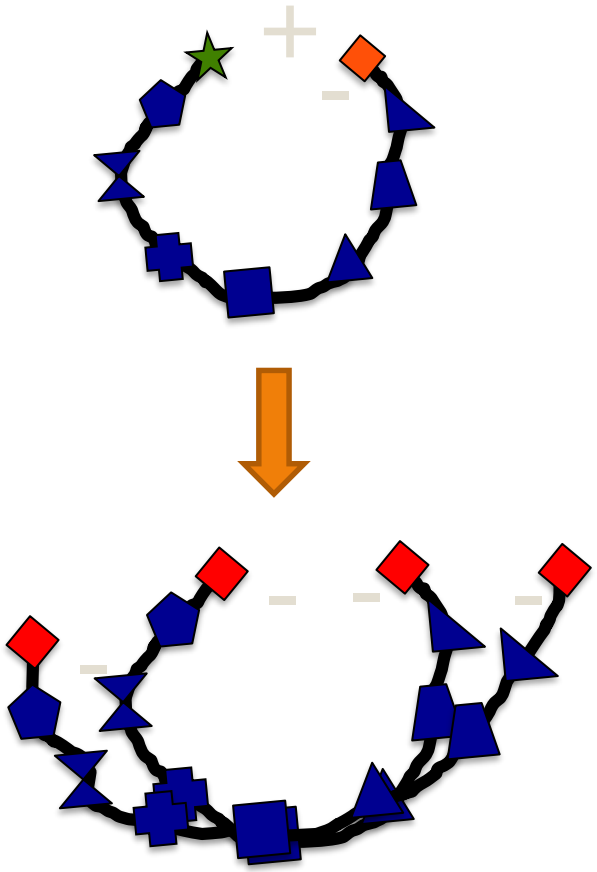


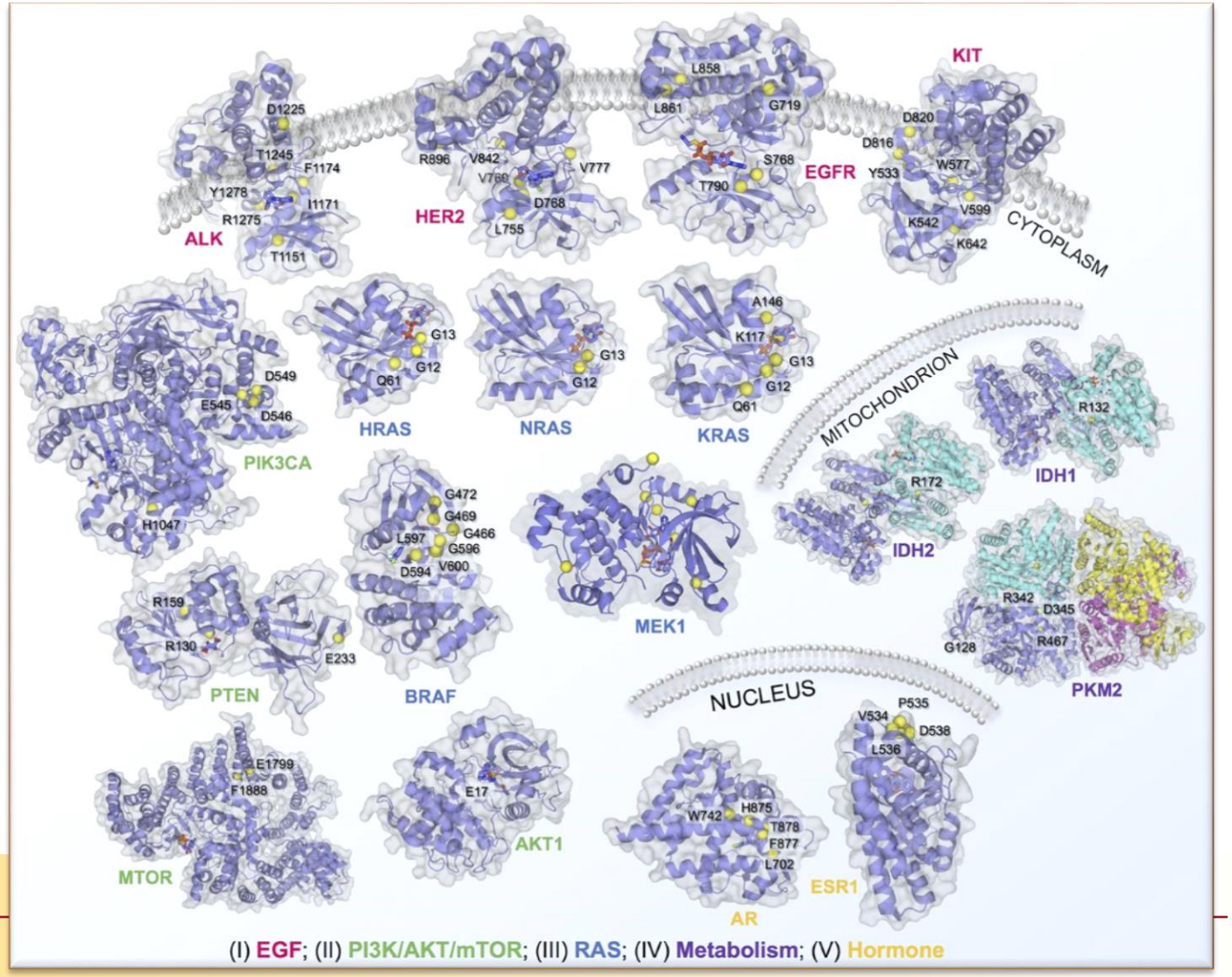
Molecular testing: *EGFR, ALK, ROS1, BRAF, RET, MET, HER2*

Personalized Therapy for Lung Cancer

Molecular testing:	Specific Drug :
EGFR	*EGFR*
ALK	*ALK*
ROS1	*ROS1*
BRAF	*BRAF*
RET	*RET*
MET	*MET*
HER2	*HER2*

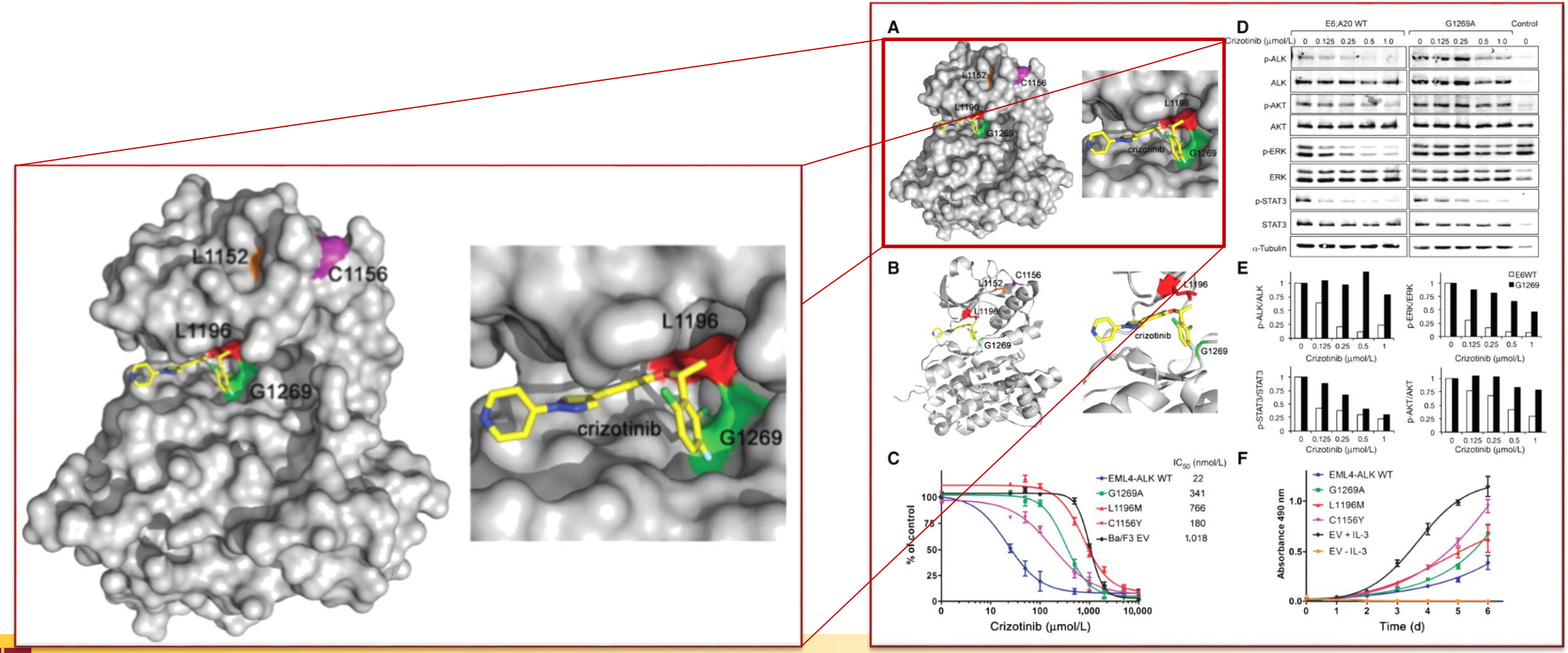
Reversing the "Altered Function" of an Oncogene





Cheng et al., Pharma. Rev., 2019

Reversing the "Altered Function" of an Oncogene

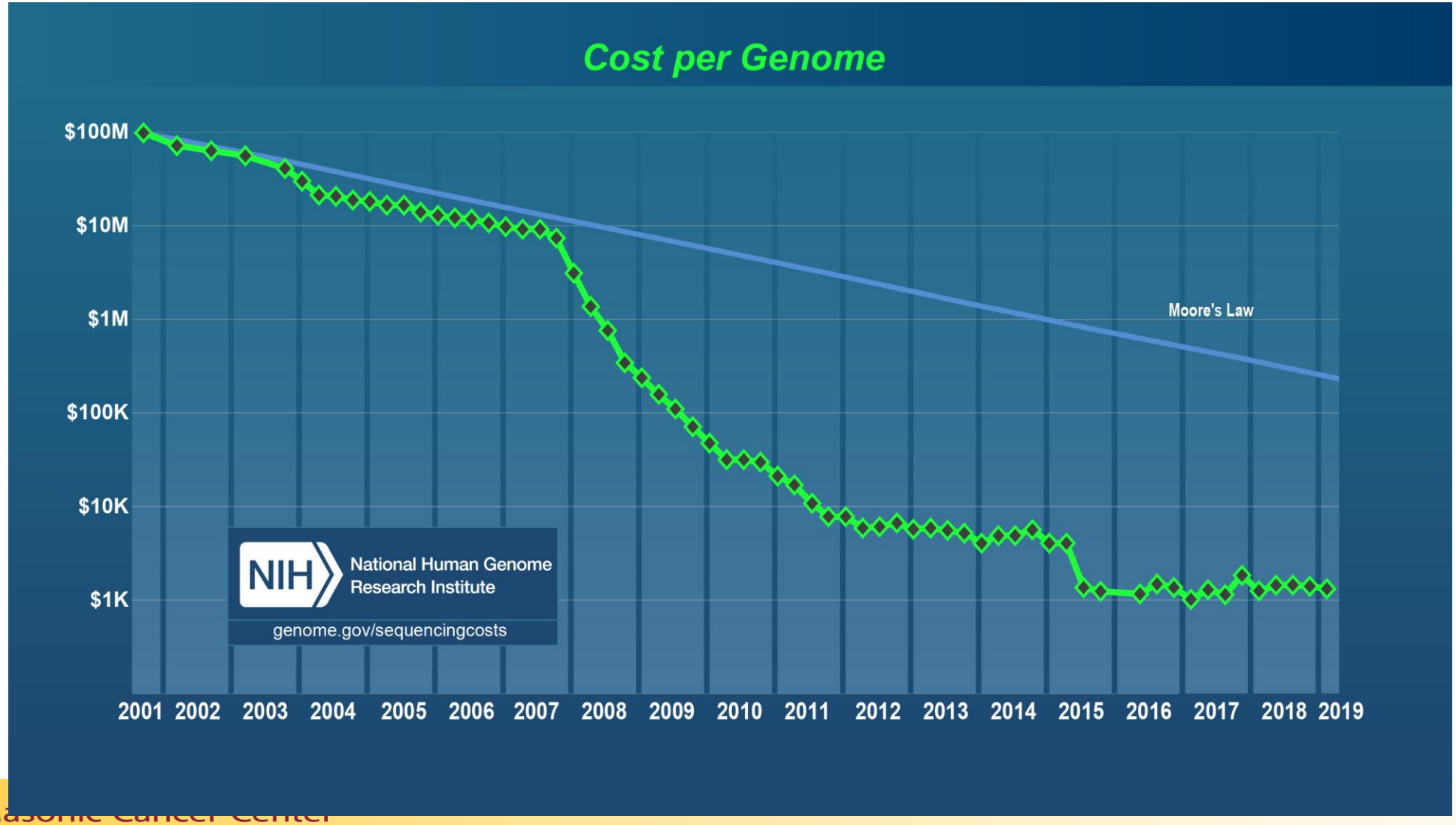


Doebele et al., Clin. Can. Res., 2012

Reversing the ”Altered Function” of an Oncogene

- Inhibits activated, mutant ALK
- Used once crizotinib fails

Cost of DNA Sequencing



The Future of Cancer Prevention and Care

- We all get sequenced?
- DNA from blood monitored for mutant DNA to detect cancer early
- Our tumors get completely sequenced – every few months during course of disease
- More “matched” therapies
- Immune therapy versus mutant proteins

Acknowledgements

- The Largaespada lab
  - Bryant Keller
  - Sue Rathe
  - Flavia Popescu
  - Kyle Williams
  - Pauline Beckmann
  - Sara Isakson
  - Julia Nikrad
  - Emily Pope
  - Minu Bhunia
  - Garrett Draper
  - Wendy Hudson
  - Alex Larsson
  - Sandi Wagner
  - Eunice Orimabisi
  - Mahathi Patchava

- Collaborators
  - Christopher Moertel, M.D. (UMN)
  - Aaron Sarver (UMN)
  - Alpay Temiz (UMN)
  - Nancy Ratner (Cincinnati Children's)
  - Gelareh Zadeh (U of Toronto)

- Funding
  - NIH/NCI, DOD
  - Children's Cancer Research Fund, American Cancer Society, Children's Tumor Foundation, Rein in Sarcoma
  - Masonic Cancer Center

OFFICE OF ACADEMIC CLINICAL AFFAIRS

University of Minnesota
Driven to Discover®

OFFICE OF ACADEMIC CLINICAL AFFAIRS

UNIVERSITY OF MINNESOTA

Driven to Discover®

@UMNclinaffairs

clinicalaffairs.umn.edu

@UMNclinicalaffairs

#UMNclinicalaffairs