Are we making any progress in the War on Cancer?

It starts with knowing what's going on.

And what have we learned about cancer?

Inspire2Live

Amsterdam, January 2020

Normal tissue

Tumor tissue

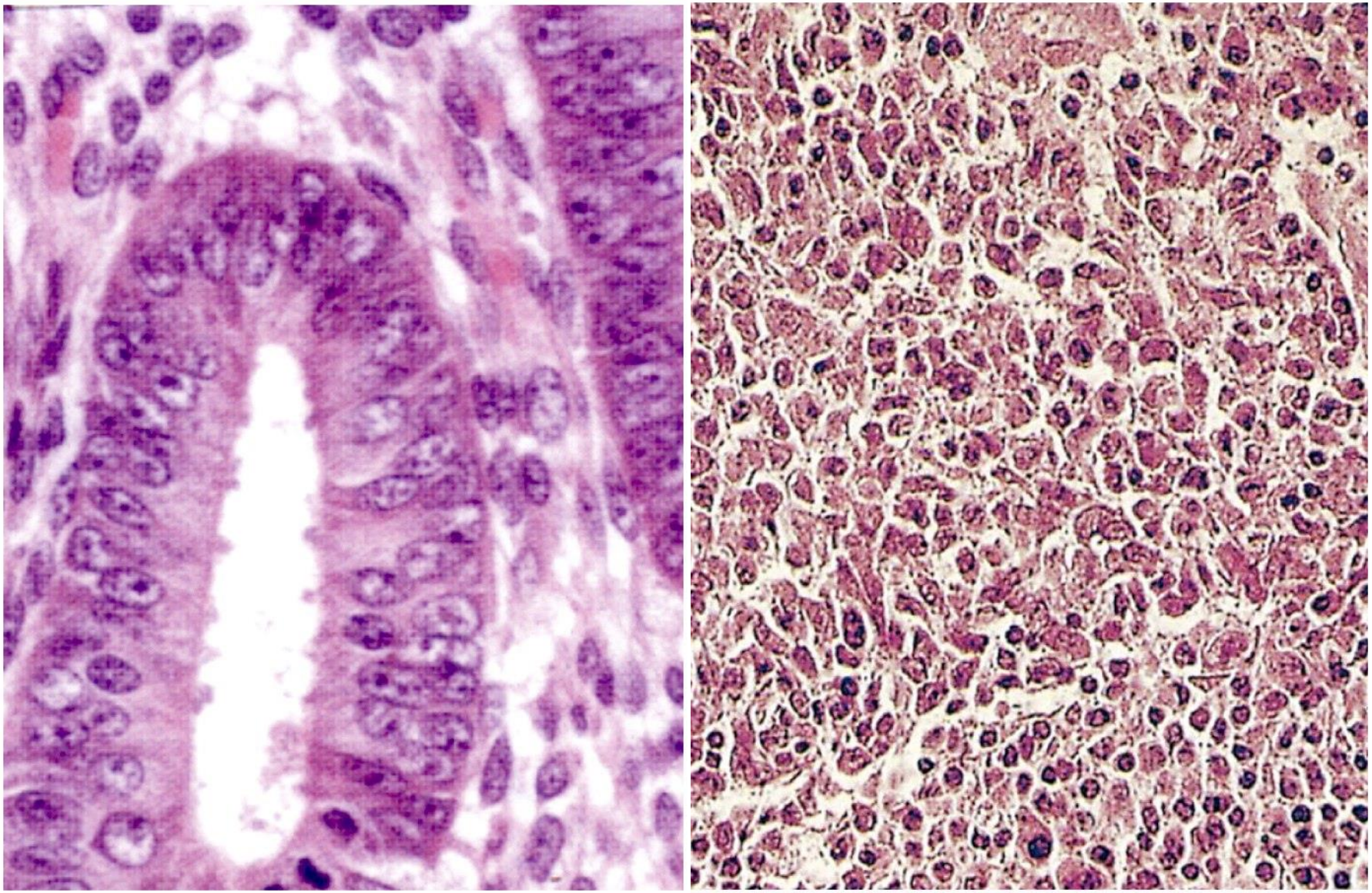
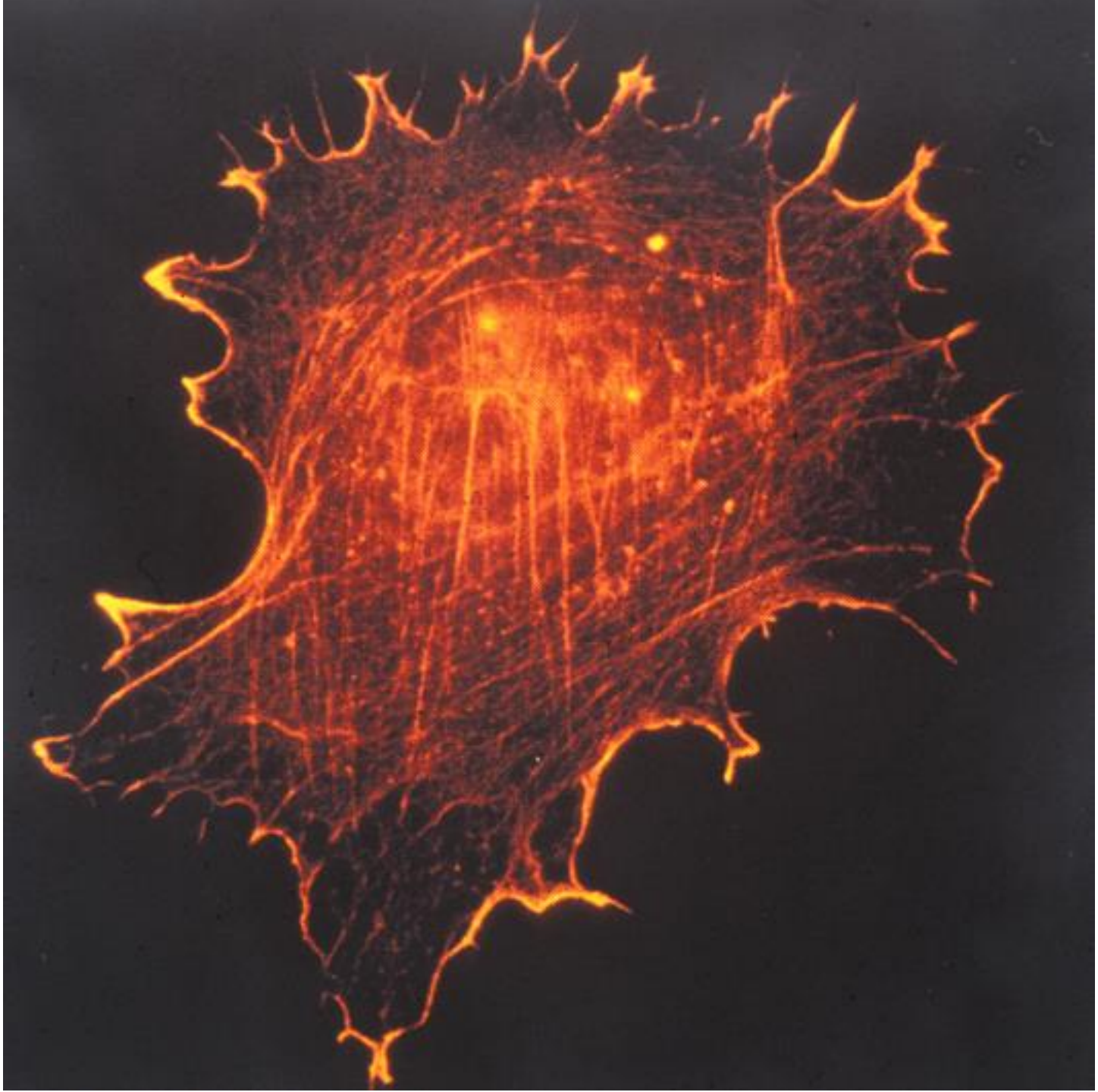
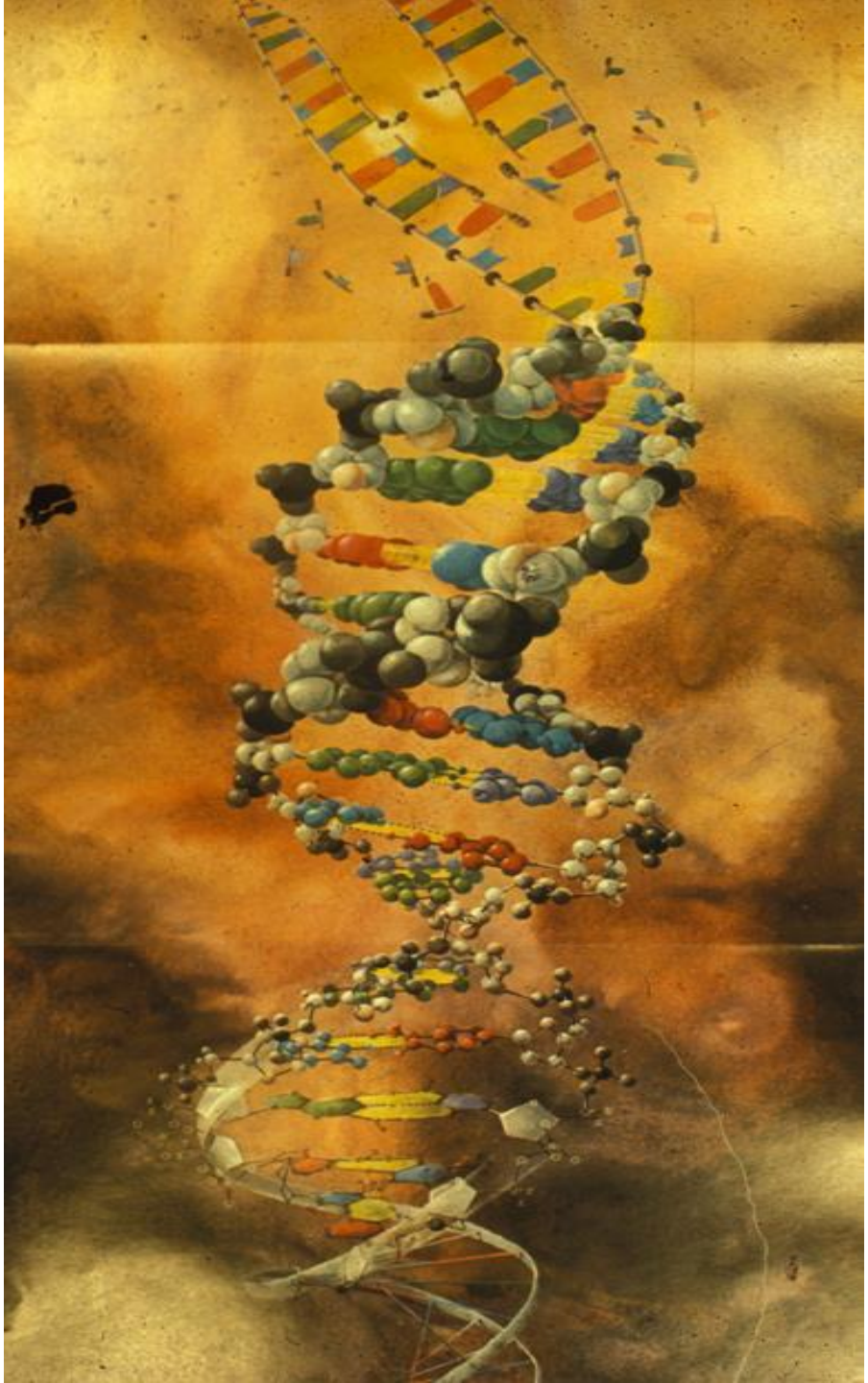
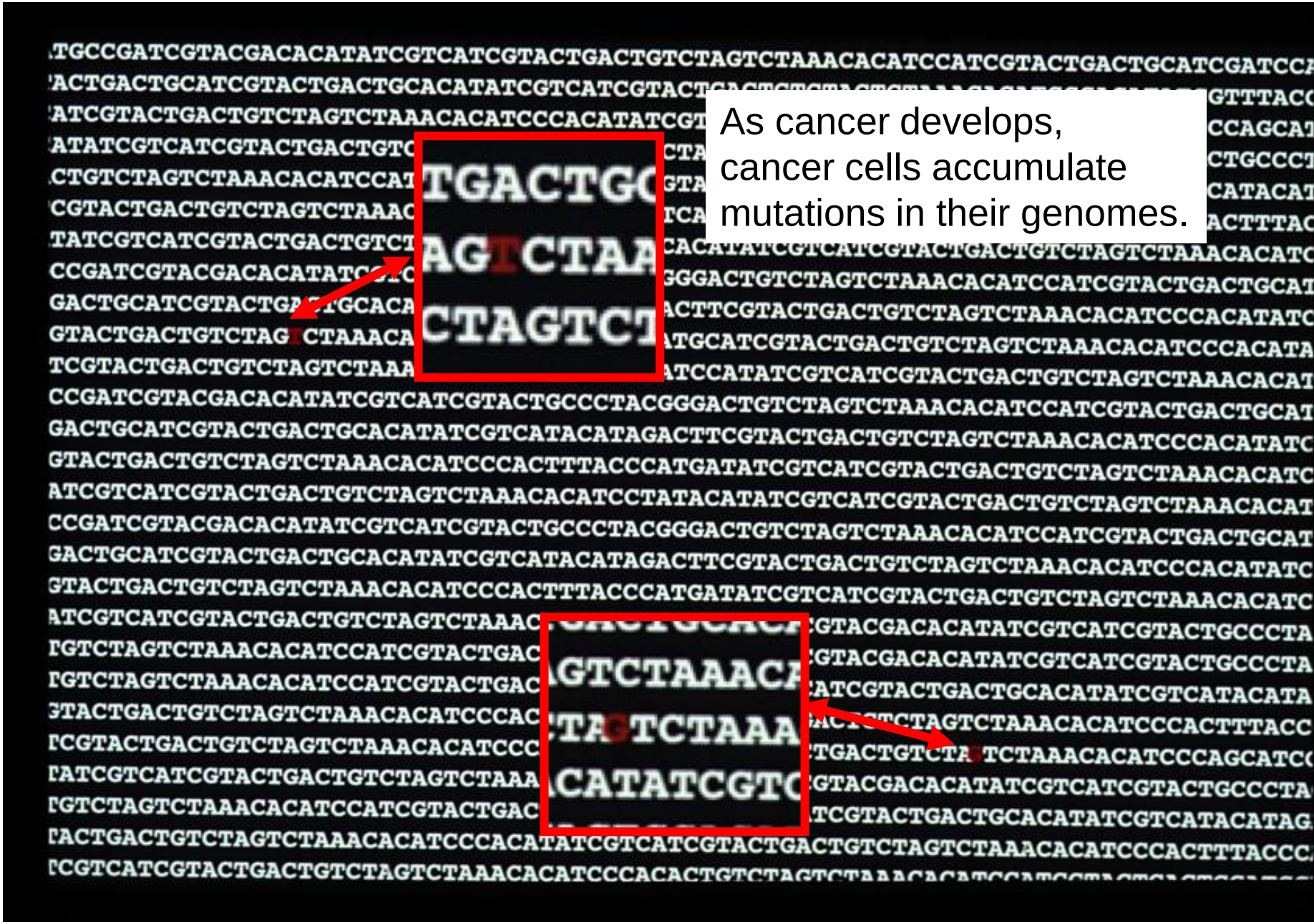


Figure 2.11 *The Biology of Cancer* (© Garland Science 2007)






As cancer develops, cancer cells accumulate mutations in their genomes.

How even a subtle change in DNA structure can wreak havoc in a cell.

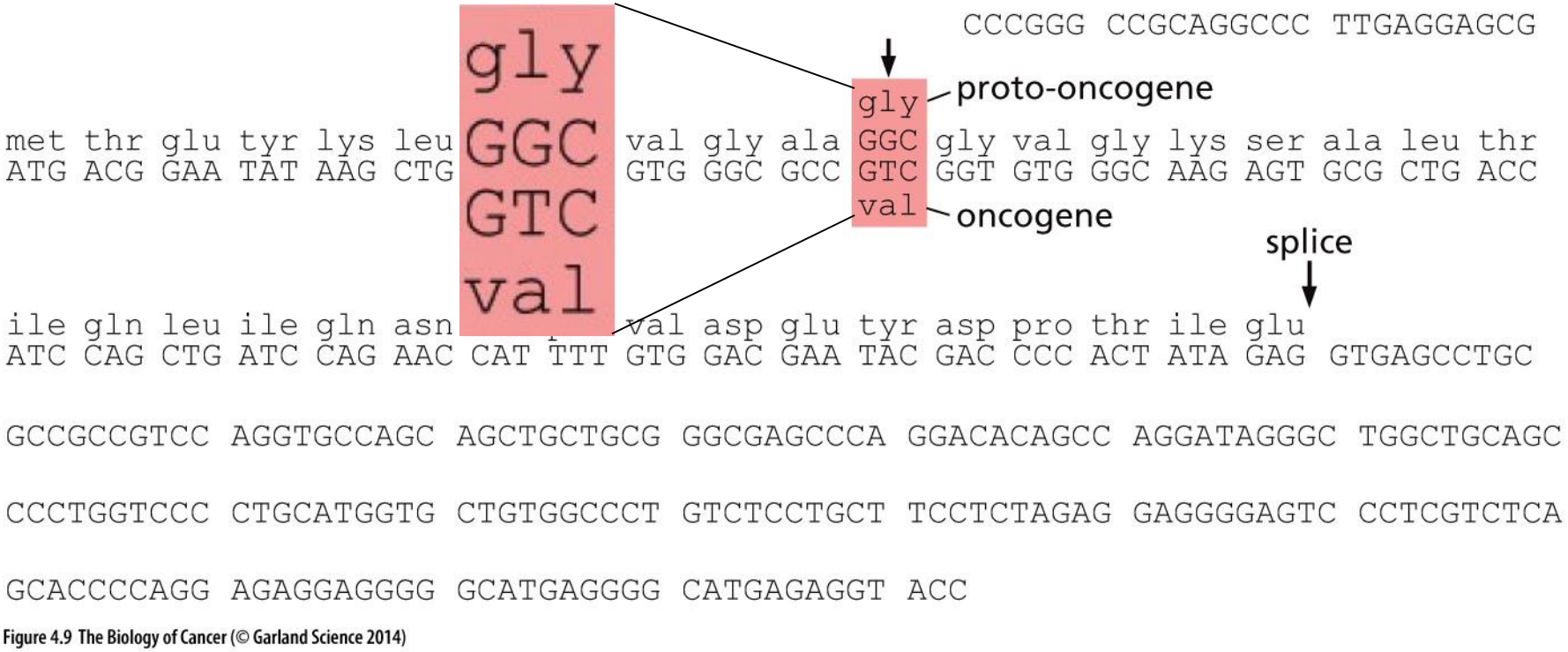
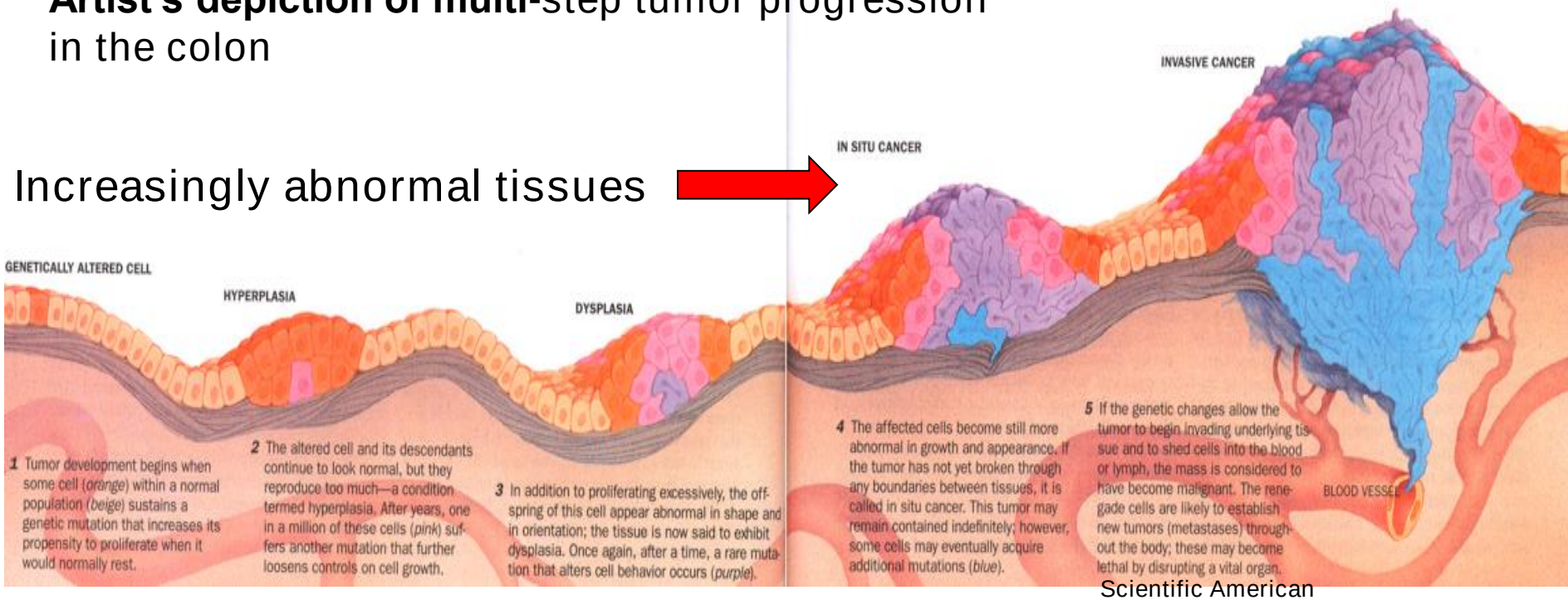


Figure 4.9 The Biology of Cancer (© Garland Science 2014)

1982: One simple point mutation out of 2 billion bases of DNA

Artist's depiction of multi-step tumor progression in the colon

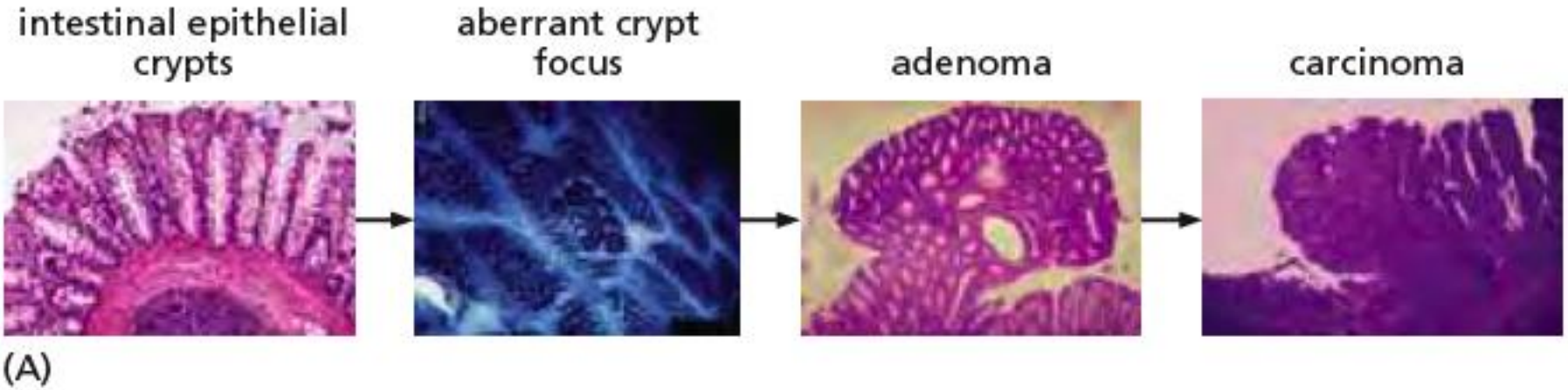
Increasingly abnormal tissues



Scientific American

Why does it take **so long** for a colon tumor to develop?

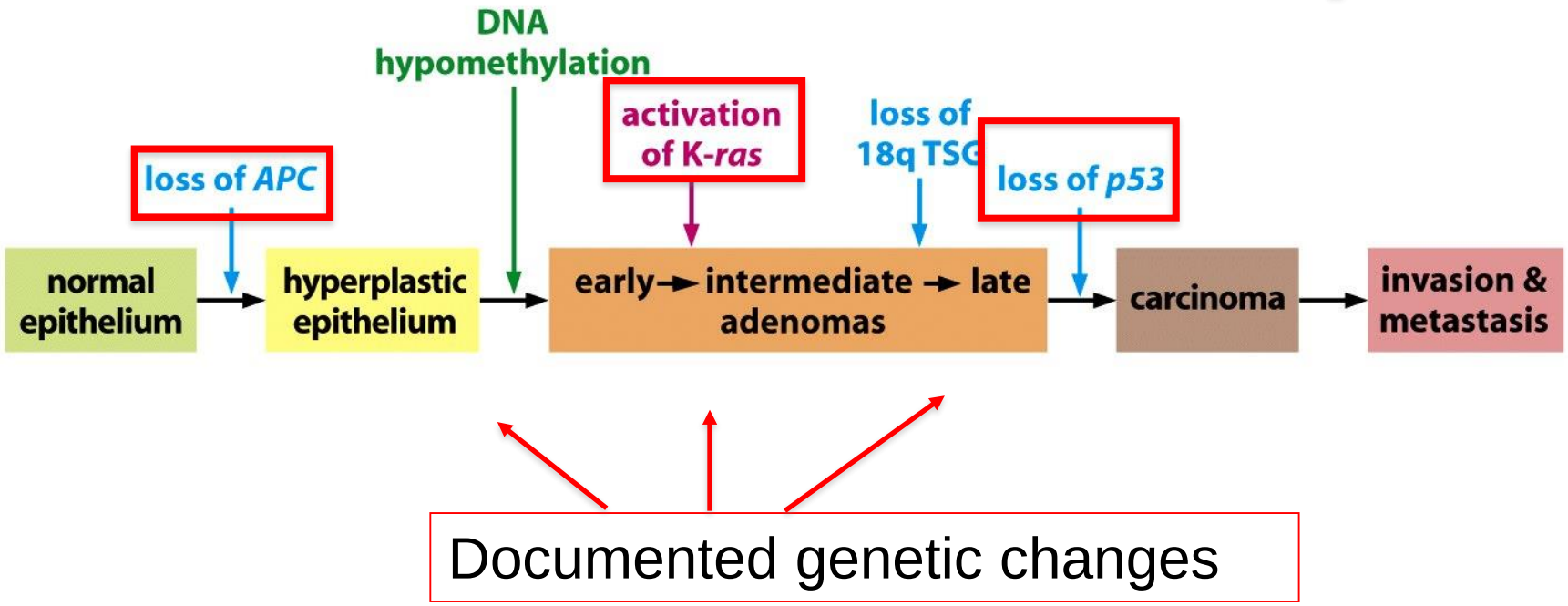
Increasingly abnormal tissues →



normal epithelium → hyperplastic epithelium → dysplasia → adenomatous polyp → carcinoma → invasion & metastasis

Each of these steps take a long time to occur, e.g., 5-10 years.

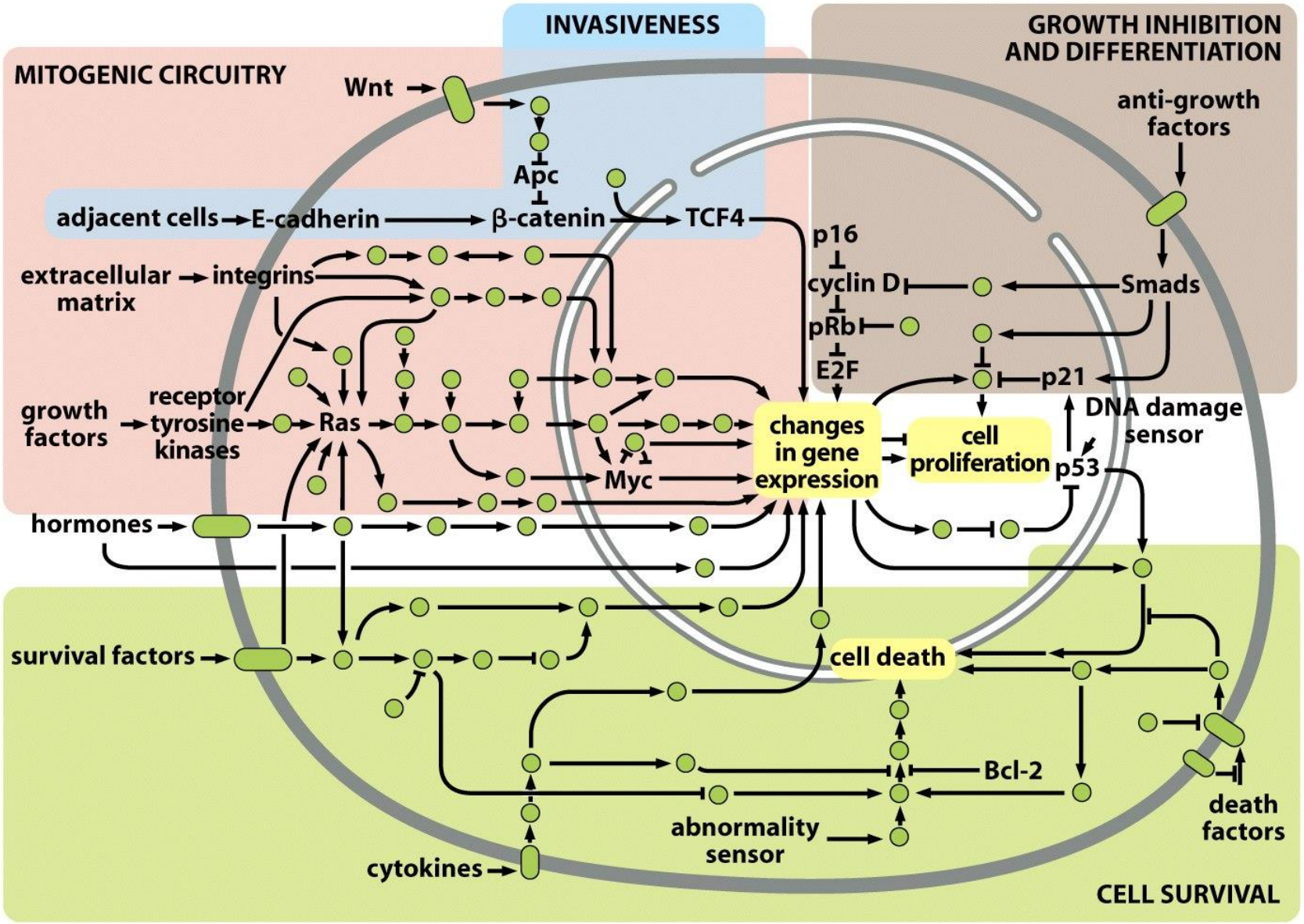
As cells [and the tumors that they form] grow increasingly abnormal, they accumulate more and more damaged genes

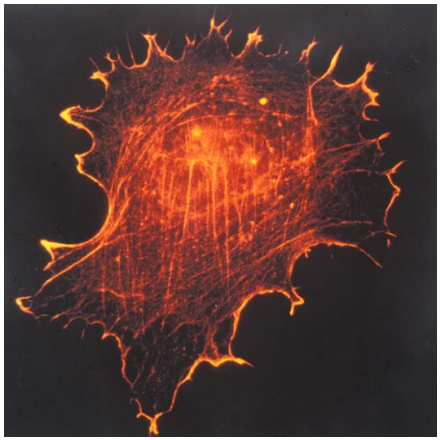


Cancer formation in the gut

Figure 11.10 The Biology of Cancer (© Garland Science 2007)

Over the past 40 years, we have learned an enormous amount about the internal circuitry governing the behavior of human cells.

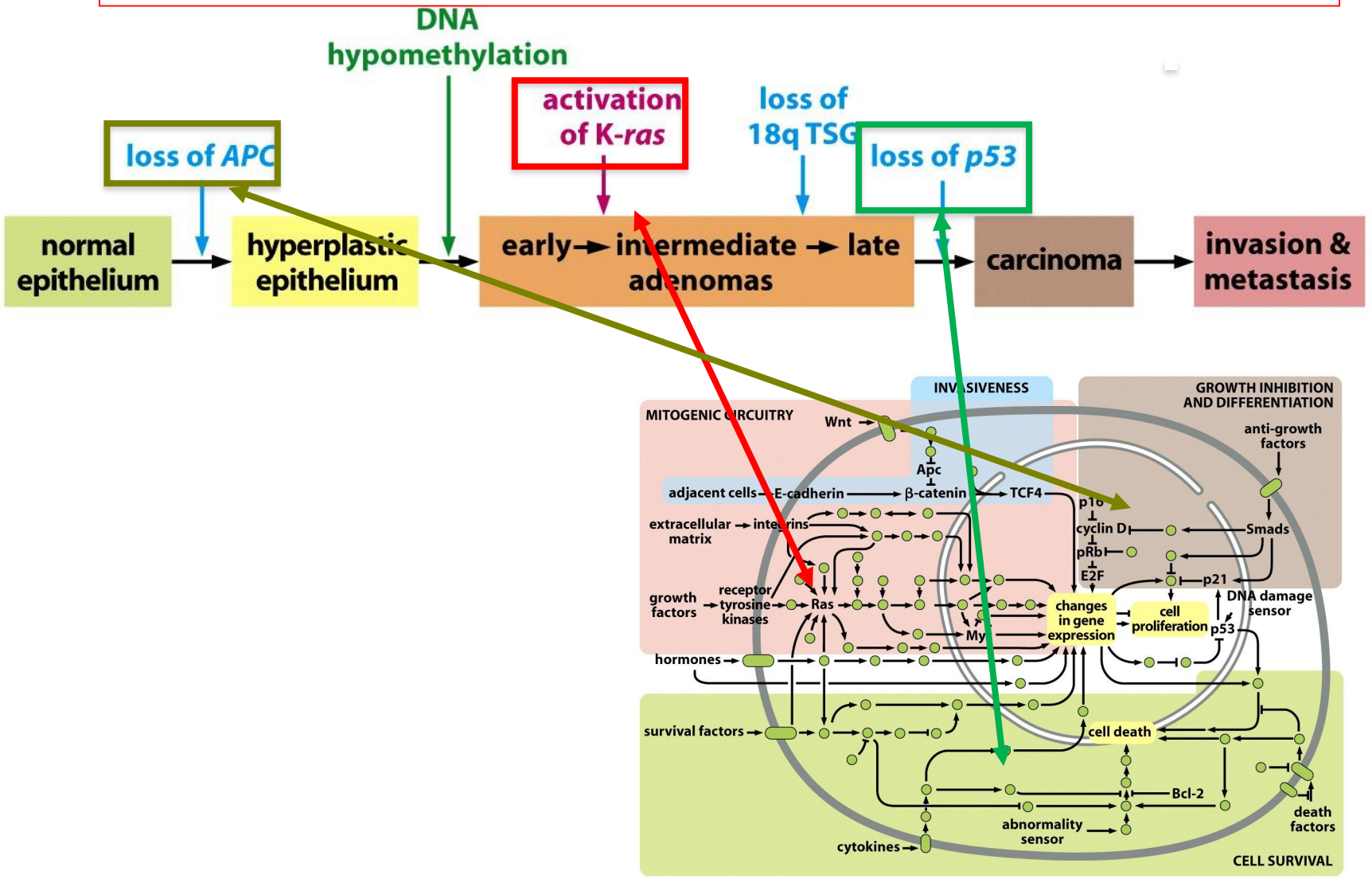




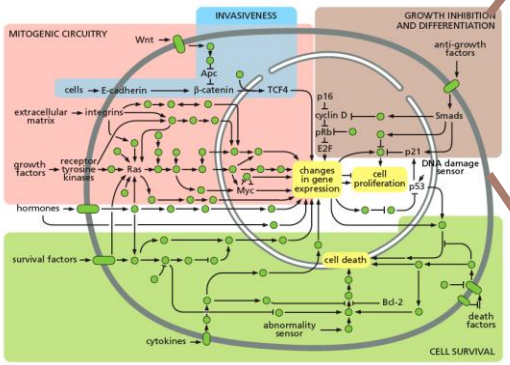
As cancer develops, the mutations cause damage to multiple control circuits operating within individual cancer cells.

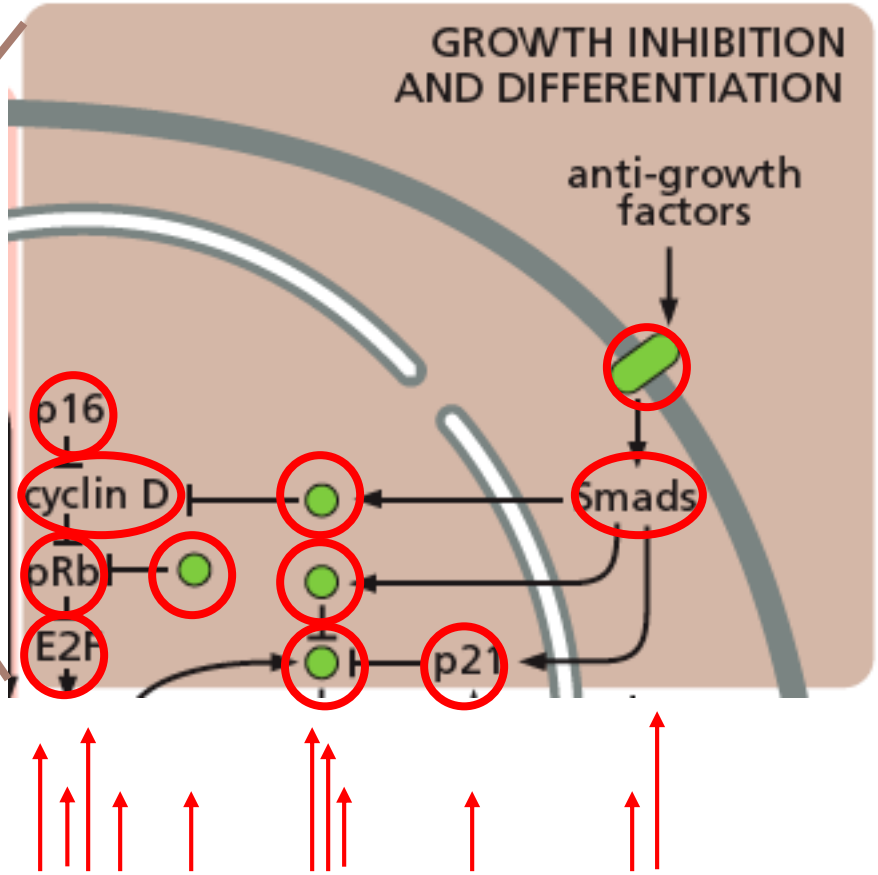
Figure 11.44 *The Biology of Cancer* (© Garland Science 2007)

As cells [and the tumors that they form] grow increasingly abnormal, they accumulate more and more damaged genes

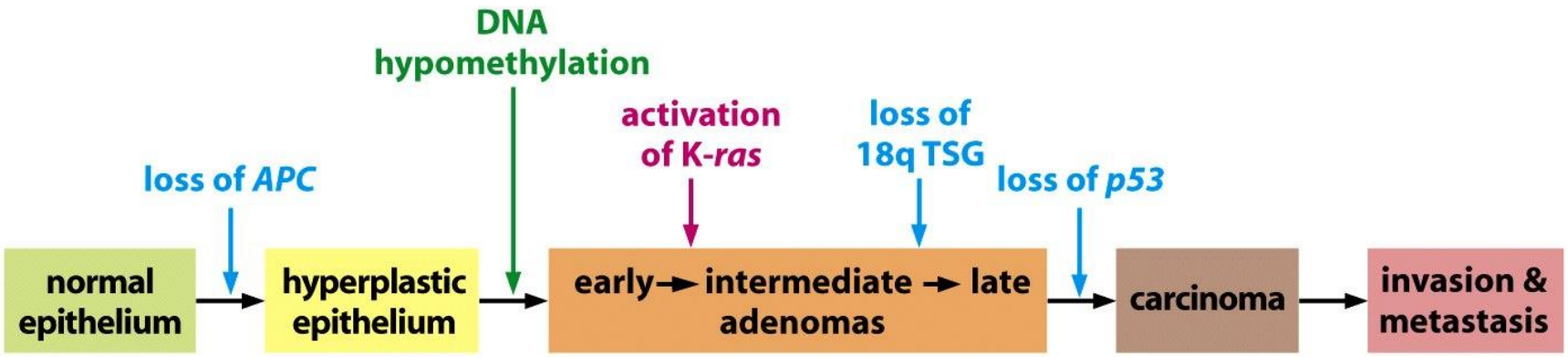


One subcircuit:





Mutations in many of these genes lead to defective proteins and therefore malfunctioning components of this subcircuit



Same process also operates in the pancreas

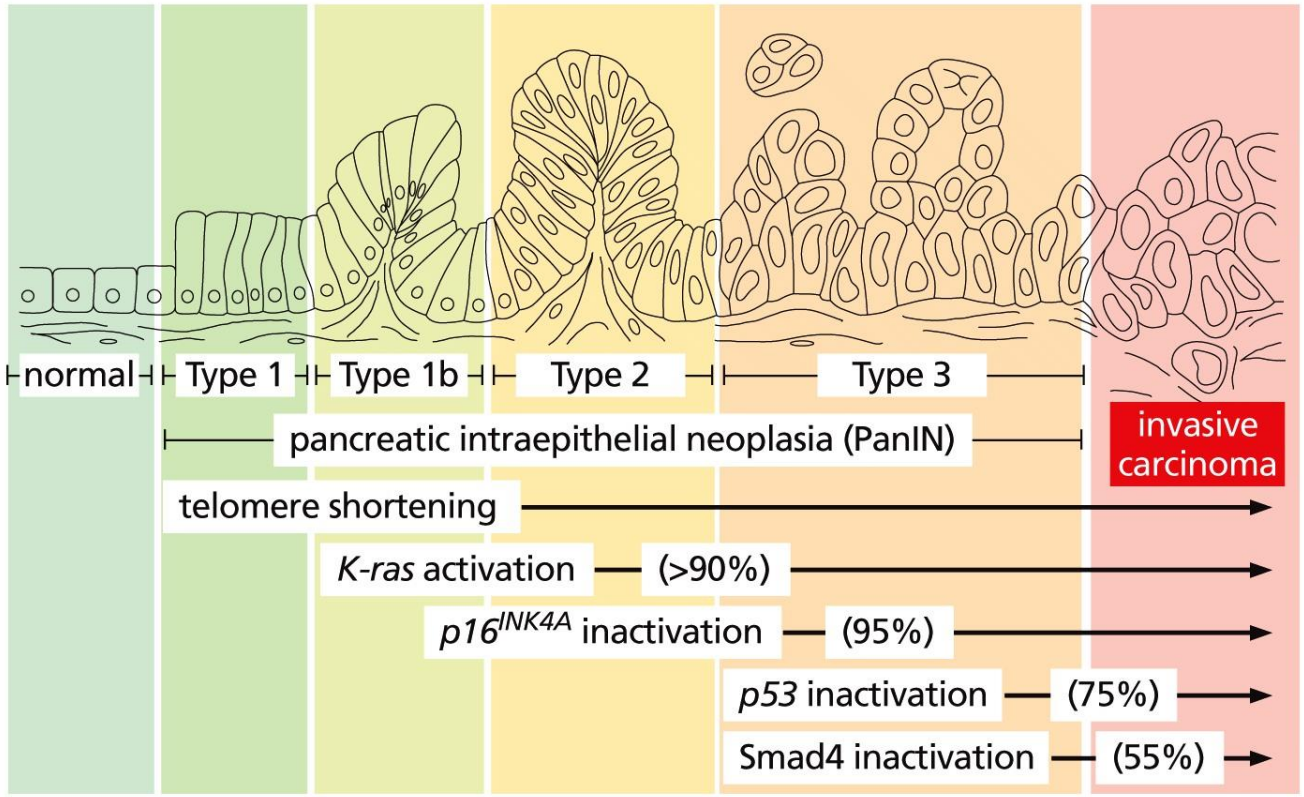
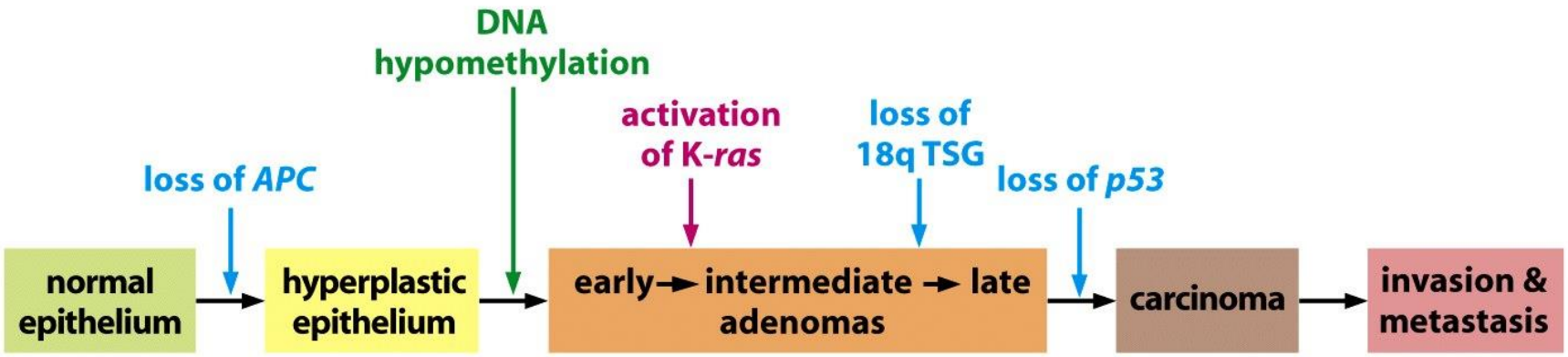


Figure 11.12b The Biology of Cancer (© Garland Science 2014)



Different colorectal carcinomas take different genetic paths
en route to full-fledged cancer formation

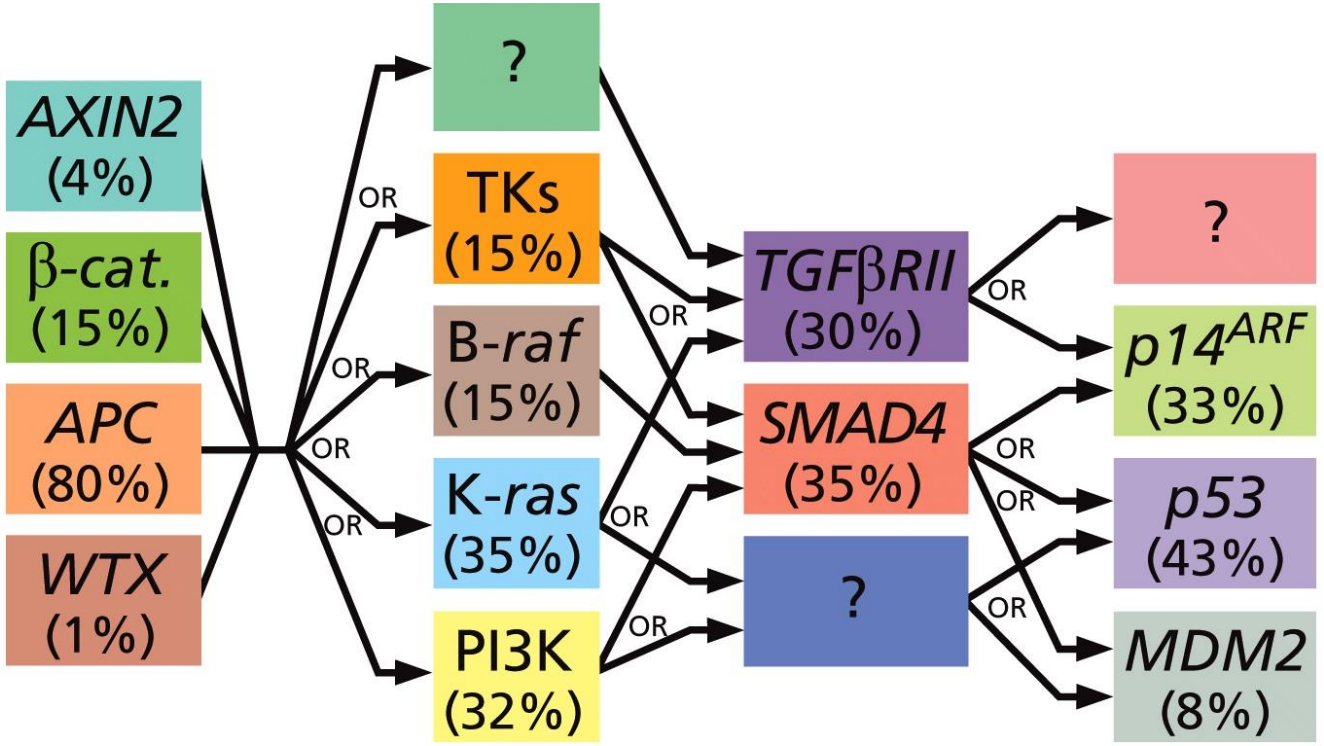
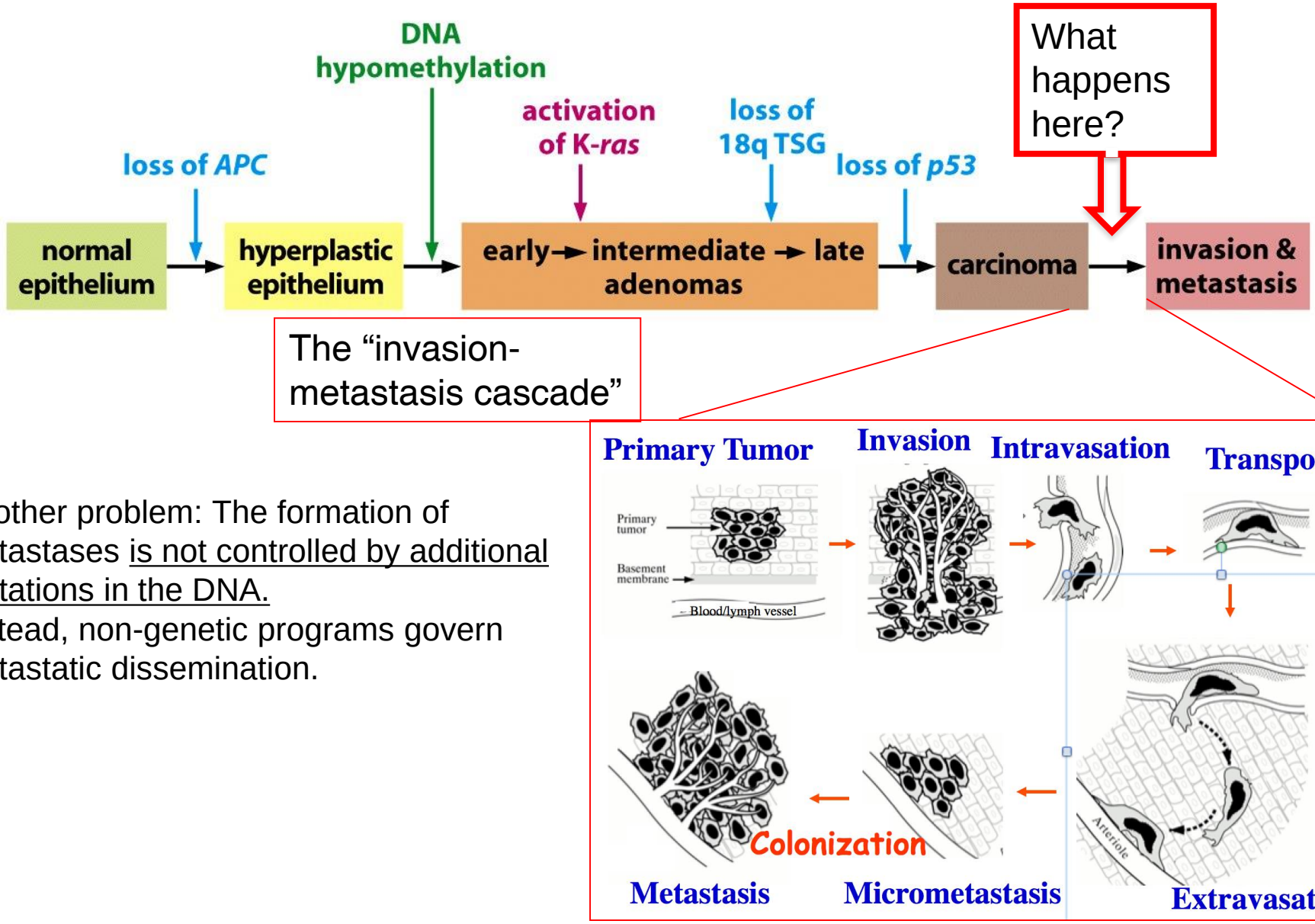


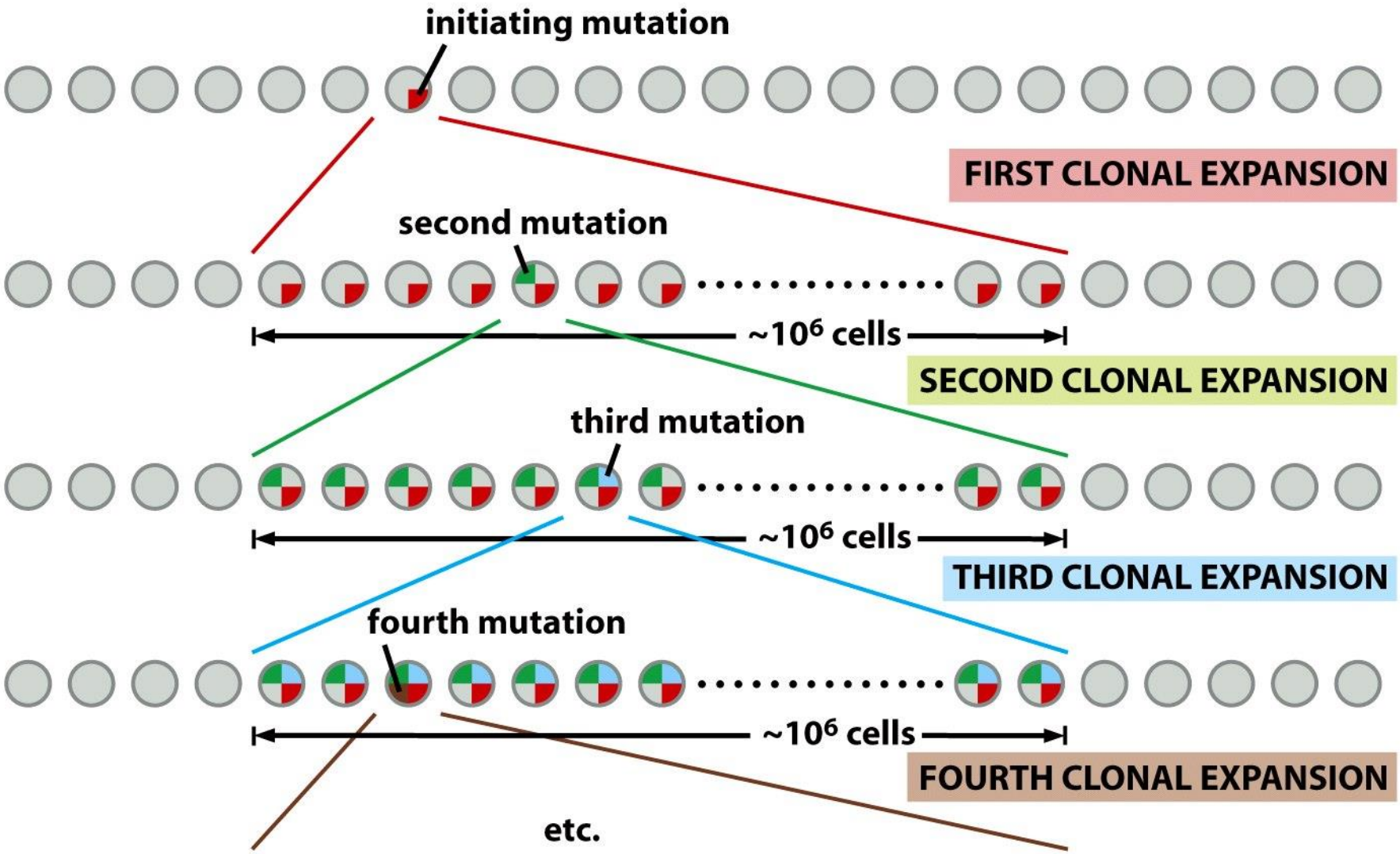
Figure 11.12a The Biology of Cancer (© Garland Science 2014)



Another problem: The formation of metastases <u>is not controlled by additional mutations in the DNA.</u>
Instead, non-genetic programs govern metastatic dissemination.

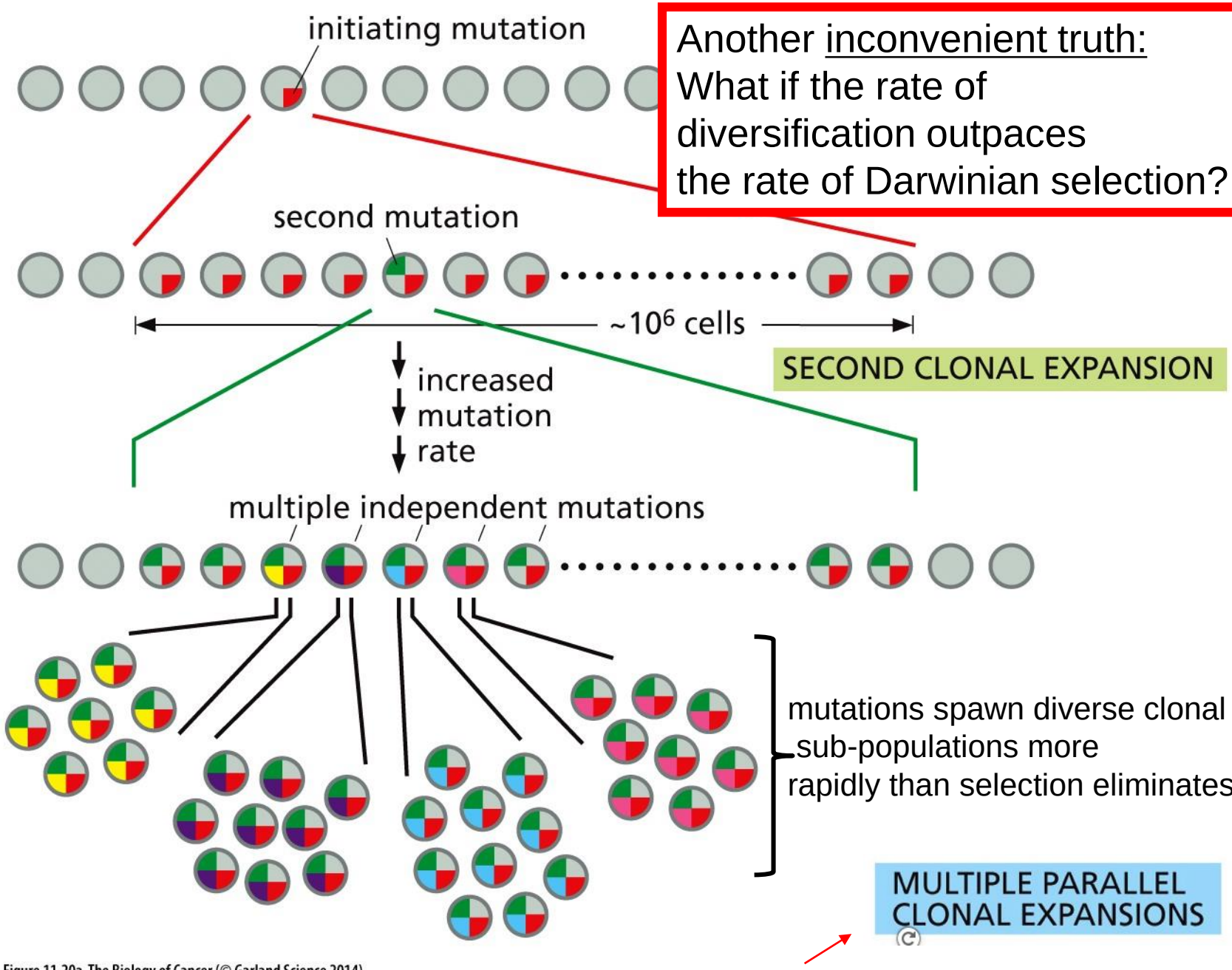
Figure 11.10 The Biology of Cancer (© Garland Science 2007)

A Darwinian model of multistep tumor progression



(Each mutation confers and additional survival or proliferation advantage.)

Figure 11.12 *The Biology of Cancer* (© Garland Science 2007)



Another inconvenient truth:
What if the rate of
diversification outpaces
the rate of Darwinian selection?

Figure 11.20a The Biology of Cancer (© Garland Science 2014)

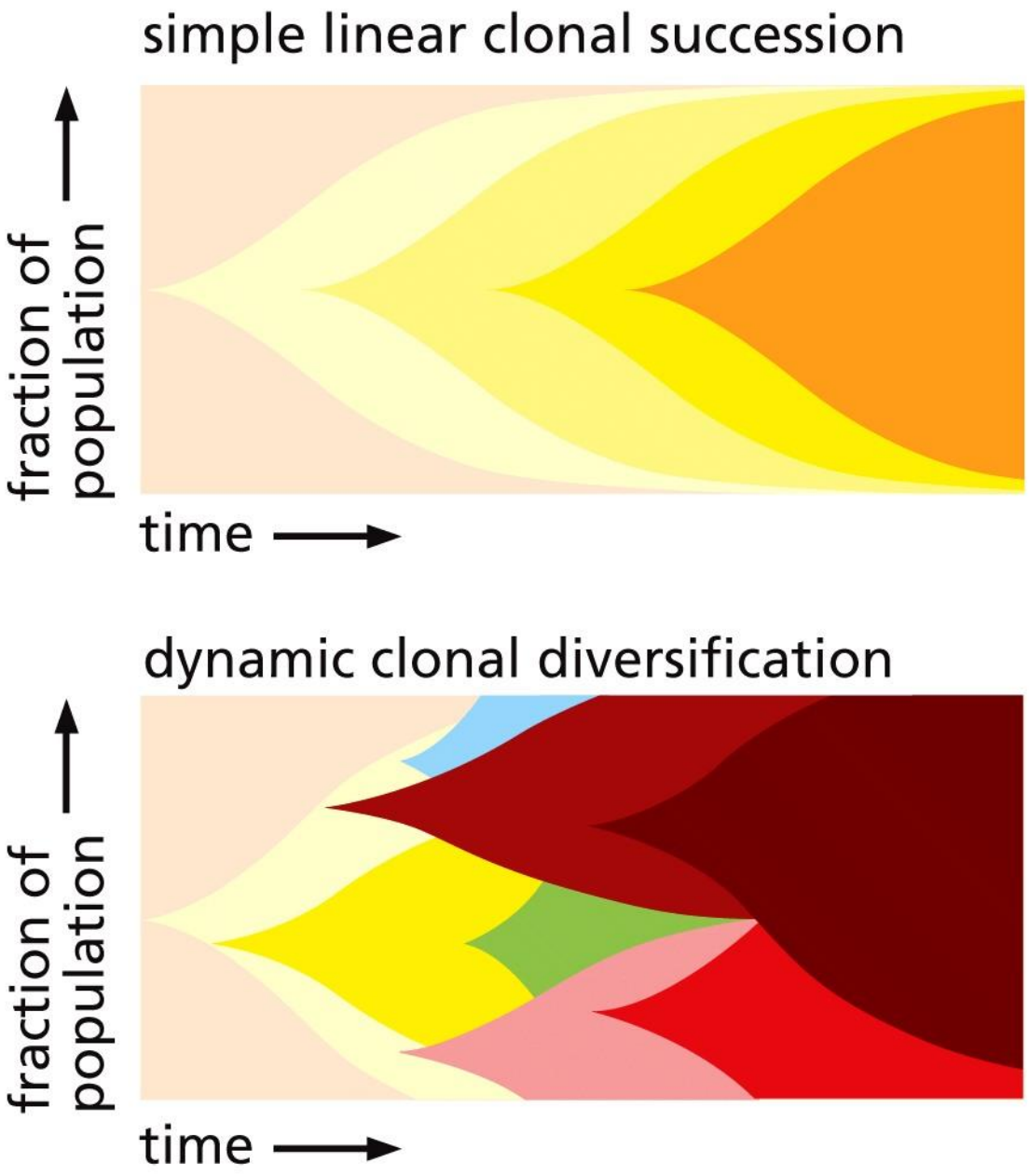
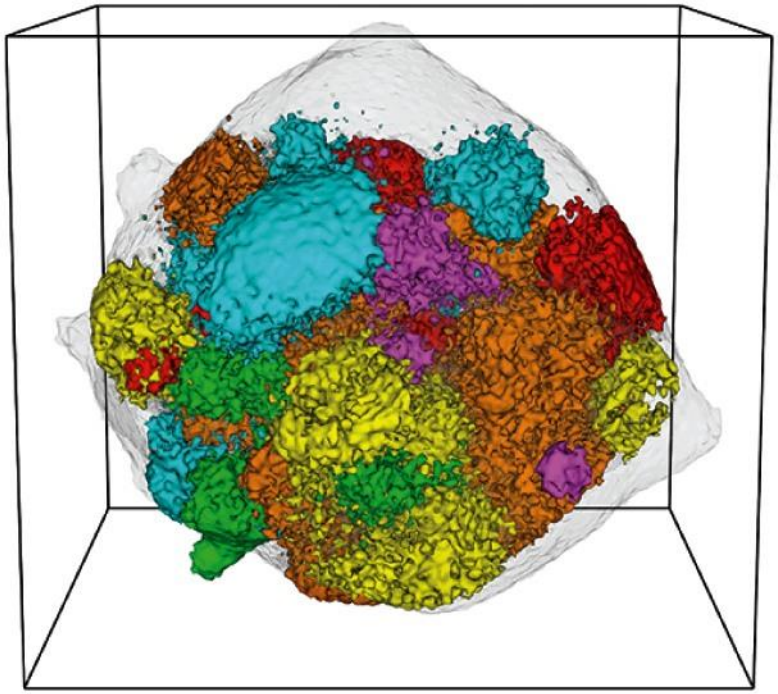


Figure 11.20b The Biology of Cancer (© Garland Science 2014)



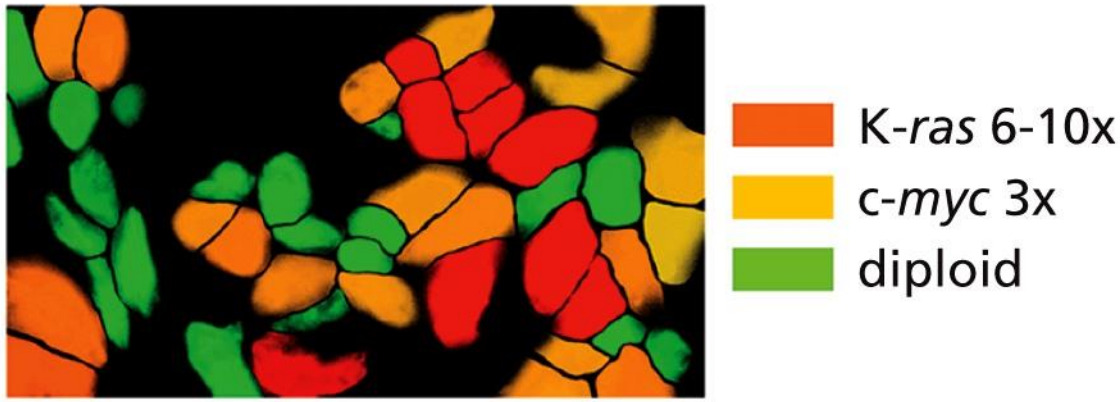


Figure 11.20c The Biology of Cancer (© Garland Science 2014)

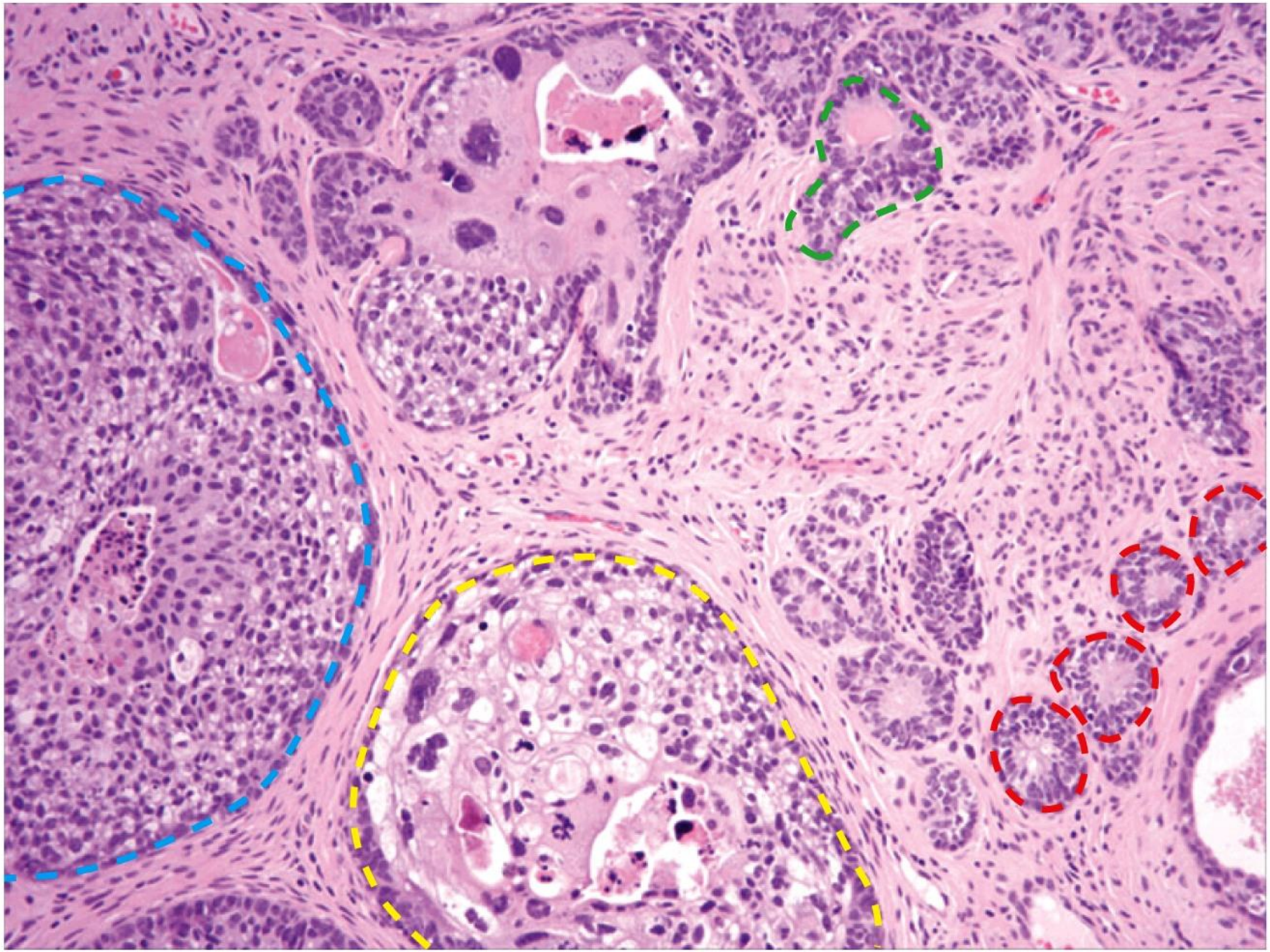
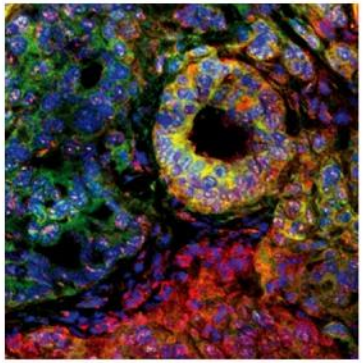


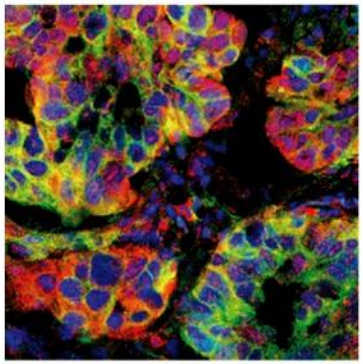
Figure 11.21a The Biology of Cancer (© Garland Science 2014)

KM12SM



Case 10 (stage 10)

EGFR



HT29

VEGFR

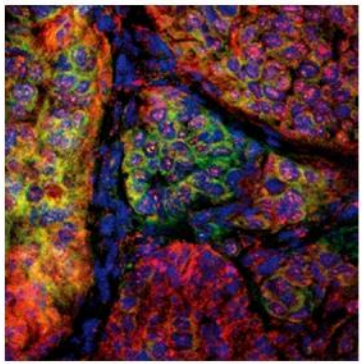
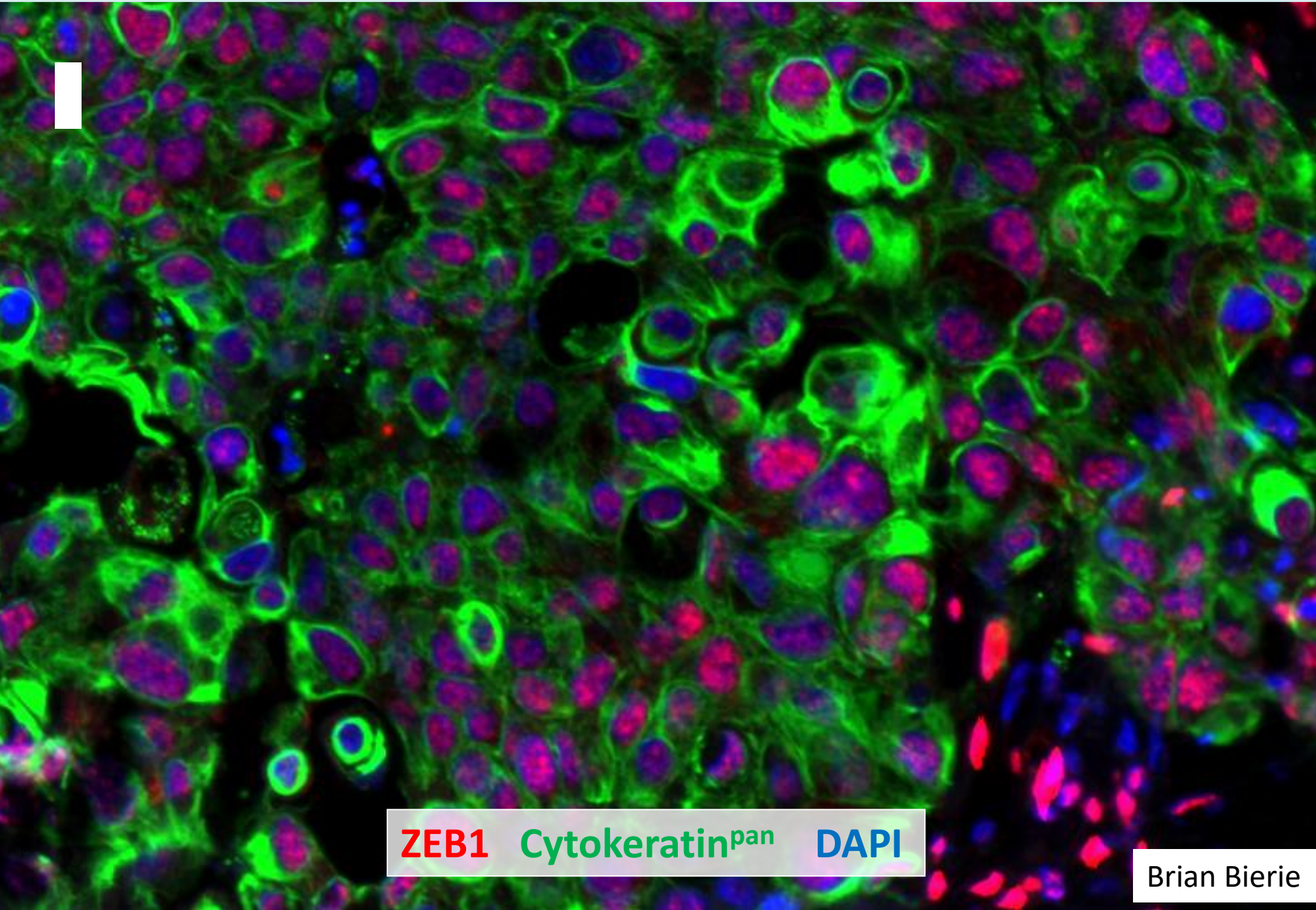


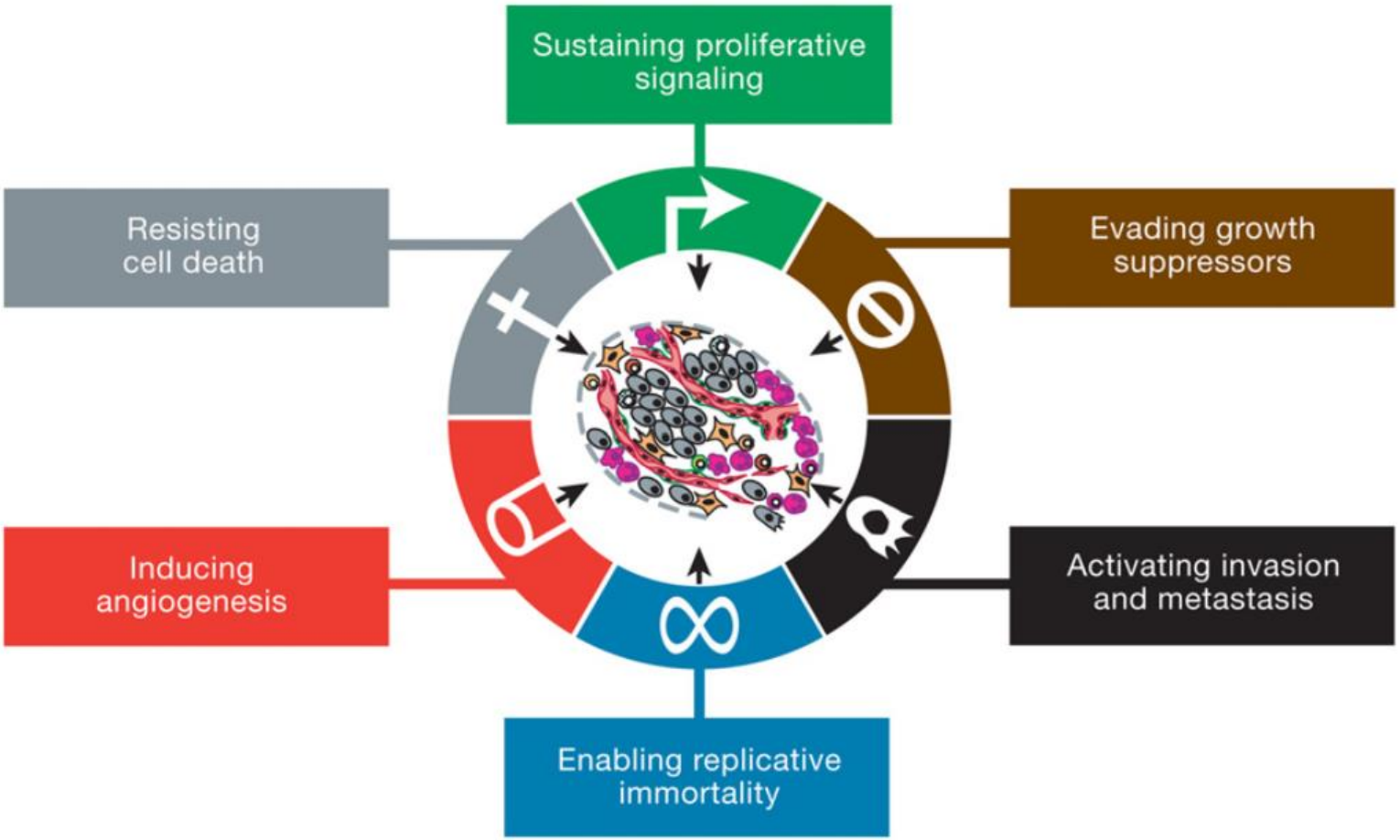
Figure 11.21b The Biology of Cancer (© Garland Science 2014)

Carcinoma cell heterogenity is a hallmark of breast cancer
Within a given tumor



Brian Bierie

How do the multiple steps required to form a human tumor
map to the multiple distinct traits that tumors develop?
In spite of this heterogeneity, are there some common shared traits??



How do the multiple steps required to form a human tumor
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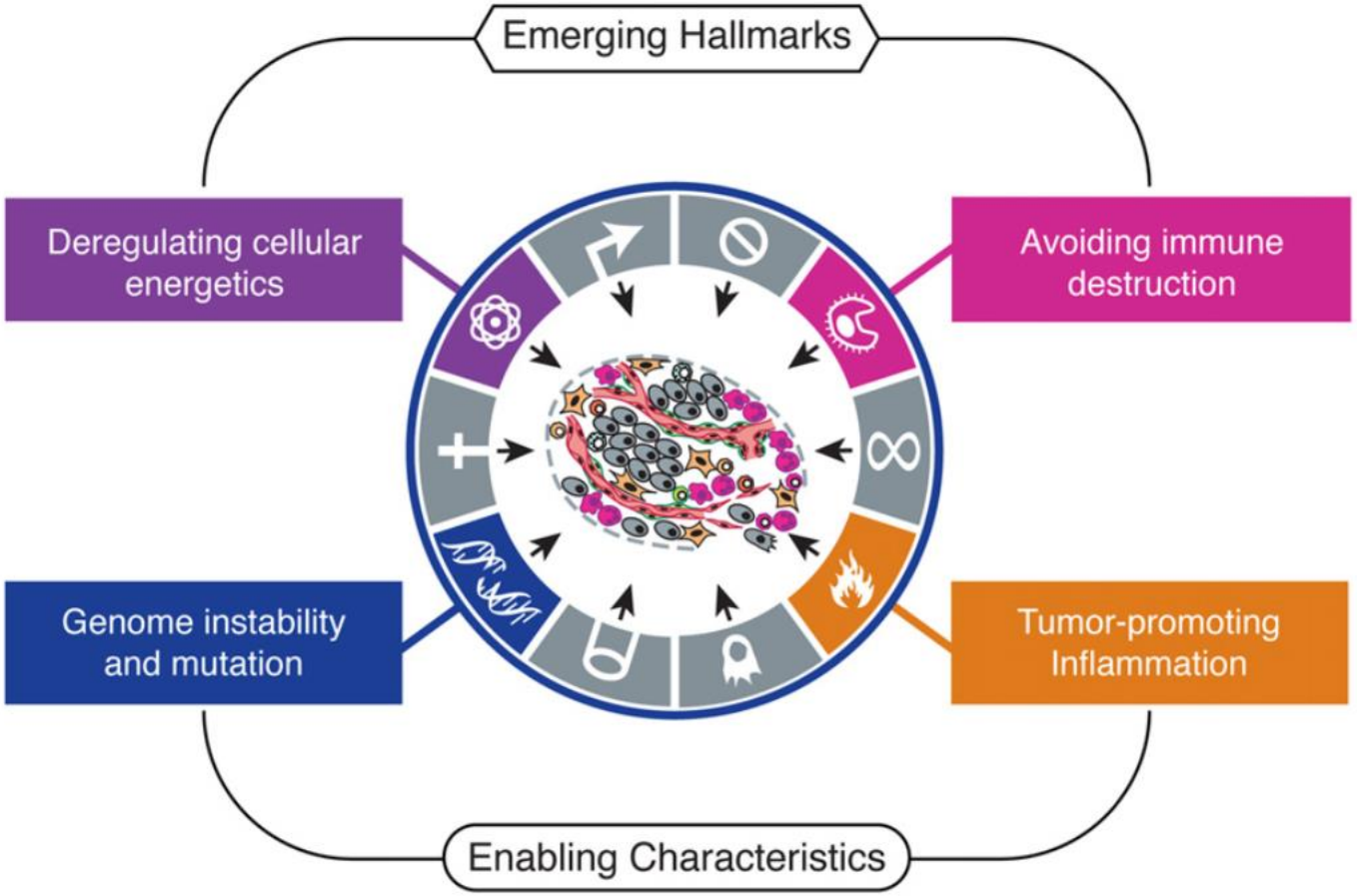
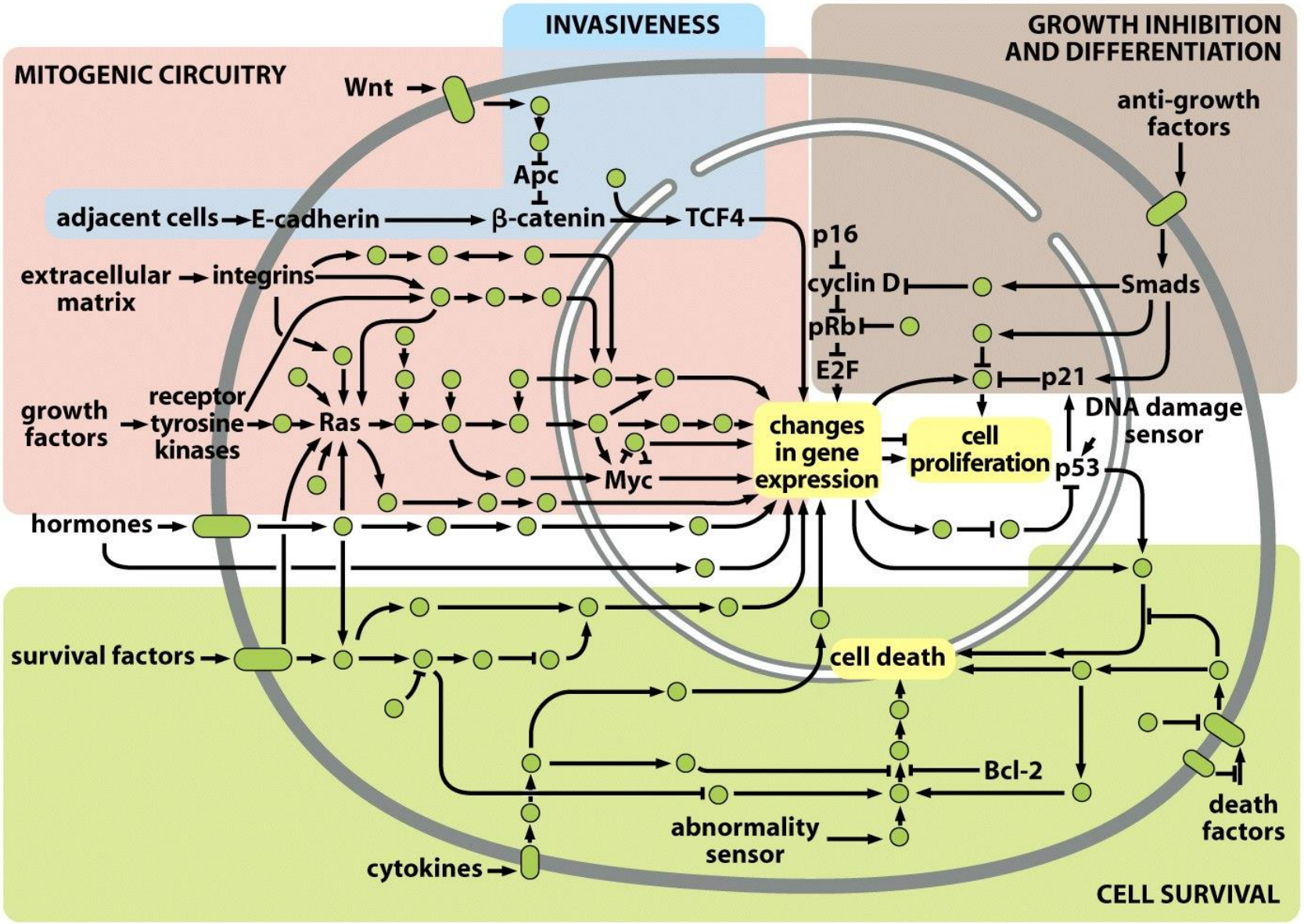
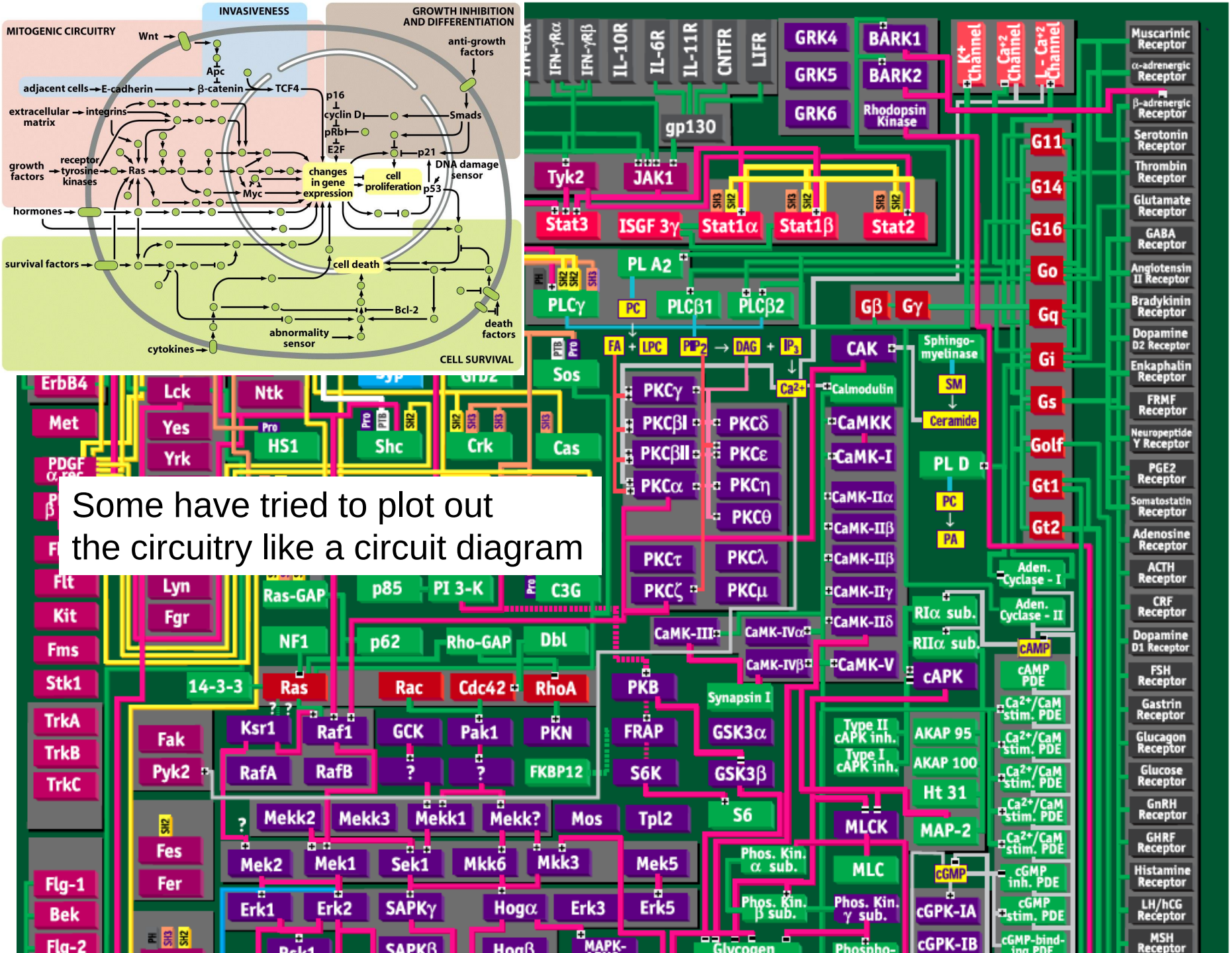
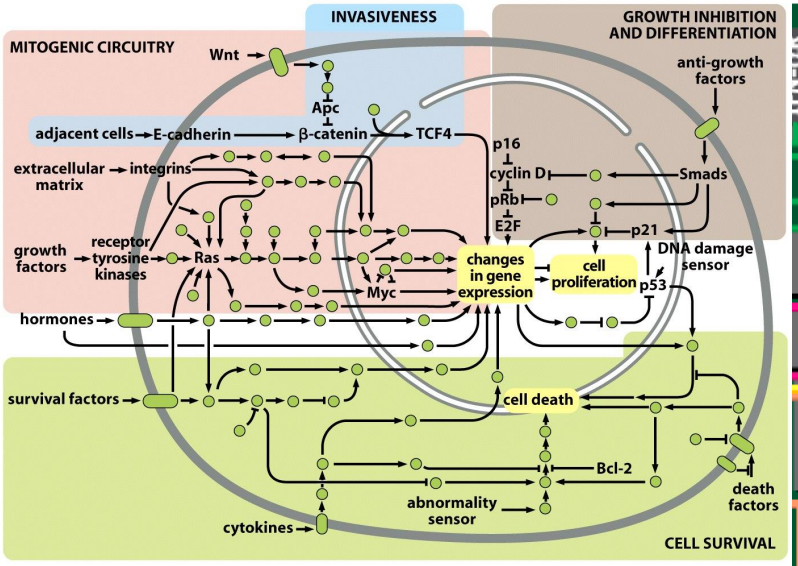


Back to the internal circuitry governing the behavior of human cells.




INVASIVENESS
GROWTH INHIBITION AND DIFFERENTIATION
MITOGENIC CIRCUITRY
Wnt
anti-growth factors
Apc
adjacent cells
E-cadherin
β-catenin
TCF4
p16
cyclin D
pRb
E2F
extracellular matrix
integrins
Smads
p21
DNA damage sensor
growth factors
receptor tyrosine kinases
Ras
Myc
changes in gene expression
cell proliferation
p53
hormones
survival factors
cell death
Bcl-2
abnormality sensor
death factors
cytokines
CELL SURVIVAL
Some have tried to plot out the circuitry like a circuit diagram
GRK4
GRK5
GRK6
BARK1
BARK2
Rhodopsin Kinase
gp130
Tyk2
JAK1
Stat3
ISGF 3γ
Stat1α
Stat1β
Stat2
PL A2
PLCγ
PC
PLCβ1
PLCβ2
Gβ
Gγ
FA
LPC
PIP2
DAG
IP3
Ca2+
CAK
Sphingo-myelinase
SM
Ceramide
Sos
Calmodulin
PKCγ
PKCβI
PKCβII
PKCα
PKCδ
PKCε
PKCη
PKCθ
CaMKK
CaMK-I
CaMK-IIα
CaMK-IIβ
CaMK-IIβ
CaMK-IIγ
CaMK-IIδ
CaMK-V
PL D
PC
PA
PKCτ
PKCζ
PKCλ
PKCμ
CaMK-III
CaMK-IVα
CaMK-IVβ
RIα sub.
RIIα sub.
cAPK
cAMP
Aden. Cyclase - I
Aden. Cyclase - II
cAMP PDE
Ca2+/CaM stim. PDE
Ca2+/CaM stim. PDE
Ca2+/CaM stim. PDE
Ca2+/CaM stim. PDE
Ca2+/CaM stim. PDE
cGMP inh. PDE
cGMP stim. PDE
cGMP-bind-ing PDE
PKB
FRAP
S6K
Synapsin I
GSK3α
GSK3β
S6
Type II cAPK inh.
Type I cAPK inh.
AKAP 95
AKAP 100
Ht 31
MAP-2
MLCK
MLC
Phos. Kin. α sub.
Phos. Kin. β sub.
Phos. Kin. γ sub.
cGMP
cGPK-IA
cGPK-IB
Glycogen
Phospho-
ErbB4
Met
PDGF α rec.
Lck
Yes
Yrk
Ntk
HS1
Shc
Crk
Cas
Lyn
Fgr
Ras-GAP
p85
PI 3-K
C3G
NF1
p62
Rho-GAP
Dbl
14-3-3
Ras
Rac
Cdc42
RhoA
Flt
Kit
Fms
Stk1
TrkA
TrkB
TrkC
Fak
Pyk2
Ksr1
Raf1
GCK
Pak1
PKN
RafA
RafB
FKBP12
Fes
Fer
Mekk2
Mekk3
Mekk1
Mekk?
Mos
Tpl2
Mek2
Mek1
Sek1
Mkk6
Mkk3
Mek5
Erk1
Erk2
SAPKγ
Hogα
Erk3
Erk5
SAPKβ
Hogβ
MAPK-
Flg-1
Bek
Flg-2
IFN-γRα
IFN-γRβ
IL-10R
IL-6R
IL-11R
CNTFR
LIFR
K+ Channel
Ca+2 Channel
L-Ca+2 Channel
G11
G14
G16
Go
Gq
Gi
Gs
Golf
Gt1
Gt2
Muscarinic Receptor
α-adrenergic Receptor
β-adrenergic Receptor
Serotonin Receptor
Thrombin Receptor
Glutamate Receptor
GABA Receptor
Angiotensin II Receptor
Bradykinin Receptor
Dopamine D2 Receptor
Enkaphalin Receptor
FRMF Receptor
Neuropeptide Y Receptor
PGE2 Receptor
Somatostatin Receptor
Adenosine Receptor
ACTH Receptor
CRF Receptor
Dopamine D1 Receptor
FSH Receptor
Gastrin Receptor
Glucagon Receptor
Glucose Receptor
GnRH Receptor
GHRF Receptor
Histamine Receptor
LH/hCG Receptor
MSH Receptor



Some have tried to plot out the circuitry like a circuit diagram

PS They went pleite!

fragment of a tumor

a cancer cell

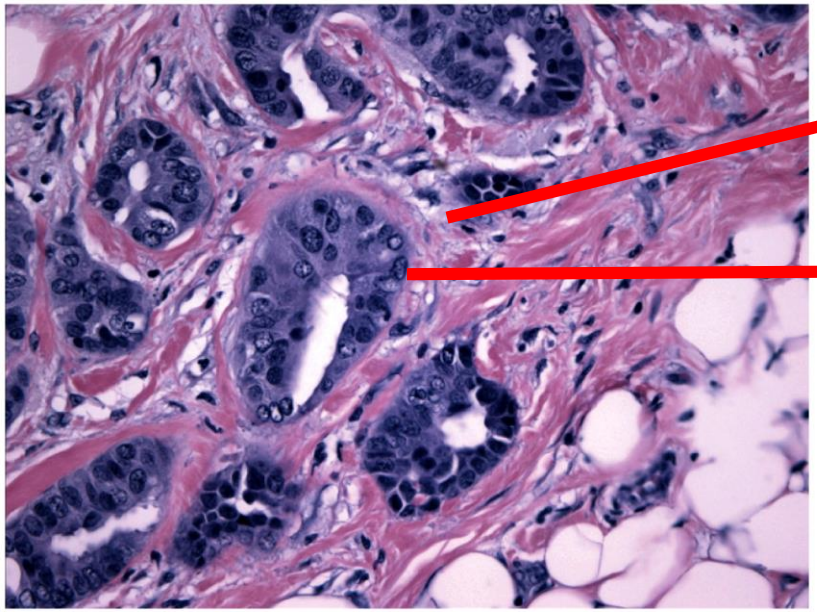
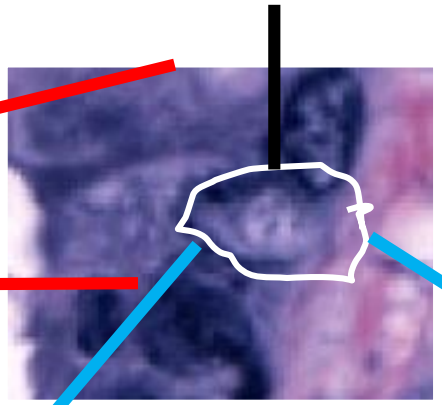
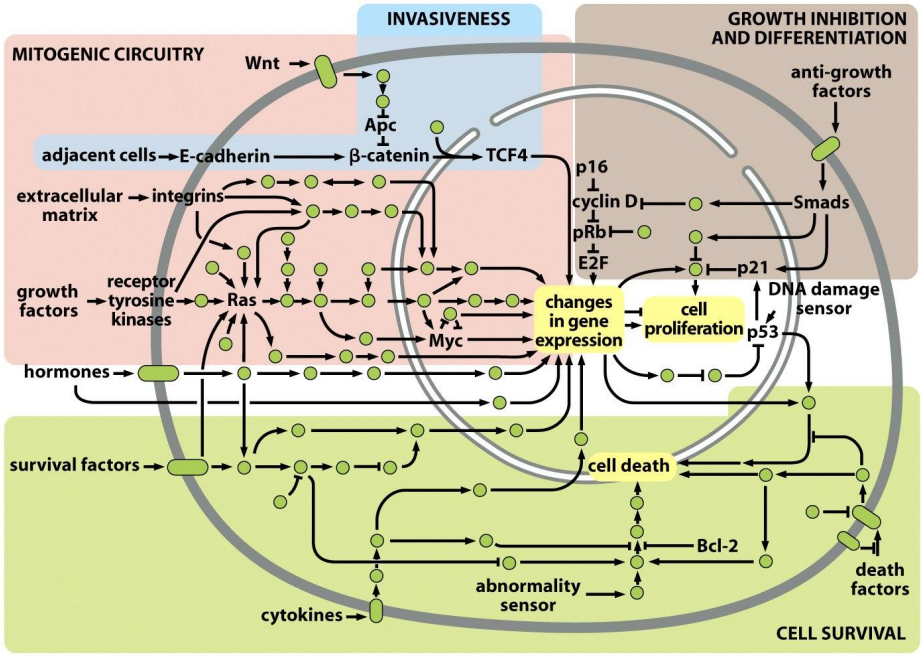
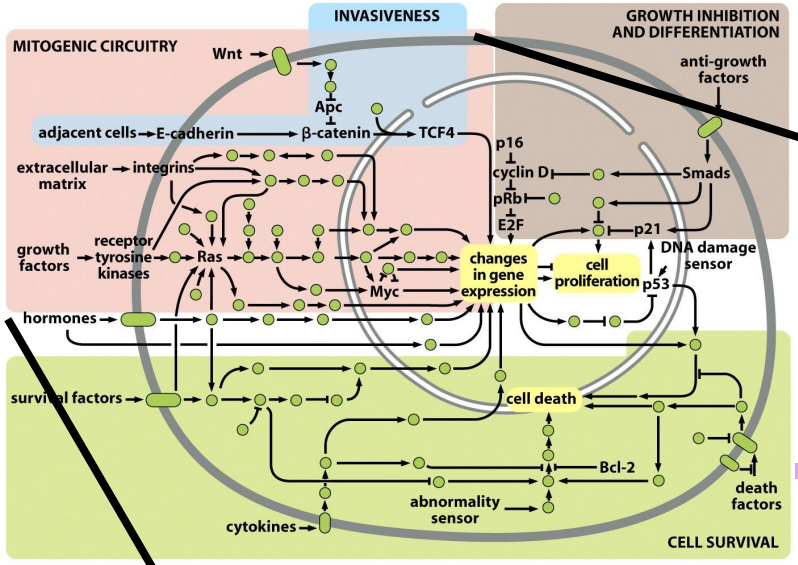


Figure 2.17b The Biology of Cancer (© Garland Science 2014)





intracellular circuitry



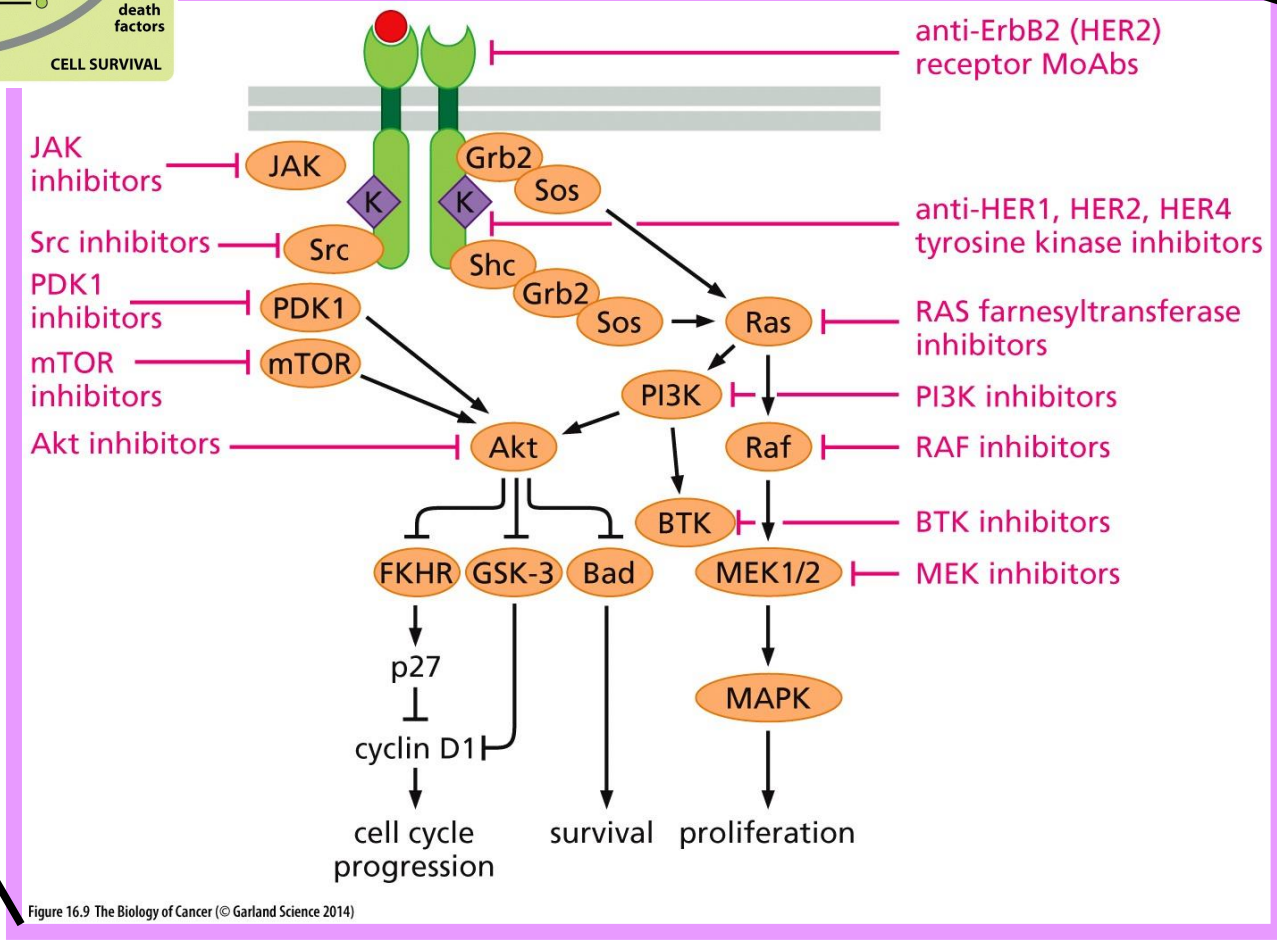
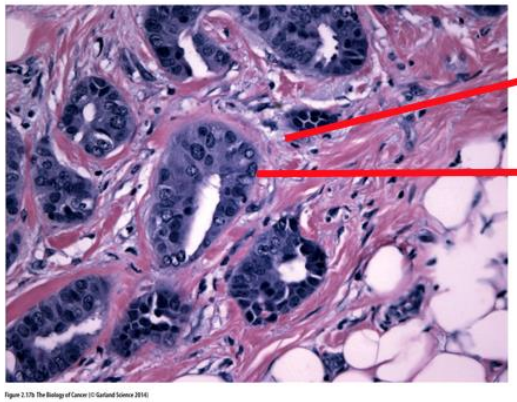
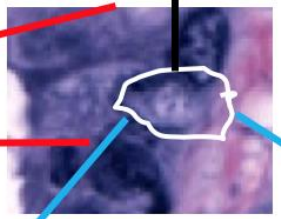


Figure 16.9 The Biology of Cancer (© Garland Science 2014)

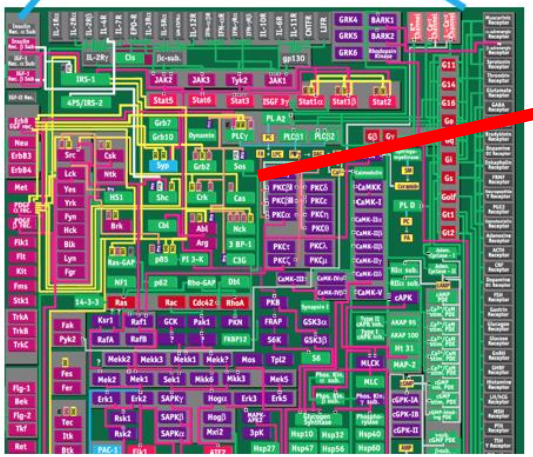
fragment of a tumor



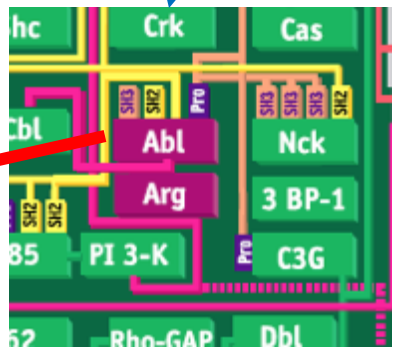
a cancer cell



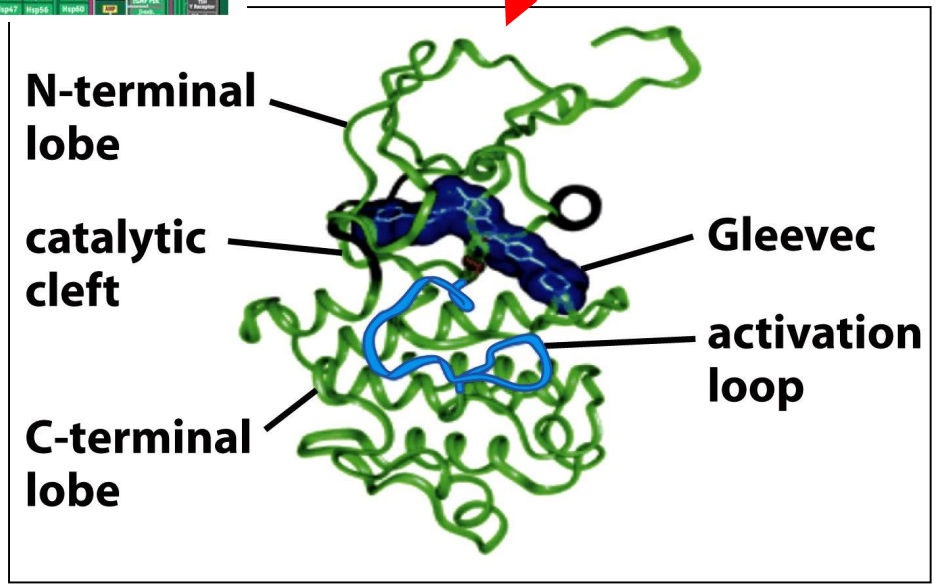
intracellular circuitry

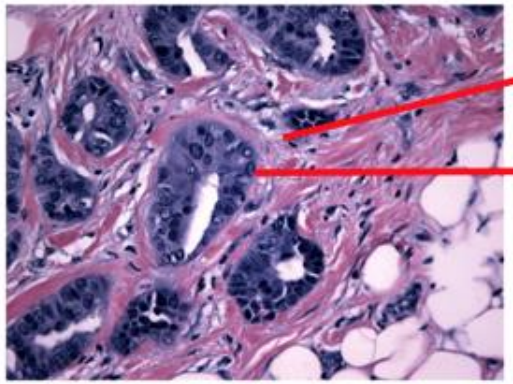


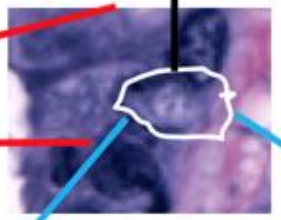
A signaling molecule
In the circuitry

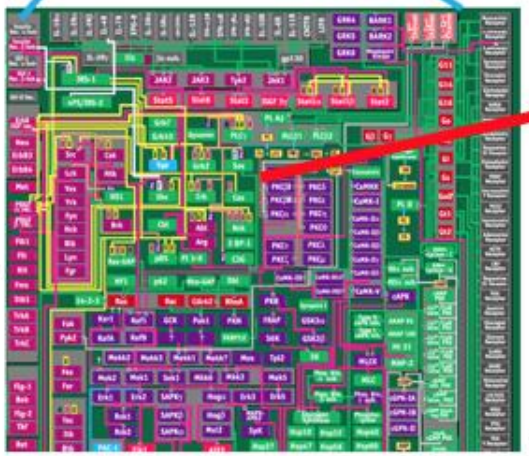


Molecular structure of the signaling molecule that misfires in **chronic myelogenous leukemia**



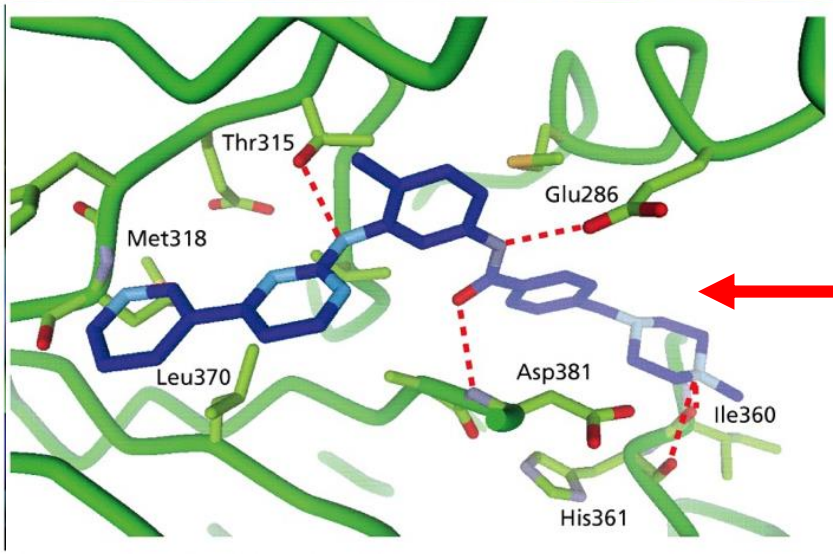


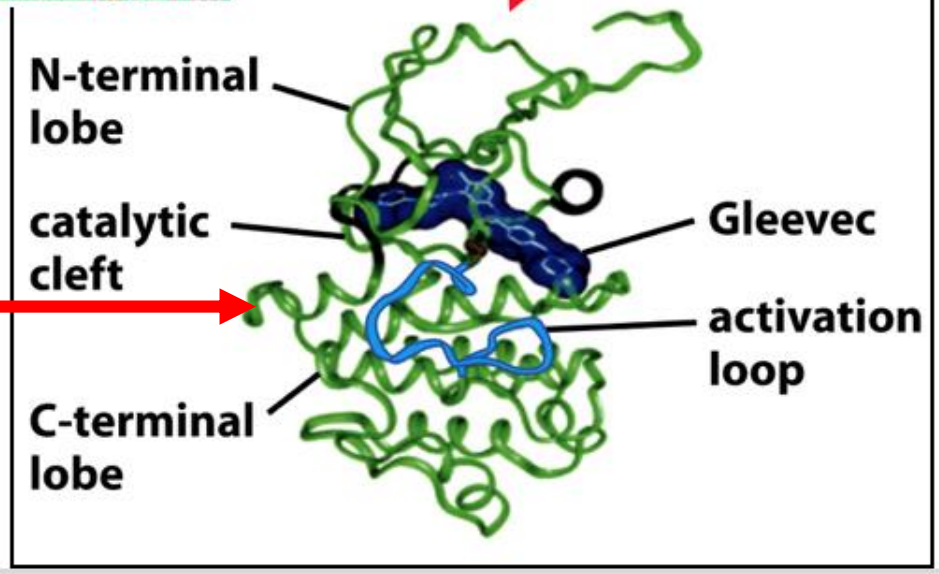




intracellular
circuitry

In the circuitry





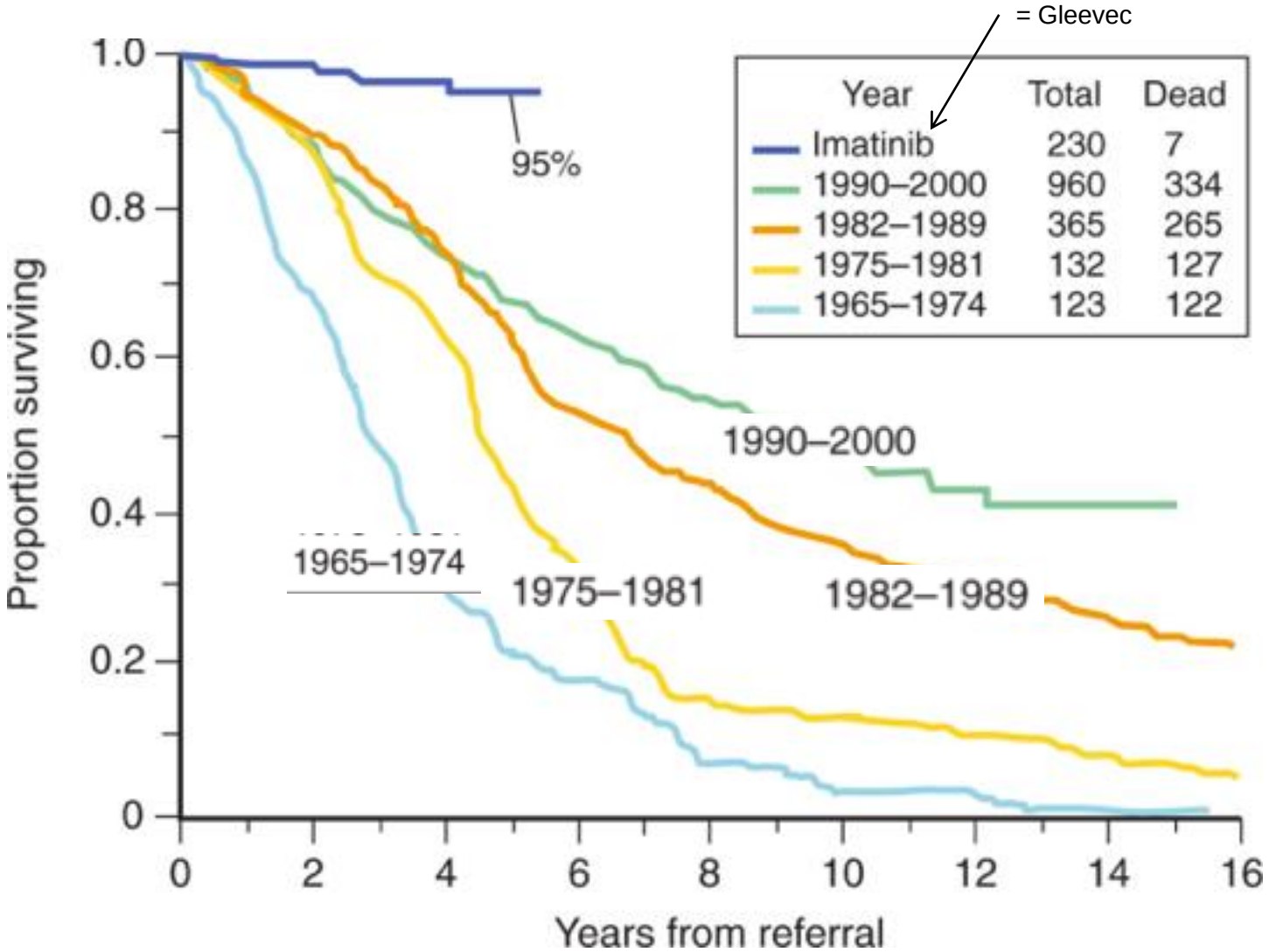
Sub-molecular structure of
the signaling molecule

Molecular structure of
the signaling molecule

A major success story:

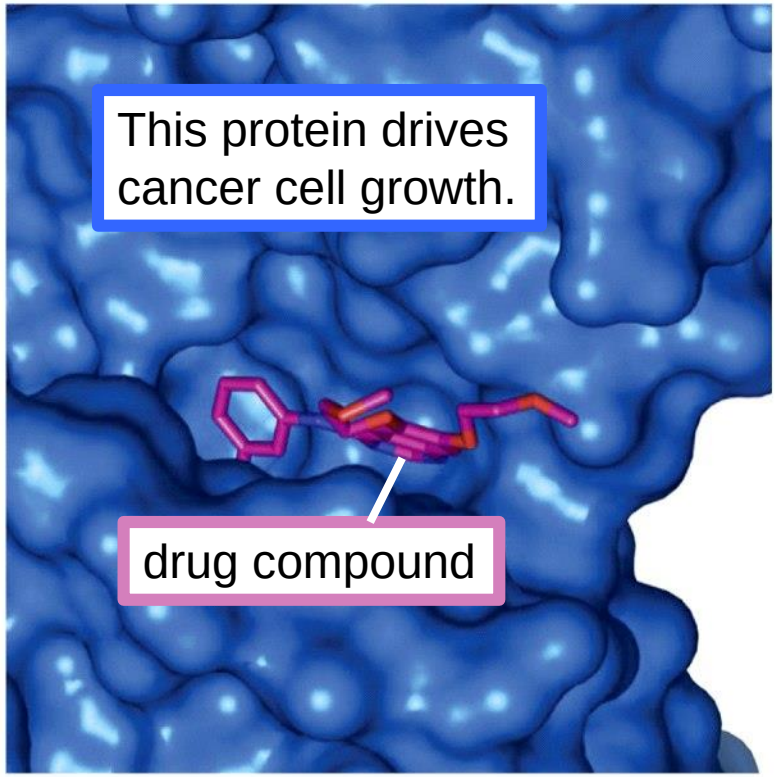
Survival of patients with chronic myelogenous leukemia

Effects of Gleevec/imatinib treatment



But there are problems, as illustrated by this drug compound that shuts down the growth of certain lung and cancer cells.

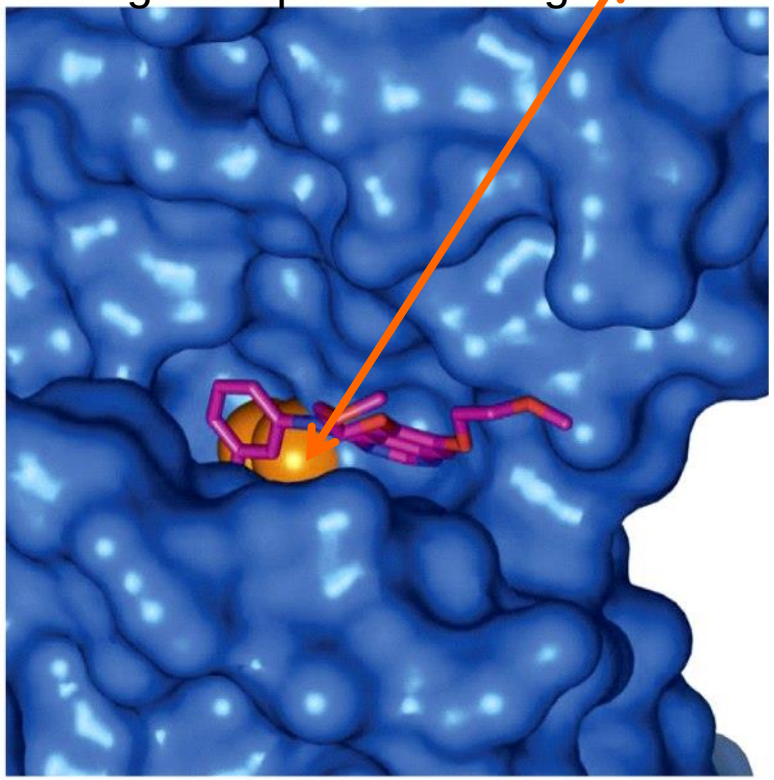
Initial responsiveness – drug works



2 years

Iressa

But later, the "target" changes and no longer responds to drug



Consequence : acquired drug resistance

Figure 16.33c *The Biology of Cancer* (© Garland Science 2007)

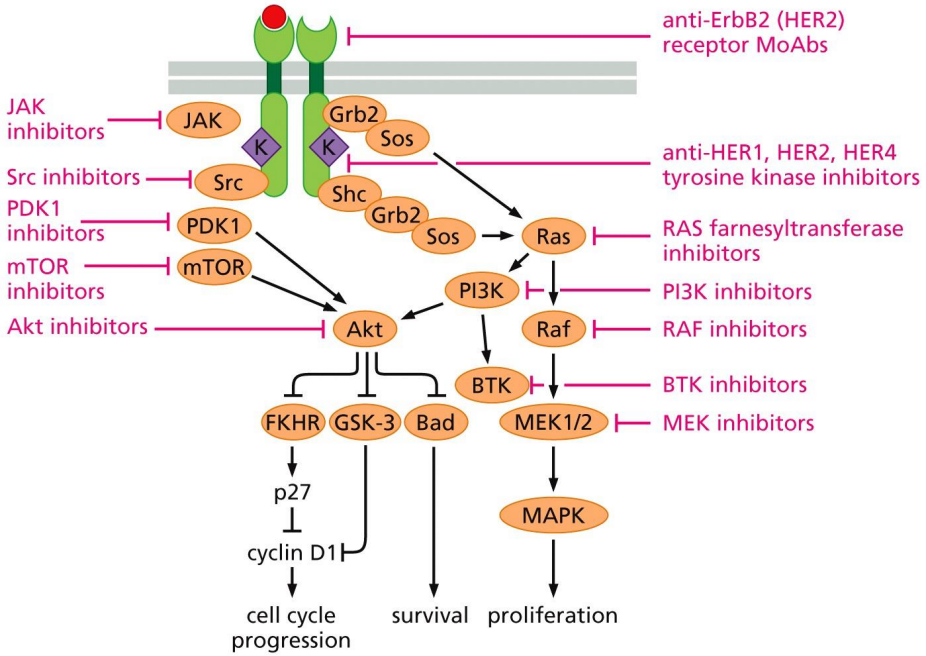


Figure 16.9 The Biology of Cancer (© Garland Science 2014)

Lung cancer regression following treatment with an "anti-receptor" drug followed by <u>eventual relapse</u>

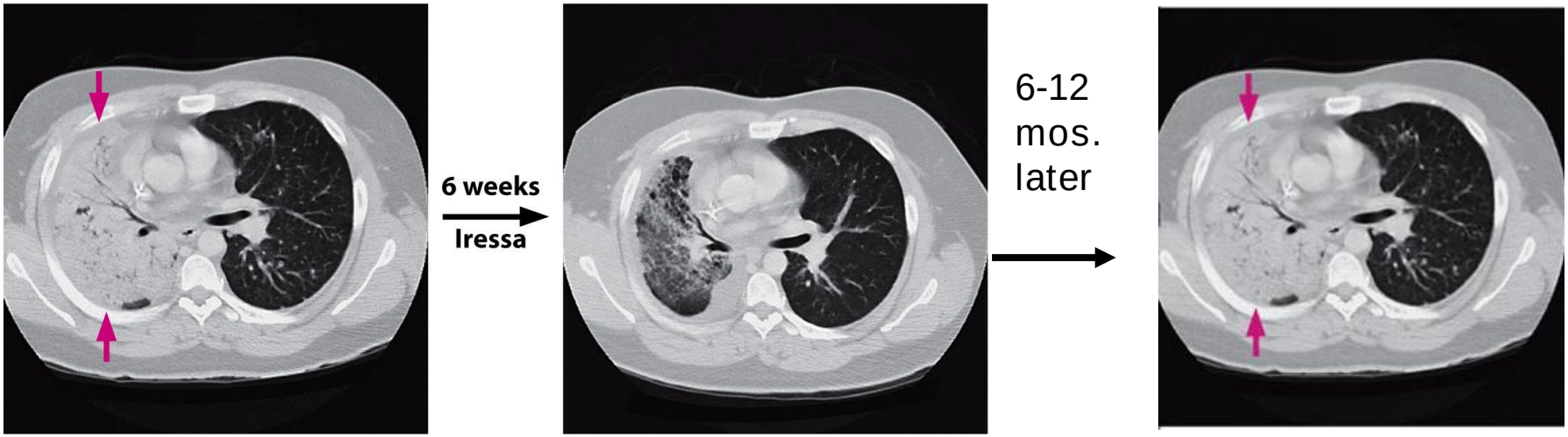


Figure 16.33a *The Biology of Cancer* (© Garland Science 2007)

The successes of Gleevec created a mirage that there would be a wave of similar successes:

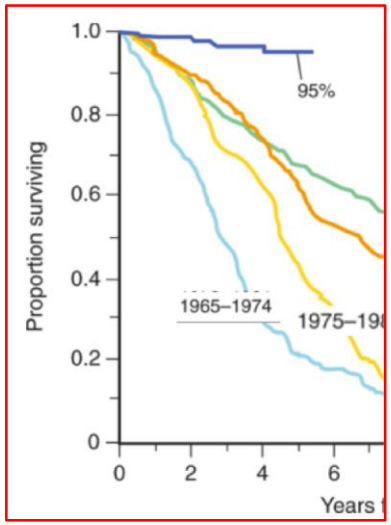
OS = overall survival

Table 1. Estimated drug costs for indications cited in the text*

Drug (brand name)	Regimen	Dose†	Amount needed†,‡	Cost per milligram or cost per tablet	Total cost‡	Increase in OS‡
Cetuximab (Erbitux)	Loading: 400 mg/m²; maintain: 250 mg/m²/wk	Loading: 600 mg; maintain: 375 mg	6975 mg	$11.52/mg	$80352	1.2 mo (1)
Bevacizumab (Avastin)	10 mg/kg every 14 d	600 mg every 14 d	13200 mg	$6.88/mg	$90816	1.5 mo§ (13)
Erlotinib (Tarceva)	150 mg daily	150 mg/d; 1 tablet per day	112 tablets	$140.64 per tablet	$15752	10 d (14)
Sorafenib (Nexavar)	400 mg twice a day	800 mg/d; 4 tablets per day	692 tablets	$49.67 per tablet	$34373	2.7 mo (15)

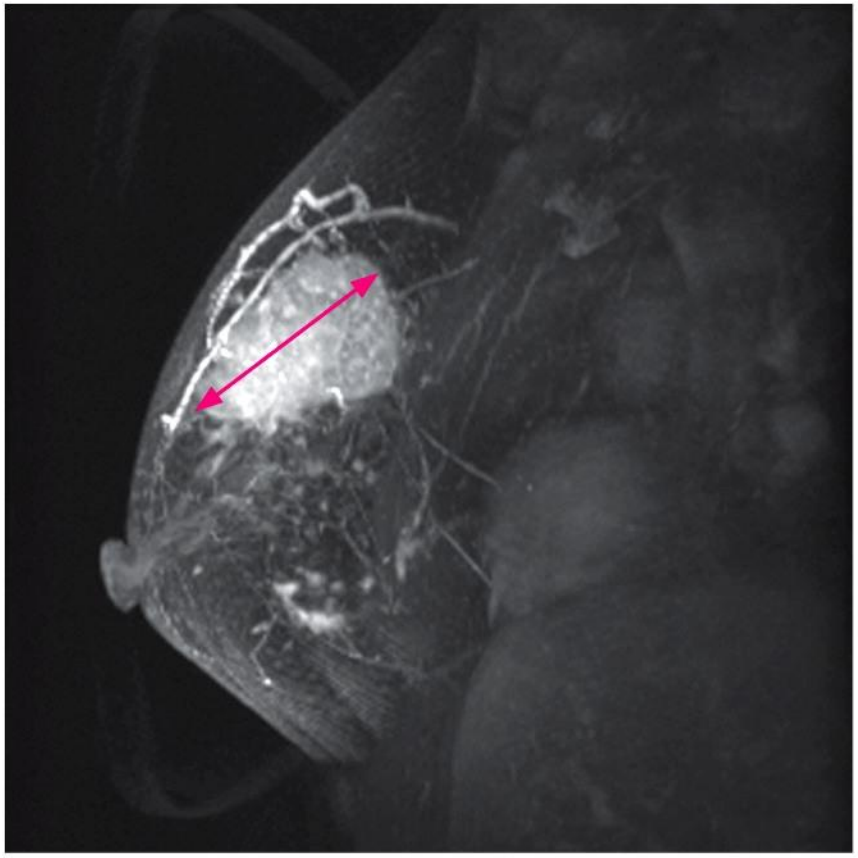
OS = overall survival

Gleevec

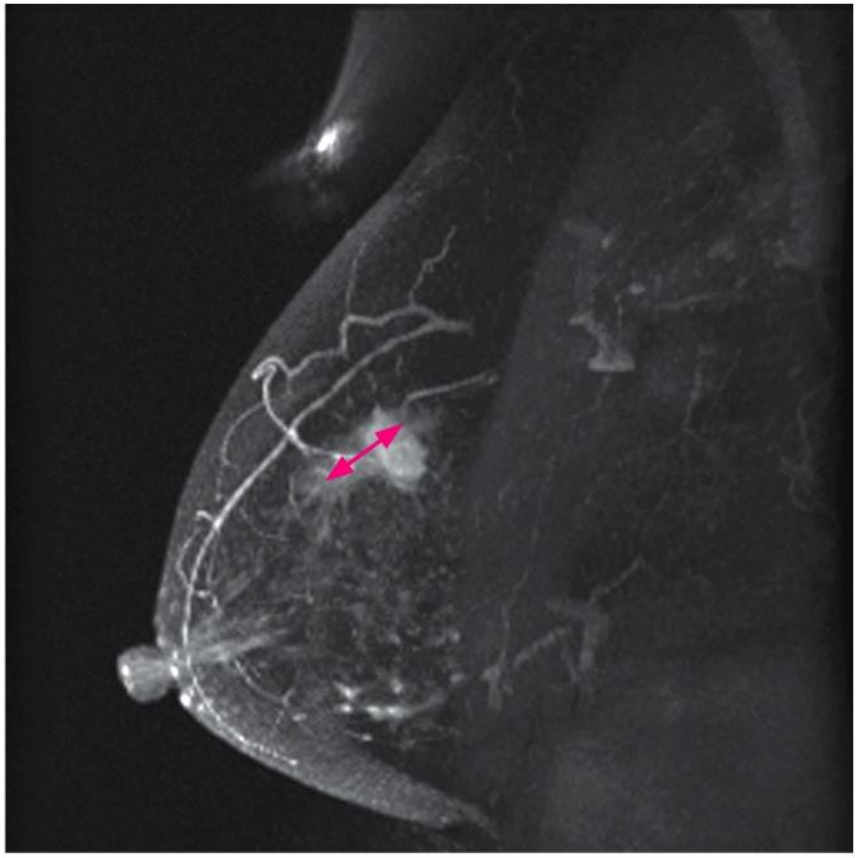


Total cost‡	Increase in OS‡
$80352	1.2 mo (1)
$90816	1.5 mo§ (13)
$15752	10 d (14)
$34373	2.7 mo (15)

Background:
How much cancer is there (incidence)? Really?



pre-chemotherapy
longest dimension = 47 mm



post-chemotherapy
longest dimension = 16 mm

Figure 16.2 The Biology of Cancer (© Garland Science 2014)

Breast Cancer

About 1 in 8 U.S. women (about 12%) will develop invasive breast cancer over the course of her lifetime. In 2017, an estimated **252,710 new cases** of invasive breast cancer are expected to be diagnosed in women in the U.S., along with **63,410 new cases** of non-invasive (in situ) breast cancer.

incidence

For women in the U.S., breast cancer death rates are higher than those for any other cancer, besides lung cancer.

About 40,610 women in the U.S. are expected to die in 2017 from breast cancer

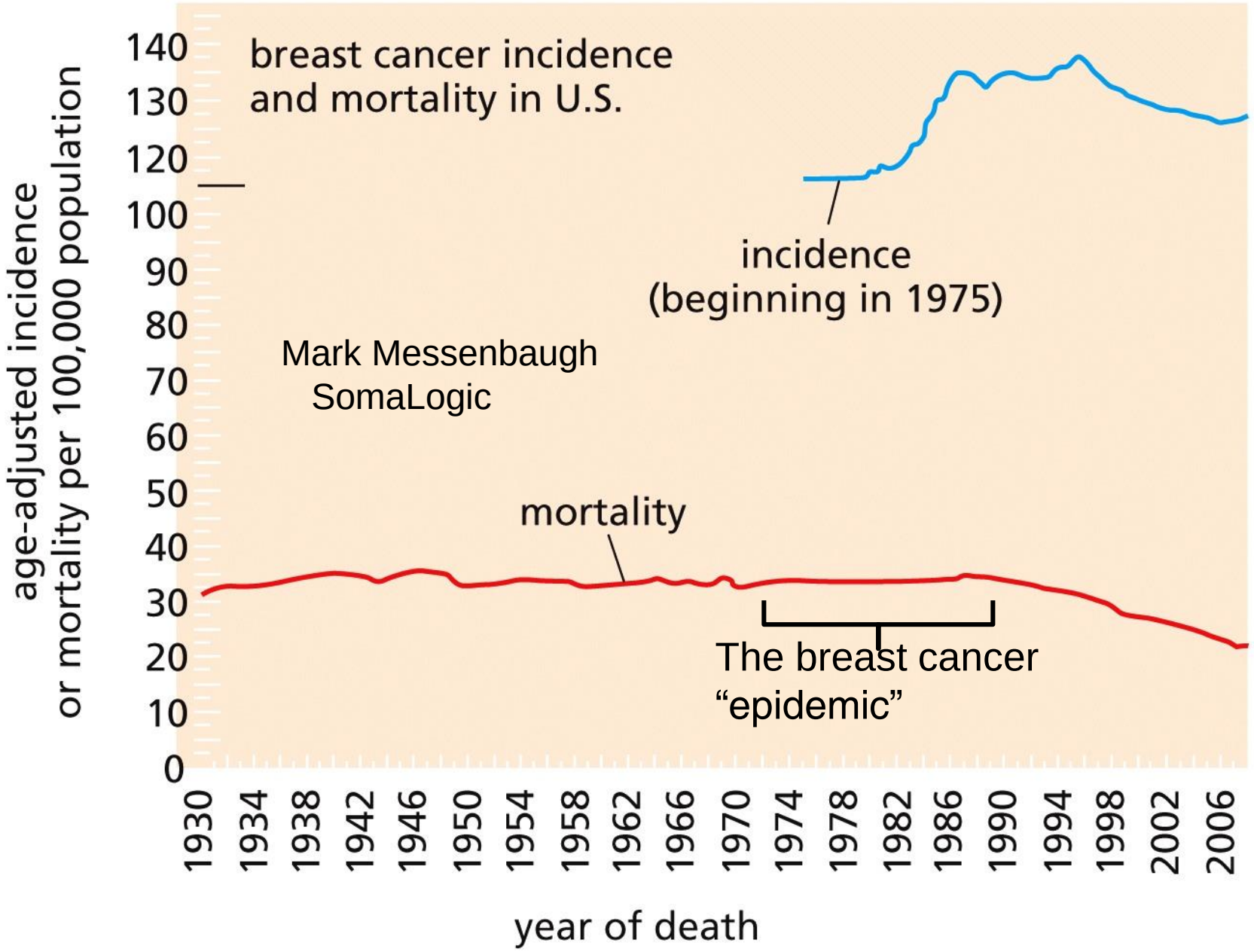


Figure 16.3 The Biology of Cancer (© Garland Science 2014)

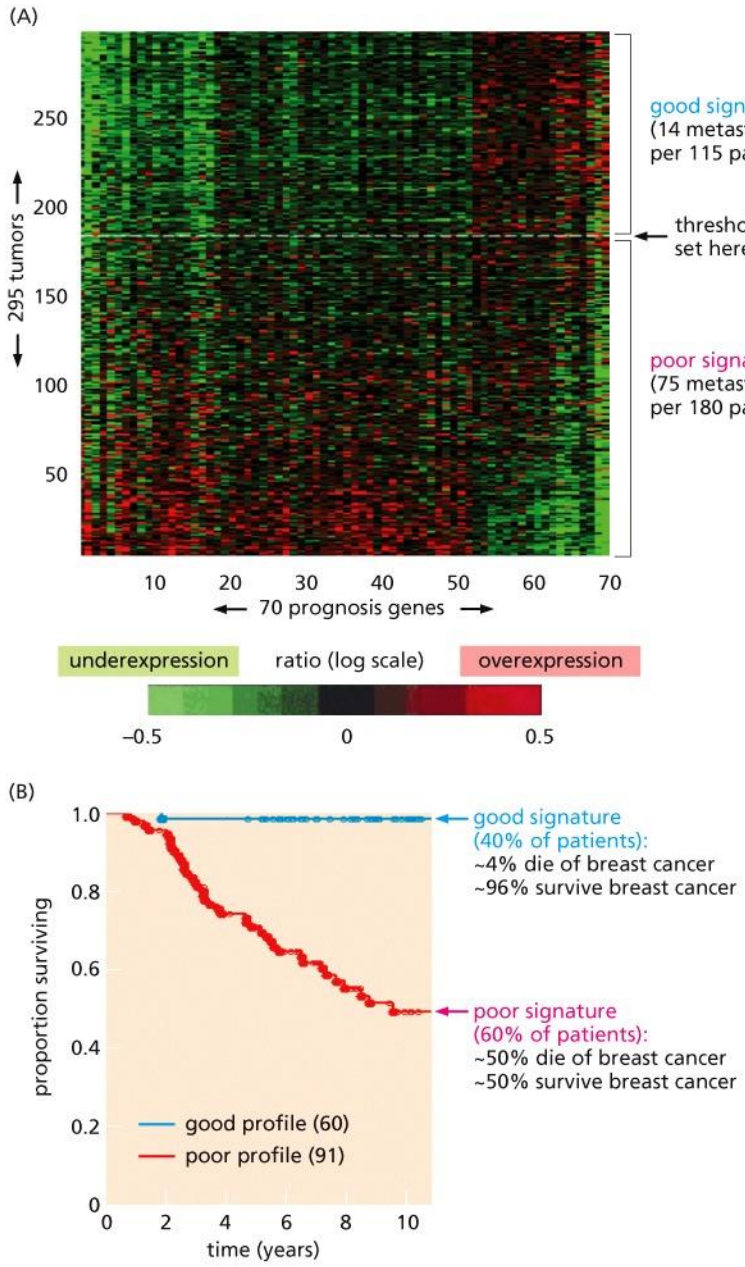
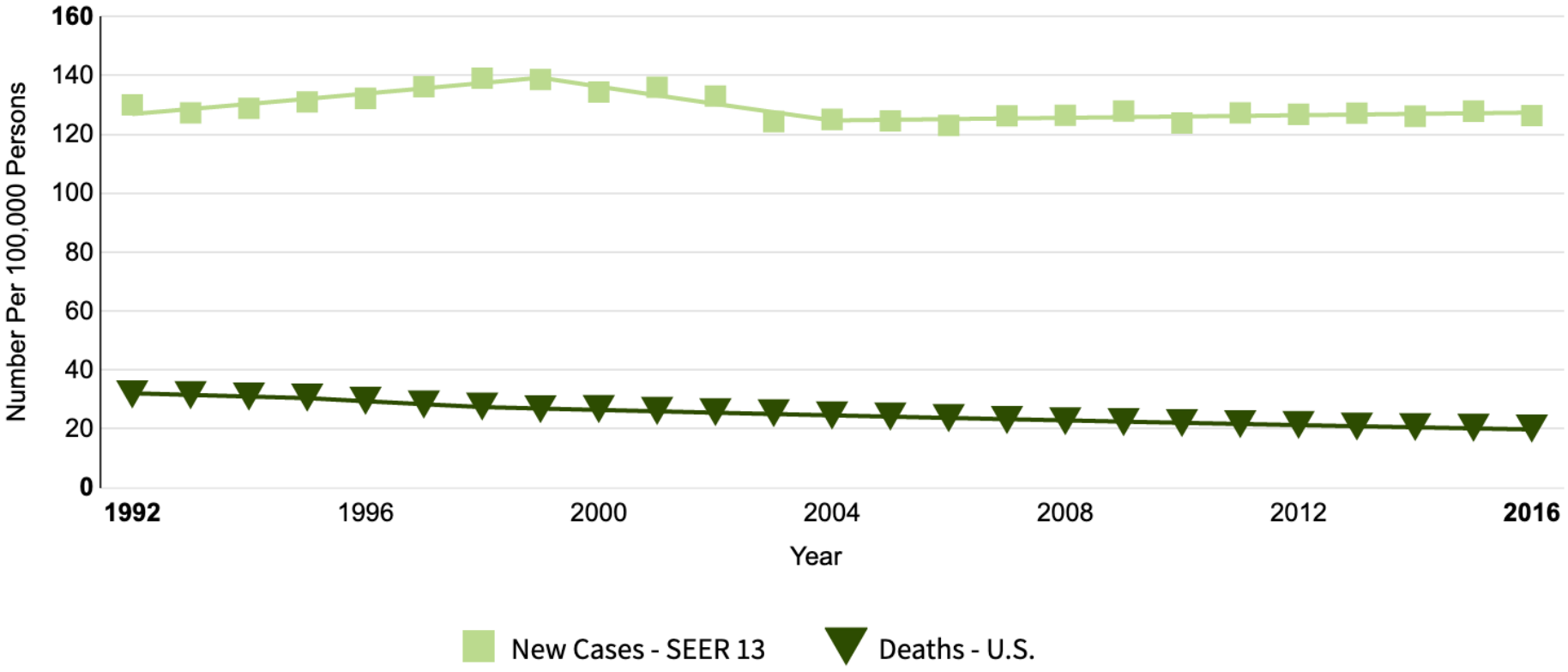


Figure 16.4 The Biology of Cancer (© Garland Science 2014)

The overall breast cancer death rate has decreased consistently since 1989, attributed both to improvements in early detection (through screening as well as increased awareness of symptoms) and treatment for a total decline of 40% through 2017. As a result of this decline, 375,900 breast cancer deaths have been averted in U.S. women through 2017.

Mortality: total decline of 40%



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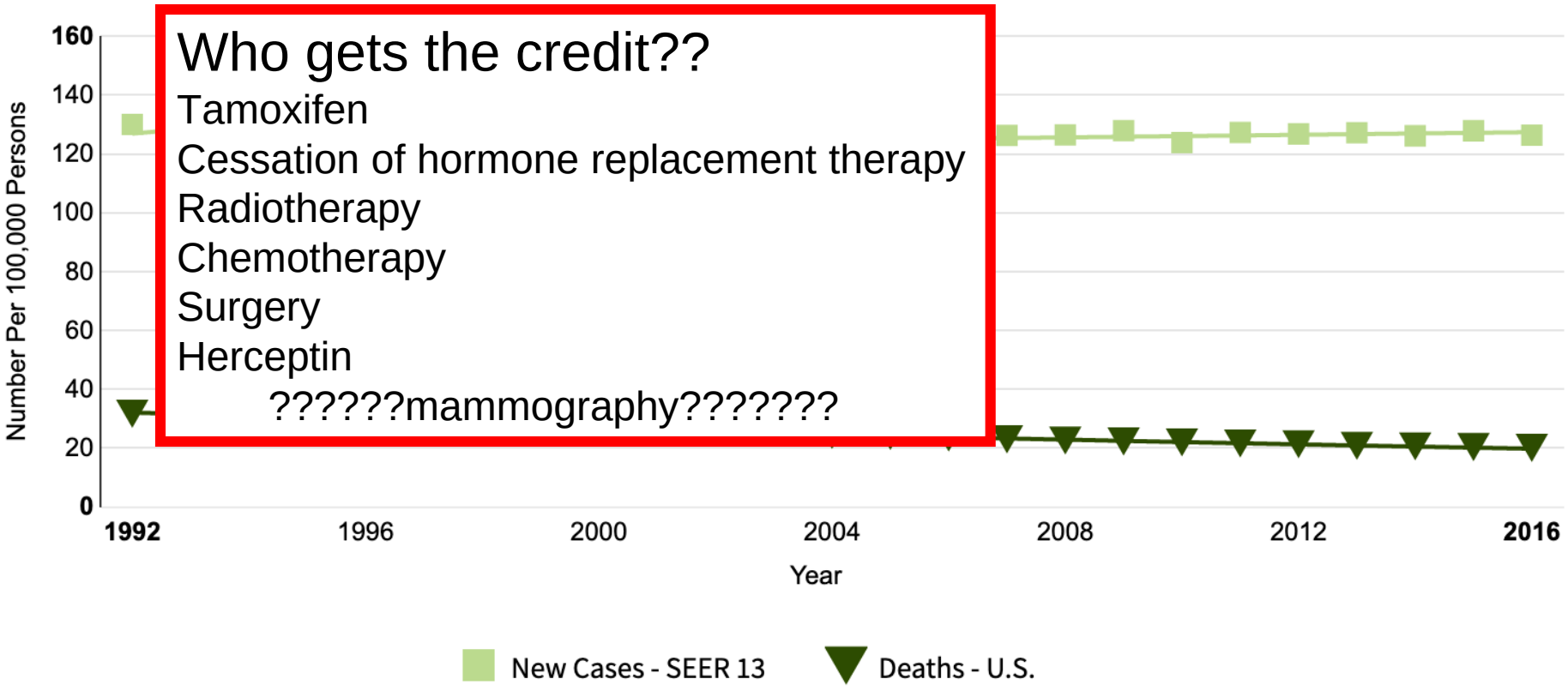


How are we doing?

Well, how are doing in our fight to stave off cancer deaths?

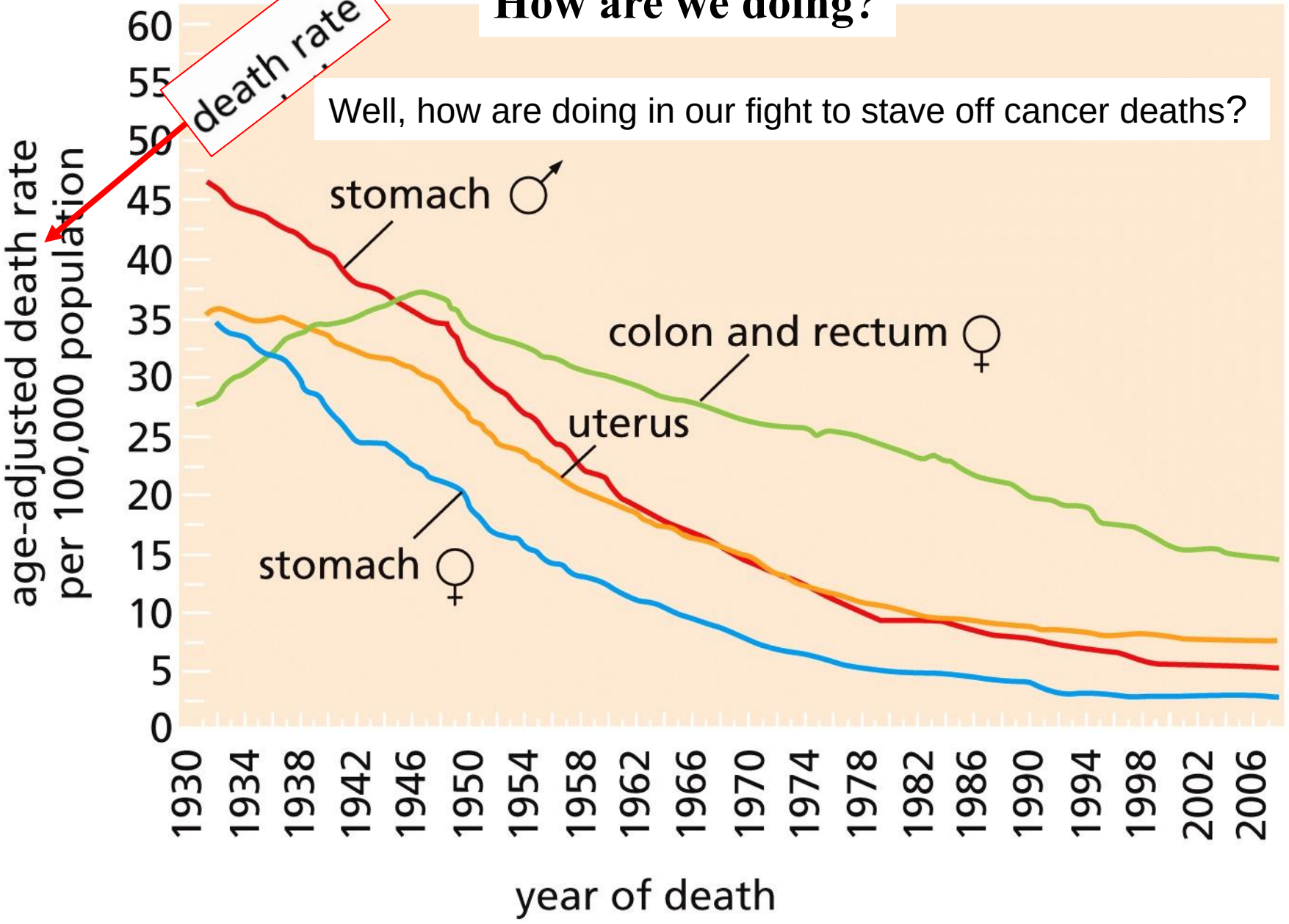


Figure 16.1a The Biology of Cancer (© Garland Science 2014)

Background

Well, how are doing in our fight to stave off cancer deaths?

Who gets the credit?

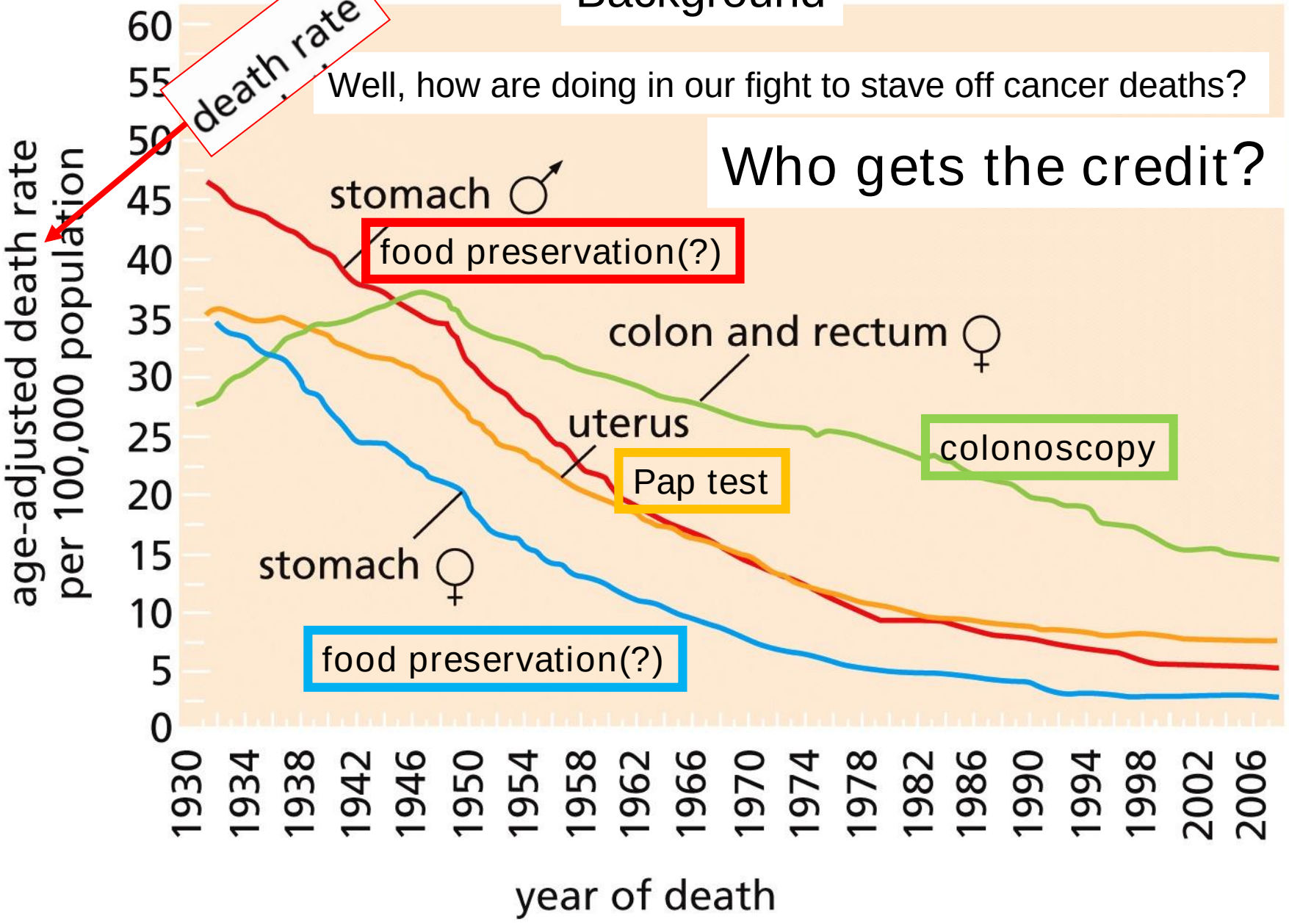


Figure 16.1a The Biology of Cancer (© Garland Science 2014)

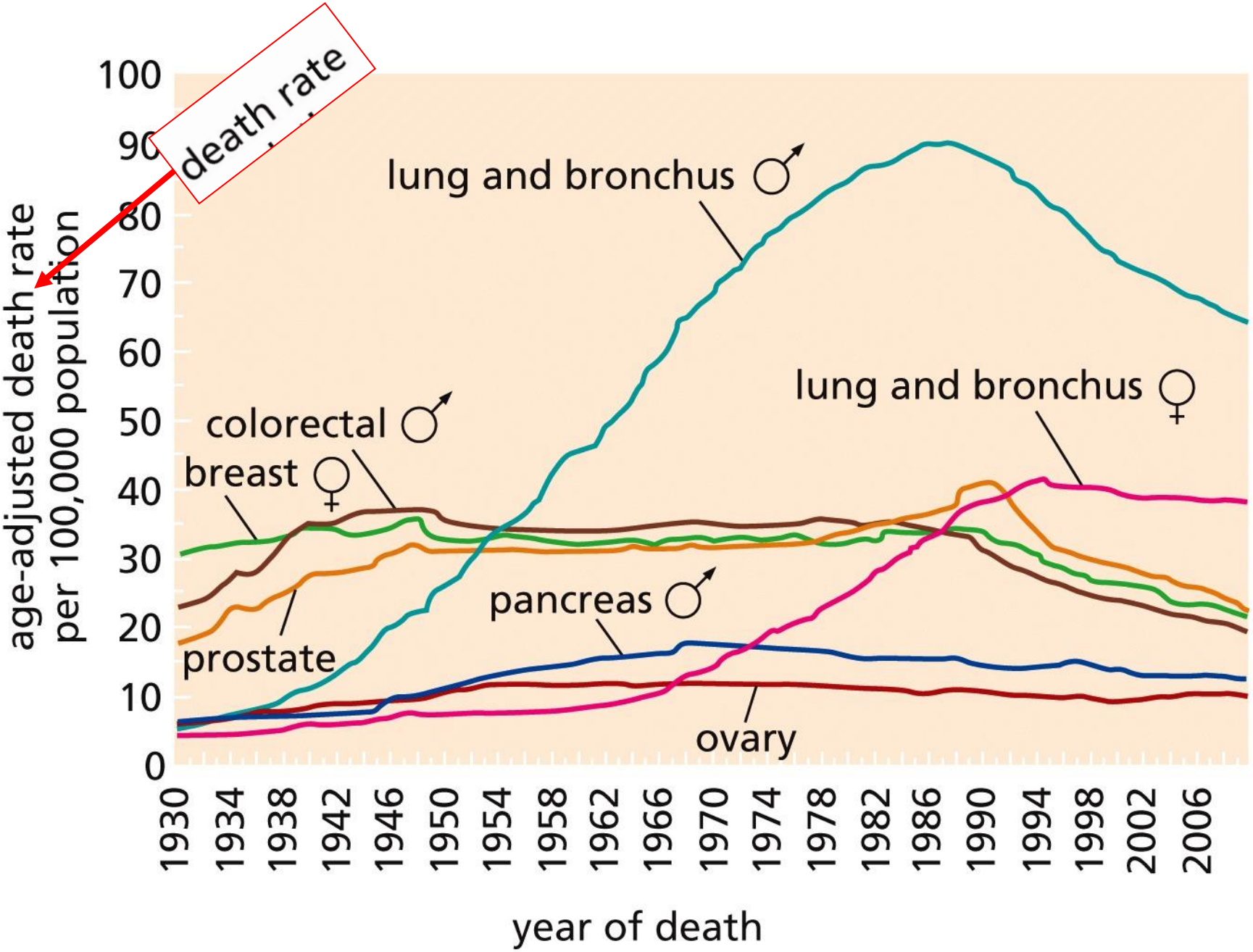


Figure 16.1b The Biology of Cancer (© Garland Science 2014)

Who gets the credit?

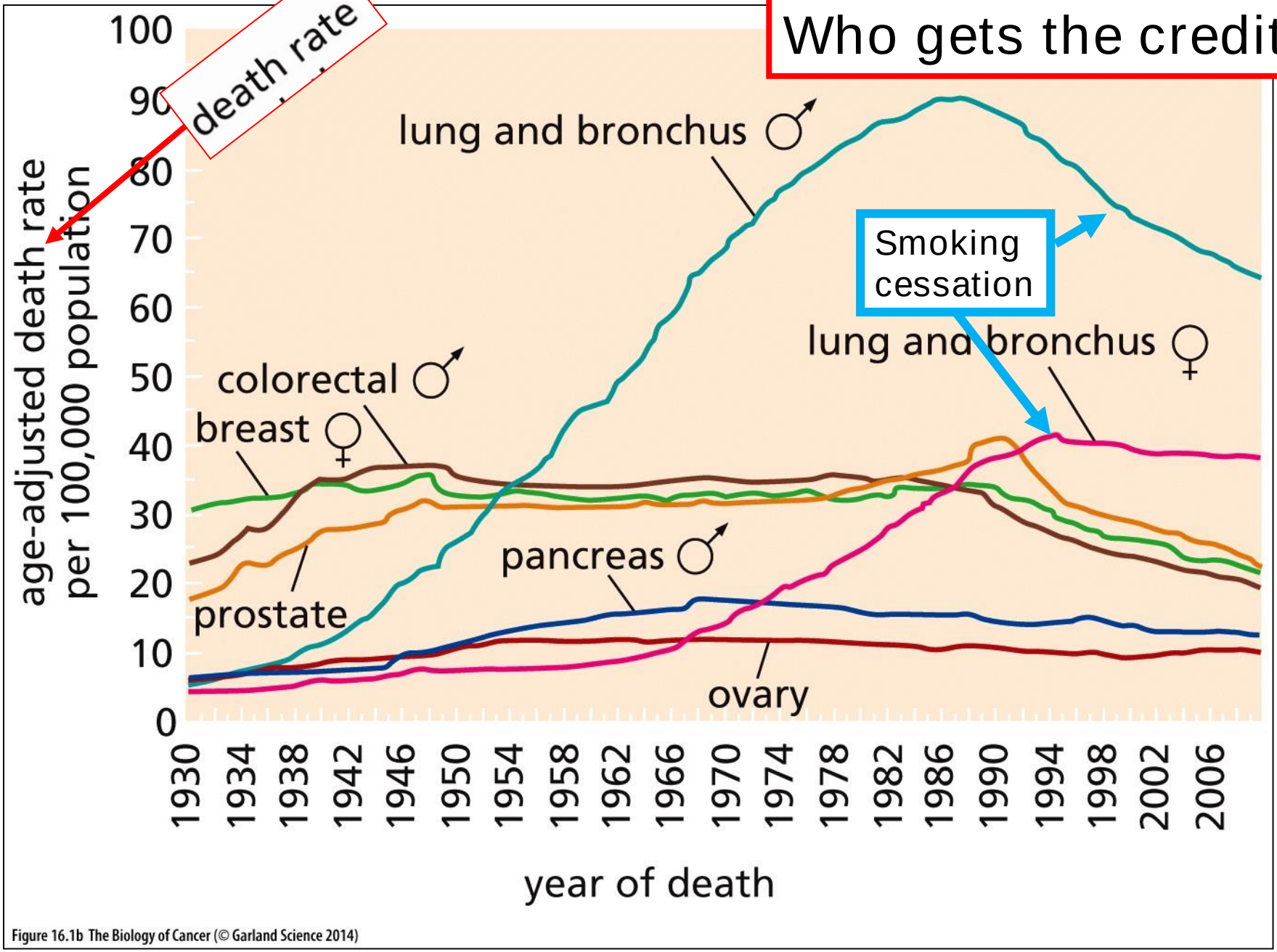
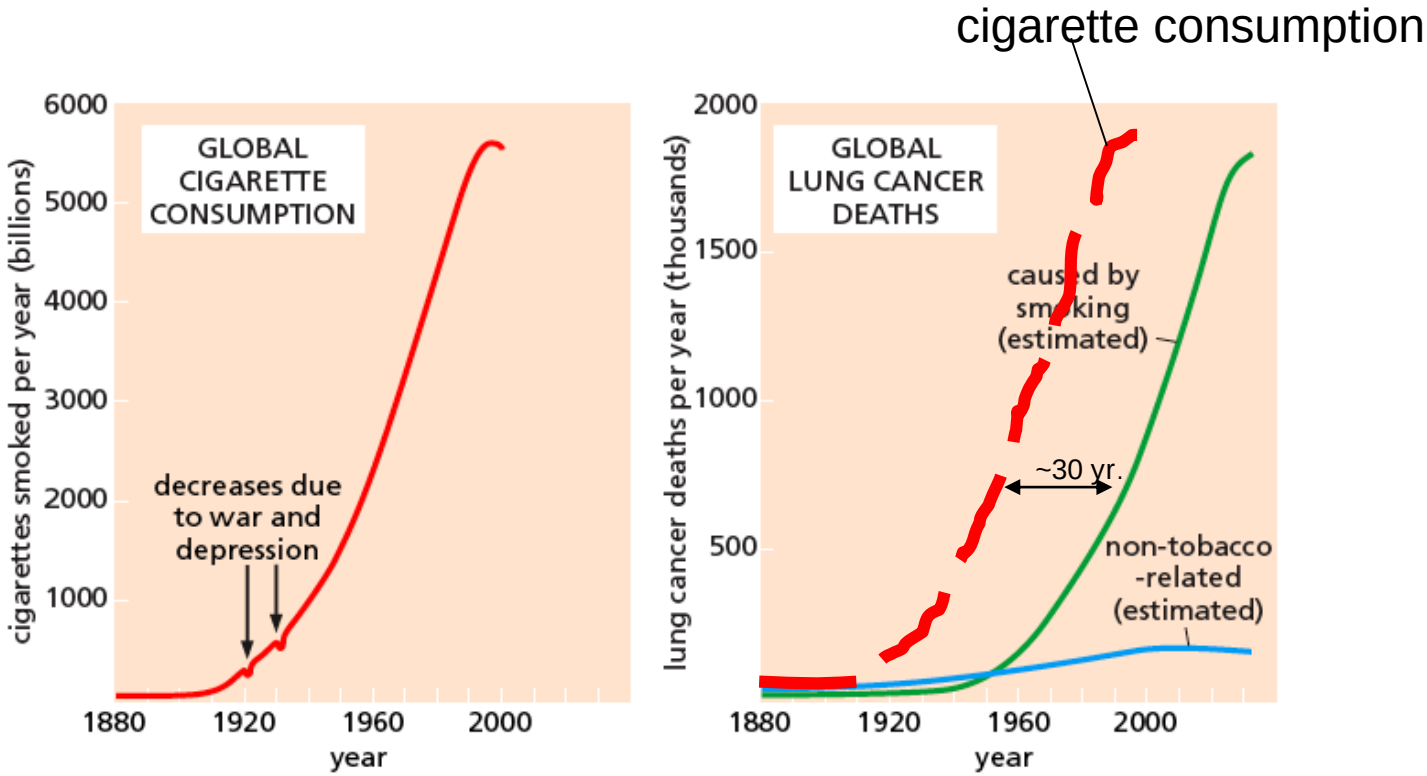


Figure 16.1b The Biology of Cancer (© Garland Science 2014)

How long does it take to develop a cancer?

A ~30 year lag between the cause and the effect



The decades-long incubation of most tumors of dictates that most cancers arise late in life

Only solution: Reduce incidence:

In the US, tobacco use is responsible for nearly 1 in 5 deaths; this equaled an estimated 443,000 premature deaths each year between 2000 and 2004.[6,7] In addition, an estimated 8.6 million people suffer from chronic conditions related to smoking, such as chronic bronchitis, emphysema, and cardiovascular diseases.[8]

Only solution: Reduce incidence:

Stunning differences in lung cancer mortality

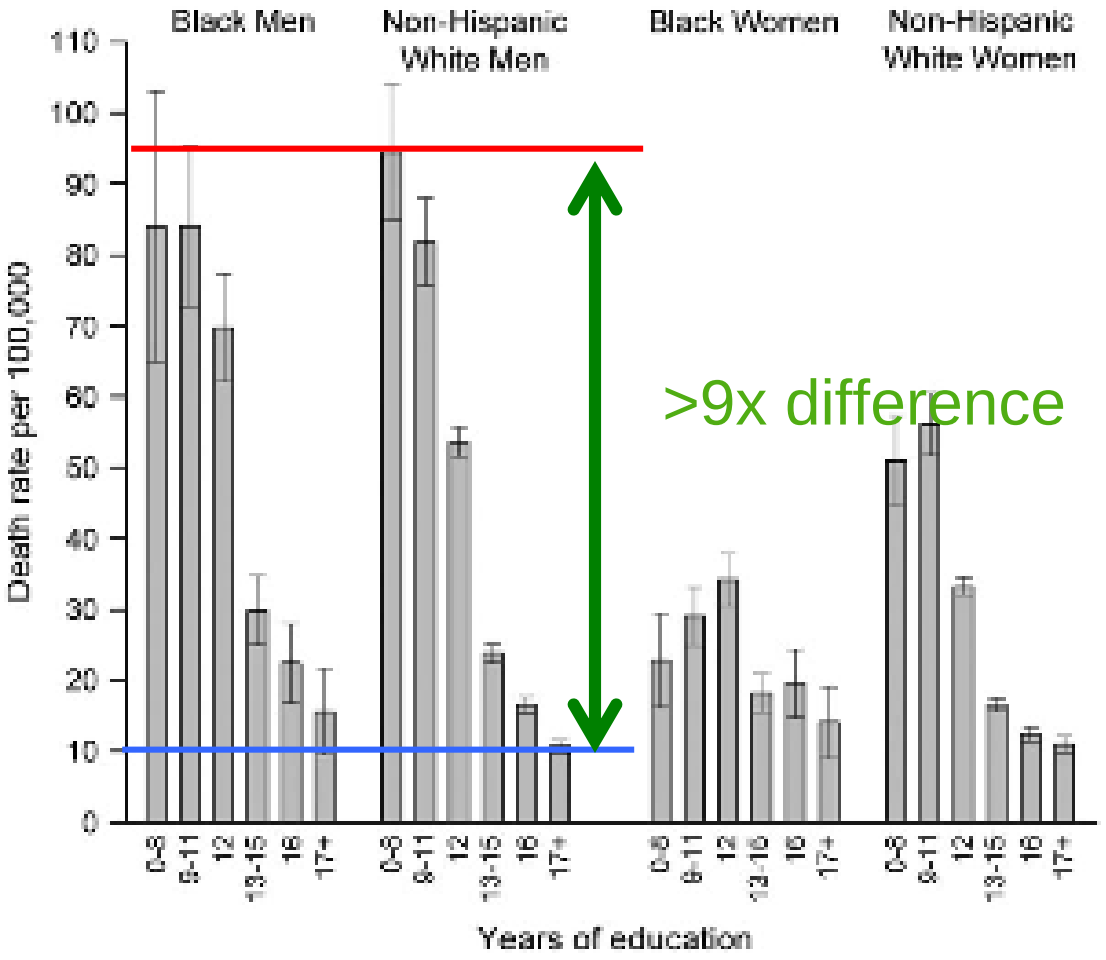


Fig. 2. Lung cancer mortality rates, by education level, sex, and race, for persons aged 25–64 years in the United States, 2001. **Error bars** correspond to 95% confidence intervals.

KEY STATE-SPECIFIC TOBACCO-RELATED DATA & RANKINGS

State	Adult Smoking Rate	Adult Smoking Rank (1=low)	Pregnant Smoking Rate[c]	Youth Smoking Rate	New Youth Smokers Per Year	Annual Adult Smoking Deaths (approx.)	Kids Now Alive Who Will Become Smokers	Kids Now Alive Who Will Die From Smoking	Smoking Caused Health Costs (millions)	Cigarette Tax (per pack)	Cigarette Tax Rank (1 = high)	FY 2019 Funding for State TC Programs (millions)	Tobacco Prevention Spending % of CDC Target
All States	**14.0%**	///	**7.2%**	**5.8%**	**98,000**	**480,000**	**17+ mill.**	**5.6 mill.**	**$170 bill.**	**$1.81**	///	**$655.0**	**19.8%**
Alabama	19.2%	41st	10.1%	**14.0%**	1,800	8,600	336,200	108,000	$1.88 bill.	$0.675	41st	$2.1	3.7%
Alaska	19.1%	39th	11.5%	**10.9%**	200	600	43,600	14,000	$438	**$2.00**	**17th**	$9.1	89.4%
Arizona	14.0%	12th	4.8%	**7.1%**	2,000	8,300	359,800	115,000	$2.38 bill.	**$2.00**	**17th**	$17.3	26.9%
Kansas	17.3%	31st	10.2%	**7.2%**	1,000	4,400	191,200	61,000	$1.12 bill.	$1.29	33rd	$0.8	3.0%
Kentucky	23.4%	50th	18.4%	**14.3%**	2,000	8,900	371,700	119,000	$1.92 bill.	$1.10	36th	$3.8	6.7%
Louisiana	20.5%	44th	6.8%	**12.3%**	1,700	7,200	307,400	98,000	$1.89 bill.	$1.08	37th	$5.4	9.0%
Texas	14.4%	13th	3.3%	11.3%	8,700	28,000	1,557,800	498,000	$8.85 bill.	**$1.41**	**29th**	$4.2	1.6%
Utah	9.0%	1st	3.0%	**3.8%**	600	1,300	120,800	39,000	$542	$1.70	25th	$7.0	36.3%
Vermont	13.7%	10th	15.5%	**9.3%**	100	1,000	31,500	10,000	$348	$3.08	7th	$3.8	45.2%

Reducing incidence: Other avoidable causes

Cancer mortality in obese vs. lean people:
Highest quartile of body mass index vs. lowest quartile

Lowest quartile: BMI of 24.9 and below; highest quartile: BMI no. is given

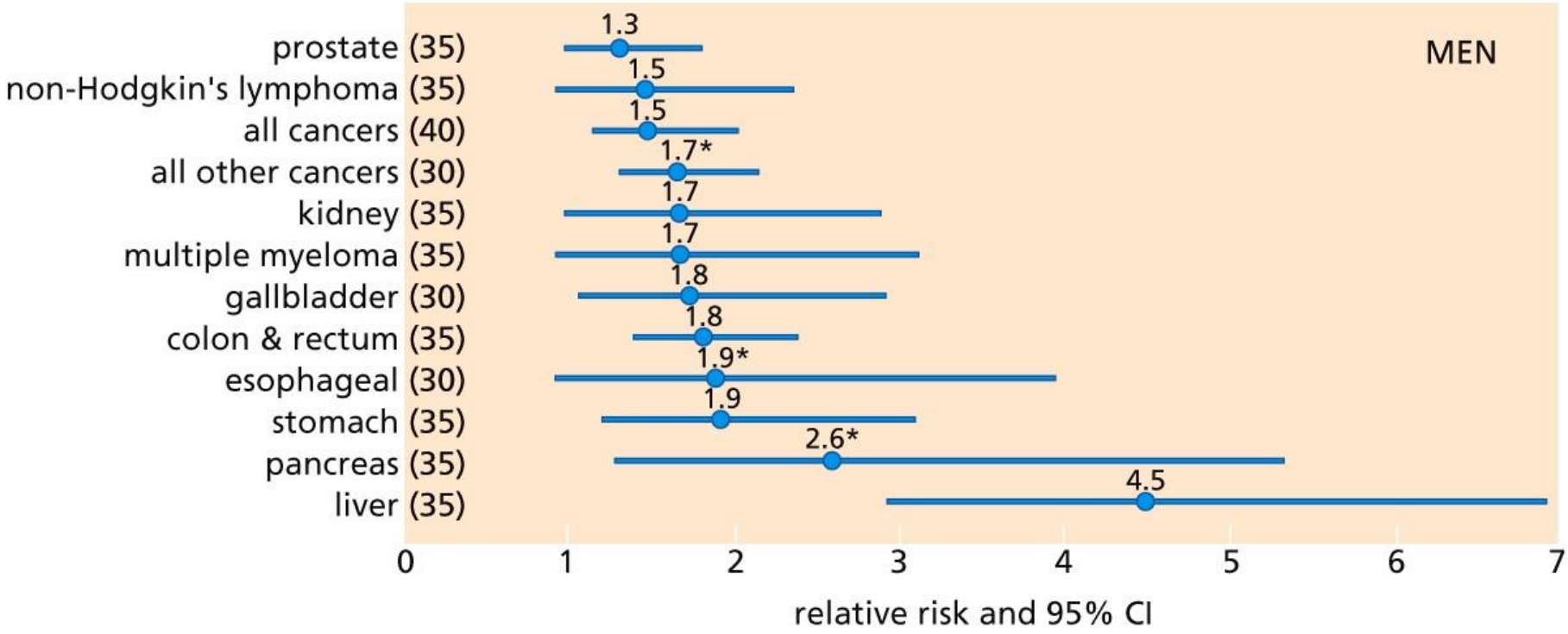
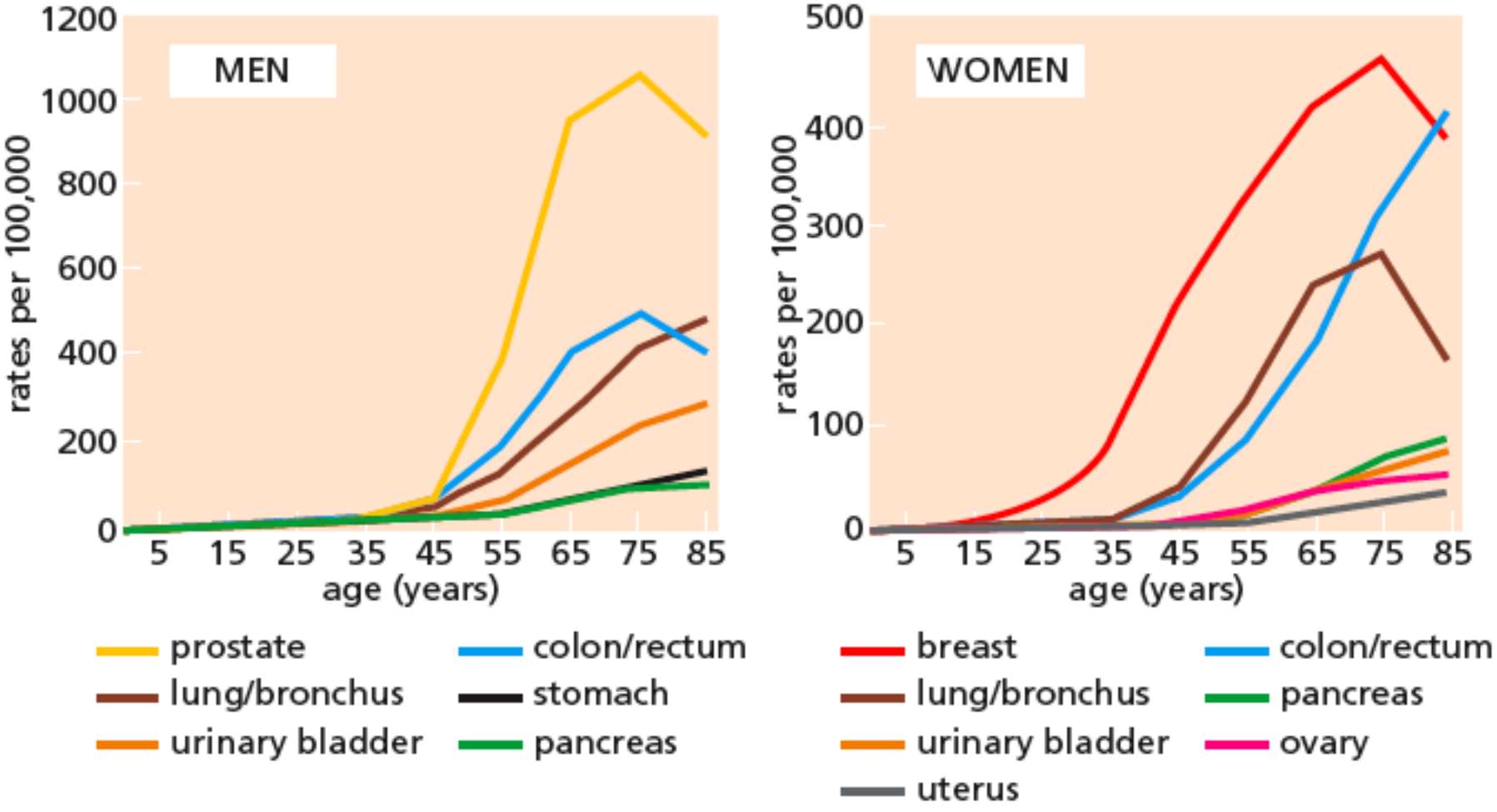


Figure 9.41a The Biology of Cancer (© Garland Science 2014)

More generally: Cancer is a disease of aging

The risk of developing cancer is different at different ages



How big is the actual problem?

Cancer annual death rates go up steeply with increasing age.

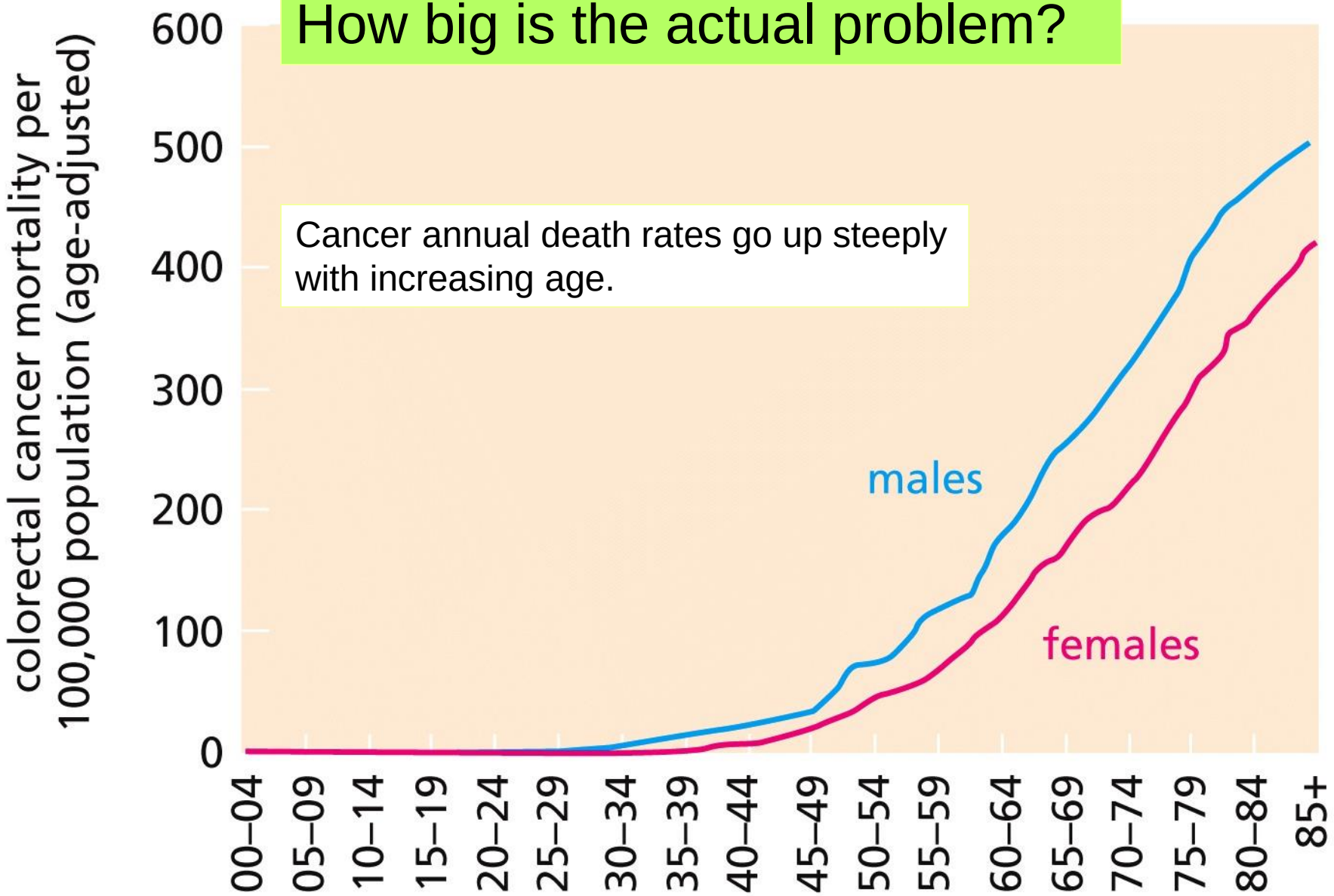
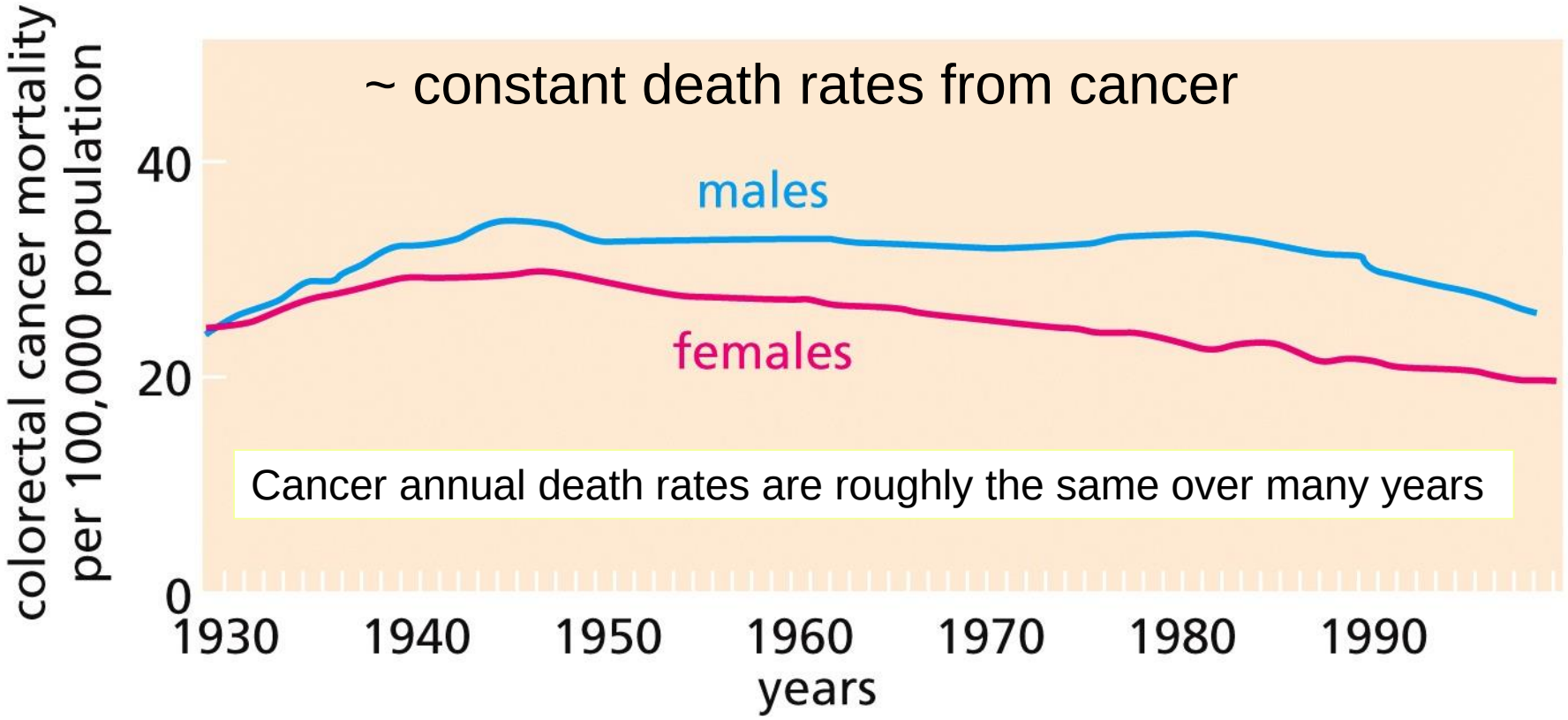


Figure 16.43c The Biology of Cancer (© Garland Science 2014)

How big is the actual problem?



Cancer annual death rates are roughly the same over many years

Figure 16.43b The Biology of Cancer (© Garland Science 2014)

How big is the actual problem?

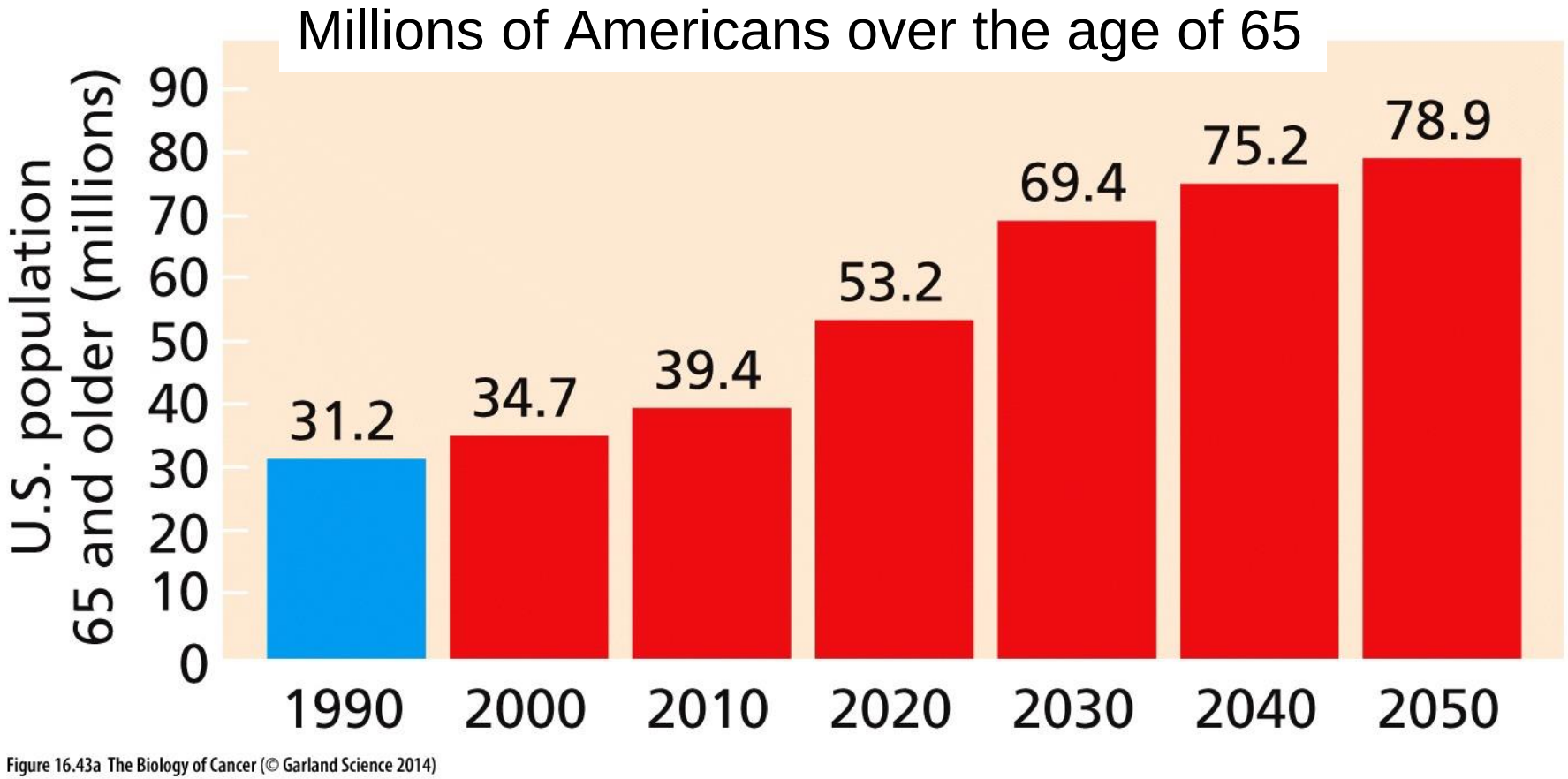


Figure 16.43a The Biology of Cancer (© Garland Science 2014)

How big is the actual problem?

Actual numbers. of deaths each year in the U.S.

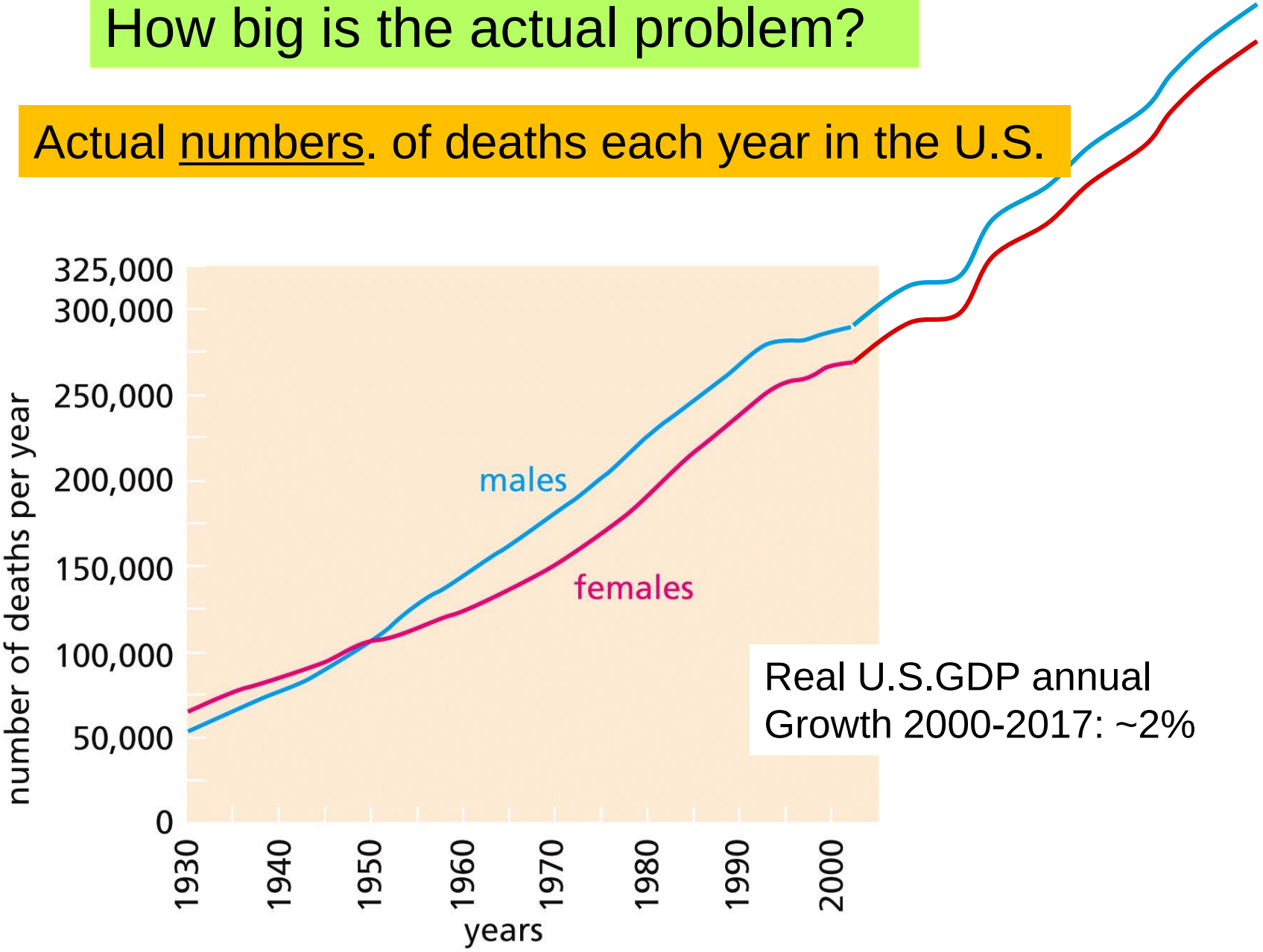


Figure 16.43d The Biology of Cancer (© Garland Science 2014)

Real U.S.GDP annual Growth 2000-2017: ~2%

Is there hope on the horizon for new therapies?

A major success story: **Gleevec** & chronic myelogenous leukemia (CML)

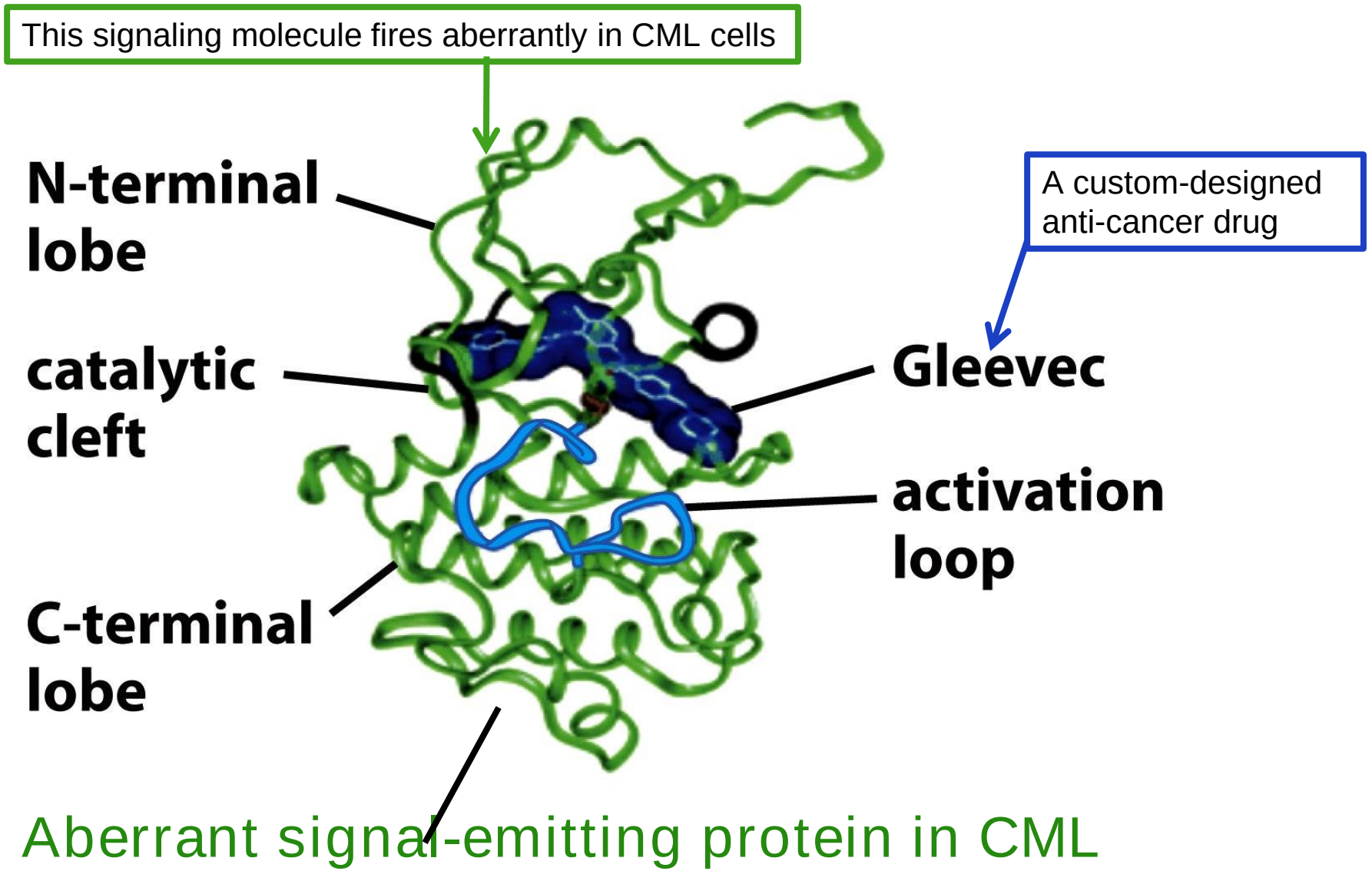
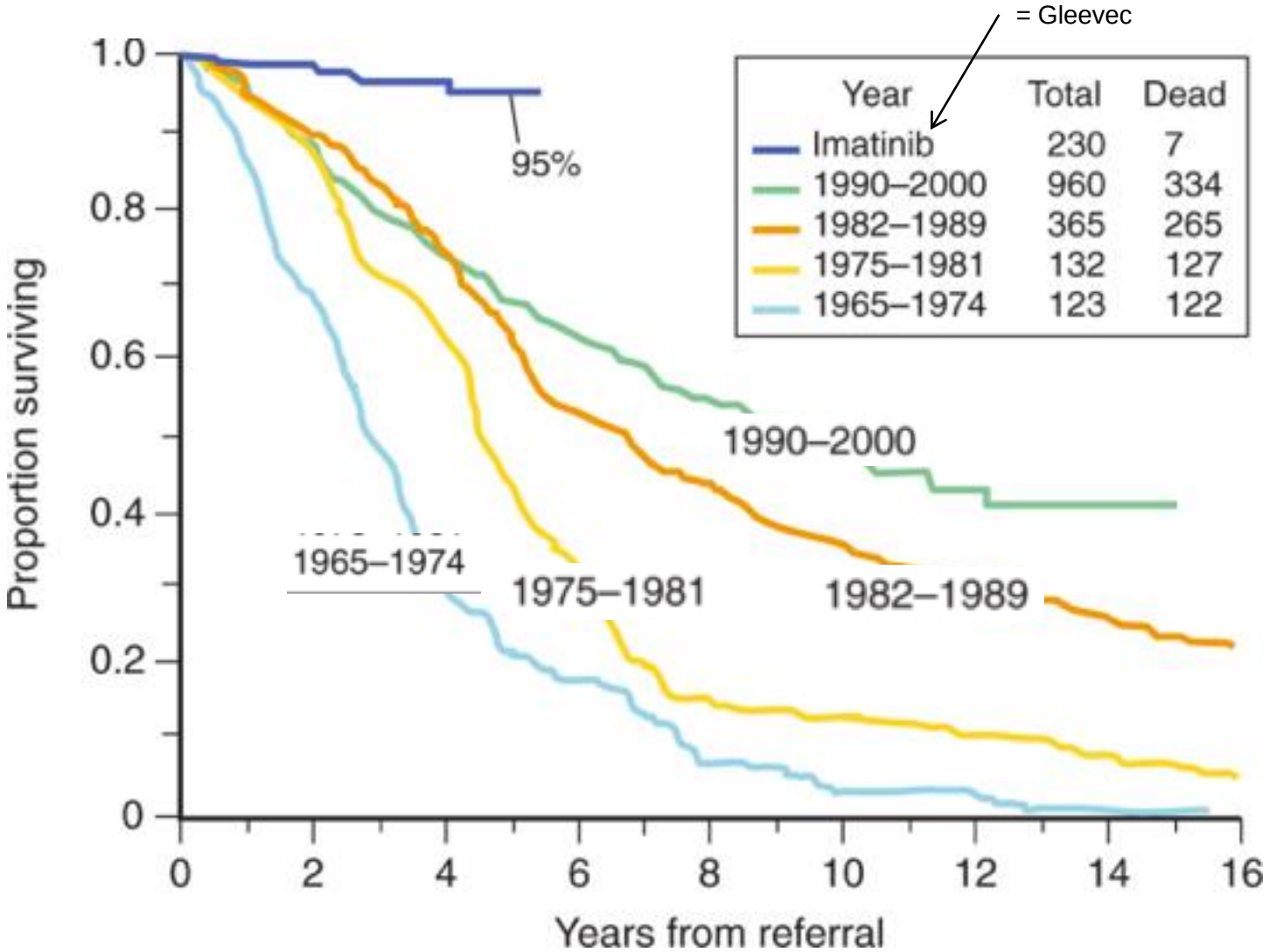


Figure 16.10b *The Biology of Cancer* (© Garland Science 2007)

A major success story:

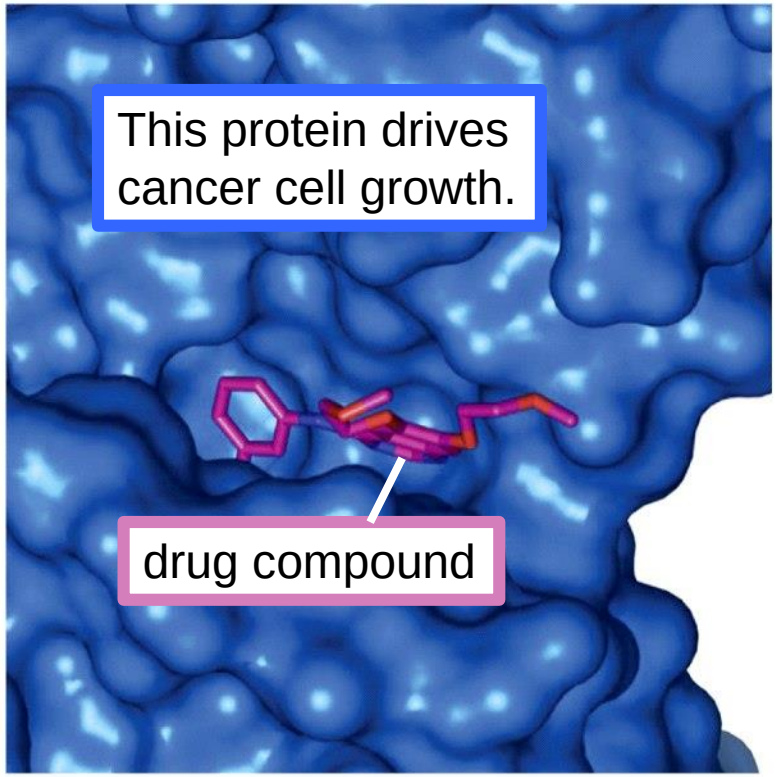
Survival of patients with chronic myelogenous leukemia

Effects of Gleevec/imatinib treatment



But there are problems, as illustrated by this drug compound that shuts down the growth of certain lung and cancer cells.

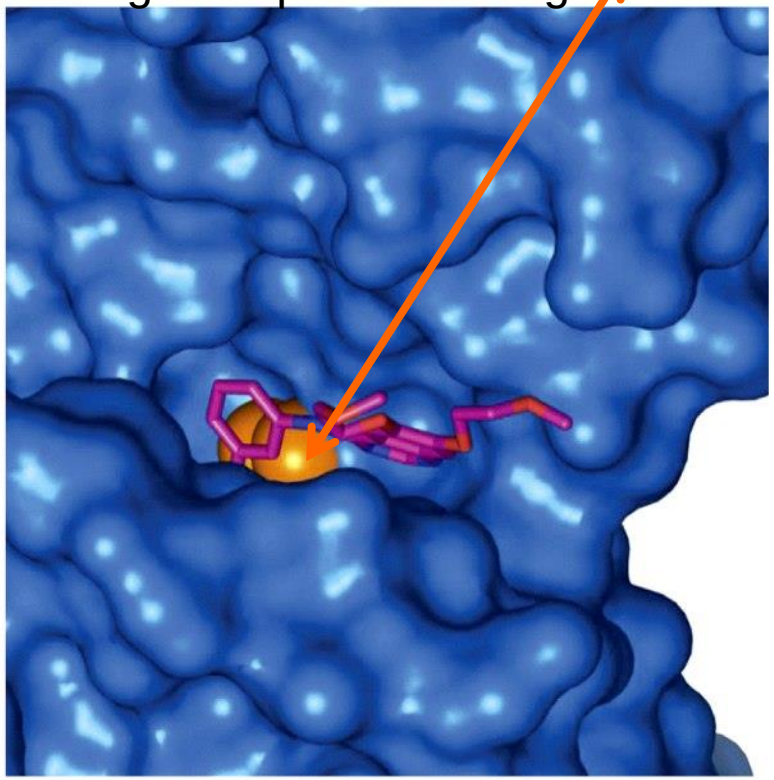
Initial responsiveness – drug works



2 years

Iressa

But later, the "target" changes and no longer responds to drug



Consequence : acquired drug resistance

Figure 16.33c *The Biology of Cancer* (© Garland Science 2007)

- About 5,980 new cases will be diagnosed with CML (3,130 in men and 2,850 in women).
- About 810 people will die of CML (550 men and 260 women).

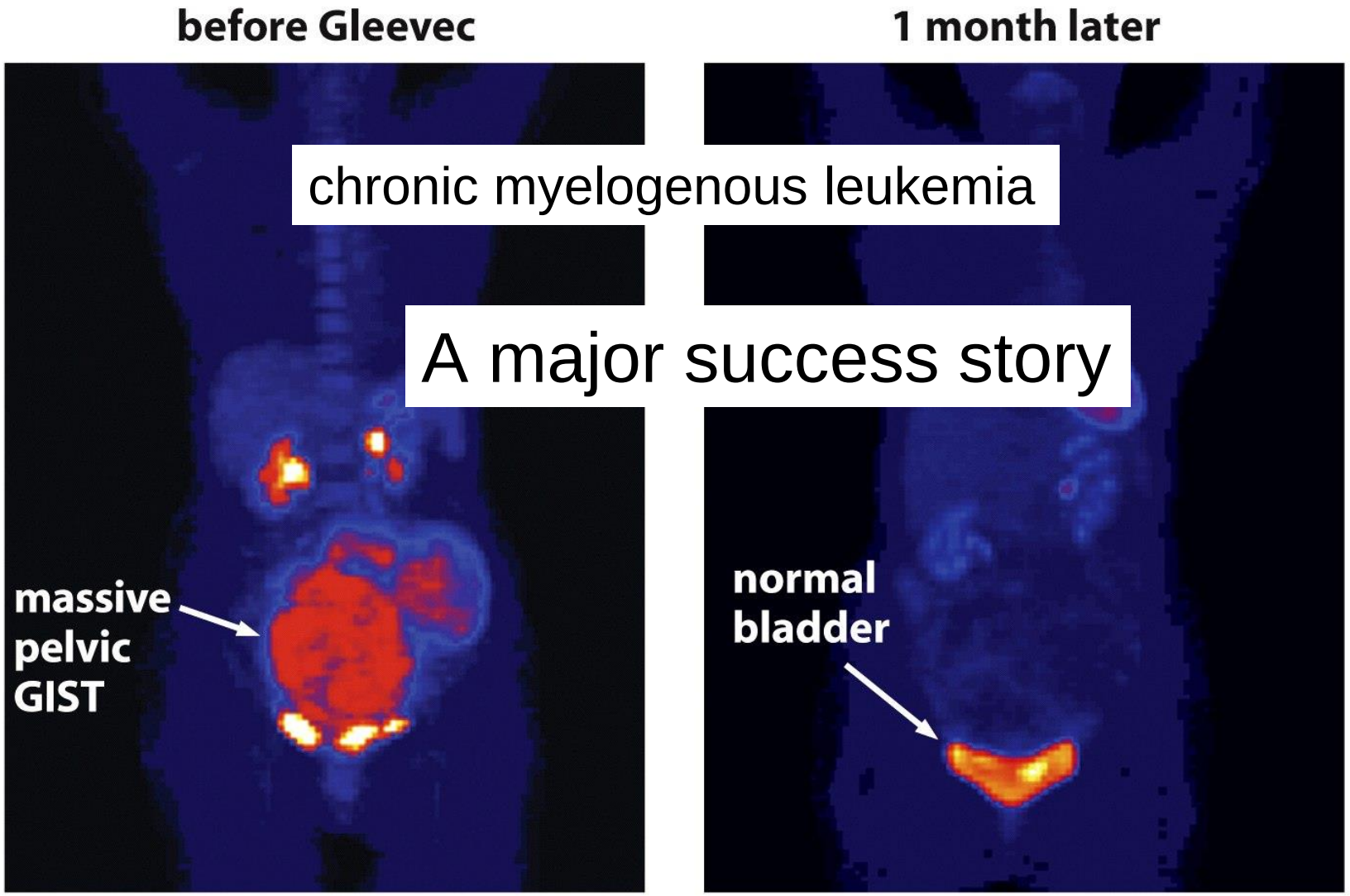


Figure 16.29 *The Biology of Cancer* (© Garland Science 2007)

The successes of Gleevec created a mirage that there would be a wave of similar successes:

OS = overall survival

Table 1. Estimated drug costs for indications cited in the text*

Drug (brand name)	Regimen	Dose†	Amount needed†,‡	Cost per milligram or cost per tablet	Total cost‡	Increase in OS‡
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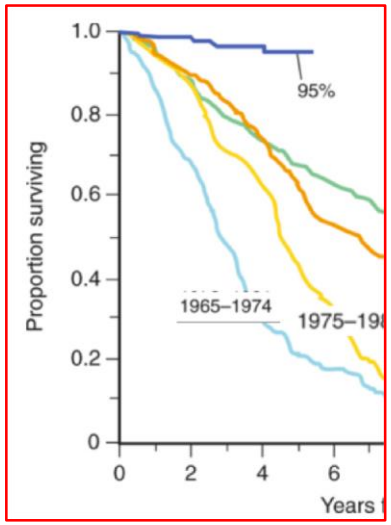
OS = overall survival

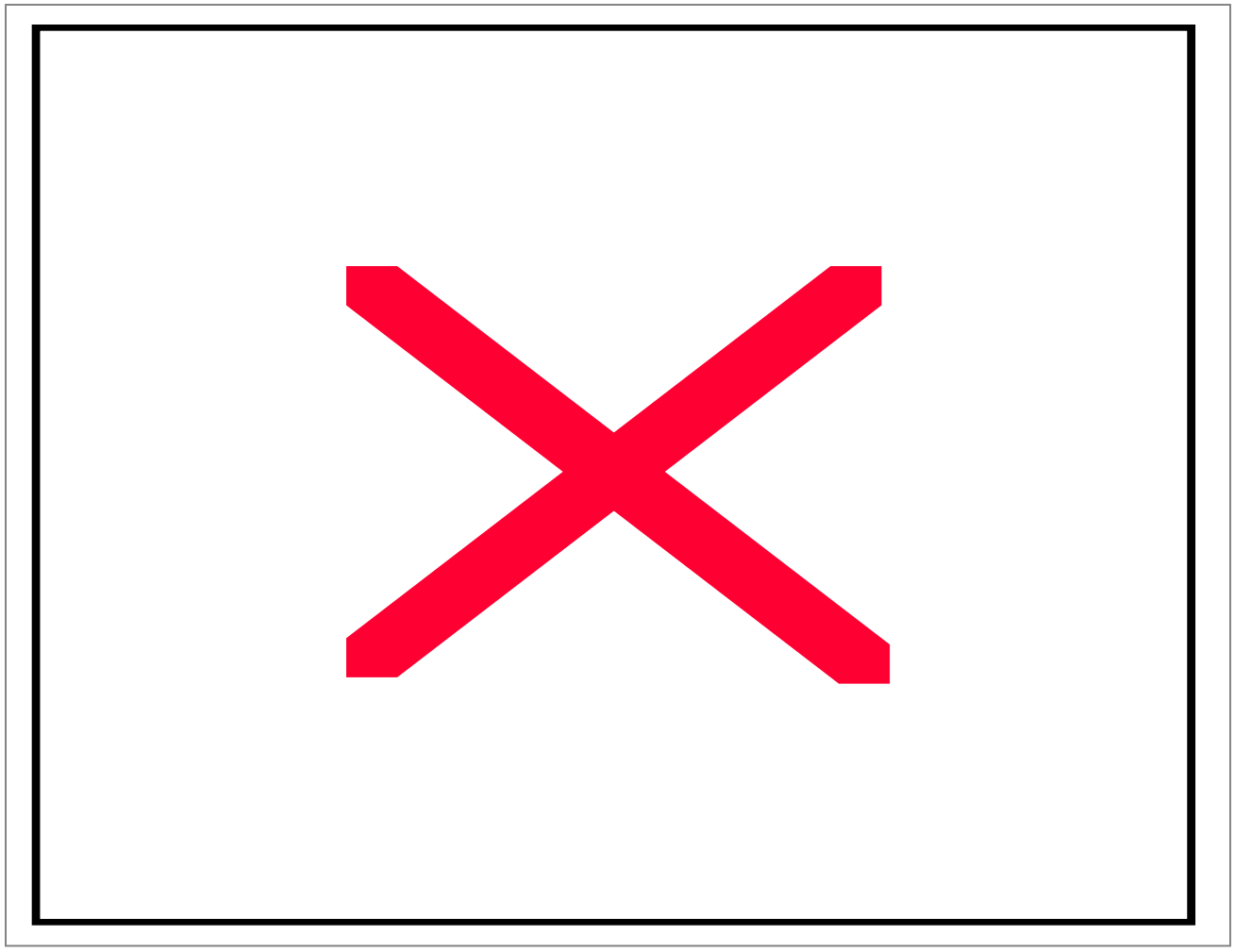
Gleevec



Total cost‡	Increase in OS‡
$80352	1.2 mo (1)
$90816	1.5 mo§ (13)
$15752	10 d (14)
$34373	2.7 mo (15)

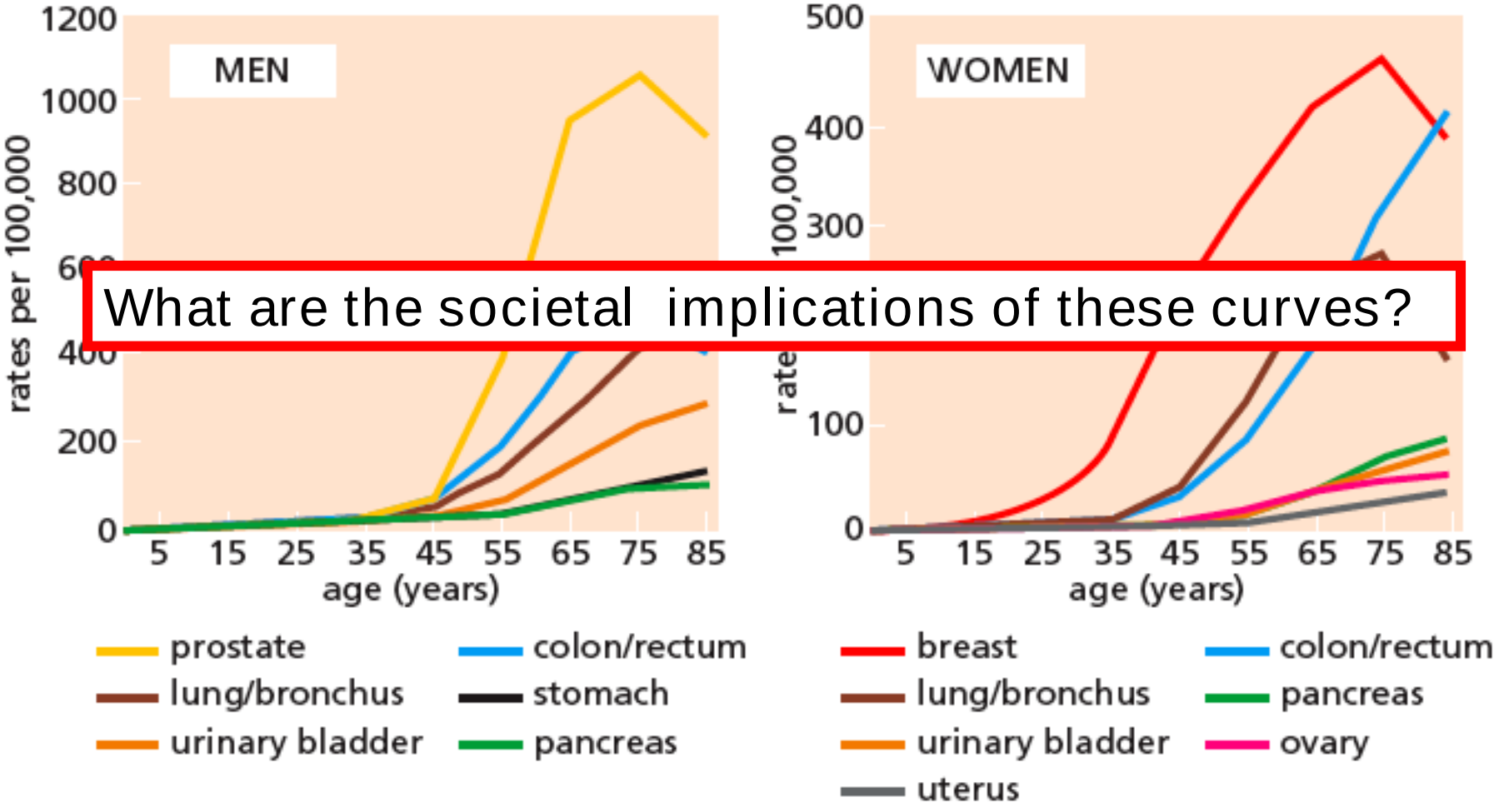
Checkpoint blockade Immunotherapy: Much hope!!!!

- Blocking these interactions using anti-CTLA4 or anti-PD1/PDL1 unleashes the “brakes” on the immune system, allowing tumor cell killing



Once again: Cancer is a disease of aging

The risk of developing cancer is different at different ages



What are the societal implications of these curves?

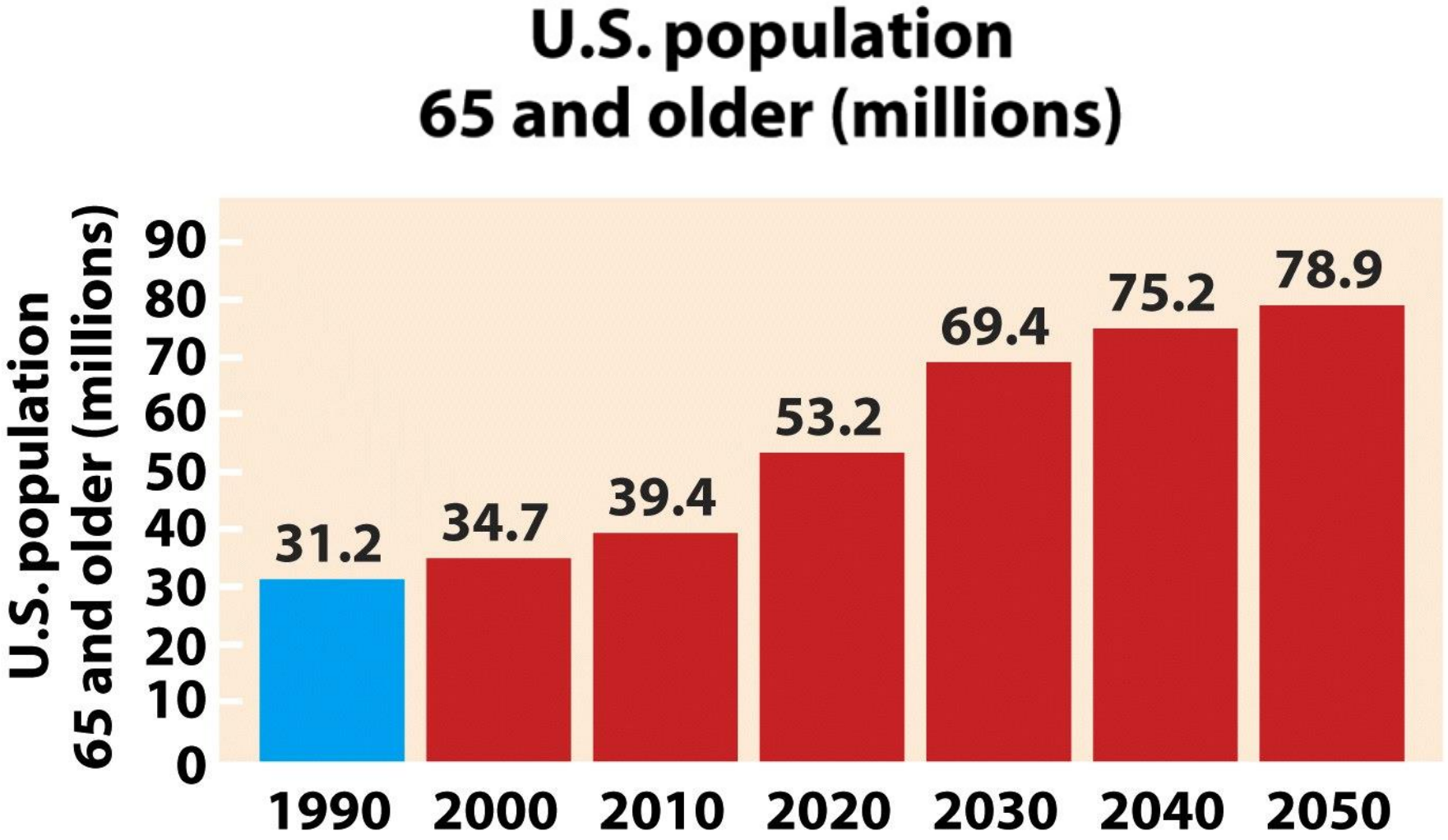


Figure 16.45a The Biology of Cancer (© Garland Science 2007)

Death rates from colorectal cancer have been decreasing but only slowly.

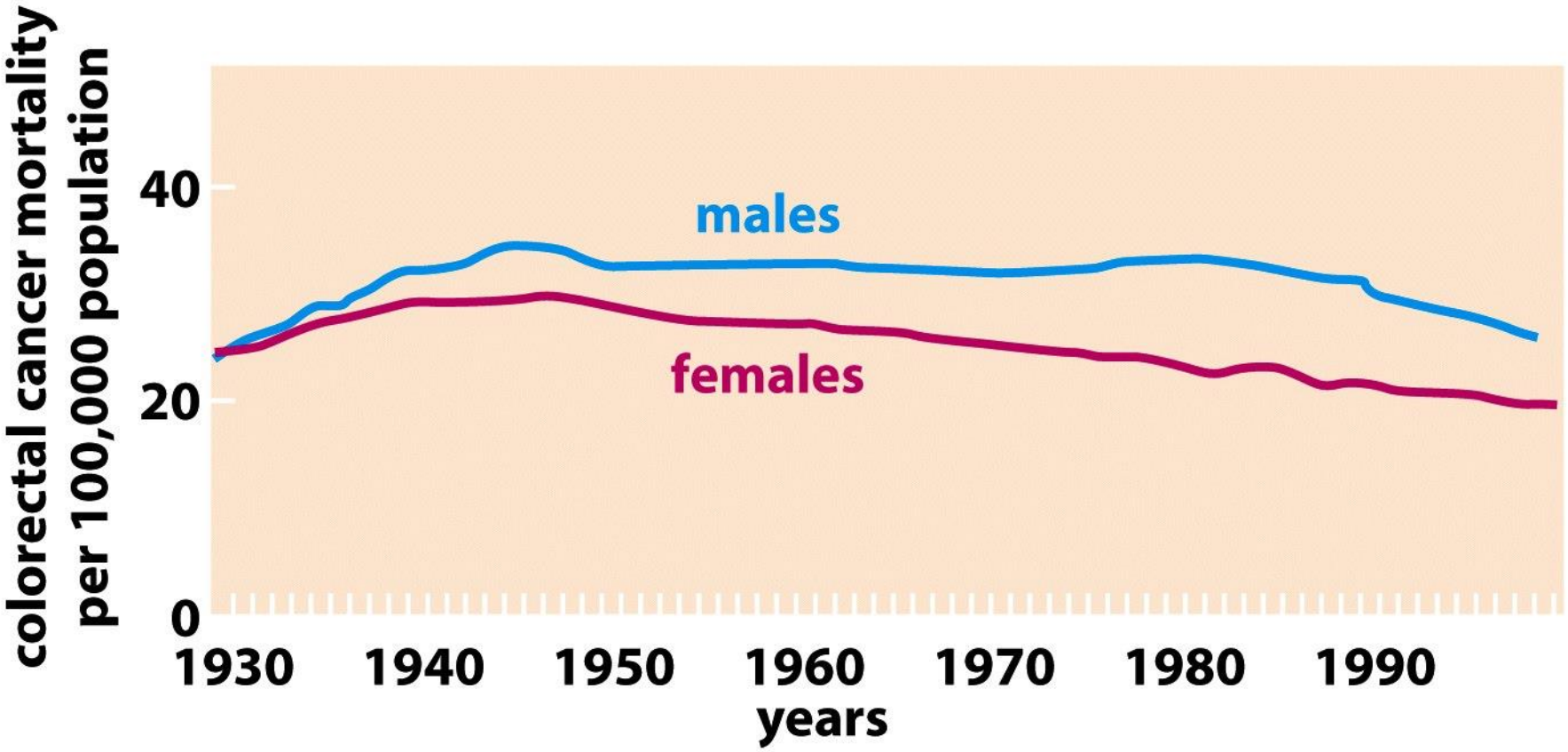
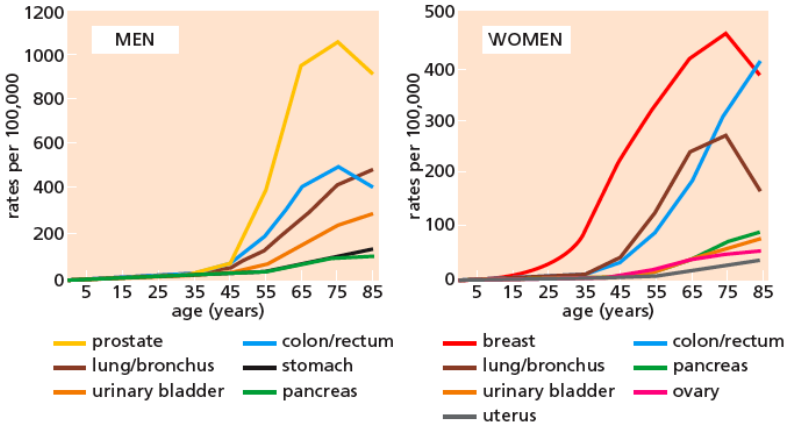
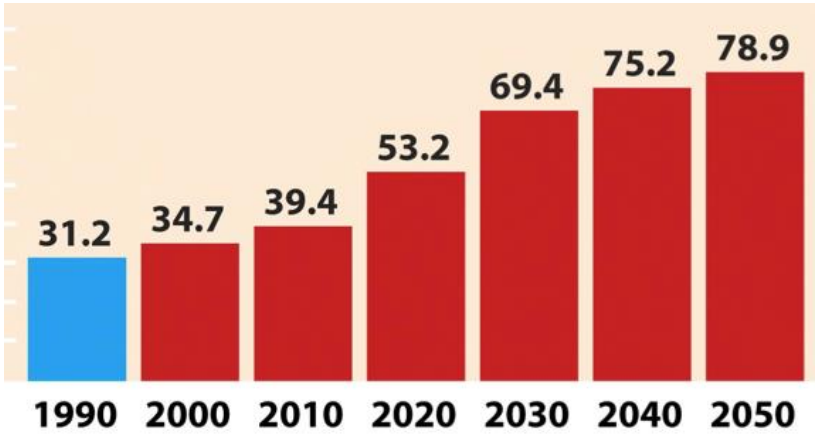
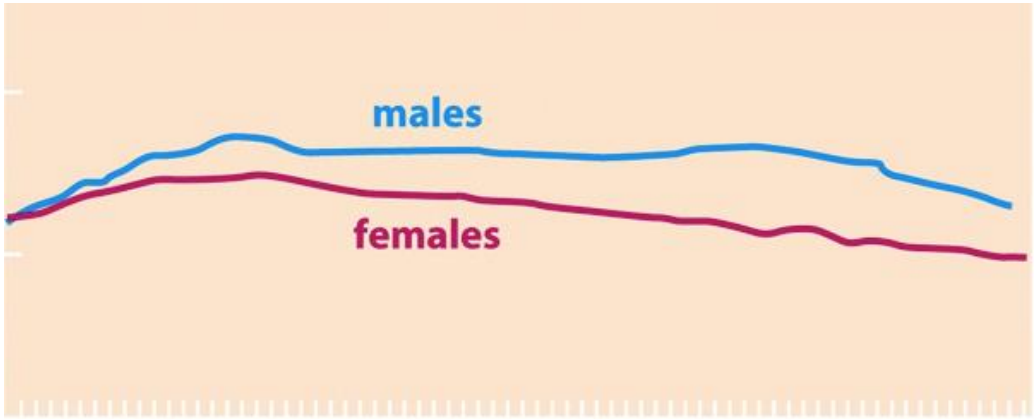


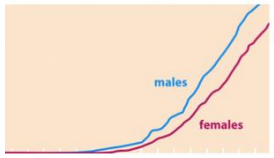
Figure 16.45b The Biology of Cancer (© Garland Science 2007)

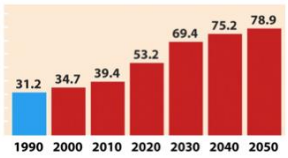
If we consider all three of these trends together…..

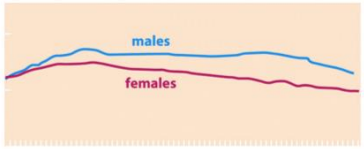








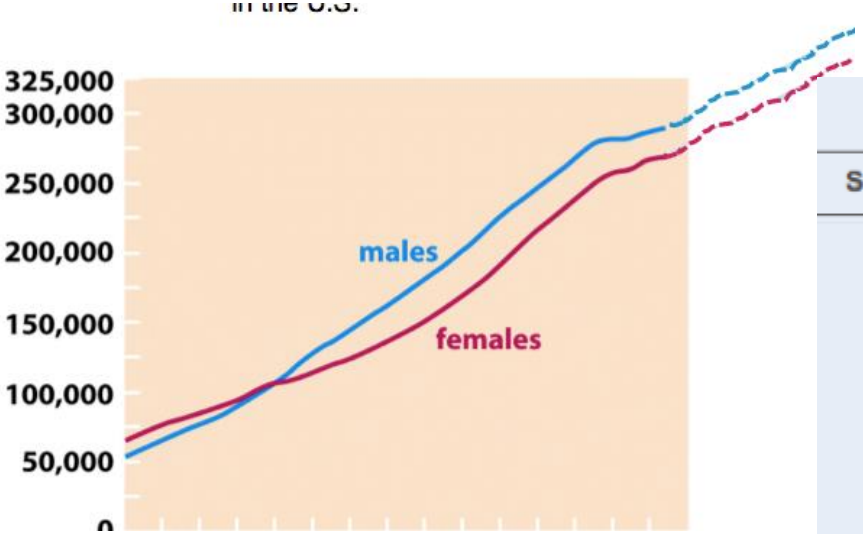




Total number of cancer-related deaths per year in the U.S.

Figure 16.45d The Biology of Cancer (© Garland Science 2007)

It’s unclear how we are going to pay for all this.



Cost of treatments

Sex	Site	Initial[1]	Continuing[1]	Last Year of Life[1] Cancer Death[2]	Last Year of Life[1] Other Cause[3]
Male	Bladder	20,960	4,677	75,772	8,446
	Brain	115,250	9,434	134,244	67,914
	Colorectal	51,812	4,595	85,671	15,068
	Esophagus	79,822	6,450	103,742	51,035
	Head/Neck	39,179	4,001	83,662	9,269
	Kidney	38,374	6,018	78,082	19,142
	Leukemia	36,036	10,249	133,183	35,941
	Lung	60,885	7,591	95,318	25,008
	Lymphoma	60,701	9,337	116,596	27,200
	Melanoma	5,437	1,951	62,436	546
	Other	41,161	7,363	97,473	25,758
	Pancreas	94,092	11,697	113,115	47,565

We will soon not be able to treat all those diagnosed with cancer because of economic factors.

It’s unclear how we are going to pay for all this.

Estimated Number* of New Cancer Cases and Deaths by Sex, US, 2014

	Estimated New Cases			Estimated Deaths		
	Both Sexes	Male	Female	Both Sexes	Male	Female
All Sites	1,665,540	855,220	810,320	585,720	310,010	275,710
Esophagus	18,170	14,660	3,510	15,450	12,450	3,000
Colon†	96,830	48,450	48,380	50,310	26,270	24,040
Lung & bronchus	224,210	116,000	108,210	159,260	86,930	72,330
Breast	235,030	2,360	232,670	40,430	430	40,000
Prostate	233,000	233,000		29,480	29,480	
Pancreas	46,420	23,530	22,890	39,590	20,170	19,420

What's the ratio of no. of deaths annually per no. of diagnosed new cases?

Pancreas 85%

Esophagus 85%

Colon 52% ← A major success!!

Lung & bronchus 87%

A major success!!

Estimated Number* of New Cancer Cases and Deaths by Sex, US, 2014

	Estimated New Cases			Estimated Deaths		
	Both Sexes	Male	Female	Both Sexes	Male	Female
All Sites	1,665,540	855,220	810,320	585,720	310,010	275,710
Esophagus	18,170	14,660	3,510	15,450	12,450	3,000
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Prostate	233,000	233,000		29,480	29,480	
Pancreas	46,420	23,530	22,890	39,590	20,170	19,420

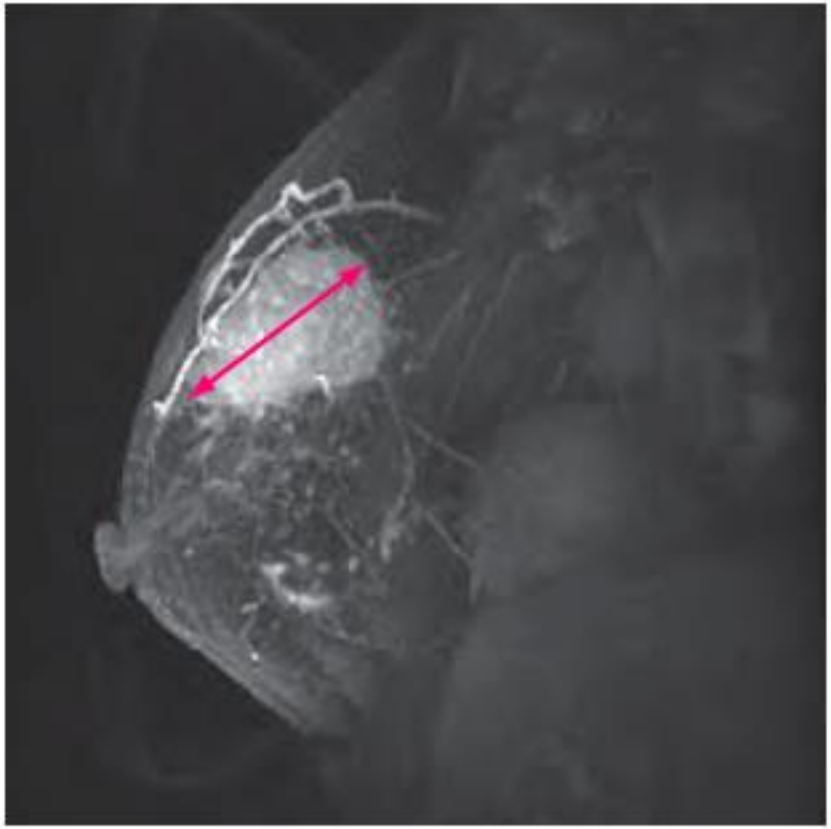
What's the ratio of no. of deaths annually per no. of diagnosed new cases?

Pancreas	85%
Esophagus	85%
Colon	52%
Lung & bronchus	87%
Breast	17%
Prostate	13%

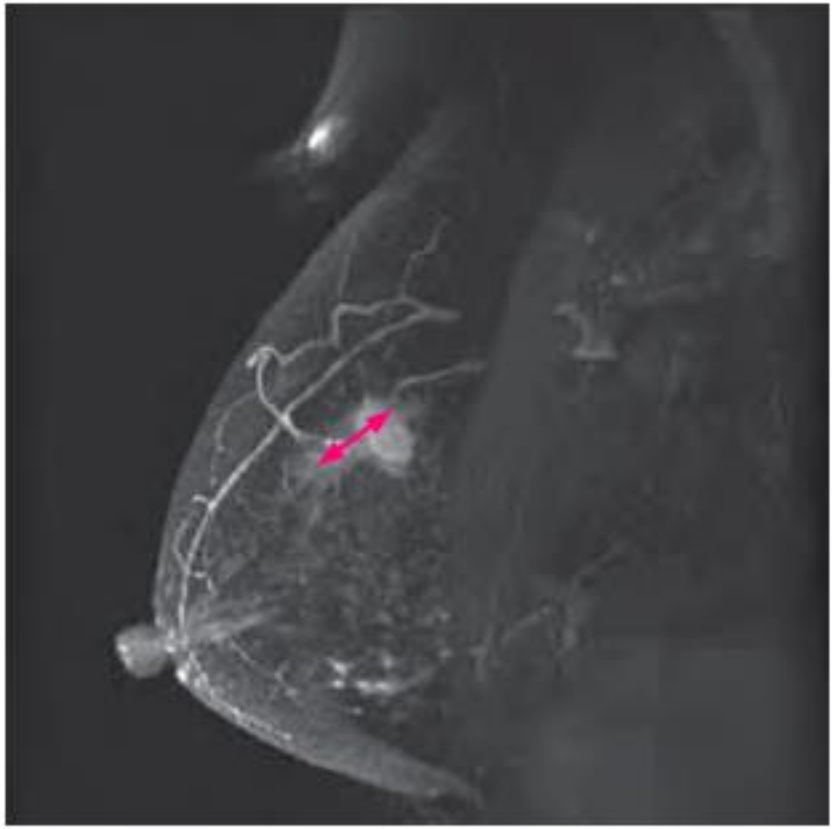
Wow! We seem to be making great progress!

A major problem at present: Overdiagnosis

These days we can find growths in the breast that would previously have eluded detection.



pre-chemotherapy
longest dimension = 47 mm



post-chemotherapy
longest dimension = 16 mm

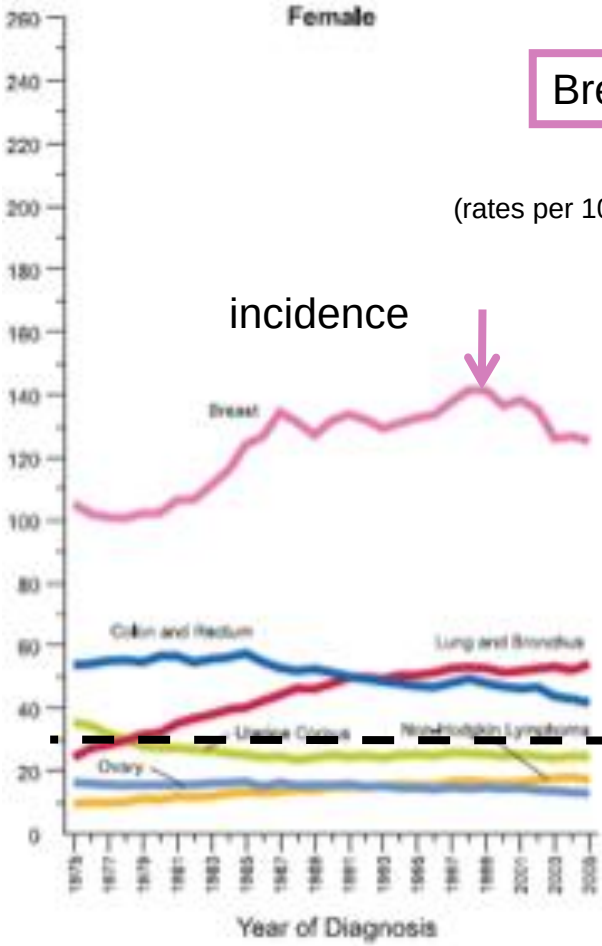
Overdiagnosis

Incidence of breast cancer is ~ 6 times higher than mortality.

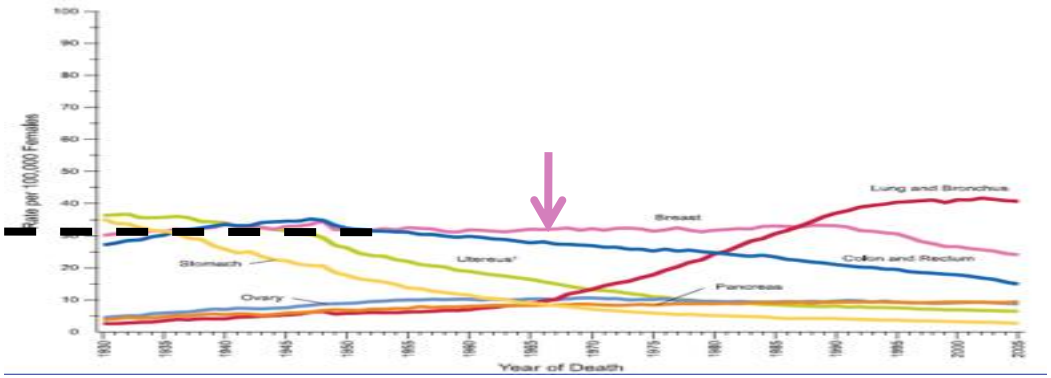
Breast cancer

(rates per 100,000 population)

incidence



mortality



Breast Cancer

About 1 in 8 U.S. women (about 12%) will develop invasive breast cancer over the course of her lifetime. In 2017, an estimated **252,710 new cases** of invasive breast cancer are expected to be diagnosed in women in the U.S., along with **63,410 new cases** of non-invasive (in situ) breast cancer.

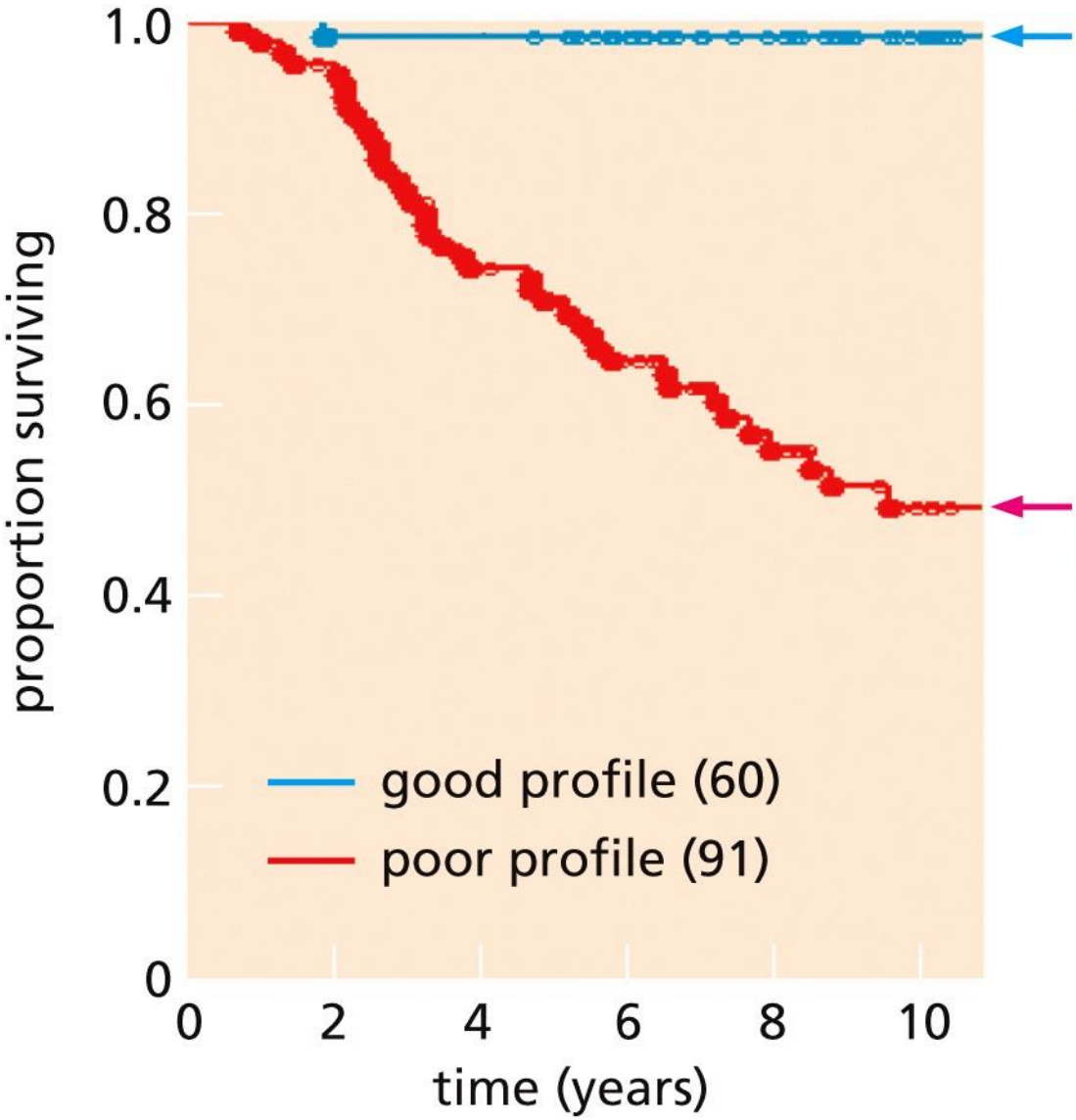
incidence

For women in the U.S., breast cancer death rates are higher than those for any other cancer, besides lung cancer.

About 40,610 women in the U.S. were expected to die in 2017 from breast cancer

mortality

How can we deal with this?
Dutch solution: don't treat all patients aggressively



good signature of tumor
(40% of patients):
~4% die of breast cancer
~96% survive breast cancer

poor signature of tumor
(60% of patients):
~50% die of breast cancer
~50% survive breast cancer

Figure 16.4b The Biology of Cancer (© Garland Science 2014)

Overdiagnosis

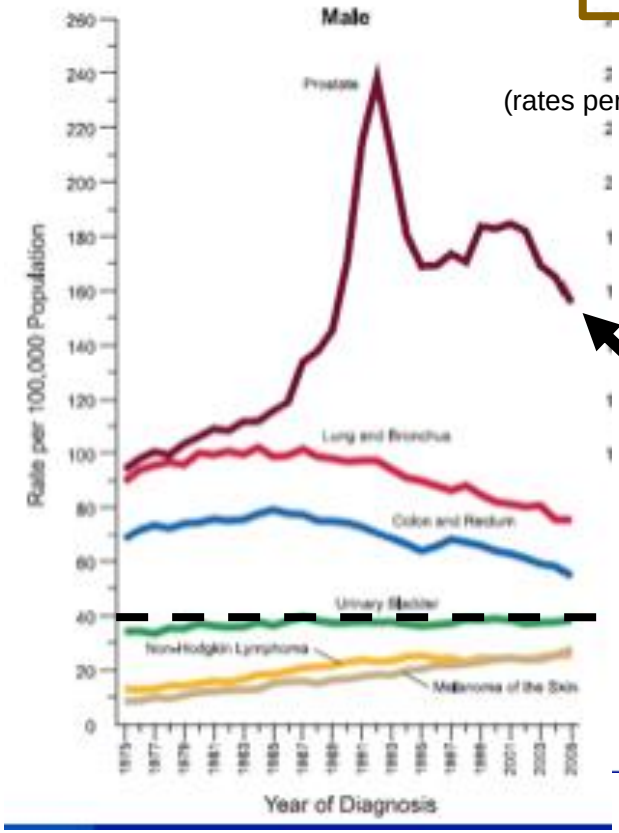
Incidence of prostate cancer is <u>many times higher</u> than mortality.

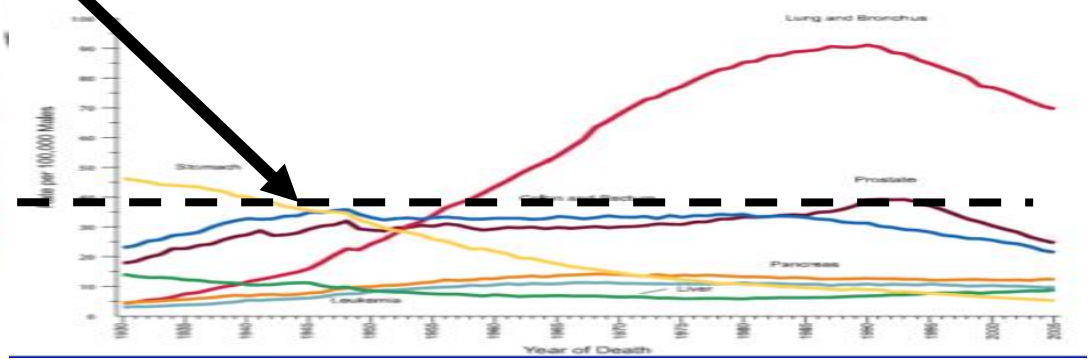
incidence

Prostate cancer

(rates per 100,000 population)

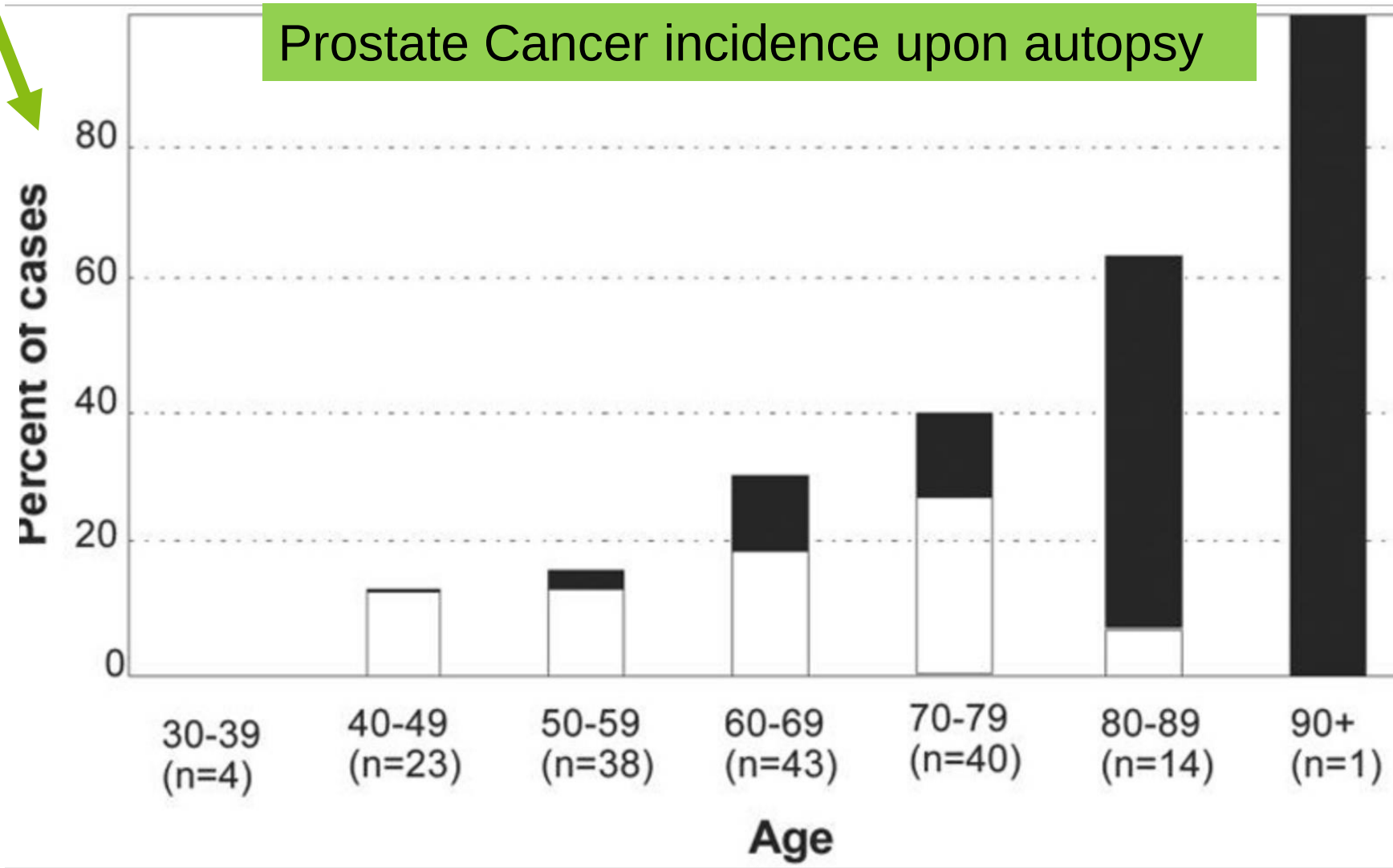
mortality





Overdiagnosis

% of men upon autopsy



~3% of men die from prostate cancer

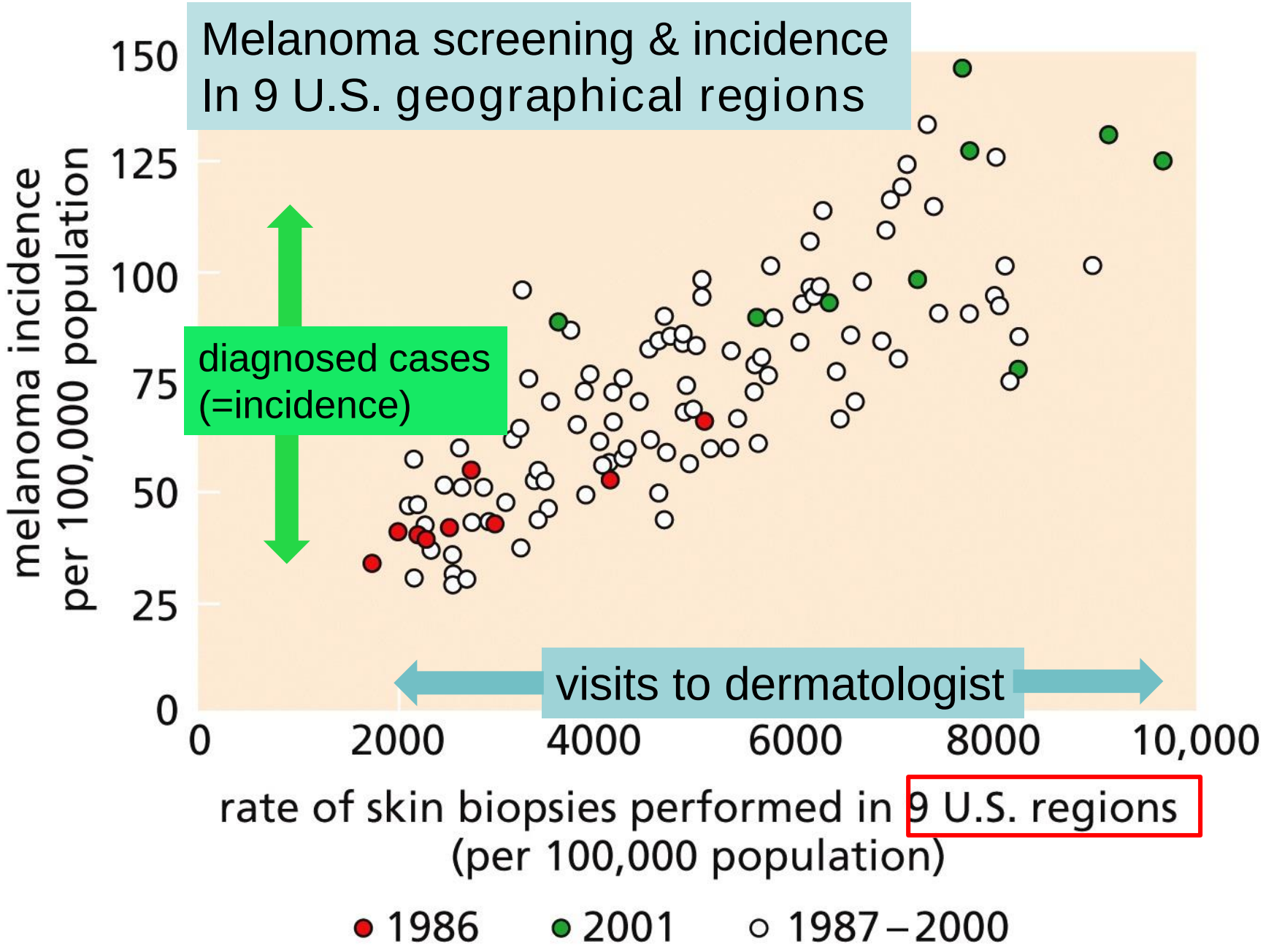


Figure 16.44b The Biology of Cancer (© Garland Science 2014)

The case of melanoma:
The melanoma epidemic

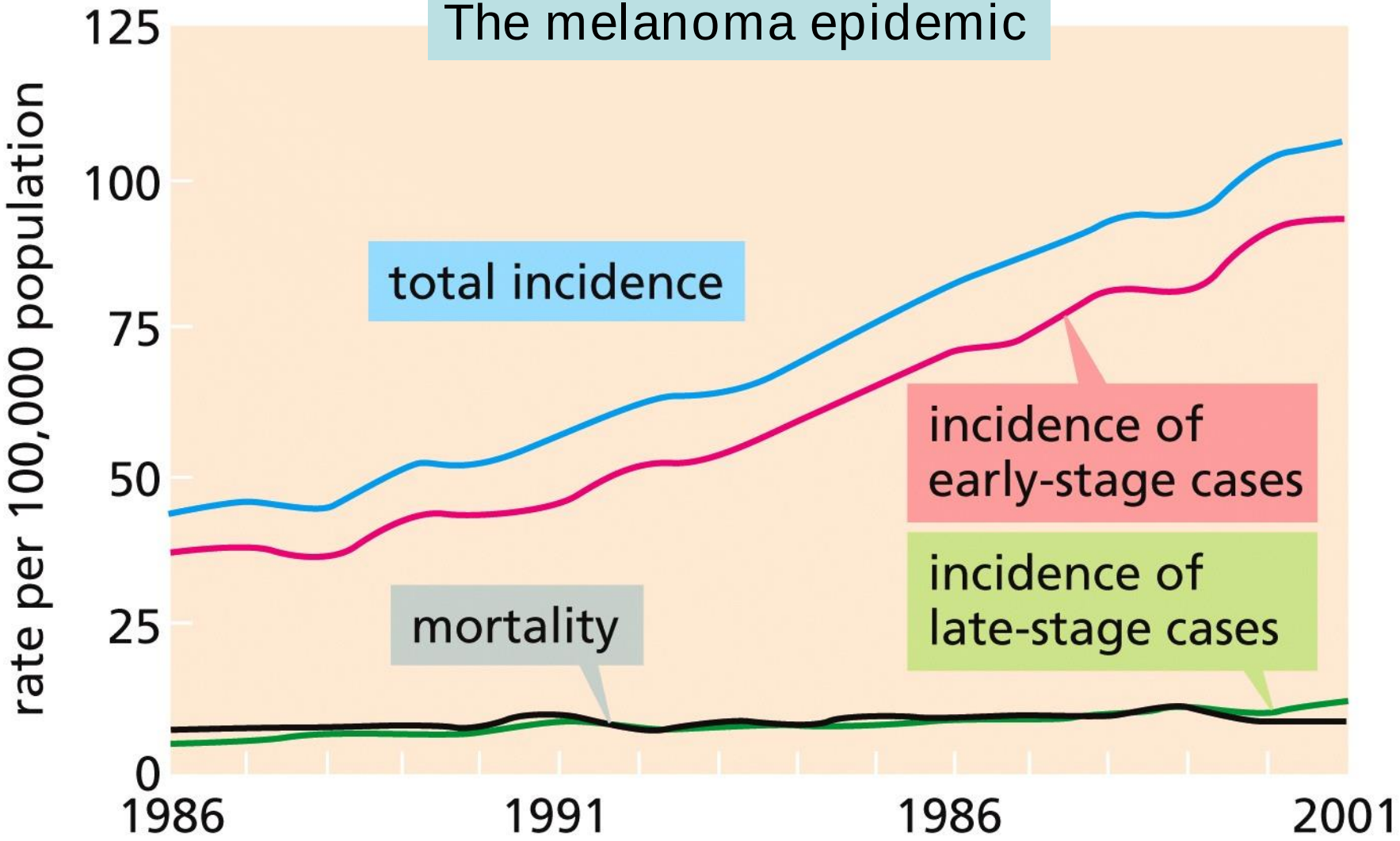


Figure 16.44a The Biology of Cancer (© Garland Science 2014)

Overdiagnosis

The melanoma circus

The more you look, the more you find.

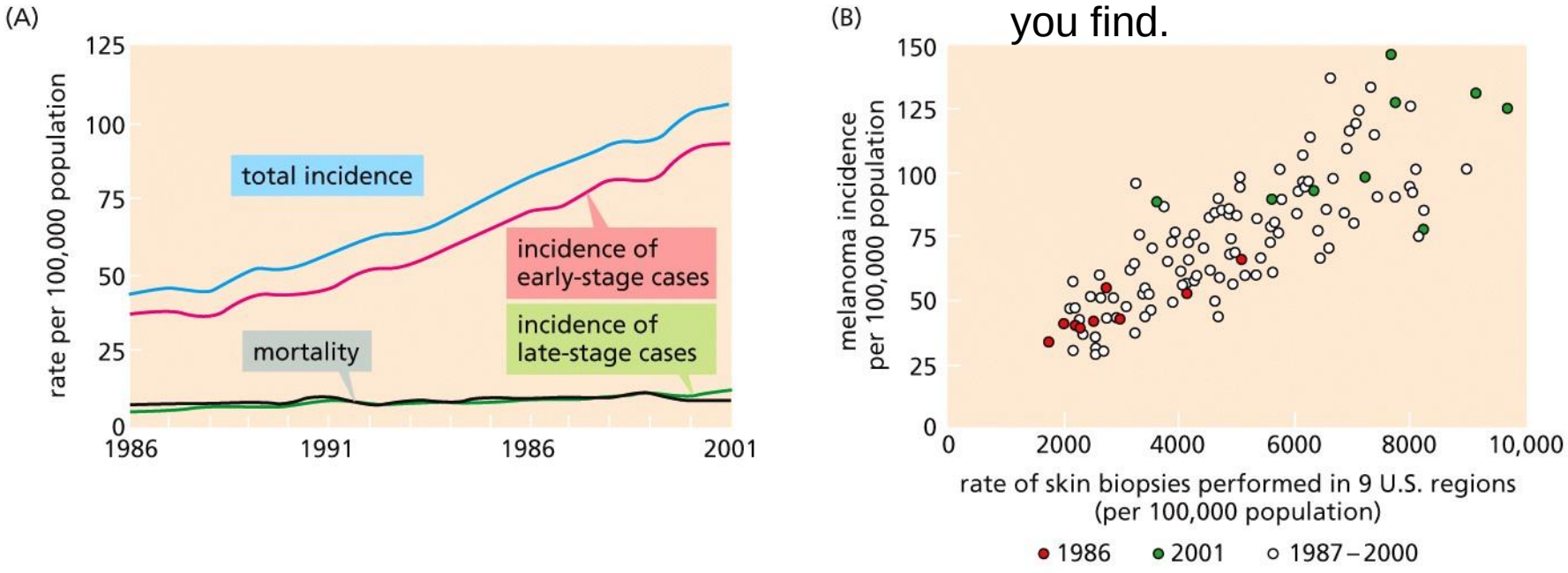


Figure 16.44 The Biology of Cancer (© Garland Science 2014)

Other confounding statements:
In this case from the Am. Cancer Society

How Many People Alive Today Have Ever Had Cancer?

Approximately 13.7 million Americans with a history of cancer were alive on January 1, 2012. Some of these individuals were cancer free, while others still had evidence of cancer and may have been undergoing treatment.

What Percentage of People Survive Cancer?

The 5-year relative survival rate for all cancers diagnosed between 2003 and 2009 is 68%, up from 49% in 1975-1977 (see page 17). The improvement in survival reflects both progress in diagnosing certain cancers at an earlier stage and improvements in treatment. Survival statistics vary greatly by cancer

Where does all this leave us?!

1. The incidence of many cancers is a cultural artifact.

2. Only a portion of these will ever be life-threatening.

3. We will soon not be able to treat all those diagnosed with cancer because of economic factors.

4. The only solution to these trends will be to reduce incidence

Only solution: Reduce incidence:

In the US, tobacco use is responsible for nearly 1 in 5 deaths; this equaled an estimated 443,000 premature deaths each year between 2000 and 2004.[6,7] In addition, an estimated 8.6 million people suffer from chronic conditions related to smoking, such as chronic bronchitis, emphysema, and cardiovascular diseases.[8]

Only solution: Reduce incidence:

Stunning differences in lung cancer mortality

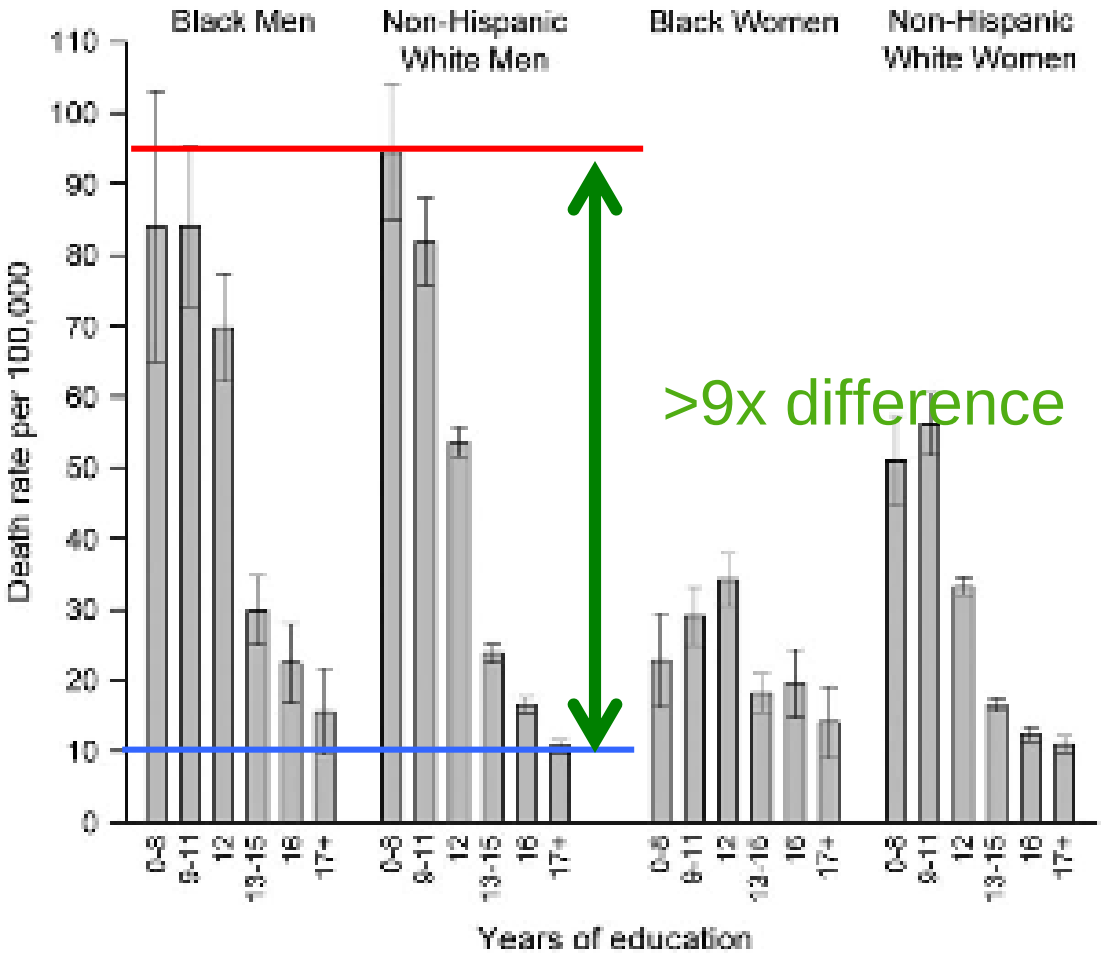
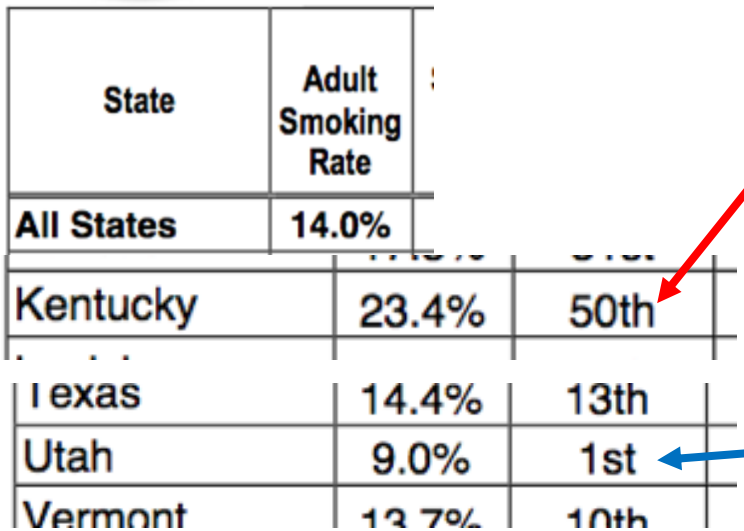


Fig. 2. Lung cancer mortality rates, by education level, sex, and race, for persons aged 25–64 years in the United States, 2001. **Error bars** correspond to 95% confidence intervals.

KEY STATE-SPECIFIC TOBACCO-RELATED DATA & RANKINGS

State	Adult Smoking Rate	Adult Smoking Rank (1=low)	Pregnant Smoking Rate	Youth Smoking Rate	New Youth Smokers Per Year	Annual Adult Smoking Deaths (approx.)	Kids Now Alive Who Will Become Smokers	Kids Now Alive Who Will Die From Smoking	Smoking Caused Health Costs (millions)	Cigarette Tax (per pack)	Cigarette Tax Rank (1 = high)	FY 2019 Funding for State TC Programs (millions)	Tobacco Prevention Spending % of CDC Target
All States	**14.0%**	///	**7.2%**	**5.8%**	**98,000**	**480,000**	**17+ mill.**	**5.6 mill.**	**$170 bill.**	**$1.81**	///	**$655.0**	**19.8%**
Alabama	19.2%	41st	10.1%	**14.0%**	1,800	8,600	336,200	108,000	$1.88 bill.	$0.675	41st	$2.1	3.7%
Alaska	19.1%	39th	11.5%	**10.9%**	200	600	43,600	14,000	$438	**$2.00**	**17th**	$9.1	89.4%
Arizona	14.0%	12th	4.8%	**7.1%**	2,000	8,300	359,800	115,000	$2.38 bill.	**$2.00**	**17th**	$17.3	26.9%
Kansas	17.3%	31st	10.2%	**7.2%**	1,000	4,400	191,200	61,000	$1.12 bill.	$1.29	33rd	$0.8	3.0%
Kentucky	23.4%	50th	18.4%	**14.3%**	2,000	8,900	371,700	119,000	$1.92 bill.	$1.10	36th	$3.8	6.7%
Louisiana	20.5%	44th	6.8%	**12.3%**	1,700	7,200	307,400	98,000	$1.89 bill.	$1.08	37th	$5.4	9.0%
Texas	14.4%	13th	3.3%	11.3%	8,700	28,000	1,557,800	498,000	$8.85 bill.	**$1.41**	**29th**	$4.2	1.6%
Utah	9.0%	1st	3.0%	**3.8%**	600	1,300	120,800	39,000	$542	$1.70	25th	$7.0	36.3%
Vermont	13.7%	10th	15.5%	**9.3%**	100	1,000	31,500	10,000	$348	$3.08	7th	$3.8	45.2%



Let's hear it for the Home Team!!

Reducing incidence: Other avoidable causes

Cancer mortality in obese vs. lean people:
Highest quartile of body mass index vs. lowest quartile

Lowest quartile: BMI of 24.9 and below; highest quartile: BMI no. is given

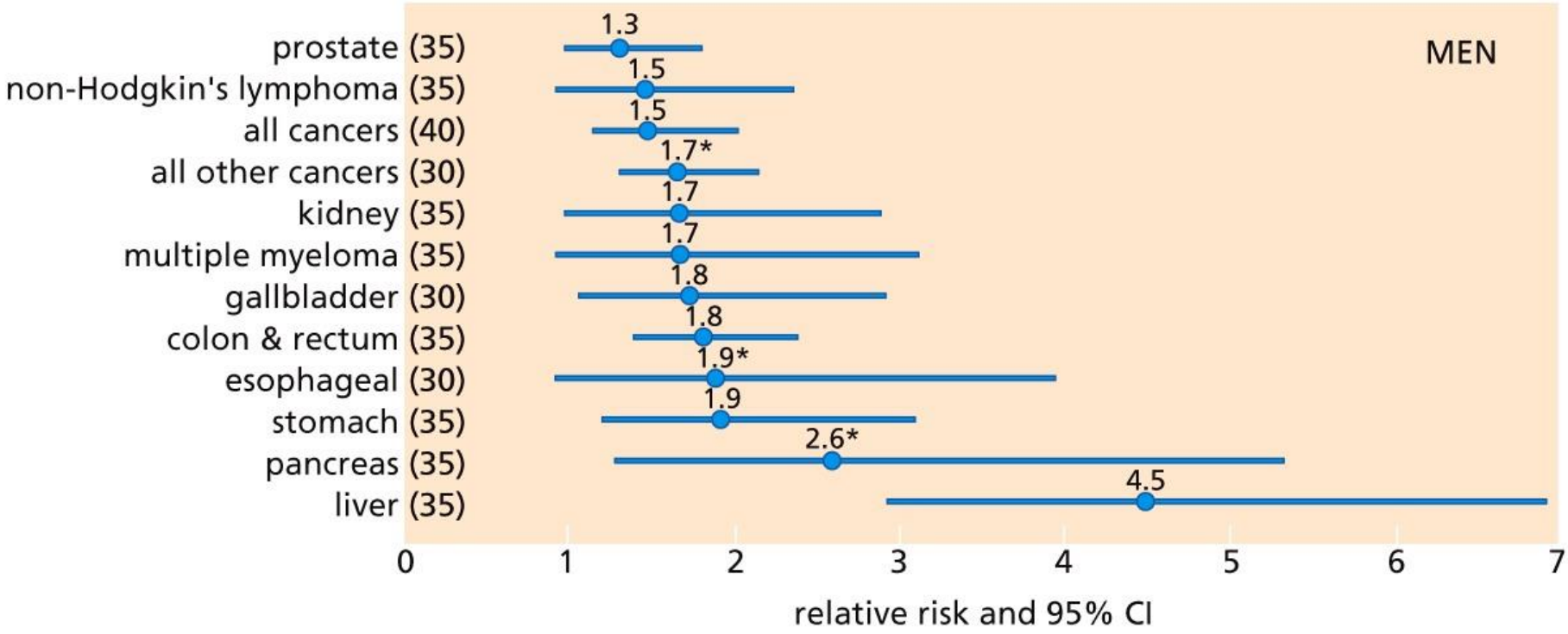


Figure 9.41a The Biology of Cancer (© Garland Science 2014)

Other avoidable causes:
Cancer mortality in obese vs. lean people:
Highest quartile of body mass index vs. lowest quartile

Lowest quartile: BMI of 24.9 and below; highest quartile: BMI no. is given

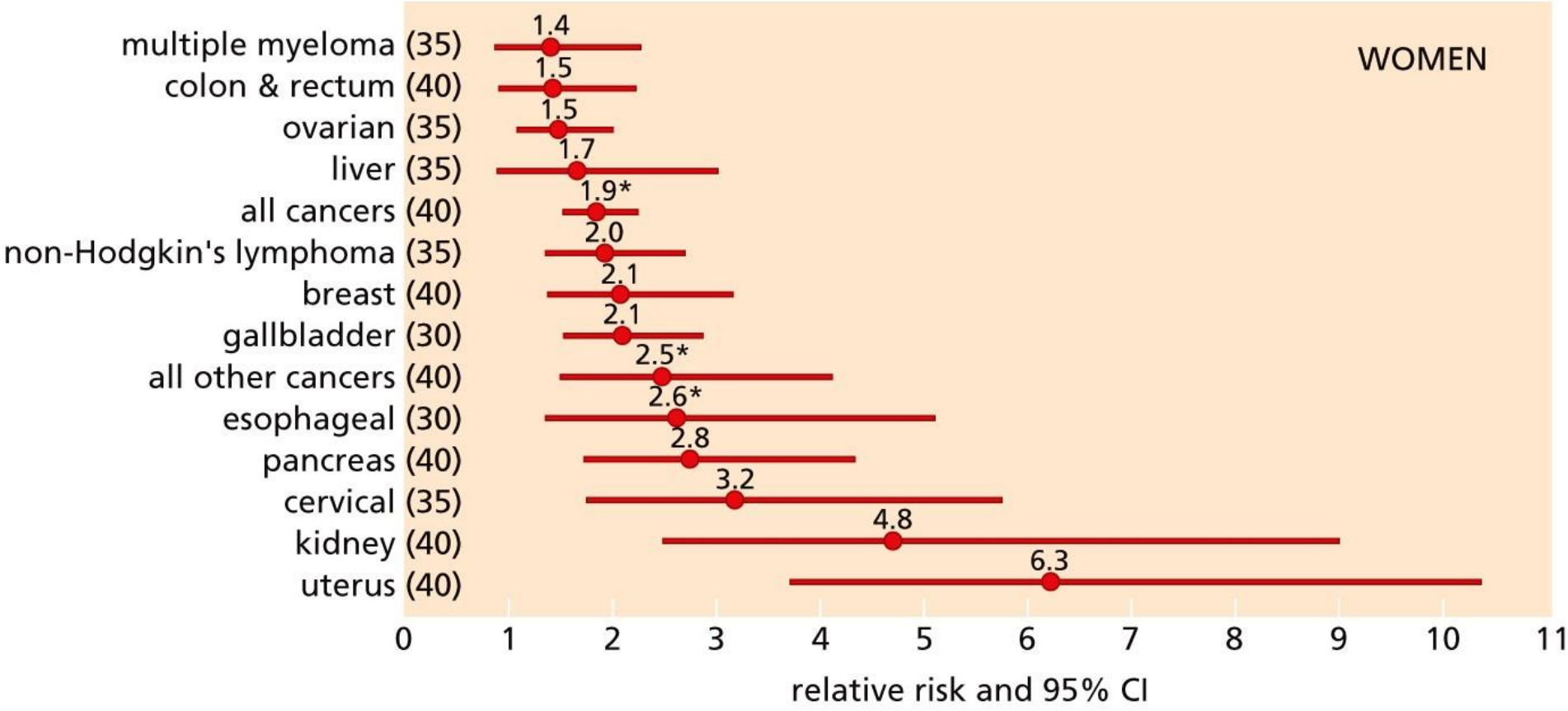


Figure 9.41b The Biology of Cancer (© Garland Science 2014)

Reducing incidence: avoidable risk factors

Table 2.7 Known or suspected causes of human cancers

Environmental and lifestyle factors known or suspected to be etiologic for human cancers in the United States[a]	
Type	**% of total cases[b]**
Cancers due to occupational exposures	1–2
Lifestyle cancers	
Tobacco-related (sites: e.g., lung, bladder, kidney)	34
Diet (low in vegetables, high in nitrates, salt) (sites: e.g., stomach, esophagus)	5
Diet (high fat, low fiber, broiled/fried foods) (sites: e.g., bowel, pancreas, prostate, breast)	37
Tobacco plus alcohol (sites: mouth, throat)	2

[a]Adapted from American Cancer Society. Cancer Facts & Figures 1990. Atlanta: American Cancer Society, Inc.
[b]A large number of cancers are thought to be provoked by a diet high in calories (see Sidebar 9.10) acting in combination with many of these lifestyl factors.
[c]Adapted from S. Wilson, L. Jones, C. Coussens and K. Hanna, eds., Cancer and the Environment: Gene–Environment Interaction. Washington, DC: National Academy Press, 2002.
[d]ER+, estrogen receptor–positive.
[e]E + P, therapy containing both estrogen and progesterone.

Through the miracle of PhotoShop!!

Native born Americans


Netherlands
Germany
Singapore
Germany
Israel
France
Germany
Japan
China
India
China
Slovakia
Germany
Australia
China
India
Netherlands
Pittsburgh
HongKong
Indonesia/
Brazil

Estimated Number* of New Cancer Cases and Deaths by Sex, US, 2014

	Estimated New Cases			Estimated Deaths		
	Both Sexes	Male	Female	Both Sexes	Male	Female
All Sites	1,665,540	855,220	810,320	585,720	310,010	275,710
Esophagus	18,170	14,660	3,510	15,450	12,450	3,000
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Pancreas	46,420	23,530	22,890	39,590	20,170	19,420

What's the ratio of no. of deaths per no. of diagnosed new cases?

Pancreas	85%
Esophagus	85%
Colon	52%
Lung & bronchus	87%

Five-year Relative Survival Rates* (%) by Stage at Diagnosis, 2003-2009

	All Stages	Local	Regional	Distant
Breast (female)	89	99	84	24
Colon & rectum	65	90	70	13
Esophagus	17	39	21	4
[illegible]	72	92	64	12
[illegible]	61	76	43	35
Liver†	16	29	10	3
Lung & bronchus	17	54	26	4
Melanoma of the skin	91	98	62	16
Oral cavity & pharynx	62	83	59	36
Ovary	44	92	72	27
Pancreas	6	24	9	2
Prostate	99	100	100	28
Stomach	28	63	28	4
Testis	95	99	96	74
Thyroid	98	100	97	55
Urinary bladder§	78	70	33	5
Uterine cervix	68	91	57	16
Uterine corpus	82	95	68	17

Death rates from disseminated tumors remain high

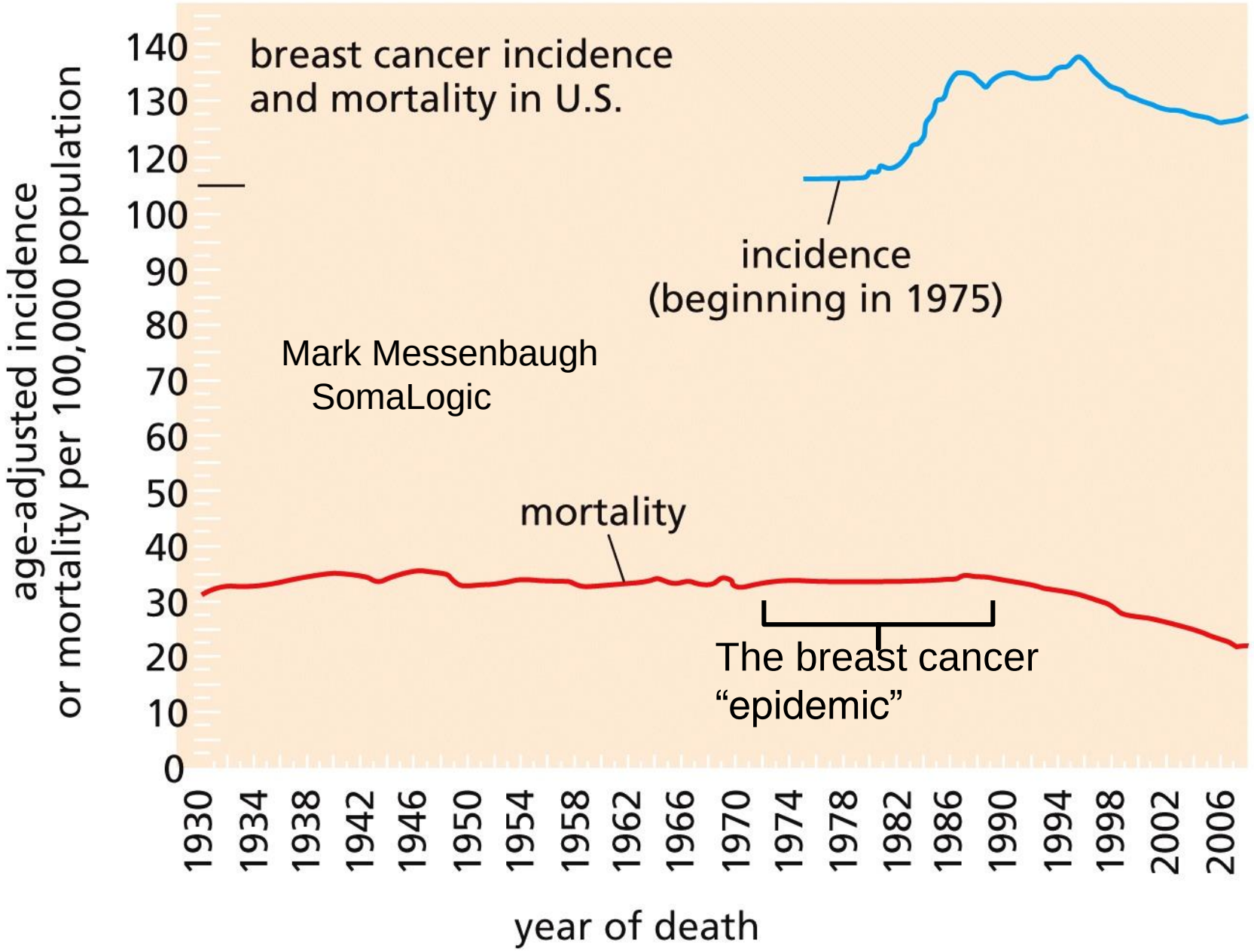
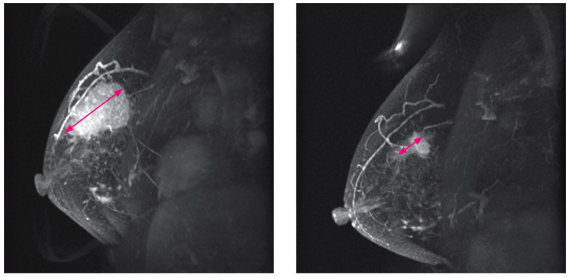


Figure 16.3 The Biology of Cancer (© Garland Science 2014)

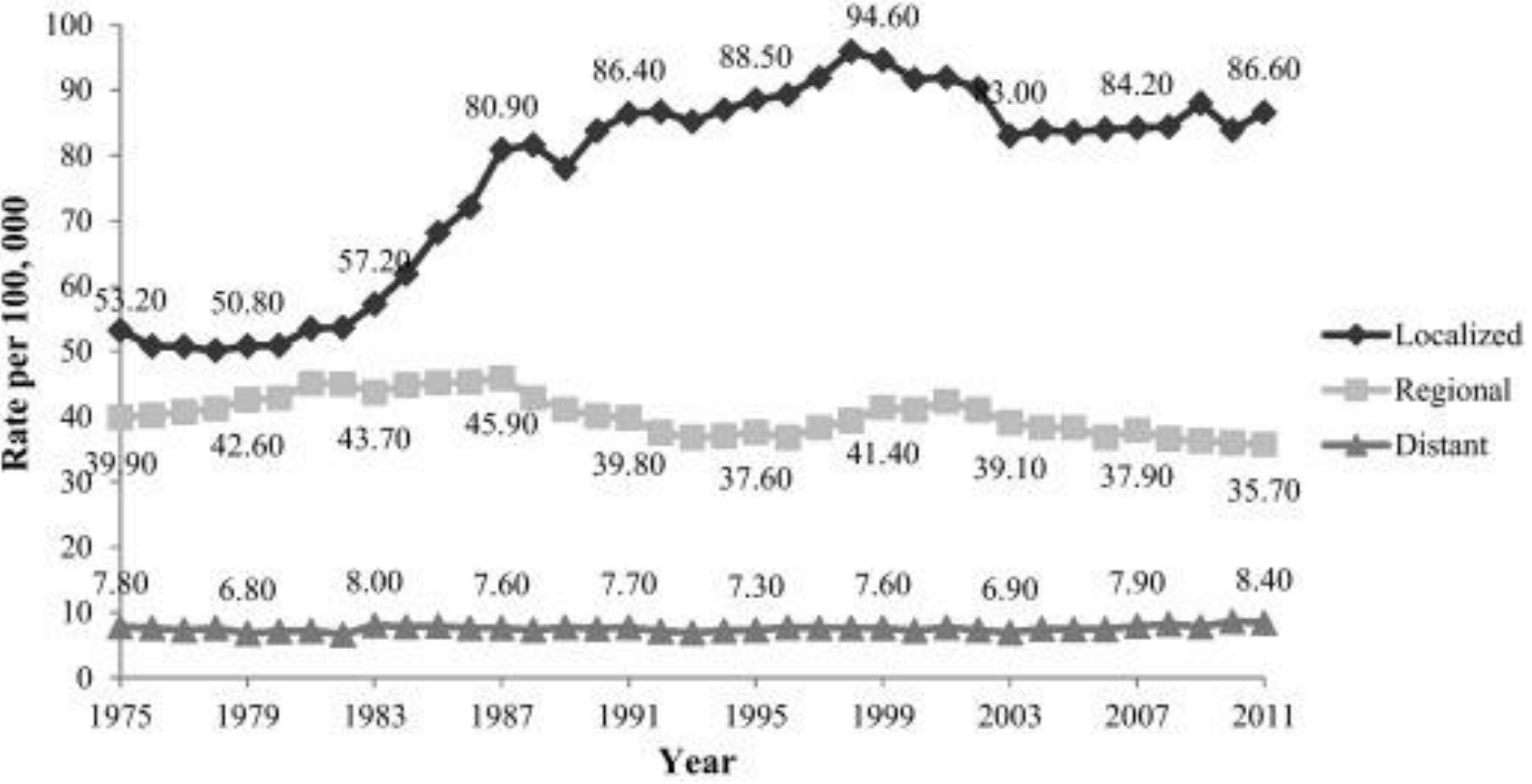
Breast cancer diagnosis



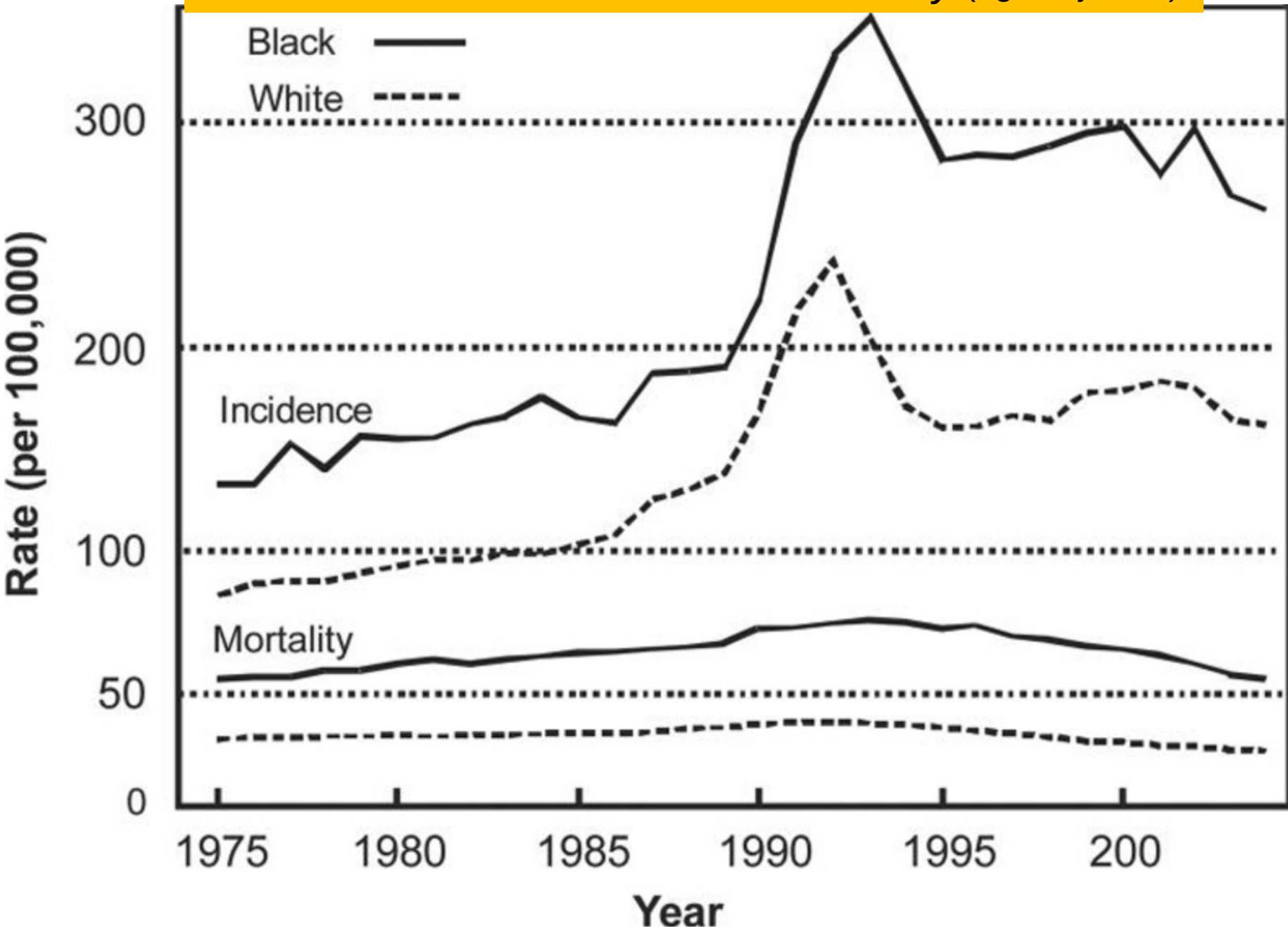
pre-chemotherapy
longest dimension = 47 mm

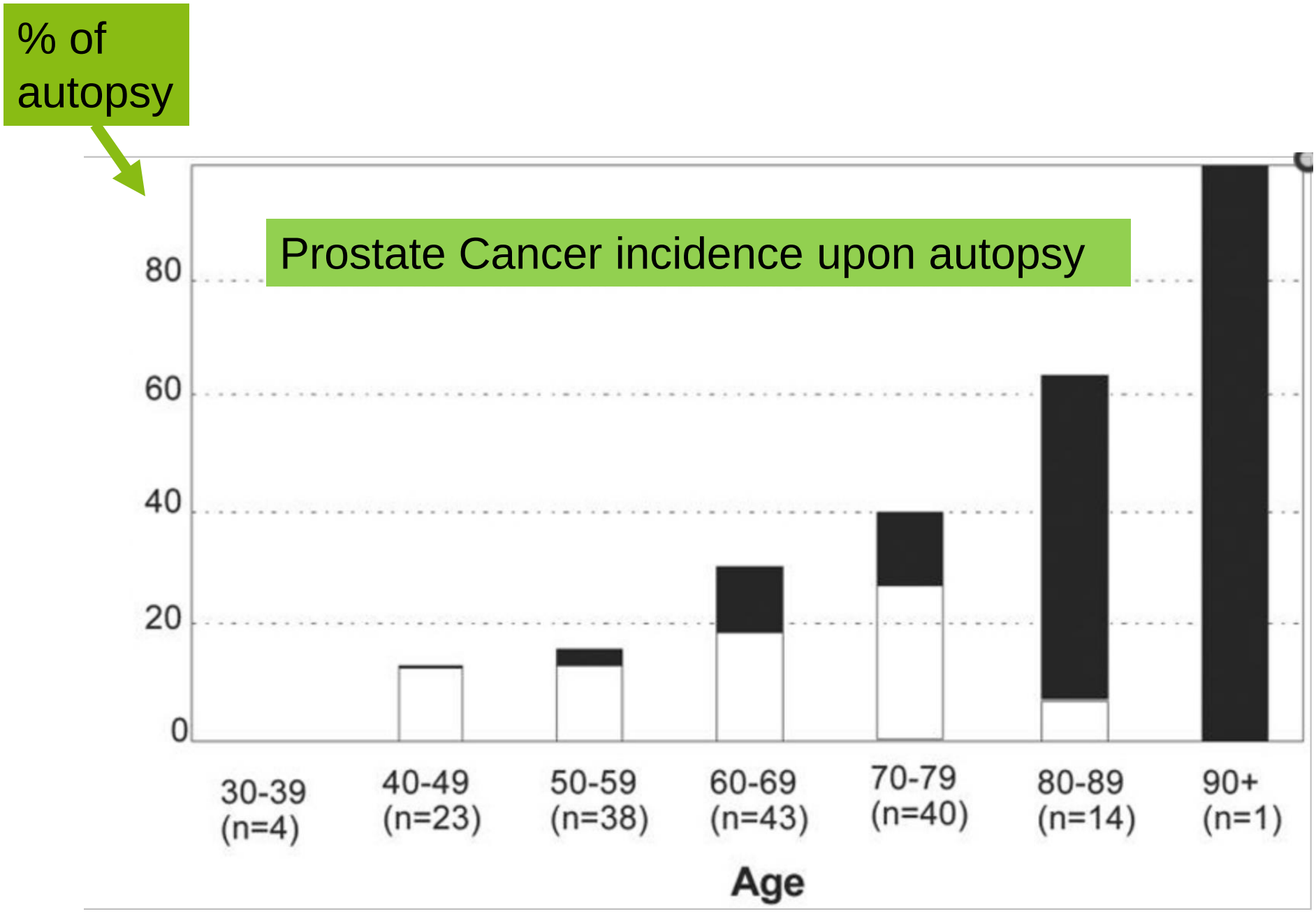
post-chemotherapy
longest dimension = 16 mm

Figure 16.2 The Biology of Cancer (© Garland Science 2014)



Prostate Cancer incidence & mortality (age adjusted)




% of autopsy
Prostate Cancer incidence upon autopsy
80
60
40
20
0
30-39 (n=4)
40-49 (n=23)
50-59 (n=38)
60-69 (n=43)
70-79 (n=40)
80-89 (n=14)
90+ (n=1)
Age

% of autopsy

Prostate Cancer incidence upon autopsy