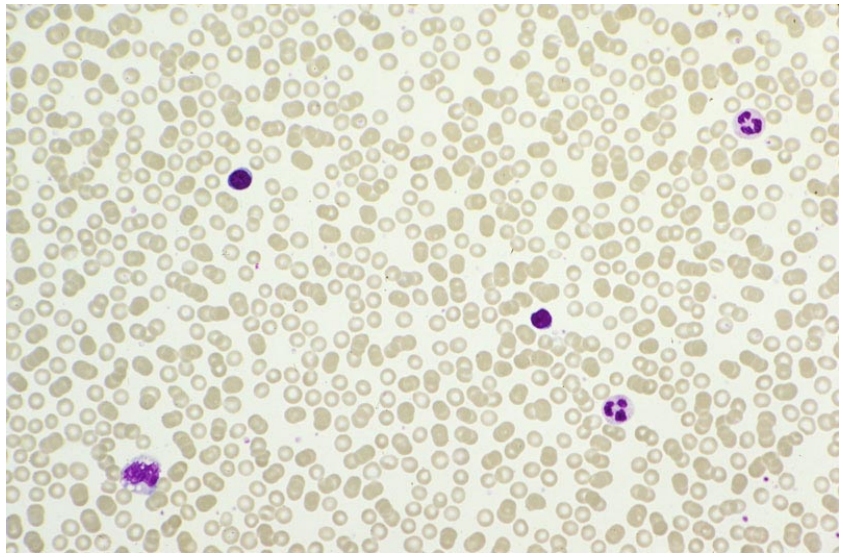
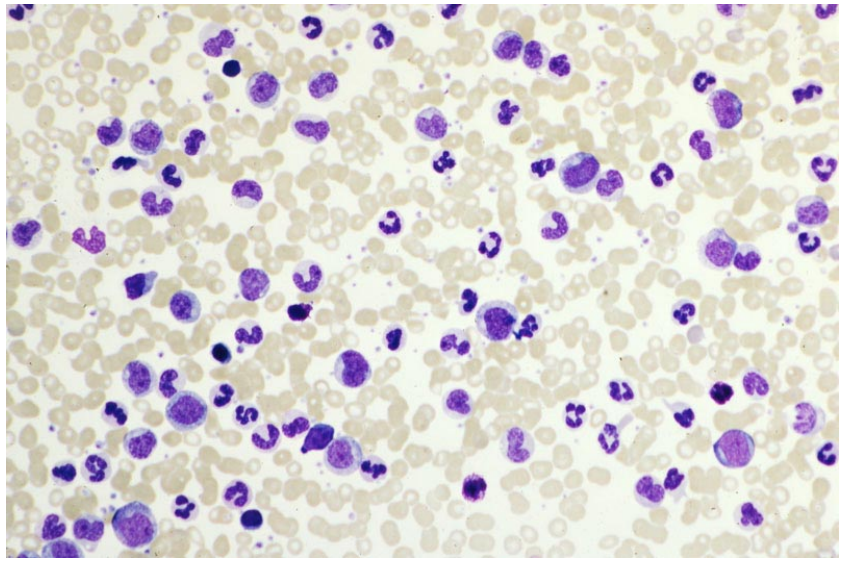
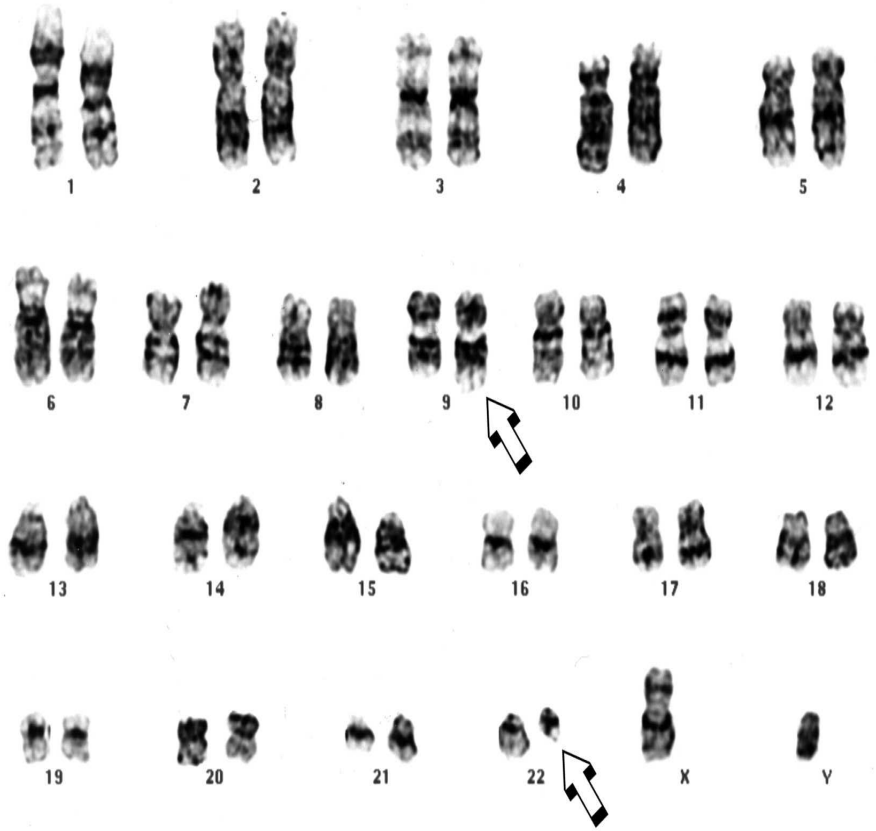
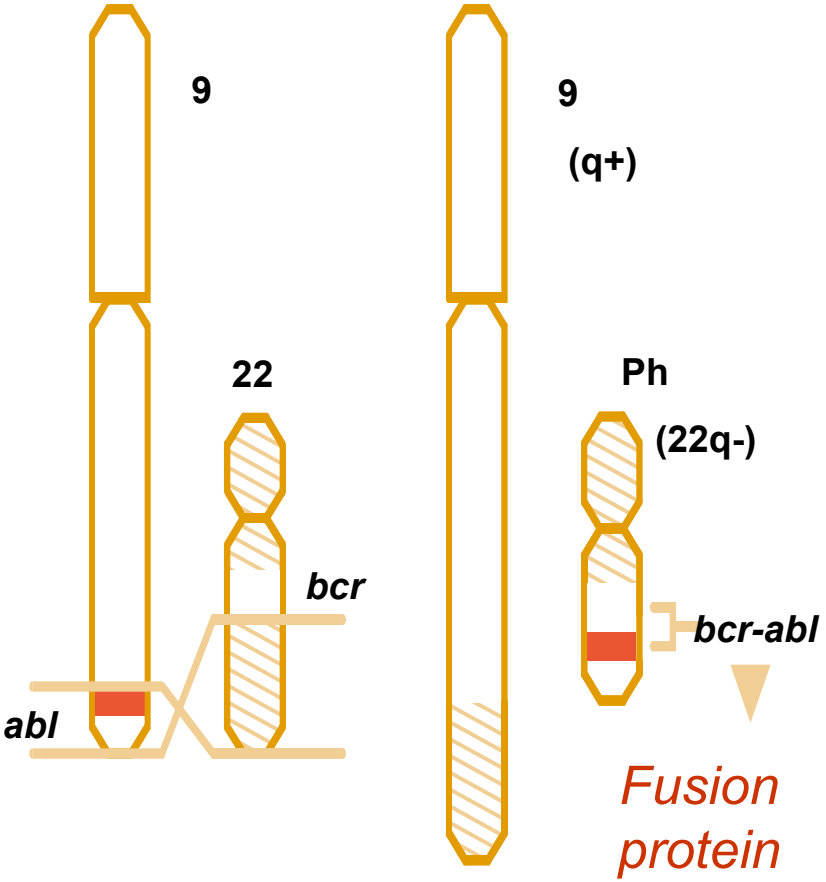
CHRONIC MYELOGENOUS LEUKEMIA





SHUFFLING THE GENETIC DECK IN CML





Fusion protein causes cancer

GLEEVEC AND BCR-ABL FUSION PROTEIN

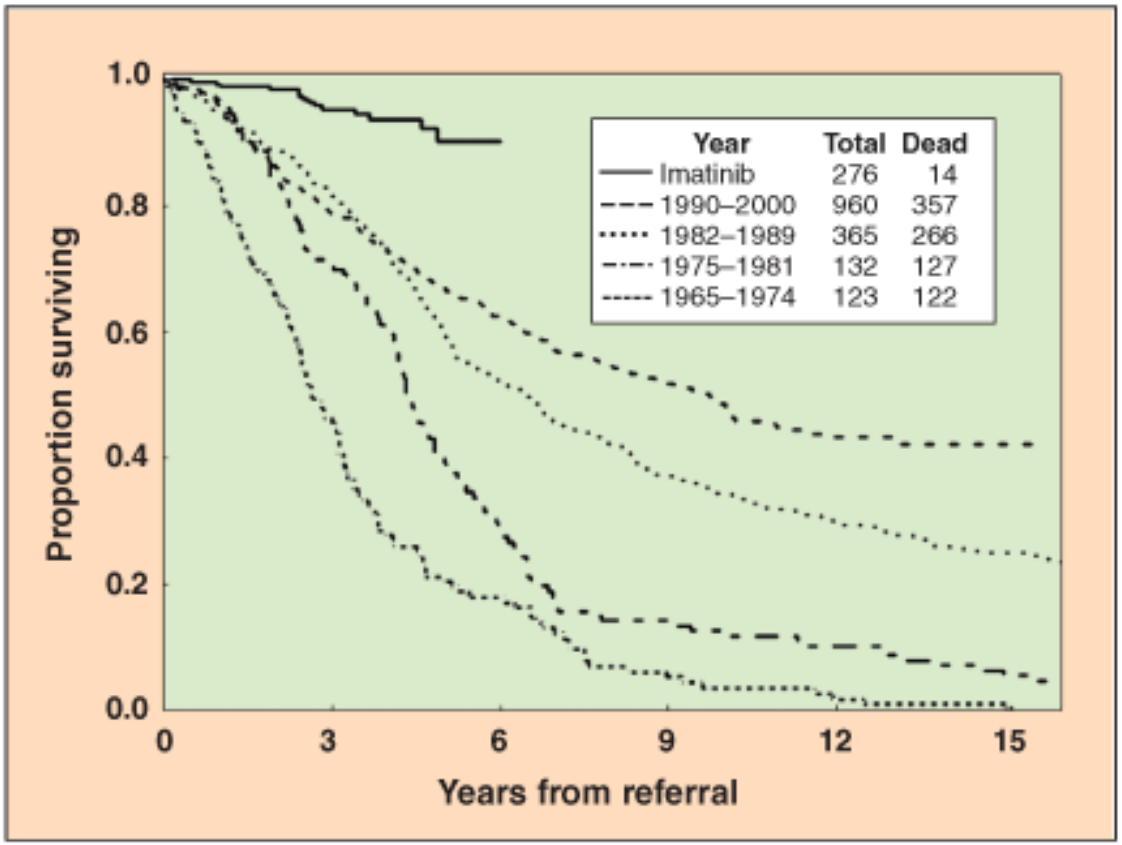


Figure 2: Survival of Chronic Myeloid Leukemia—Survival of patients treated at the University of Texas M.D. Anderson Cancer Center since 1965, by year of therapy and with the advent of imatinib.

GENETIC MEDICINE

A. ***Genetic diseases***

B. Genetic testing

C. Genetics and cancer

D. Genome and treatment

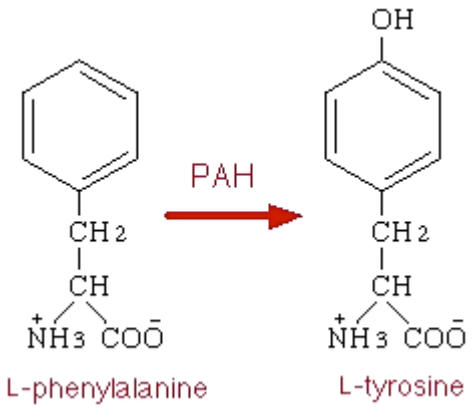
GENE AND PROTEIN

Gene (DNA)

↓

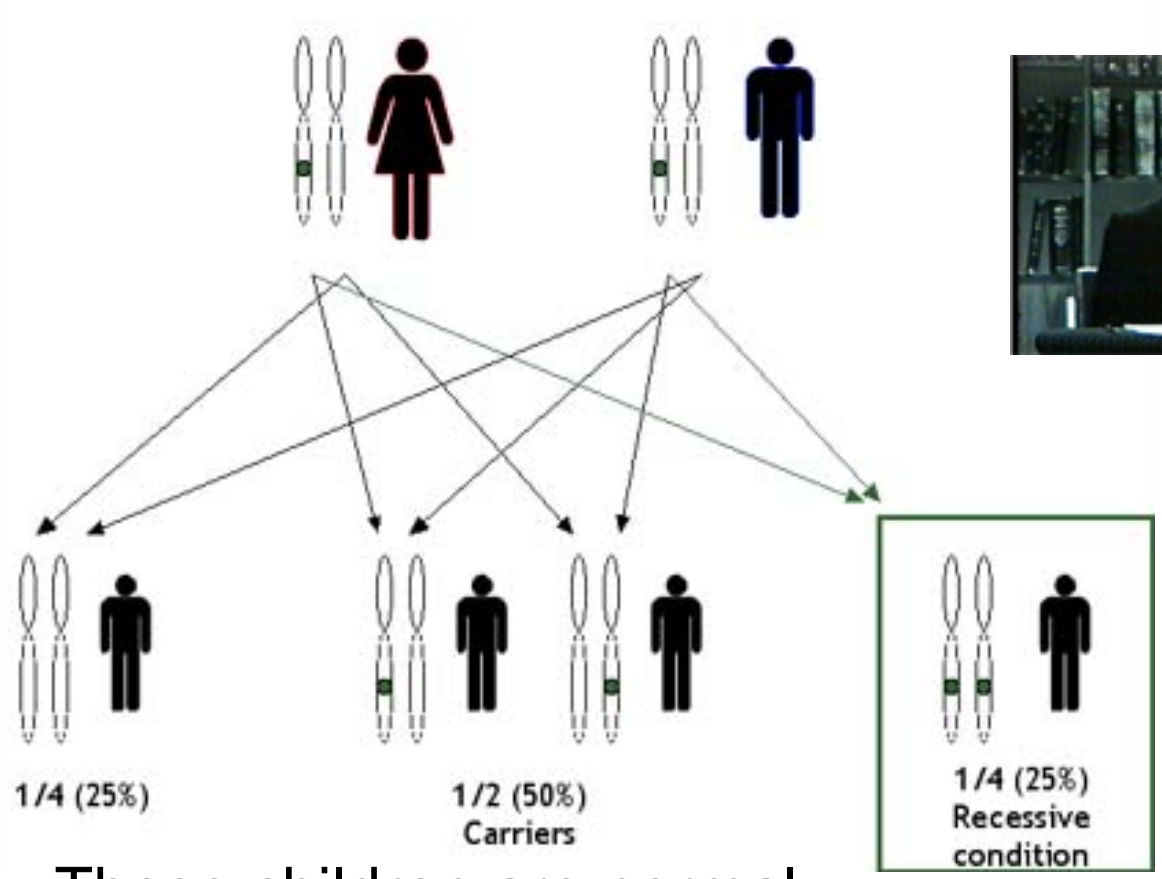
protein

Substance A ----------→ Substance B



A GENETIC DISEASE

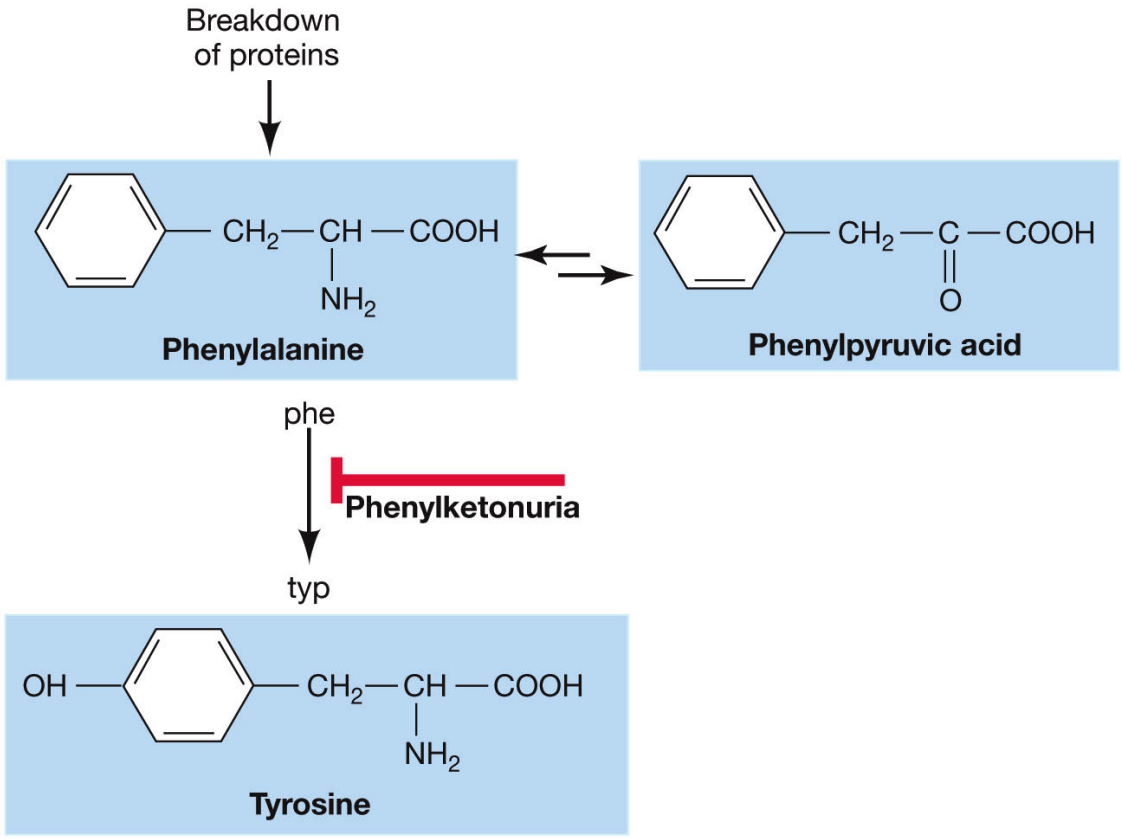
Parents are both normal



This child has PKU

These children are normal

A GENETIC DISEASE: PROTEIN

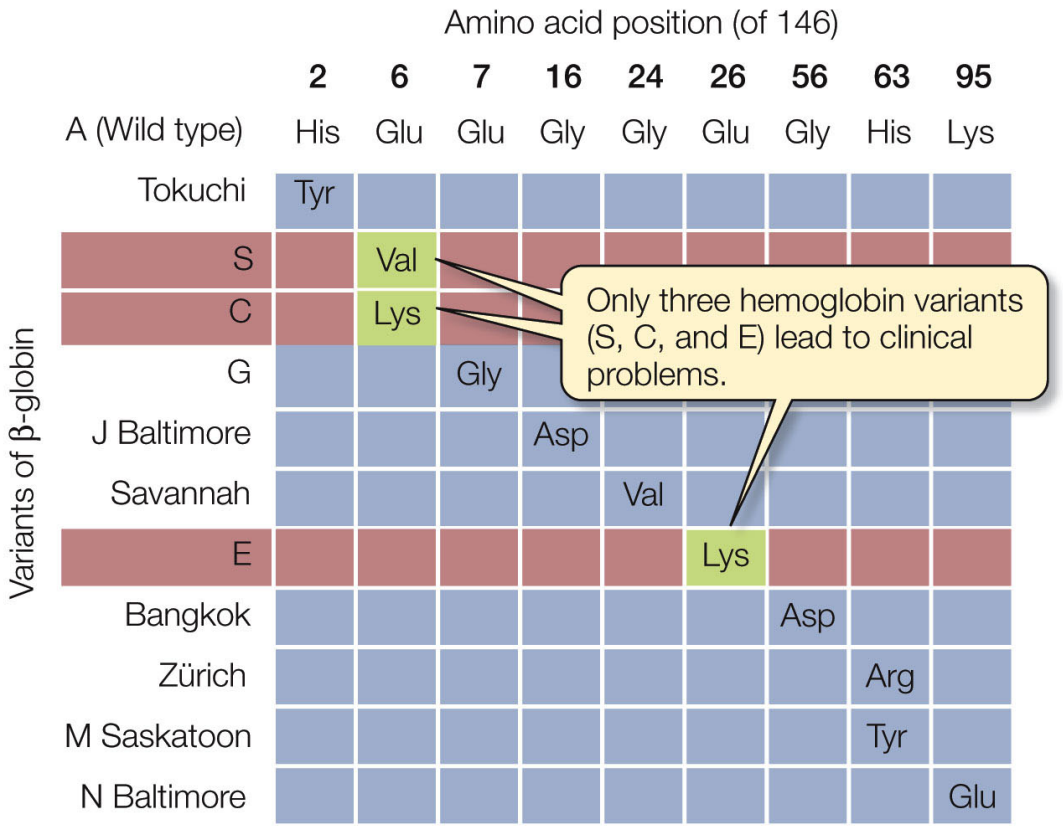


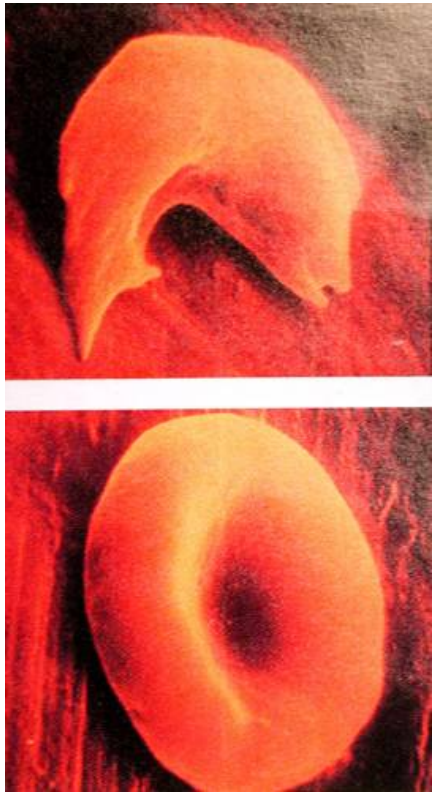
Phenotype: Mental retardation
1 birth in 14,000

A GENETIC DISEASE: DNA

	Normal	*PKU*
Length of protein	451 amino acids	451 amino acids
DNA at codon 408	xxx**C**GGxxx xxx**G**CCxxx	xxx**T**GGxxx xxx**A**CCxxx
Amino acid at pos. 408	arginine	tryptophan
Protein works?	Yes	No

GENETIC VARIATION OF HEMOGLOBIN



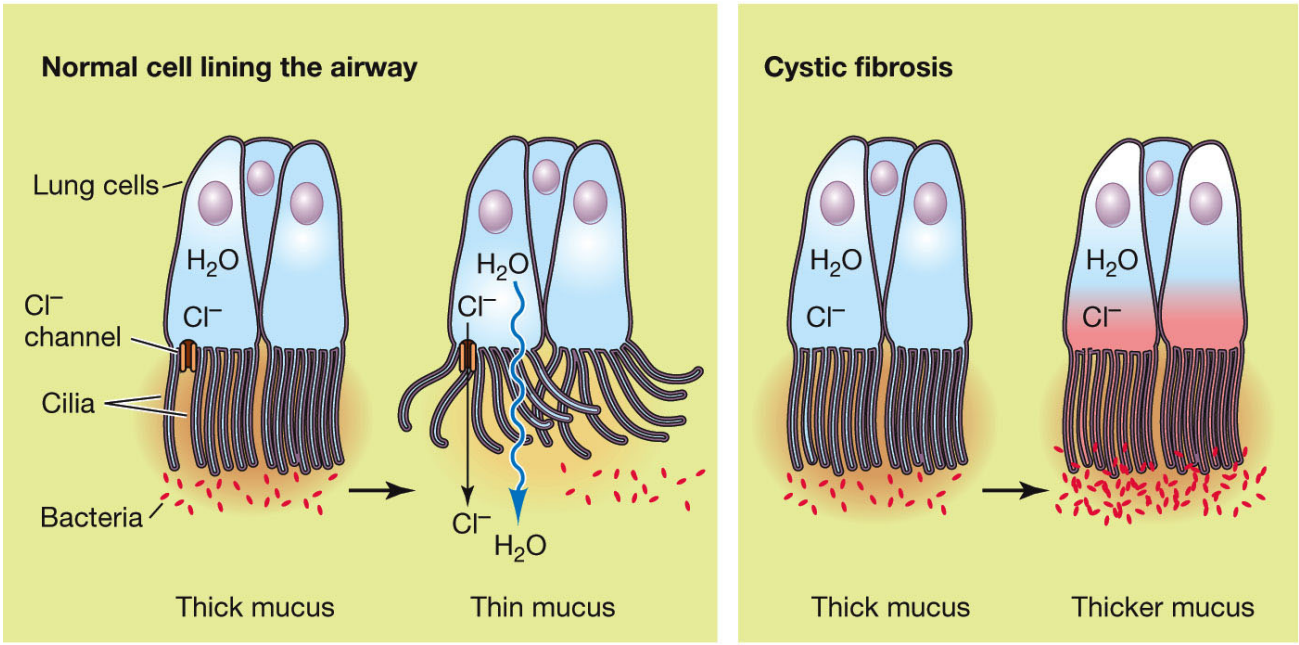


For hemoglobin S, one birth in

100 in African-Americans

A GENETIC DISEASE

Cystic fibrosis



1 birth in 4,000

GENETIC MEDICINE

A. Genetic diseases

B. ***Genetic testing***

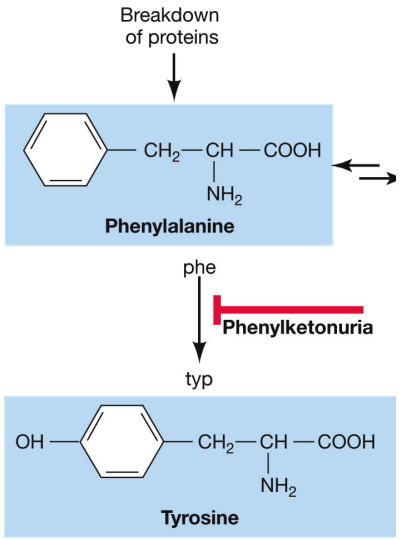
C. Genetics and cancer

D. Genome and treatment

GENETIC TESTING BY PHENOTYPE

Newborn screening for phenylketonuria

Blood sample from 2-4 day old infant



Measure phenylalanine in blood and look for very high level

Legally required

BENEFIT OF TESTING

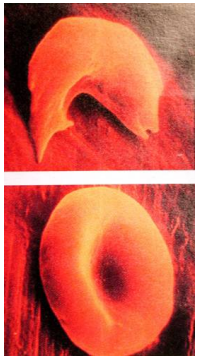
- Can diagnose the baby in time to treat and avoid all clinical consequences of the disease

  Treatment: Restrict phenylalanine in the diet. Result: no mental retardation

- Can test siblings of affected child to see if they are carriers for the disease (1 in 70 in the general population are carriers)

GENETIC TESTING BY DNA

	Sickle-cell anemia
Protein phenotype	hemoglobin
Length chain	146 amino acids
Normal	Pos. 6: glutamic acid
Disease	Pos. 6: valine
Length gene	1512 bp
Normal gene	Pos. 6: GAG
Disease gene	Pos. 6: GTG



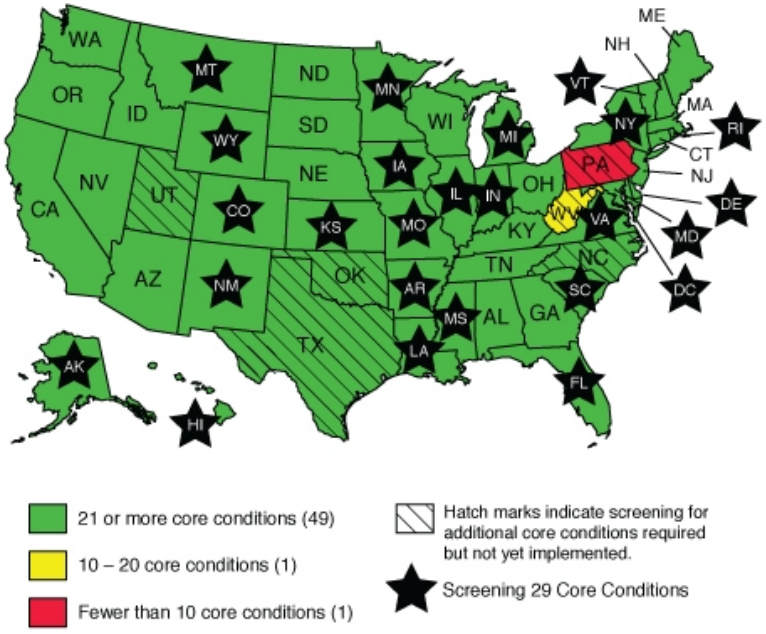
- Do not need red blood cells
- Can be done on any tissue at any time

Examine DNA for the specific change

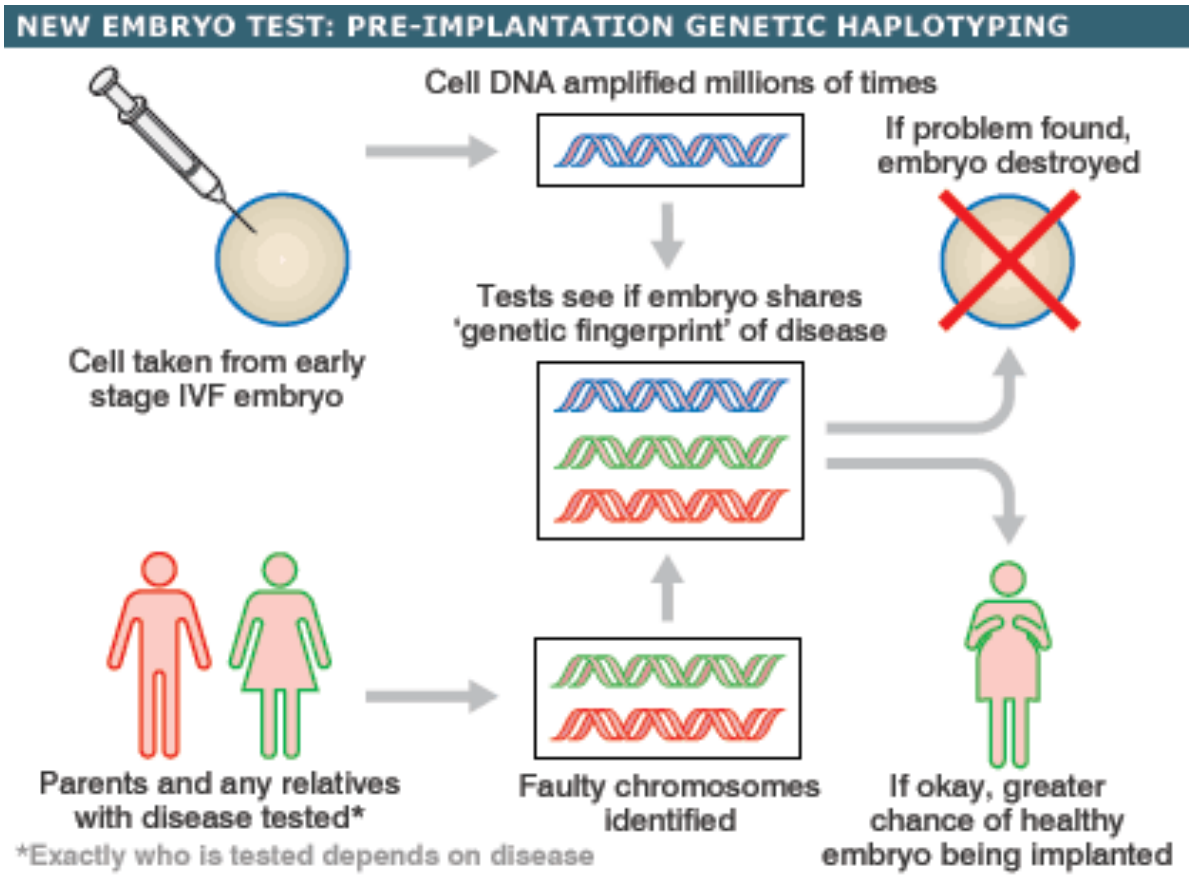
BENEFIT OF TESTING

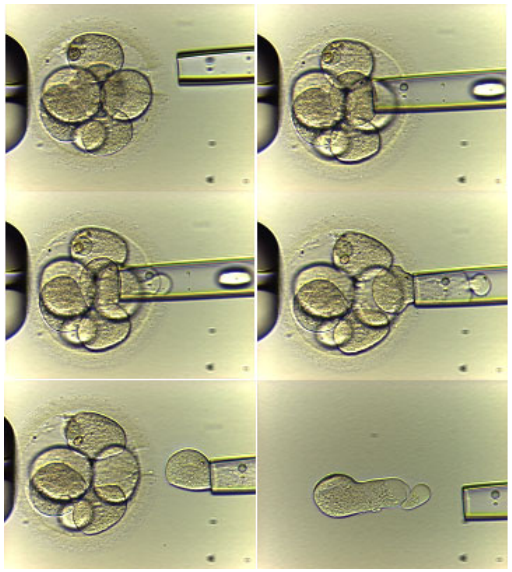
- Can use same blood drop in newborn screening for PKU or test at any time
- Can initiate therapy
- Genetic counseling for family

GENETIC TESTING OF NEWBORNS



PREIMPLANTATION TESTING





CARRIER TESTING

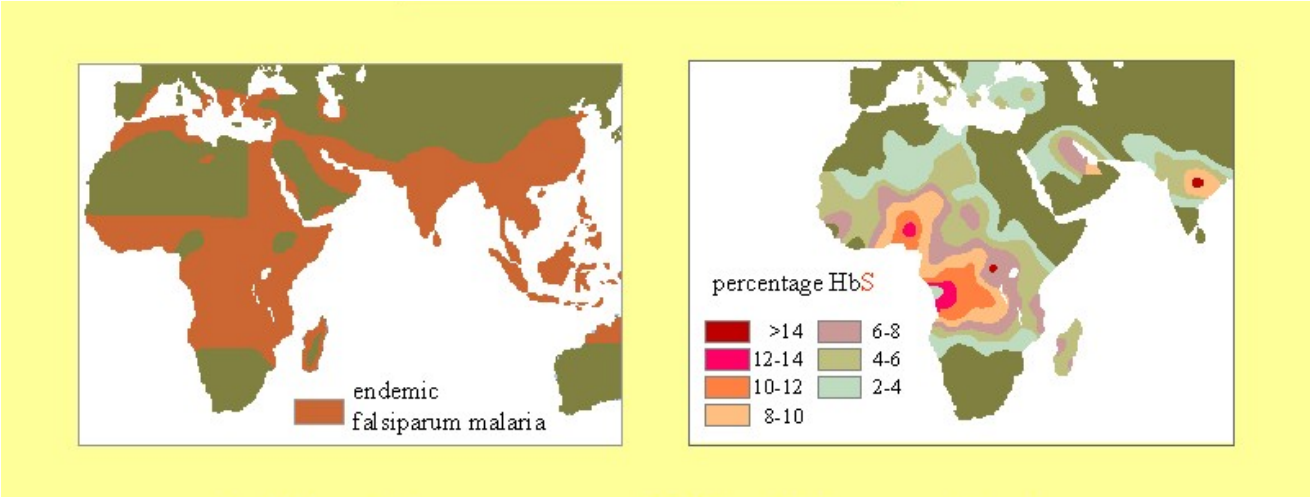
Achondrogenesis Type 1B
Achromatopsia
Alkaptonuria
Alpha-1 Antitrypsin Deficiency
Andermann Syndrome
ARSACS
Aspartylglycosaminuria
Ataxia With Vitamin E Deficiency
Ataxia-Telangiectasia
Autosomal Recessive Polycystic Kidney Disease
Bardet-Biedl Syndrome, BBS1-Related
Bardet-Biedl Syndrome, BBS10-Related
Beta Thalassemia
Biotinidase Deficiency
Bloom Syndrome
Canavan Disease
Carnitine Palmitoyltransferase IA Deficiency
Carnitine Palmitoyltransferase II Deficiency
Cartilage-Hair Hypoplasia
Choroideremia
CLN5-Related Neuronal Ceroid Lipofuscinosis
Congenital Disorder of Glycosylation Type Ia
Congenital Disorder of Glycosylation Type Ib
Congenital Finnish Nephrosis
Cystic Fibrosis
Cystinosis
Diastrophic Dysplasia
Factor V Leiden Thrombophilia
Factor XI Deficiency
Familial Dysautonomia
Familial Mediterranean Fever
Fanconi Anemia Type C
Fumarase Deficiency
Galactosemia
Gaucher Disease
GJB2-Related DFNB 1 Nonsyndromic Hearing Loss and Deafness
Glucose-6-Phosphate Dehydrogenase Deficiency
Glutaric Acidemia Type 1
Glycogen Storage Disease Type Ia
Glycogen Storage Disease Type Ib
Glycogen Storage Disease Type III
Glycogen Storage Disease Type V
GRACILE Syndrome
Hereditary Fructose Intolerance
Hereditary Thymine-Uraciluria
Herlitz Junctional Epidermolysis Bullosa, LAMA3-Related
Herlitz Junctional Epidermolysis Bullosa, LAMB3-Related

- Hexosaminidase A Deficiency
- HFE-Associated Hereditary Hemochromatosis
- Homocystinuria Caused by Cystathionine Beta-Synthase Deficiency
- Hurler Syndrome
- Hyperornithinemia-Hyperammonemia-Homocitrullinuria Syndrome
- Hypophosphatasia, Autosomal Recessive
- Inclusion Body Myopathy 2
- Infantile Refsum Disease
- Isovaleric Acidemia
- Krabbe Disease
- Leigh Syndrome, French-Canadian Type
- Limb-Girdle Muscular Dystrophy Type 2E
- Long Chain 3-Hydroxyacyl-CoA Dehydrogenase Deficiency
- Maple Syrup Urine Disease Type 1B
- Maple Syrup Urine Disease Type 3
- Medium Chain Acyl-CoA Dehydrogenase Deficiency
- Metachromatic Leukodystrophy
- Mucolipidosis IV
- Muscle-Eye-Brain Disease
- MYH-Associated Polyposis
- Niemann-Pick Disease Type A
- Niemann-Pick Disease Type C
- Nijmegen Breakage Syndrome
- Northern Epilepsy
- Pendred Syndrome
- Phenylalanine Hydroxylase Deficiency
- Polyglandular Autoimmune Syndrome Type 1
- Pompe Disease
- PPT1-Related Neuronal Ceroid Lipofuscinosis
- Primary Hyperoxaluria Type 1
- Primary Hyperoxaluria Type 2
- Pycnodysostosis
- Recessive Multiple Epiphyseal Dysplasia
- Rhizomelic Chondrodysplasia Punctata Type 1
- Salla Disease
- Segawa Syndrome
- Short Chain Acyl-CoA Dehydrogenase Deficiency
- Sickle Cell Disease
- Sjogren-Larsson Syndrome
- Smith-Lemli-Opitz Syndrome
- Spinal Muscular Atrophy
- Tay-Sachs Disease
- TPP1-Related Neuronal Ceroid Lipofuscinosis
- Tyrosinemia Type I
- Usher Syndrome Type 1F
- Usher Syndrome Type 3
- Wilson Disease
- X-Linked Juvenile Retinoschisis

EVOLUTION AND THE GENOME: NATURAL SELECTION OF A DISEASE GENE

Malaria

Sickle-cell disease



GENETIC TESTING OF SPECIFIC POPULATIONS

	Overall US: carriers	Jews in US: carriers
Canavan disease	1 in 800	1 in 40
Familial dysautonomia	1 in 3000	1 in 30
Gaucher disease	1 in 200	1 in 16
Niemann-Pick disease	1 in 400	1 in 80
Tay-Sachs disease	1 in 250	1 in 25

JEWISH GENETIC DISEASES EDUCATION AND SCREENING EVENT

SUNDAY, MARCH 14, 2010

10:00 AM - 4:00 PM

INA LEVINE JEWISH COMMUNITY CAMPUS

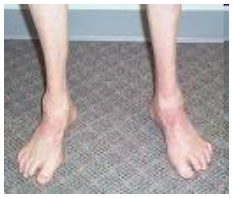
12701 N. SCOTTSDALE ROAD

L'DOR From Generation To Generation V'DOR

Jewish Genetic Diseases Center of Greater Phoenix

WHOLE GENOME SEQUENCING AND DISEASE

Charcot-Marie-Tooth Disease: inherited; 1 in 2,500 births (common)



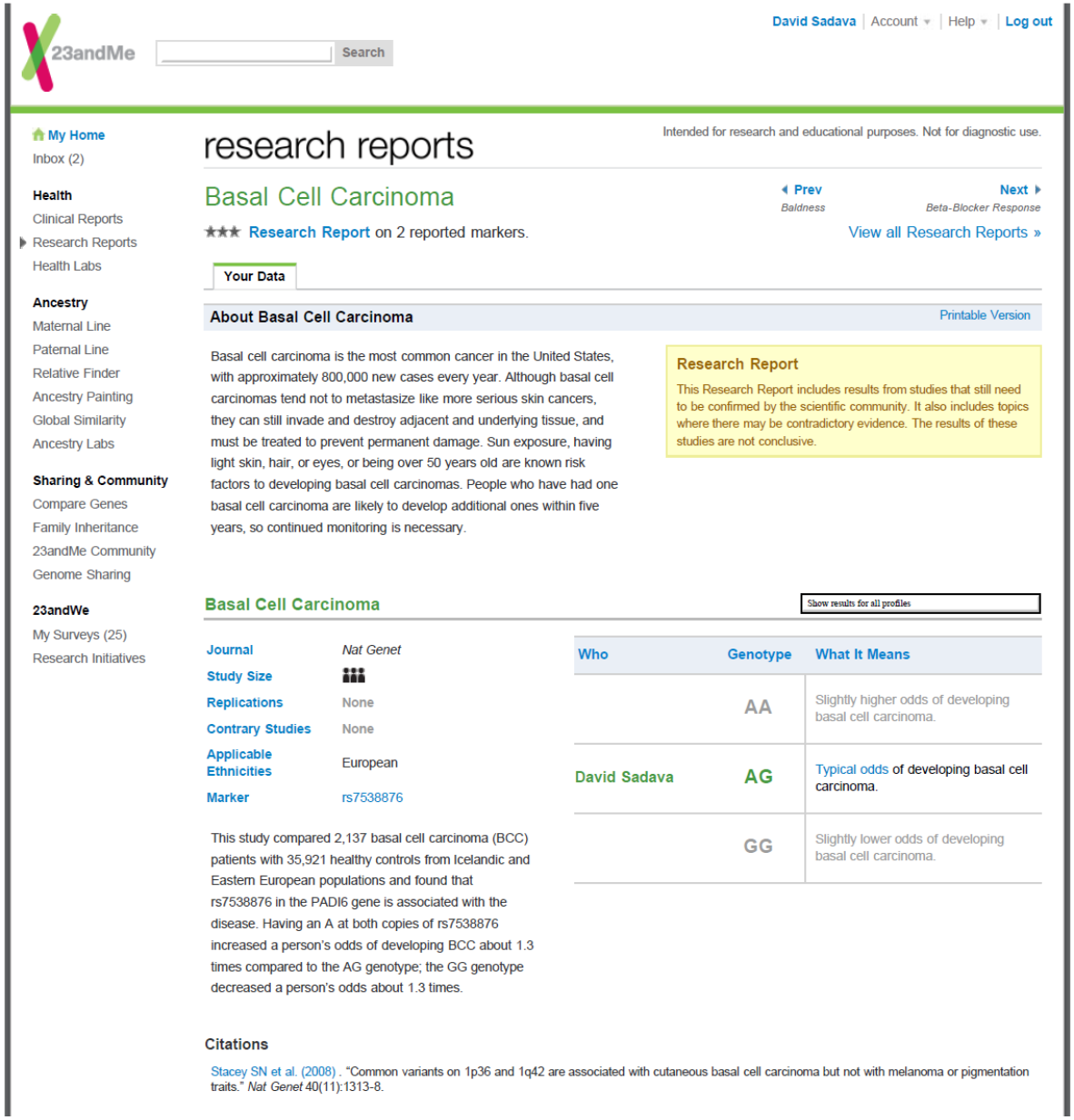
Variable symptoms: neurological;
foot drop, limb weakness,
hammer toes, carpal tunnel

Treated with physical therapy

Method: sequenced entire genome of patient (2010)
looked for mutations in some candidate genes
found one mutated: *SH3TC2* (expressed in nervous system)
found same mutation in family: carriers

Significance: First gene for disease identified by whole genome sequencing
Target for therapy

GENETIC TESTING BY SNP



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Basal Cell Carcinoma

Prev *Baldness* | Next *Beta-Blocker Response*

★★★ Research Report on 2 reported markers.

View all Research Reports »

Your Data

About Basal Cell Carcinoma Printable Version

Basal cell carcinoma is the most common cancer in the United States, with approximately 800,000 new cases every year. Although basal cell carcinomas tend not to metastasize like more serious skin cancers, they can still invade and destroy adjacent and underlying tissue, and must be treated to prevent permanent damage. Sun exposure, having light skin, hair, or eyes, or being over 50 years old are known risk factors to developing basal cell carcinomas. People who have had one basal cell carcinoma are likely to develop additional ones within five years, so continued monitoring is necessary.

Research Report

This Research Report includes results from studies that still need to be confirmed by the scientific community. It also includes topics where there may be contradictory evidence. The results of these studies are not conclusive.

Basal Cell Carcinoma

Show results for all profiles

Journal	*Nat Genet*
Study Size	
Replications	None
Contrary Studies	None
Applicable Ethnicities	European
Marker	rs7538876

This study compared 2,137 basal cell carcinoma (BCC) patients with 35,921 healthy controls from Icelandic and Eastern European populations and found that rs7538876 in the PADI6 gene is associated with the disease. Having an A at both copies of rs7538876 increased a person's odds of developing BCC about 1.3 times compared to the AG genotype; the GG genotype decreased a person's odds about 1.3 times.

Who	Genotype	What It Means
	AA	Slightly higher odds of developing basal cell carcinoma.
David Sadava	AG	Typical odds of developing basal cell carcinoma.
	GG	Slightly lower odds of developing basal cell carcinoma.

Citations

Stacey SN et al. (2008) . "Common variants on 1p36 and 1q42 are associated with cutaneous basal cell carcinoma but not with melanoma or pigmentation traits." *Nat Genet* 40(11):1313-8.

GENETIC MEDICINE

A. Genetic diseases

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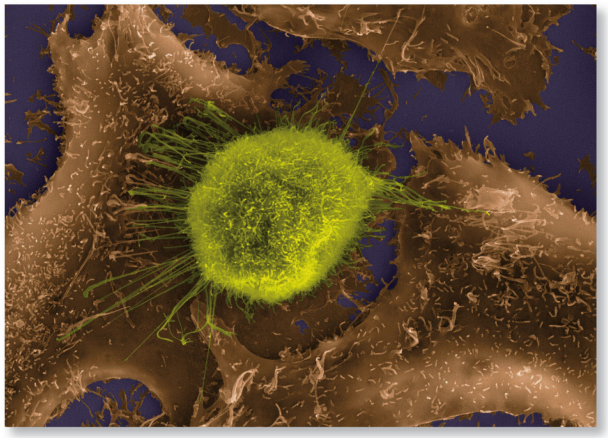
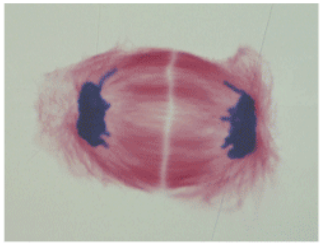
C. ***Genetics and cancer***

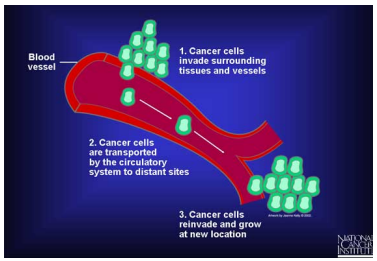
D. Genome and treatment

SMALL-CELL LUNG CARCINOMA CELL WITH NORMAL CELLS

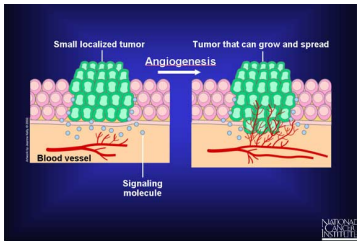




Inappropriate cell reproduction



Metastasis



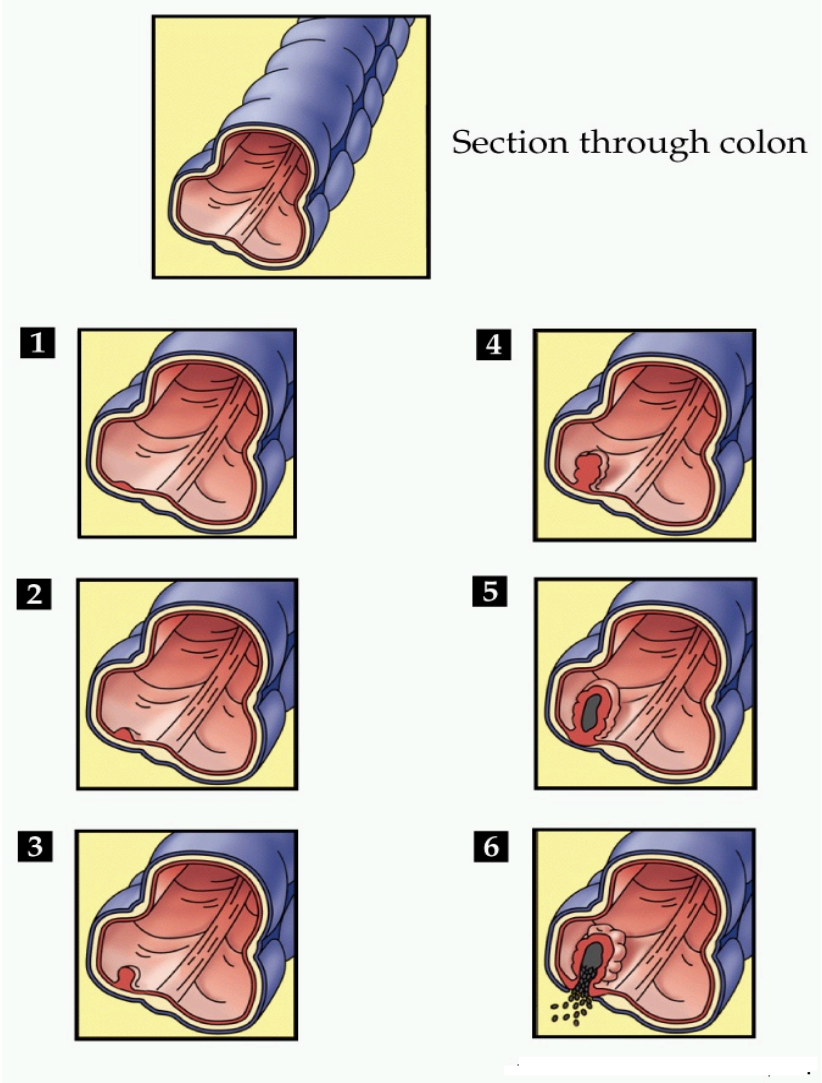
Angiogenesis

GENES CHANGED IN CANCER

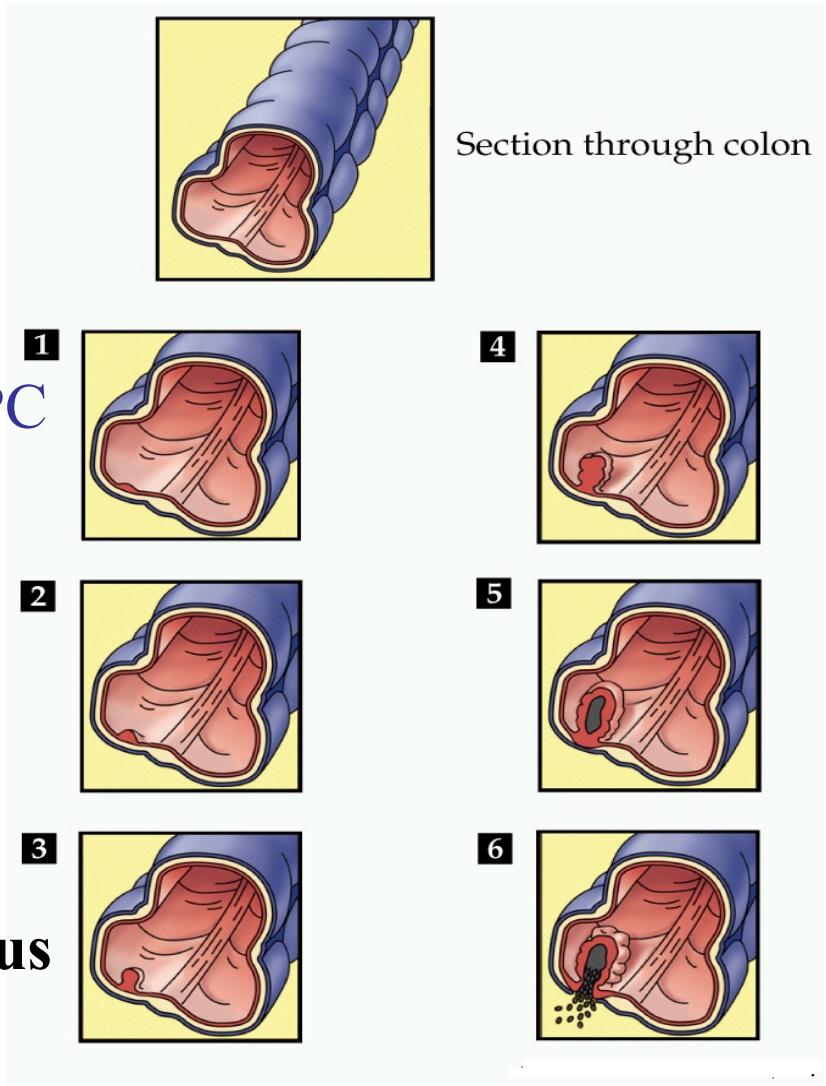
ONCOGENES:
"Gas pedals" to stimulate cell reproduction

TUMOR SUPPRESSOR GENES:
"Brakes" cut off so reproduction is allowed to occur

THE PATH TO COLON CANCER



THE PATH TO COLON CANCER



Mutation in APC gene: **Polyp**

Mutation in ras gene: **Precancerous lesion**

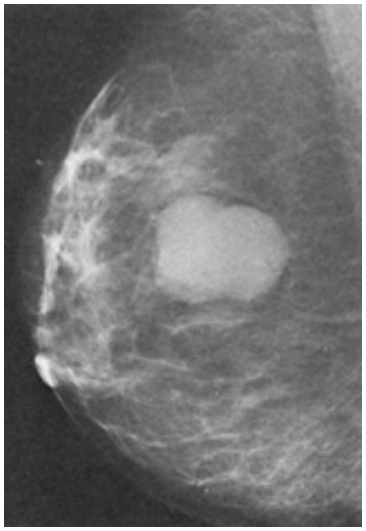
Mutation in DCC gene: **Adenoma**

Mutation in p53 gene: **Carcinoma**

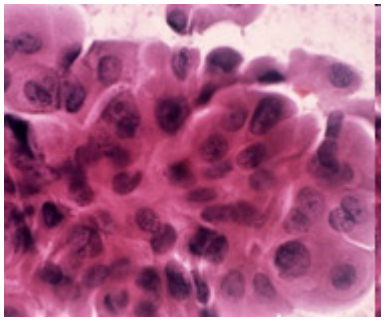
Mutation in anti-metastasis genes: **Metastatic tumor**

BREAST CANCER

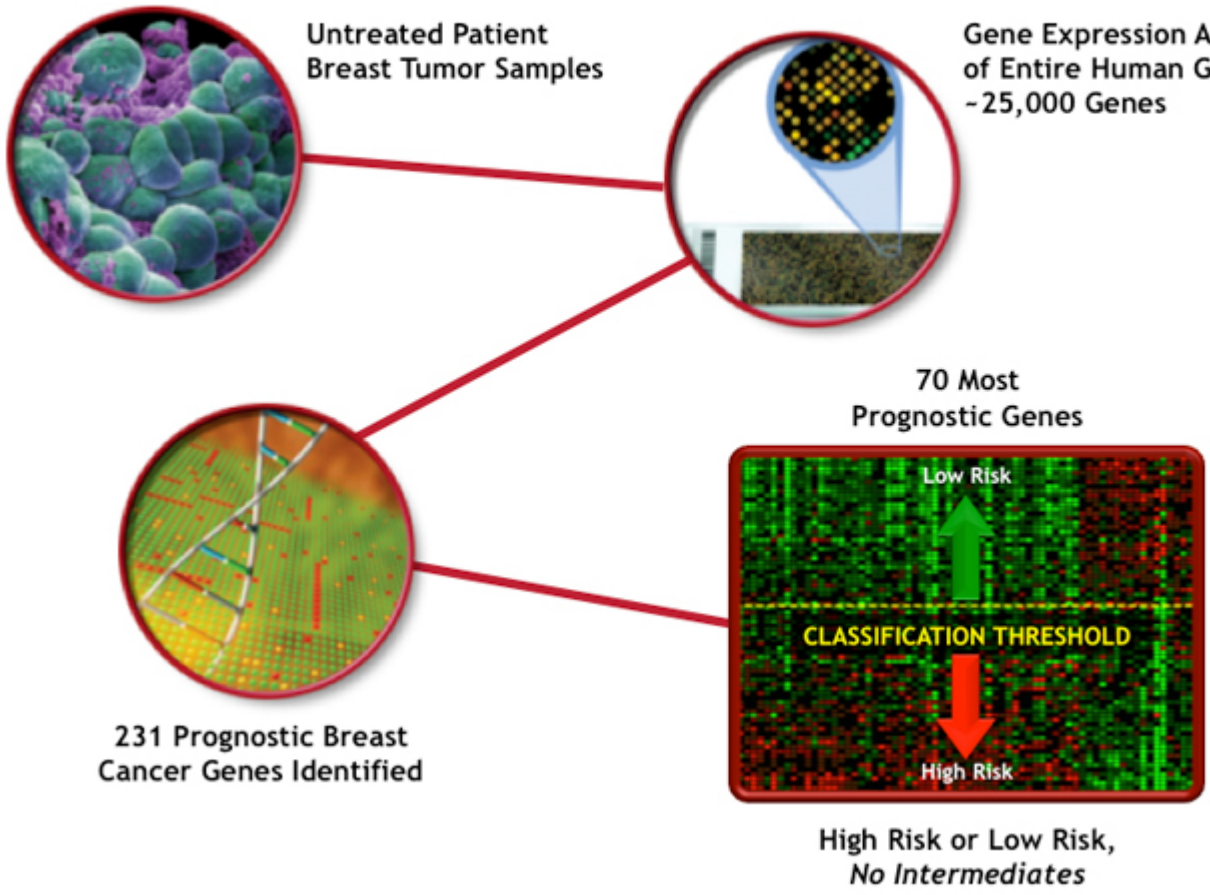
192,370 new cases,
40,170 deaths,
USA, 2009



Problem: Prognosis after surgery



GENE EXPRESSION SIGNATURE FOR BREAST CANCER



GENETIC MEDICINE

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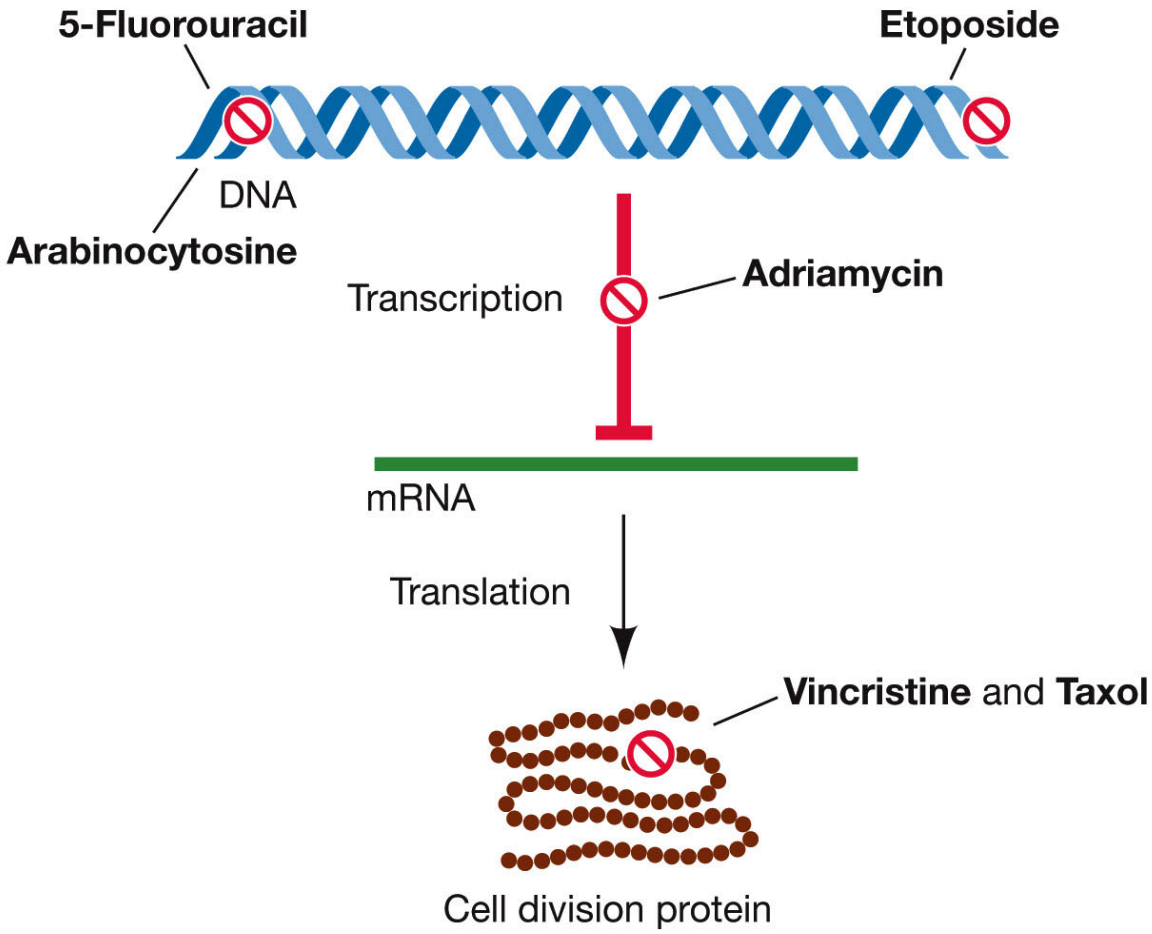
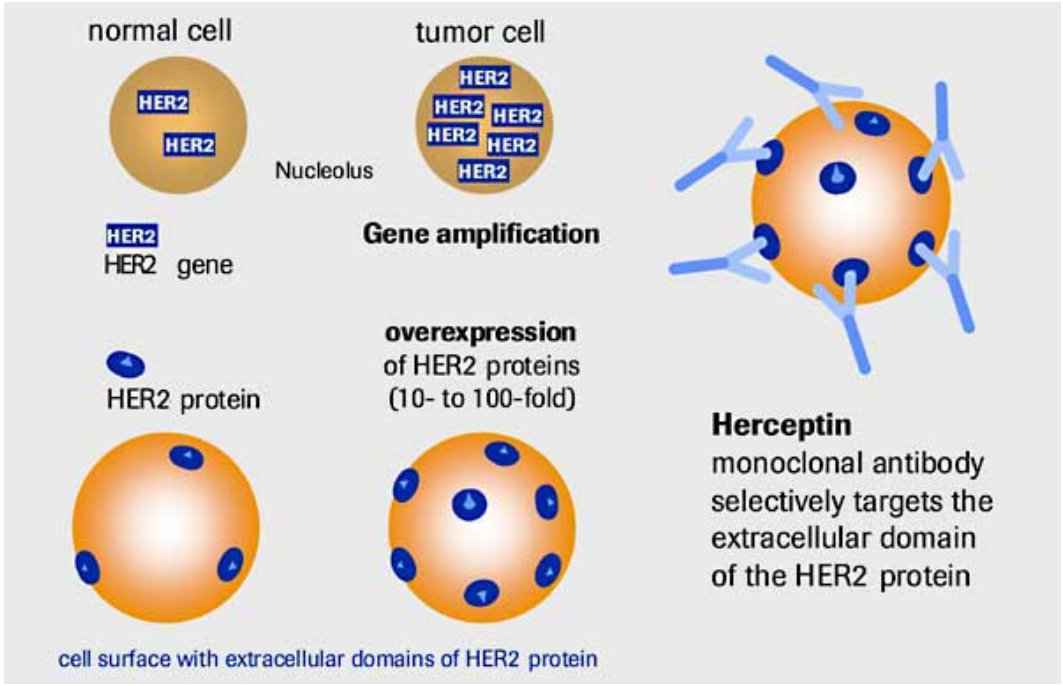
C. Genetics and cancer

D. ***Genome and treatment***

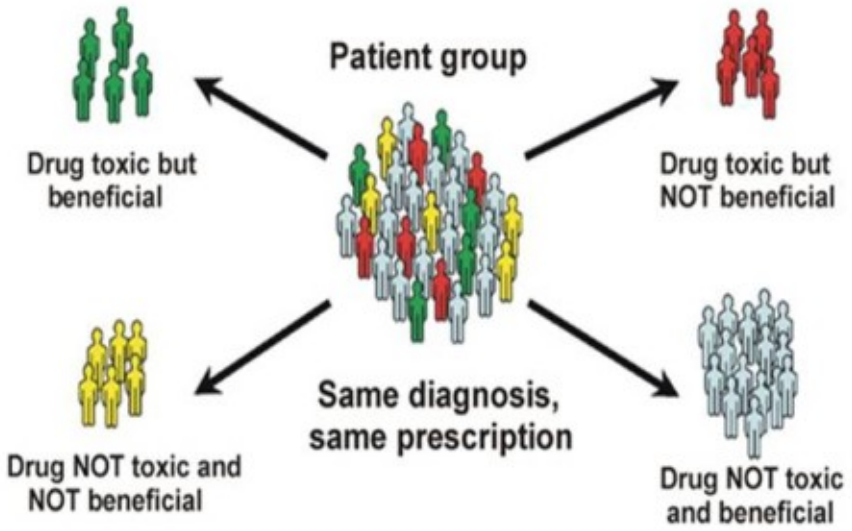
CHEMOTHERAPY FOR CANCER: GENERAL



CHEMOTHERAPY FOR CANCER: SPECIFIC



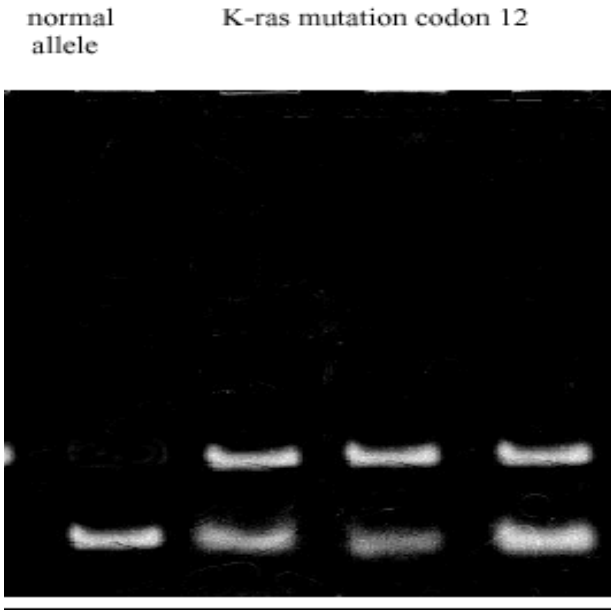
PHARMACOGENOMICS



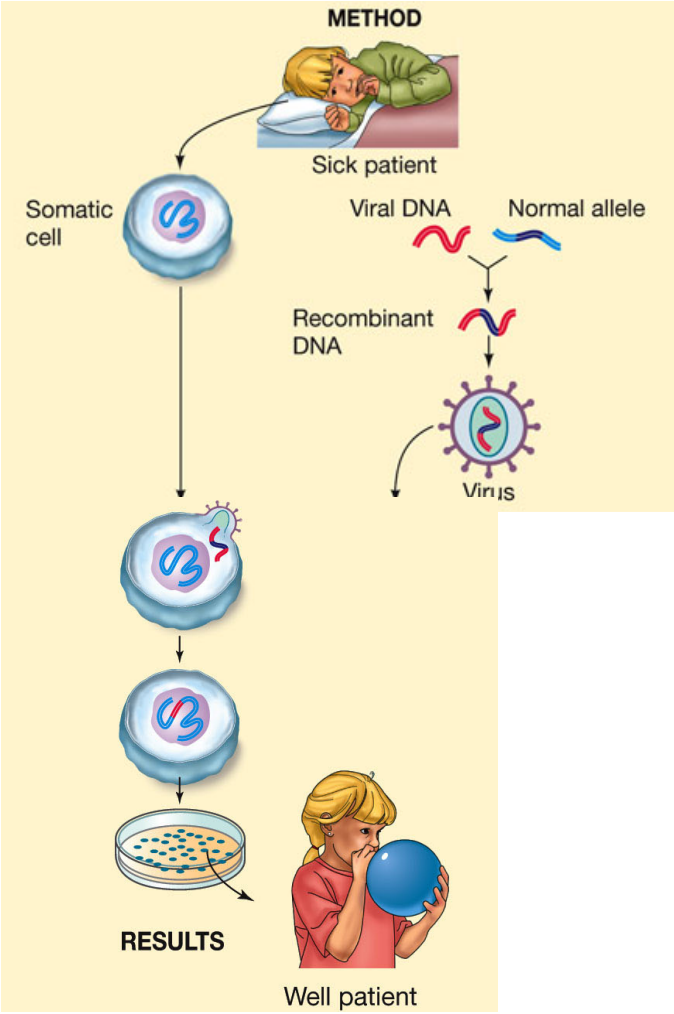
Identify patient groups by SNP

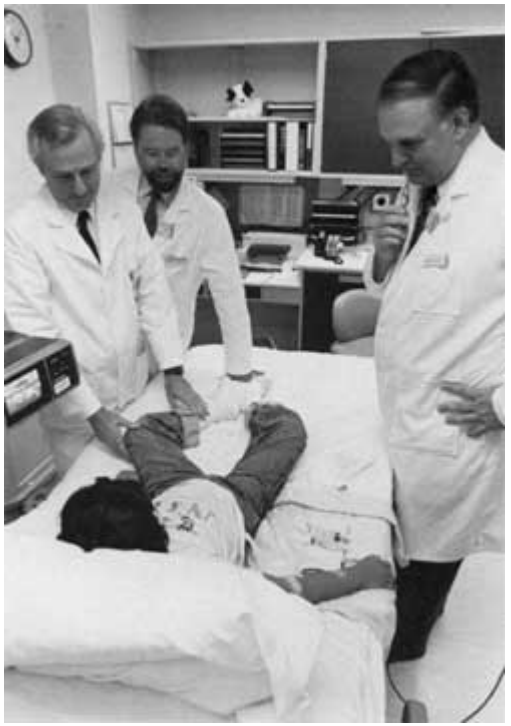
PHARMACOGENOMICS: CANCER

- *KRAS* DNA mutation makes protein less susceptible to treatment with cetuximab
- Genetic test on tumor tissue to choose treatment



GENE THERAPY FOR IMMUNODEFICIENCY





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