Public Health in the High Definition Precision Health Care Era

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American Institute of Dental Public Health Colloquium

San Antonio, Texas

January 25th and 26th 2018

"...I am painting what I see!" Rene Magritte

High Definition Precision Dental Public Health Care

- Concepts: Phenotype + Genotype + Environment= Precision or Personalized Health Care
- President Obama' Initiative "Precision Medicine" State-of-the-Union, January 20th, 2015
- *So, what's happening by January 2018? How are we (society and health care professionals) preparing for "Precision Health Care"?*

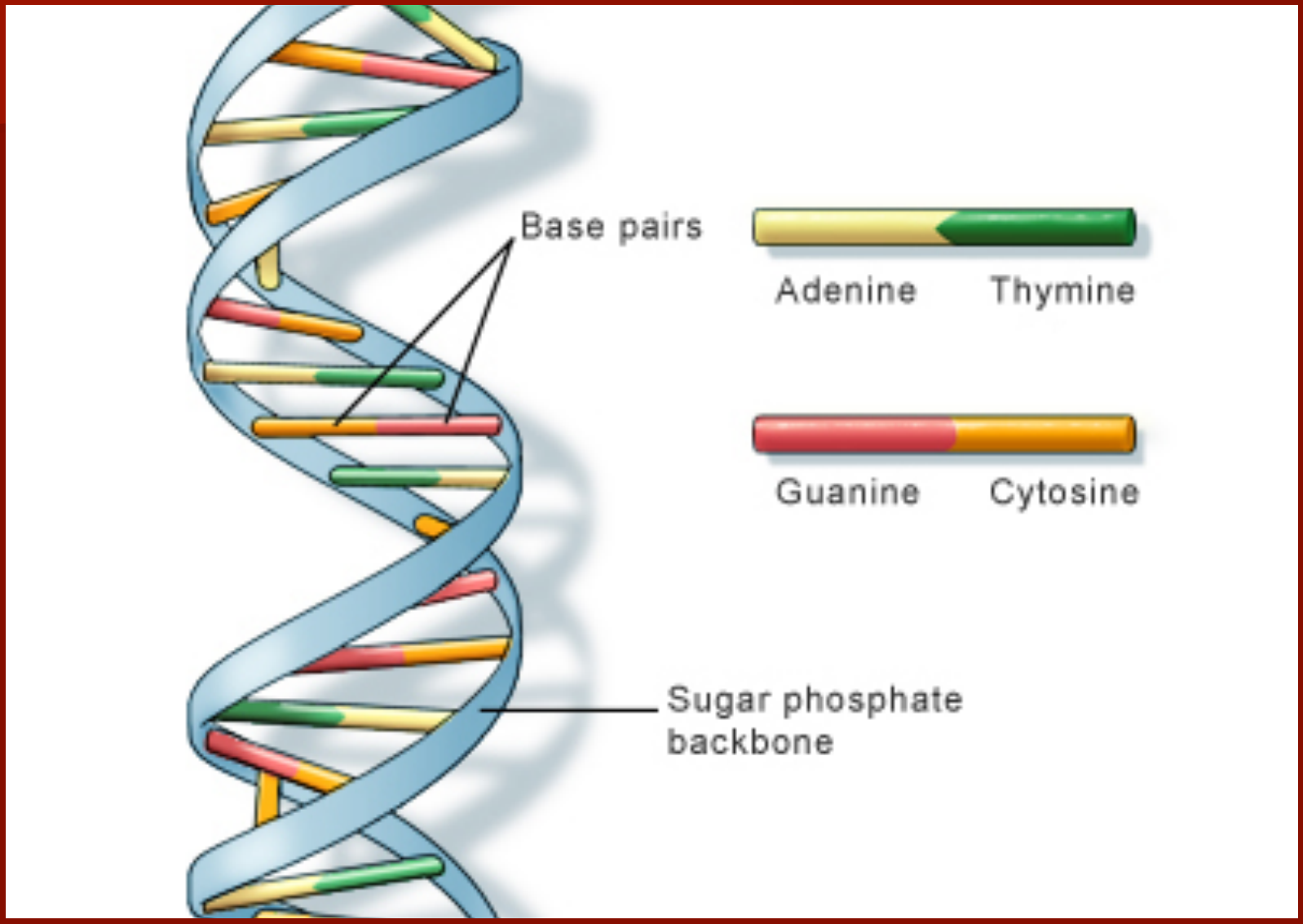
Rosalind Franklin made the seminal discovery based on x-ray diffraction studies of adenoviral DNA (1952): "base-pairing, A to T and C to G, maybe double helix?"

Norman Simmons (dentist, postdoc) prepared the adenoviral DNA preparations

…from Rosiland Franklin's x-ray crystallography data to Watson and Crick's 3D model of deoxyribonucleic acid…

Sixty-five years ago, February 28th, 1953, two young scientists walked into the Eagle pub in Cambridge, England, and announced that they had discovered the secret of life…James Watson & Francis Crick based on data from Rosalind Franklin and Norman Simmons

DNA (deoxyribonucleic acid), Genetics and Genomics



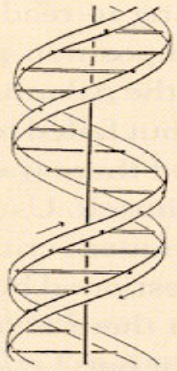
MOLECULAR STRUCTURE OF NUCLEIC ACIDS

A Structure for Deoxyribose Nucleic Acid

WE wish to suggest a structure for the salt of deoxyribose nucleic acid (D.N.A.). This structure has novel features which are of considerable biological interest.

A structure for nucleic acid has already been proposed by Pauling and Corey[1]. They kindly made their manuscript available to us in advance of publication. Their model consists of three intertwined chains, with the phosphates near the fibre axis, and the bases on the outside. In our opinion, this structure is unsatisfactory for two reasons: (1) We believe that the material which gives the X-ray diagrams is the salt, not the free acid. Without the acidic hydrogen atoms it is not clear what forces would hold the structure together, especially as the negatively charged phosphates near the axis will repel each other. (2) Some of the van der Waals distances appear to be too small.

Another three-chain structure has also been suggested by Fraser (in the press). In his model the phosphates are on the outside and the bases on the inside, linked together by hydrogen bonds. This structure as described is rather ill-defined, and for this reason we shall not comment on it.



This figure is purely diagrammatic. The two ribbons symbolize the two phosphate–sugar chains, and the horizontal rods the pairs of bases holding the chains together. The vertical line marks the fibre axis

We wish to put forward a radically different structure for the salt of deoxyribose nucleic acid. This structure has two helical chains each coiled round the same axis (see diagram). We have made the usual chemical assumptions, namely, that each chain consists of phosphate diester groups joining β-D-deoxyribofuranose residues with 3′,5′ linkages. The two chains (but not their bases) are related by a dyad perpendicular to the fibre axis. Both chains follow right-handed helices, but owing to the dyad the sequences of the atoms in the two chains run in opposite directions. Each chain loosely resembles Furberg's[2] model No. 1; that is, the bases are on the inside of the helix and the phosphates on the outside. The configuration of the sugar and the atoms near it is close to Furberg's 'standard configuration', the sugar being roughly perpendicular to the attached base. There is a residue on each chain every 3·4 A. in the *z*-direction. We have assumed an angle of 36° between adjacent residues in the same chain, so that the structure repeats after 10 residues on each chain, that is, after 34 A. The distance of a phosphorus atom from the fibre axis is 10 A. As the phosphates are on the outside, cations have easy access to them.

The structure is an open one, and its water content is rather high. At lower water contents we would expect the bases to tilt so that the structure could become more compact.

The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases. The planes of the bases are perpendicular to the fibre axis. They are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side with identical *z*-co-ordinates. One of the pair must be a purine and the other a pyrimidine for bonding to occur. The hydrogen bonds are made as follows: purine position 1 to pyrimidine position 1; purine position 6 to pyrimidine position 6.

If it is assumed that the bases only occur in the structure in the most plausible tautomeric forms (that is, with the keto rather than the enol configurations) it is found that only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine).

In other words, if an adenine forms one member of a pair, on either chain, then on these assumptions the other member must be thymine; similarly for guanine and cytosine. The sequence of bases on a single chain does not appear to be restricted in any way. However, if only specific pairs of bases can be formed, it follows that if the sequence of bases on one chain is given, then the sequence on the other chain is automatically determined.

It has been found experimentally[3,4] that the ratio of the amounts of adenine to thymine, and the ratio of guanine to cytosine, are always very close to unity for deoxyribose nucleic acid.

It is probably impossible to build this structure with a ribose sugar in place of the deoxyribose, as the extra oxygen atom would make too close a van der Waals contact.

The previously published X-ray data[5,6] on deoxyribose nucleic acid are insufficient for a rigorous test of our structure. So far as we can tell, it is roughly compatible with the experimental data, but it must be regarded as unproved until it has been checked against more exact results. Some of these are given in the following communications. We were not aware of the details of the results presented there when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.

It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material.

Full details of the structure, including the conditions assumed in building it, together with a set of co-ordinates for the atoms, will be published elsewhere.

We are much indebted to Dr. Jerry Donohue for constant advice and criticism, especially on interatomic distances. We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at King's College, London. One of us (J. D. W.) has been aided by a fellowship from the National Foundation for Infantile Paralysis.

J. D. WATSON
F. H. C. CRICK

Medical Research Council Unit for the Study of the Molecular Structure of Biological Systems,
Cavendish Laboratory, Cambridge.
April 2.

[1] Pauling, L., and Corey, R. B., *Nature*, **171**, 346 (1953); *Proc. U.S. Nat. Acad. Sci.*, **39**, 84 (1953).
[2] Furberg, S., *Acta Chem. Scand.*, **6**, 634 (1952).
[3] Chargaff, E., for references see Zamenhof, S., Brawerman, G., and Chargaff, E., *Biochim. et Biophys. Acta*, **9**, 402 (1952).
[4] Wyatt, G. R., *J. Gen. Physiol.*, **36**, 201 (1952).
[5] Astbury, W. T., Symp. Soc. Exp. Biol. 1, Nucleic Acid, 66 (Camb. Univ. Press, 1947).
[6] Wilkins, M. H. F., and Randall, J. T., *Biochim. et Biophys. Acta*, **10**, 192 (1953).

The Human Genome Project 1988 – 2003 (and beyond)

- **Sequencing & assembly of the human genome**
- **Translating genomics for health care providers, policy makers & consumers**
- **Genes & individualized therapeutics**
- **SNPs and population screening**
- **Genomics (microbial, plant, animal & human) and impact on biotechnology & evolution**
- **CRISPR/Cas9 System and Gene-Editing (2012-)**

June 26th, 2000 at White House Ceremony

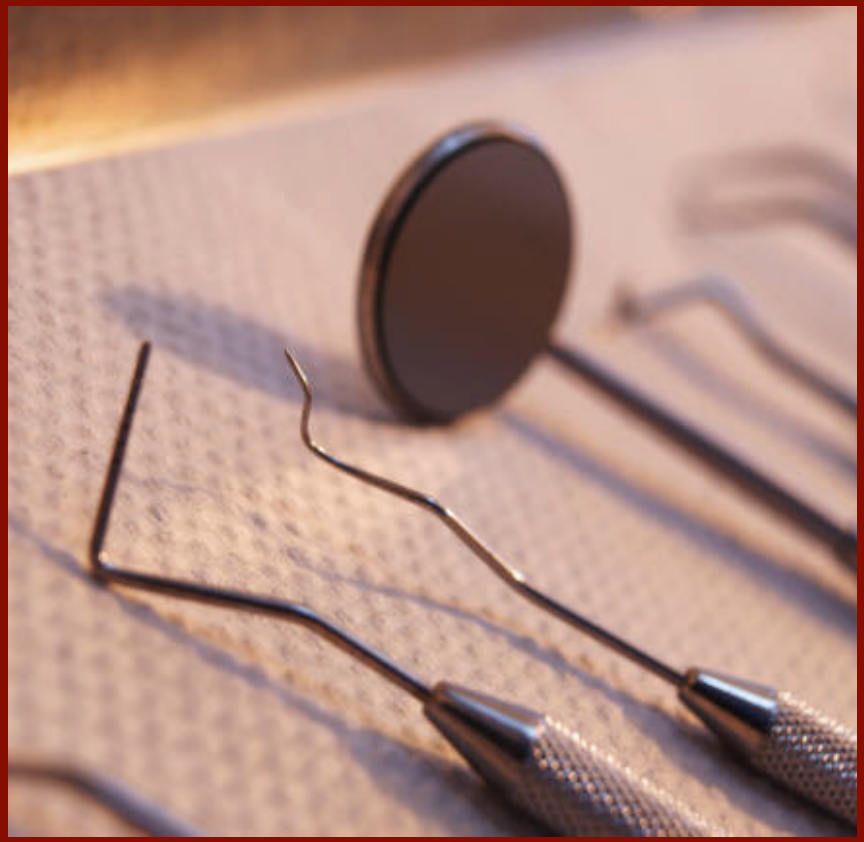
"A 95% draft of the map of life is completed!"

Craig Venter (Celera), President Clinton & Francis Collins (NIH)

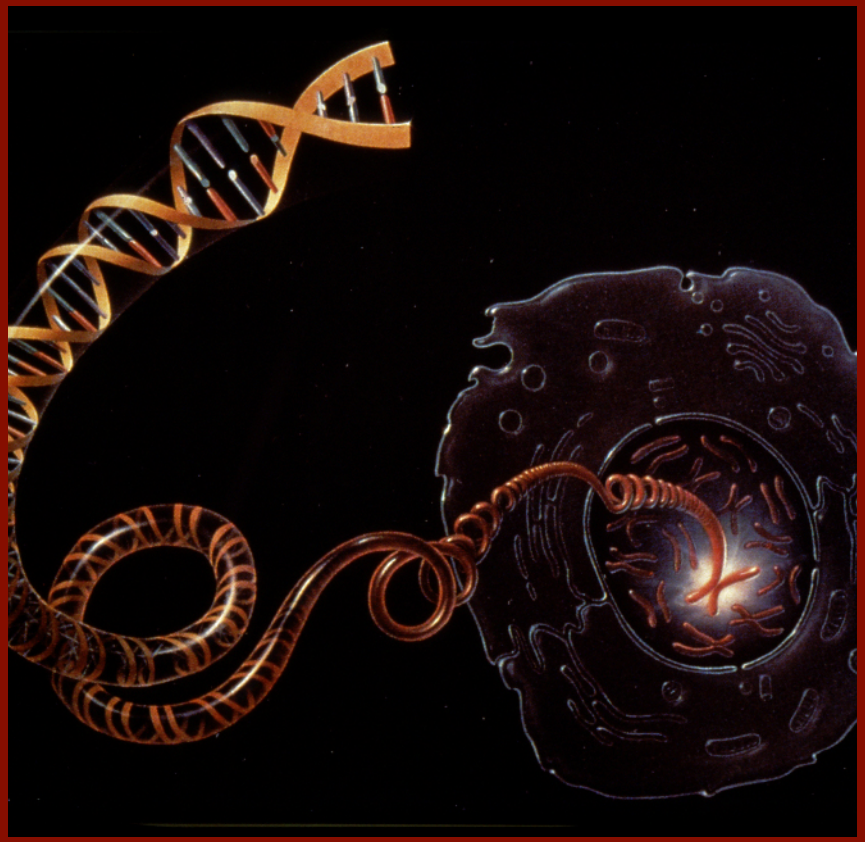
PHENOTYPE + GENOTYPE

from single nucleotide to patient, family & population traits

Phenomics



Genomics



What's *Phenotype* versus *Genotype*?

Phenotype? The physical, behavioral, and biochemical characteristics of an organism as the result of the interactions between genes and environment. Examples are height, weight, facial features, skin color, personality, oral and writing attributes, wound healing, responses to drugs, immunity, blood type, blood chemistry, etc.

Genotype or Genome? The genetic makeup of an organism with reference to a single trait (Mendelian Inheritance), set of traits, or an entire complex of traits (Human Complex Diseases & Disorders); the sum total of genes transmitted from parent to offspring. Human genome is DNA inherited from parents that reside in the *nucleus* of each somatic cell + the DNA specifically inherited from our mothers located within the *mitochondria* found in all somatic cells.

Human Biome? A term that includes nuclear DNA, mitochondrial DNA, and the associated microbial DNA found within many hundreds of families of virus, bacteria and yeast organisms living within and upon humans (*microbial genome*).

DECODING THE HUMAN GENOME: ENTER HIGH DEFINITION PRECISION DENTAL PUBLIC HEALTH

- **TNFSF4: Heart Attacks**
- **LCT: Lactose Intolerance**
- **CLOCK: Evening Preference**
- **SLC6A3: Substance Abuse**
- **CHRNA6: Linked to Tobacco Addiction**
- **OCA2: Blue Eyes**
- **Multiple genes for inflammation (Human Complex Diseases), cancers, & wound healing**

NextSeq 500 Desktop Sequencer (from Illumina, San Diego)

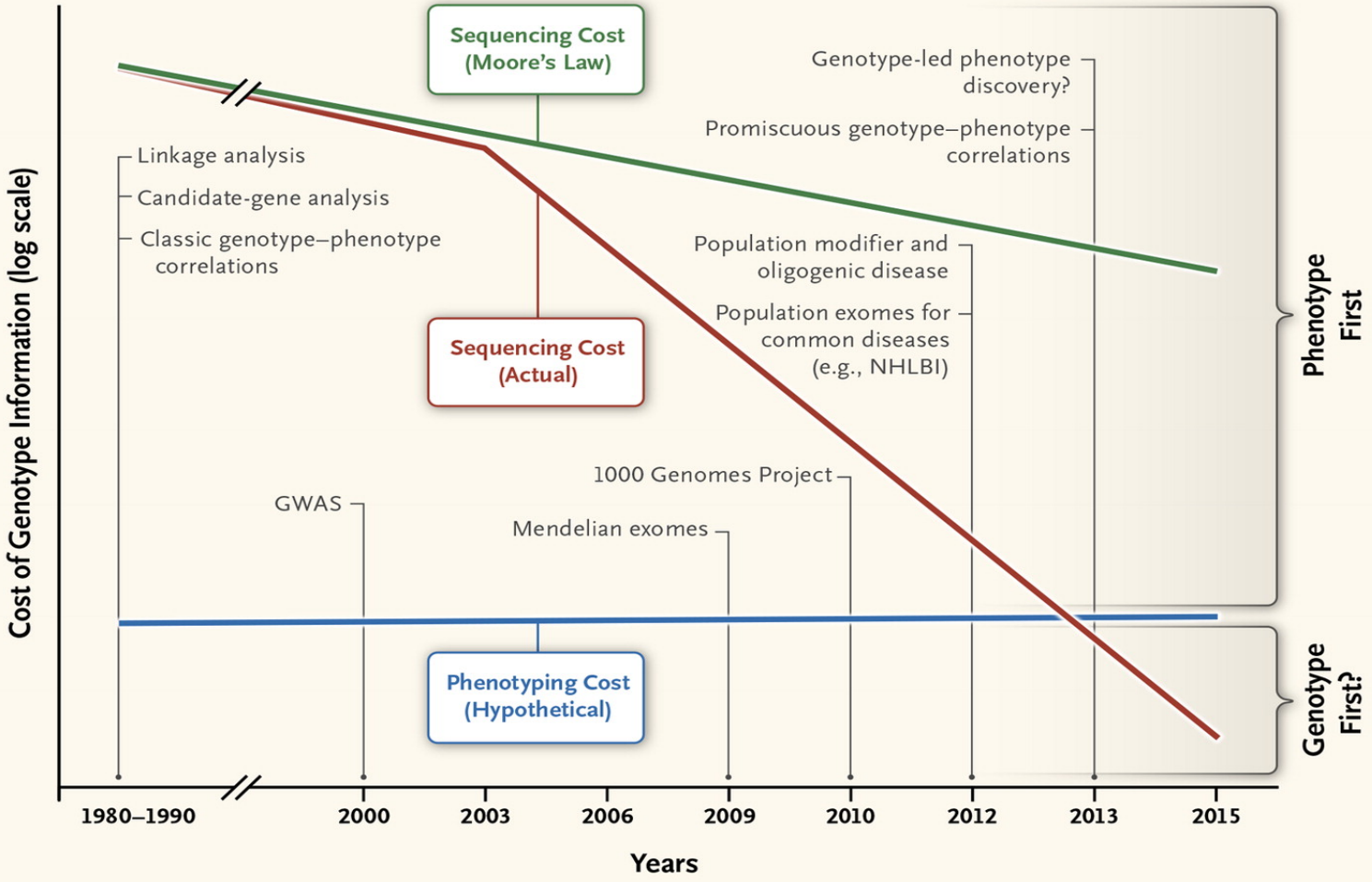
- Faster (complete genome 8-12 hrs)
- Cheaper (< $1,000 per human genome)
- Smarter (precise, efficient, accurate)
- DNA and RNA sequencing
- FDA approved in late 2013
- In 2017, now utilized in inherited disease detection, genetic variance and risk assessments, stratification of patients within large populations, and cancer diagnostics for treatment/chemotherapy selections (pharmacogenomics)

In 2013, global DNA sequencing was $4.6 billion

In 2017, global DNA sequencing was $10.096 billion

USA and China are > 75% of global DNA sequencing for microbiome, plant and animal genomes, and human genomics

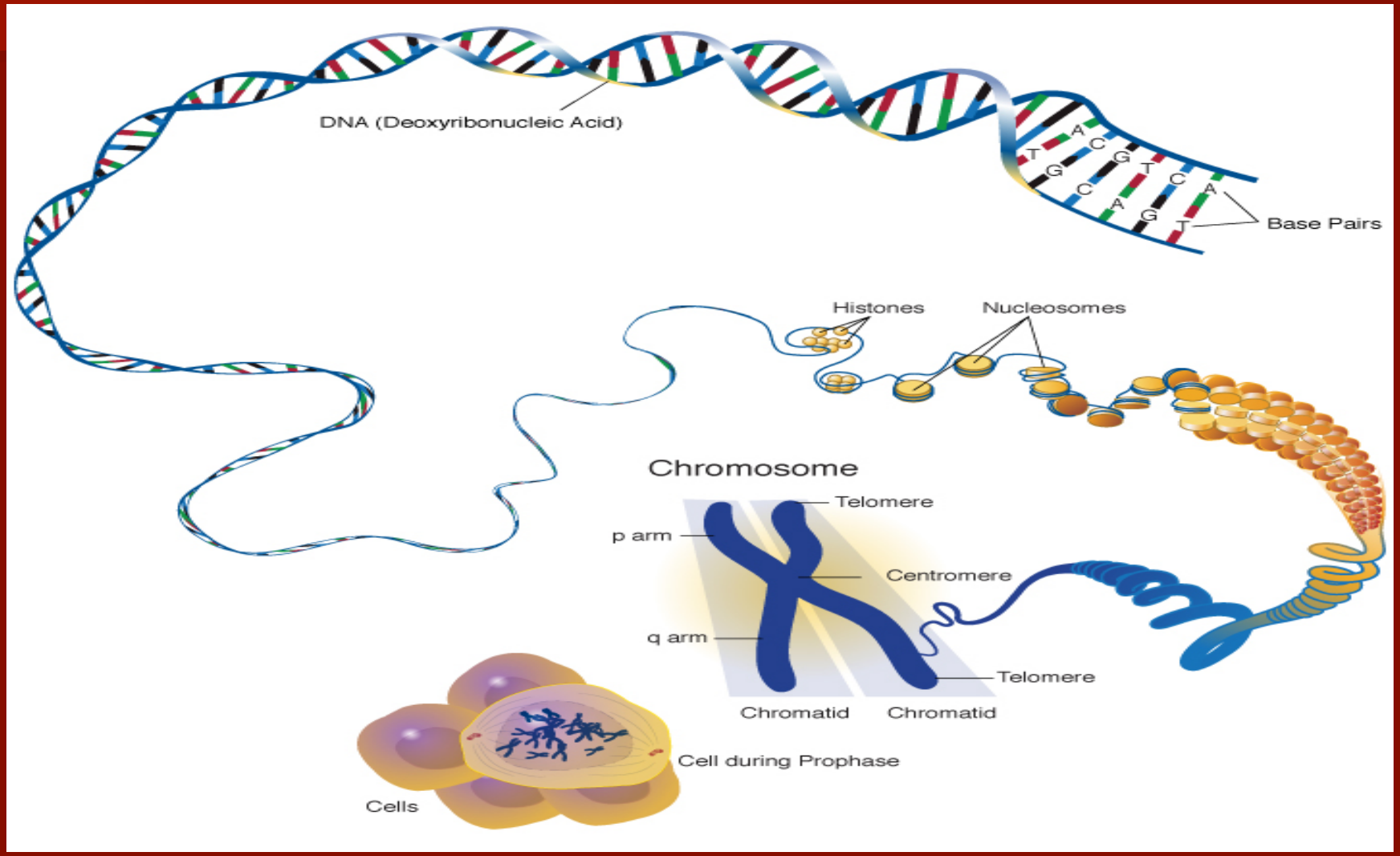
The Decreasing Cost of Genotype Information



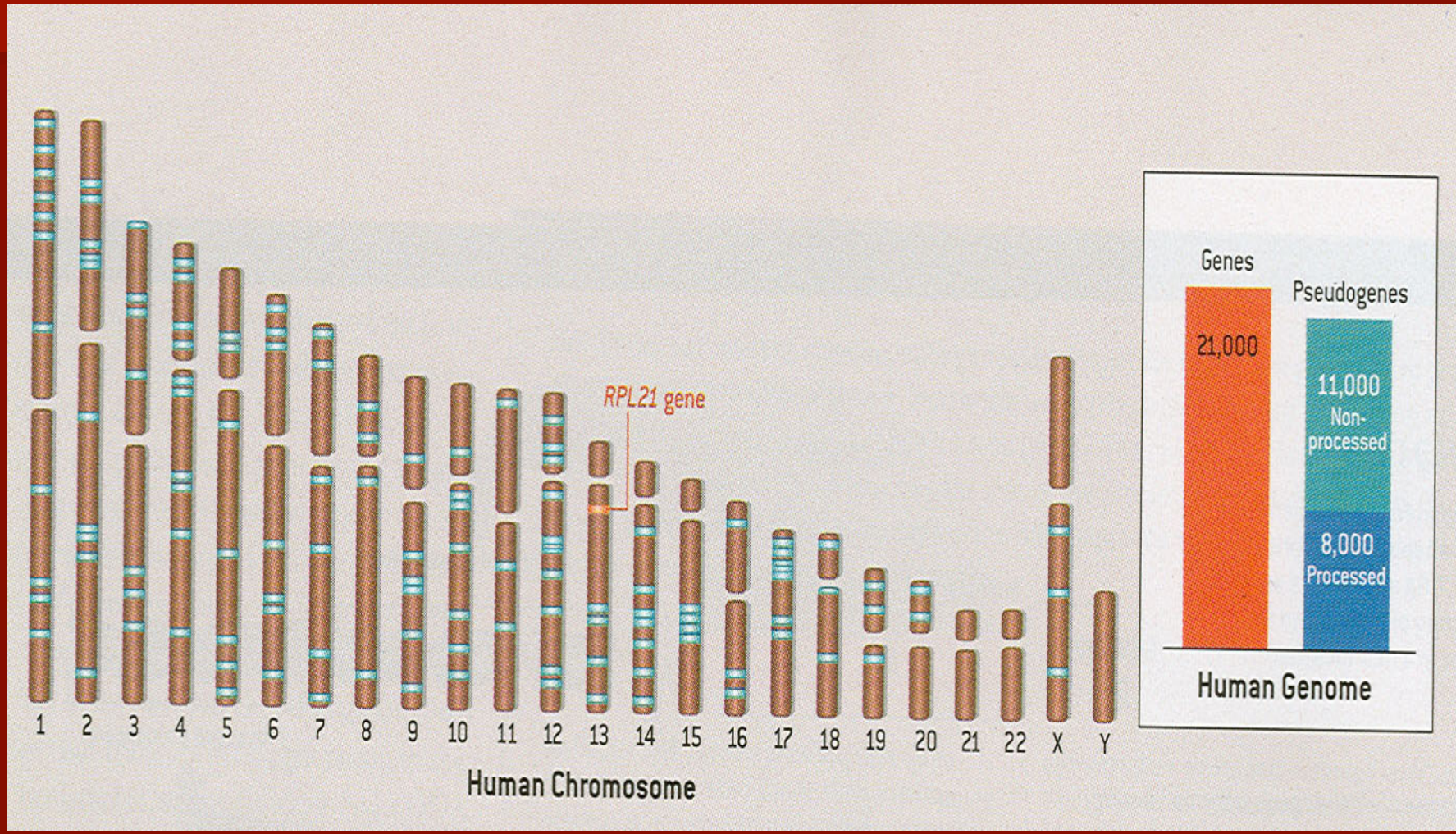
Lu JT et al. N Engl J Med 2014;371:593-596.

The NEW ENGLAND JOURNAL of MEDICINE

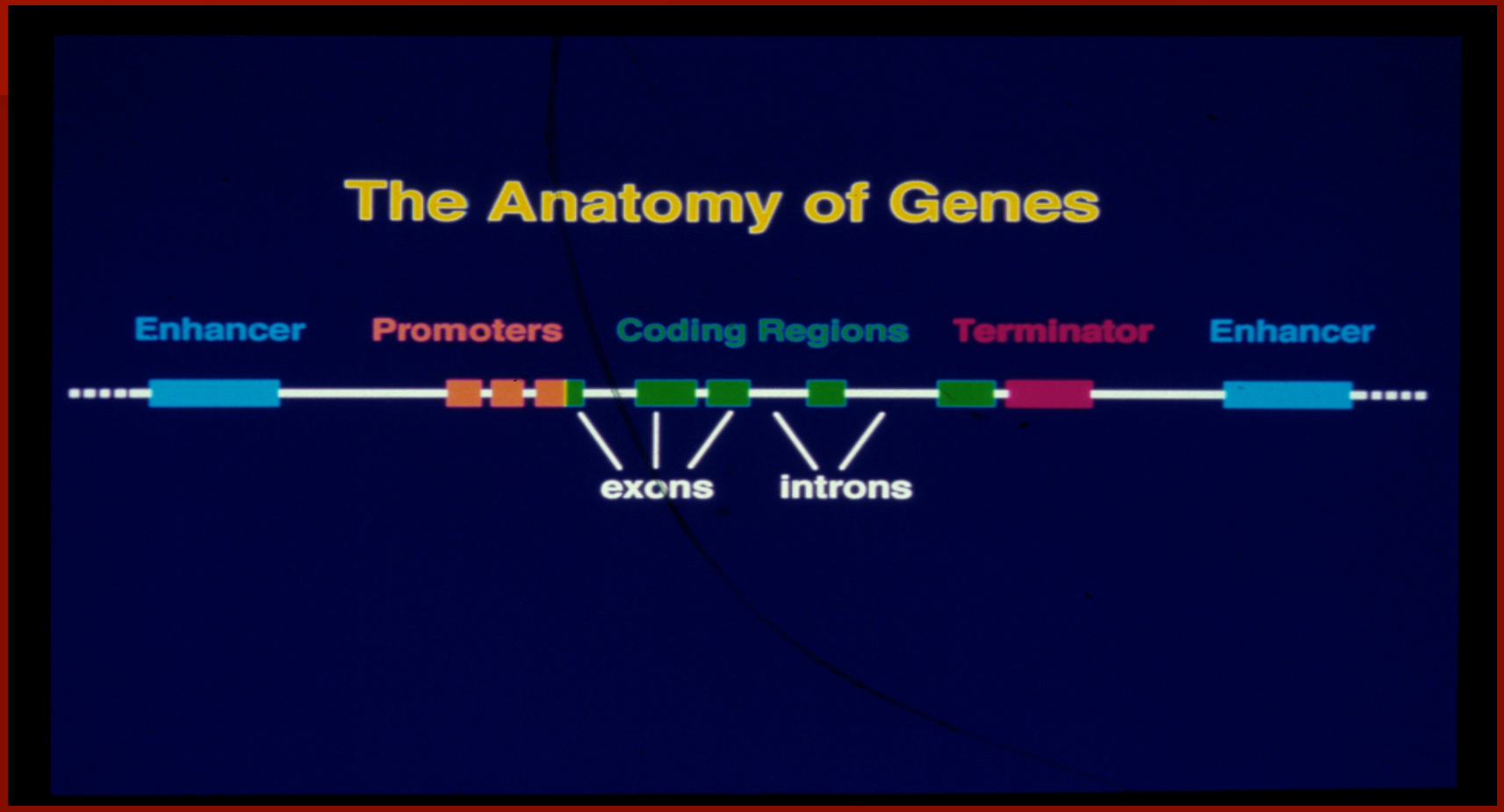
Human Genomics



Human Genomic Math: 21,000 genes & 19,000 pseudogenes

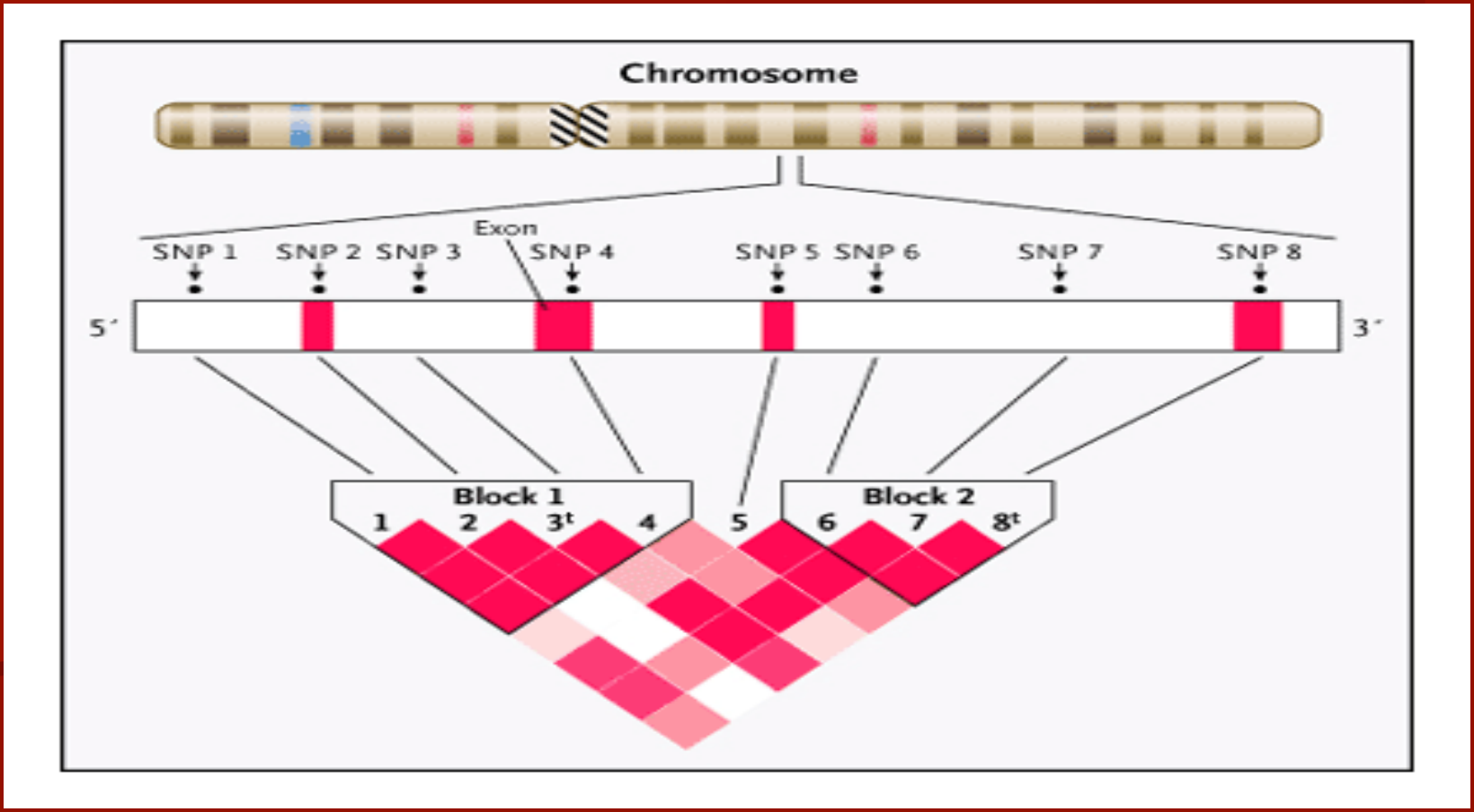


Genomics and Precision Health Care



As of 2017, >3 million regulatory regions discovered and >15 million transcription factor recognition elements have been found

SNPs (single nucleotide polymorphisms) are tools to identify minor genetic variance within genome-wide scans



Human Genetic Variations, and Variation in DNA Sequences (less than 0.1% of Human Genome)

aattggaagc aaatgacatc acagcaggtc agagaaaaag ggtt cca
gagtagtagg tctttggcat taggagcttg agcccagacg
gcccgagaga ccatgcagag gtcgcctctg gaaaaggcc
ttcagctgga ccagaccaat tttgaggaaa ggatac
atataccaaa tcccttctgt tgattctgct gaca
tgggatagag agctggcttc aaagaaaaat cc aa
ttttctgga gatttatgtt ctatggaatc ctt
gtacagcctc tcttactggg aagaatcat gctt
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gagttgttac aggcgt cgc cttctgtgga cttggtttcc
caggctgggc tagg agaat gatgatgaag tacagagatc agag cagt
gaaagacttg tga tac tc agaaatgatt aatcttgttaa ggcatactgc
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cggaaggcag cctatgtgag atacttcaat agctcagcct tcttcttctc agggttcttt
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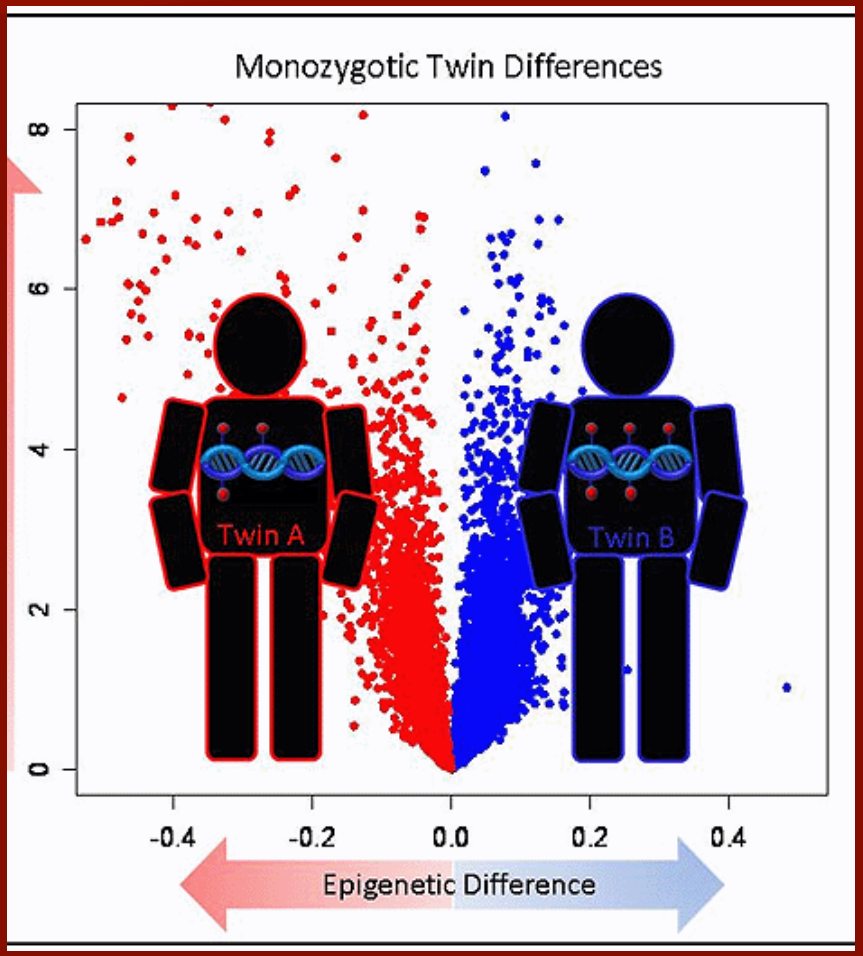
ccttcagagg gtaaaattaa gcacagtgga agaatttcat tctgttctca gttttcctgg
attatgcctg gcaccattaa agaaaatatc atCTTtggtg tttcctatga tgaatatag
tacagaagcg tcatcaaagc atgccaacta gaagaggaca tctccaagtt tgcagagaaa
gacaatatag ttcttggaga aggtggaatc acactgagtg gaggtcaacg agcaagaatt

agaatttca
at[T/C]gt
aagaggaca

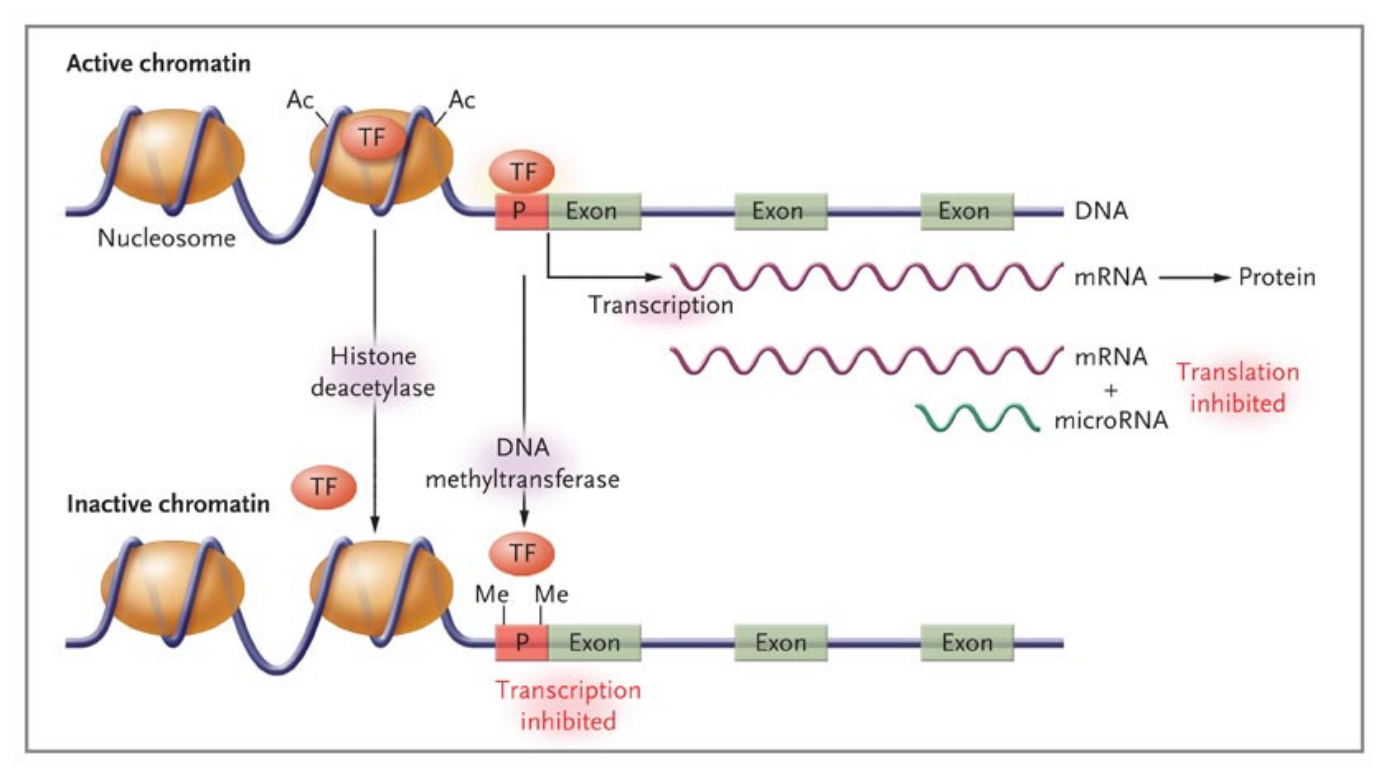
3.2 billion letters of human DNA encoded within 21,009 genes

1 Base per 1,000 Shows Single Nucleotide Polymorphism

Monozygotic Twins Differ as Much as 30% By 60 Years of Age



Regulation of Gene Expression through Epigenetic Processes (Epigenome)



Gluckman P et al. N Engl J Med 2008;359:61-73

Epigenetic changes can switch genes on or off by DNA methylation, histone modifications, and RNA-associated silencing

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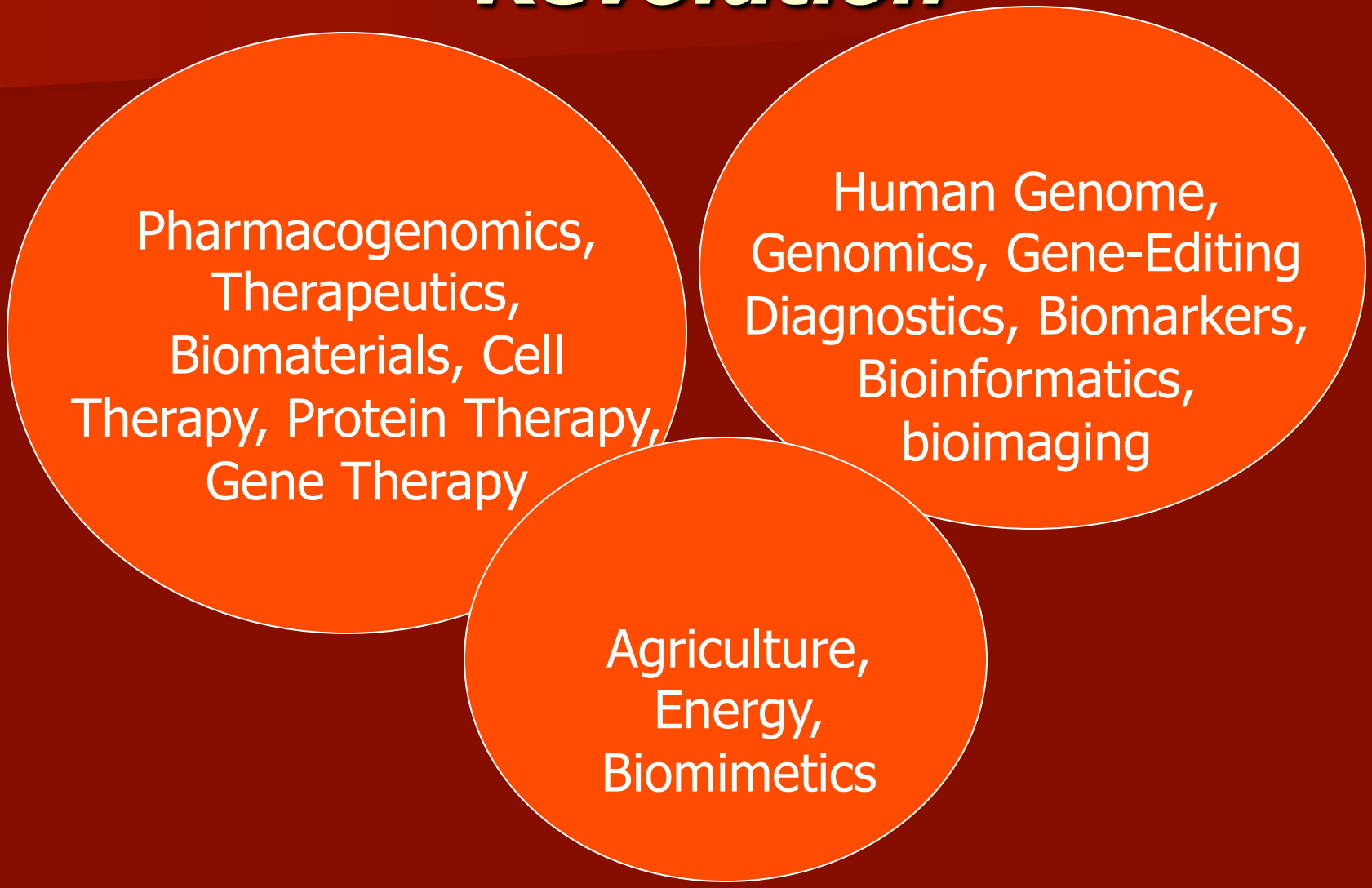
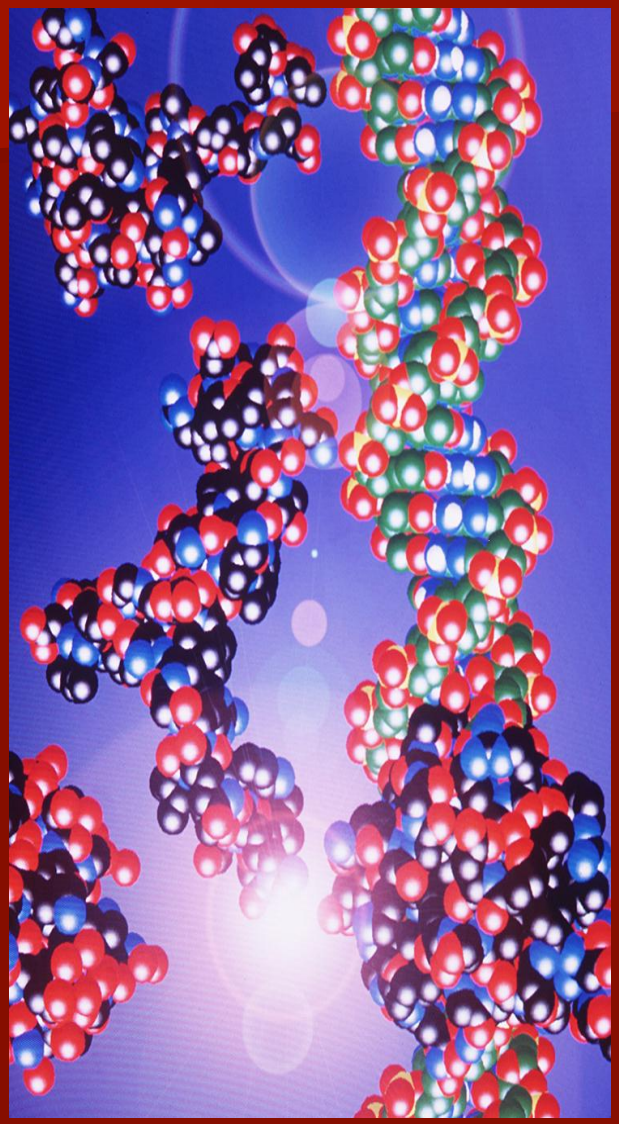
Fruits of the Biological Revolution



Evolutionary Continuity



- All humans are 99.9% similar and therefore 0.1% different (3 million base differences)
- The difference between a human and chimp is 0.1%
- Humans have the same number of genes as found in chimps, mice & fish (21,000)
- Human genome shares 96% homology with chimps & 90% with mice and rats
- Human genome shares 85% homology with zebrafish
- Human genome shares 7% homology with *E.coli*

Genomes of People From Europe, Asia, and North America Contain 2% Neanderthal DNA

- Evidence suggests interbreeding between Neanderthals and Homo Sapiens
- Conserved genes for Toll-like receptor gene cluster (innate immunity) and skin pigmentation
- Neanderthals became extinct 40,000 years ago with 99.7% DNA homology; interbreeding approximately 50,000 to 60,000 years ago.

President Obama's State of Union Address January 20th 2015 ($215 million in FY 2016)

1. Determine risk for diseases by integrating environmental exposures, genetic factors and gene-environment interactions
2. Identify causes of gene variation in response to therapeutics (pharmacogenomics)
3. Discover biomarkers that signal increased or decreased risk for diseases
4. Use mobile health (*mHealth*) technologies to correlate activity, physiological measures and environmental exposures
5. New classifications based on evidence
6. Empower participants to improve health
7. Create a platform to enable clinical trials of gene-targeted therapies

NIH Funding July 2016

- NIH launches largest-ever study of breast cancer genetics in black women (20,000) for $12 million (African-American Consortia)
- NIH awards $75 million to begin study of a million American volunteers who give consent to have their phenotypes measured in a myriad of ways and to correlate with their genotype (phenomics)

  Each grant $5 million: Columbia; Northwestern; University of Arizona; University of Pittsburgh; California University Consortium, Geisinger Health System, New England Consortium, Trans-American Consortium, (Baylor, Minnesota, Michigan, Massachusetts), and VA

  $14 million: data analytics to Vanderbilt & Broad Inst.

  $20 million: Scripps Res Inst, mobile & web applications
- FDA drafts guidance to regulatory path for DNA sequencing that determines risk as well as diagnosis

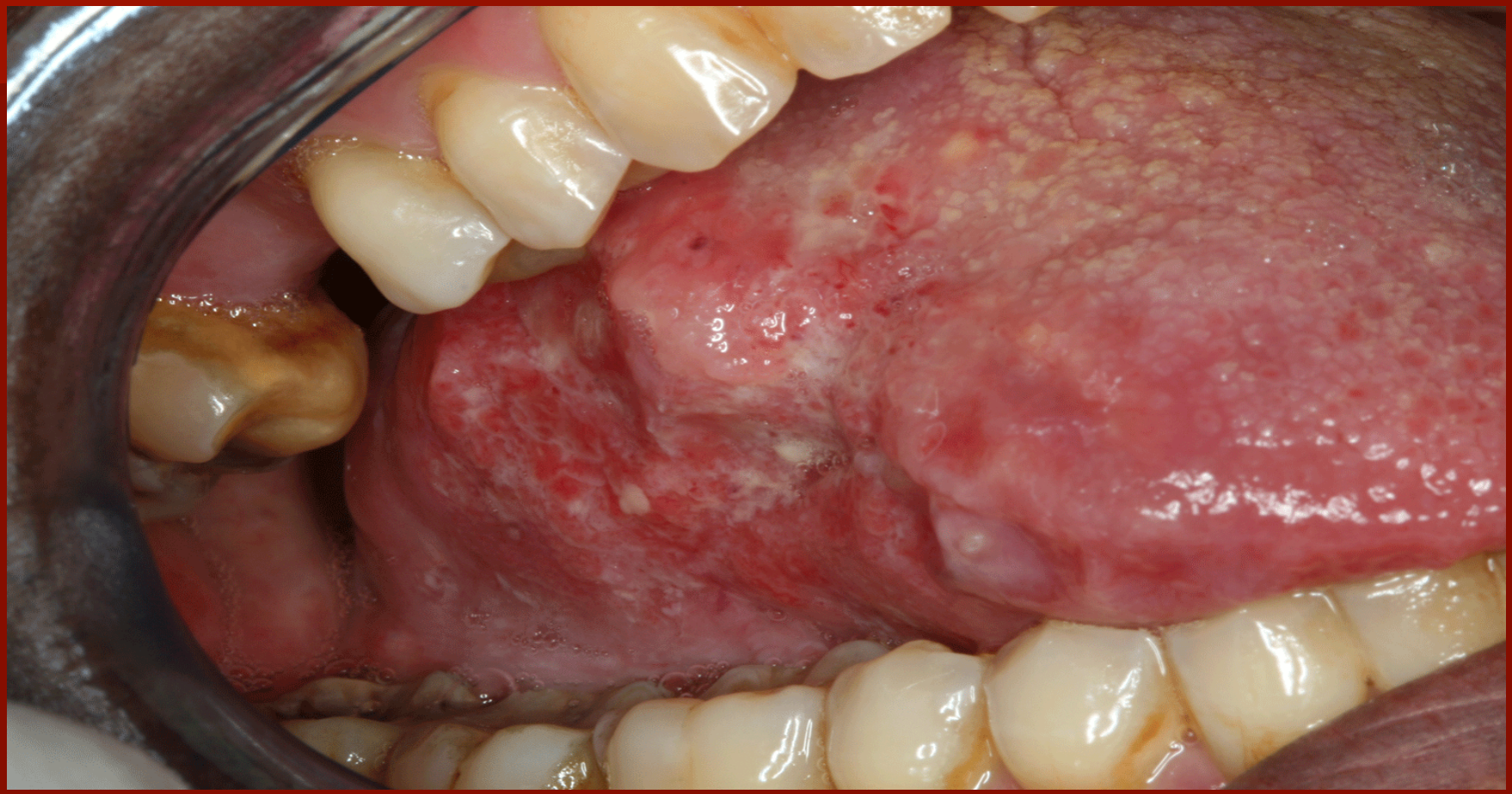
Wednesday September 7th, 2016

Scientific Road Map to Achieve ***Cancer Moonshot*** Goals (NCI)

1. Engage patients to contribute tumor profile data to expand knowledge about what therapies work, in whom, and in which types of cancer
2. Establish cancer immunotherapy clinical trials network to evaluate therapeutic approach
3. Discover agents to overcome drug resistance
4. Create national sharing of cancer data enterprise
5. Improve understanding of oncoproteins in pediatric cancers
6. Accelerate development of guidelines for routine patient reporting symptoms to minimize side-effects
7. Reduce cancer risk and cancer health disparities
8. Predict response to therapy via retrospective analysis of patient samples
9. Create 3-D maps of human tumor progression and evolution and document sequence of genetic mutations
10. Develop new enabling cancer technologies to characterize tumors

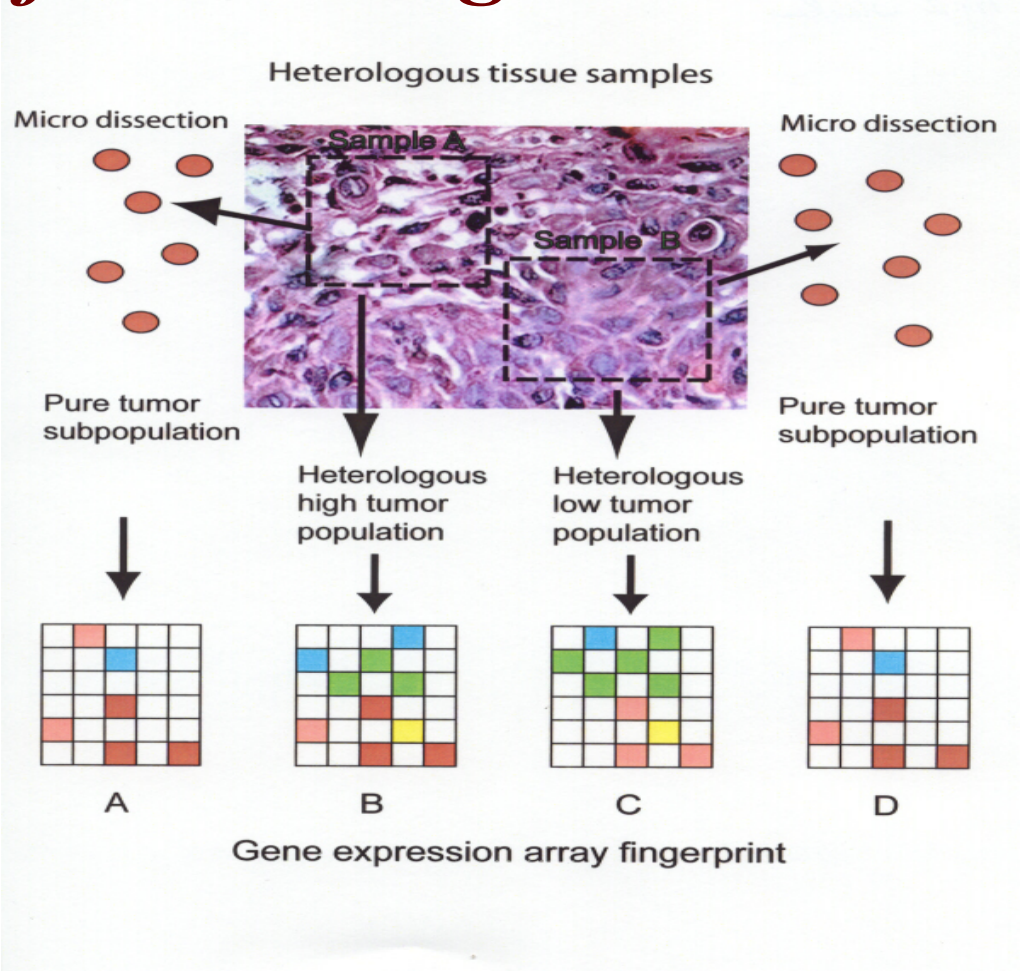
Oral Cancers in Adolescents & Adults

[tobacco products, UV light, HPV-16 (viral oncogene exon 7) & sexual behaviors]



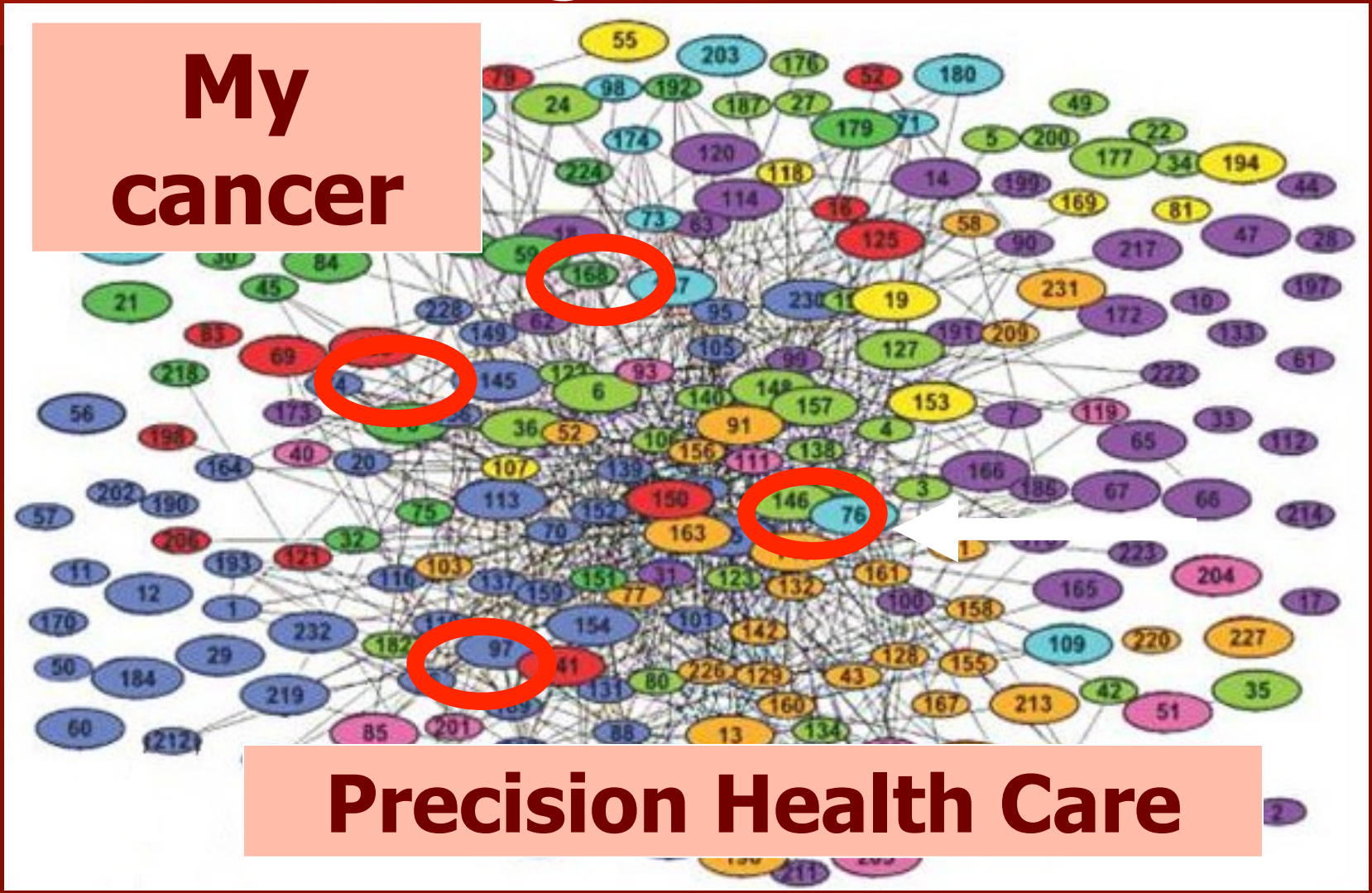
Head & neck cancer is the sixth most common cancer worldwide - - - 650,000 new cases diagnosed each year.

Discovery of gene variations in same sample from malignant lesion/tumor



Changing Knowledge & Therapy

Understanding at cellular level



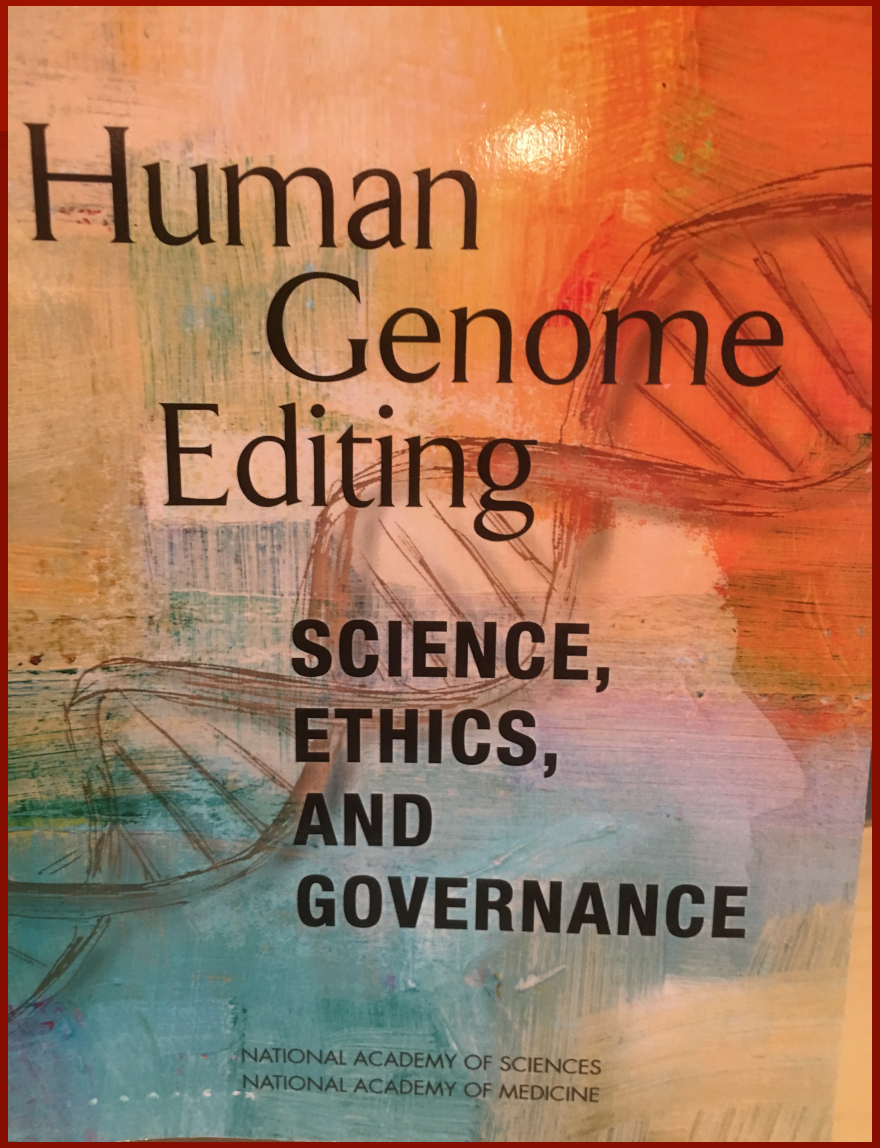
Genotype + Phenotype + Environment + Behaviors = Precision Health Care in 21st Century

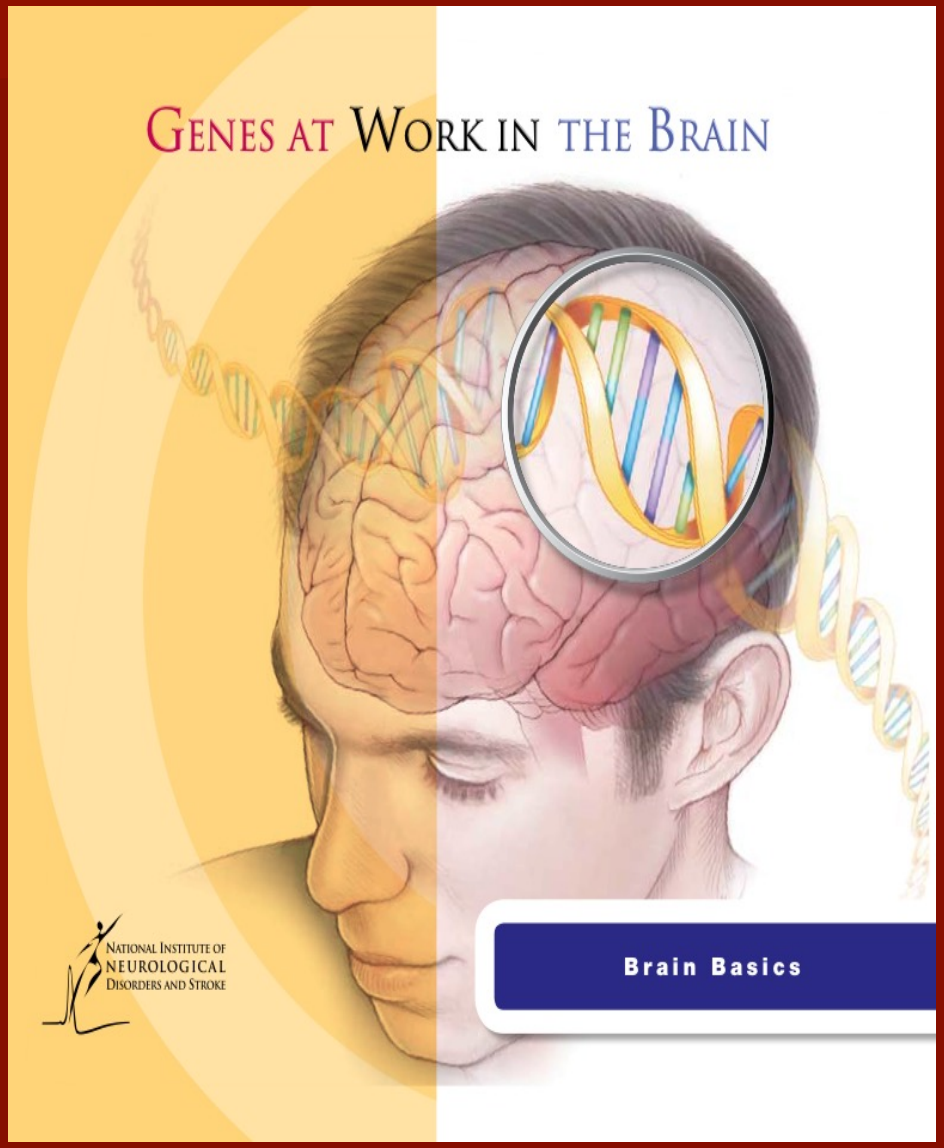
Personalized health care and pharmacogenomics to improve risk, diagnosis, stratification of patients "at risk," and treatment for specific diseases and disorders

Pharmacogenomics

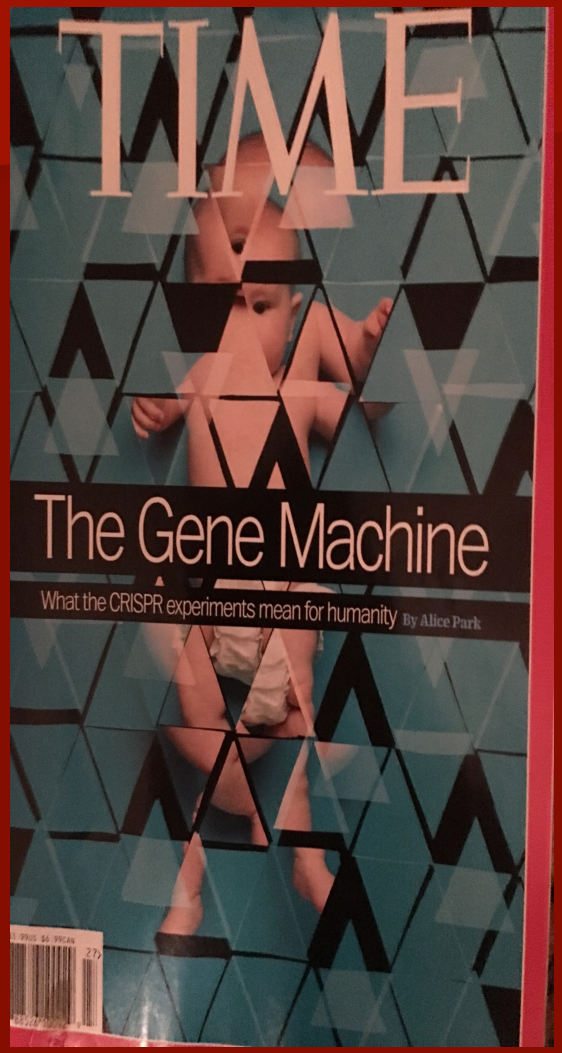
Gene-directed therapeutics

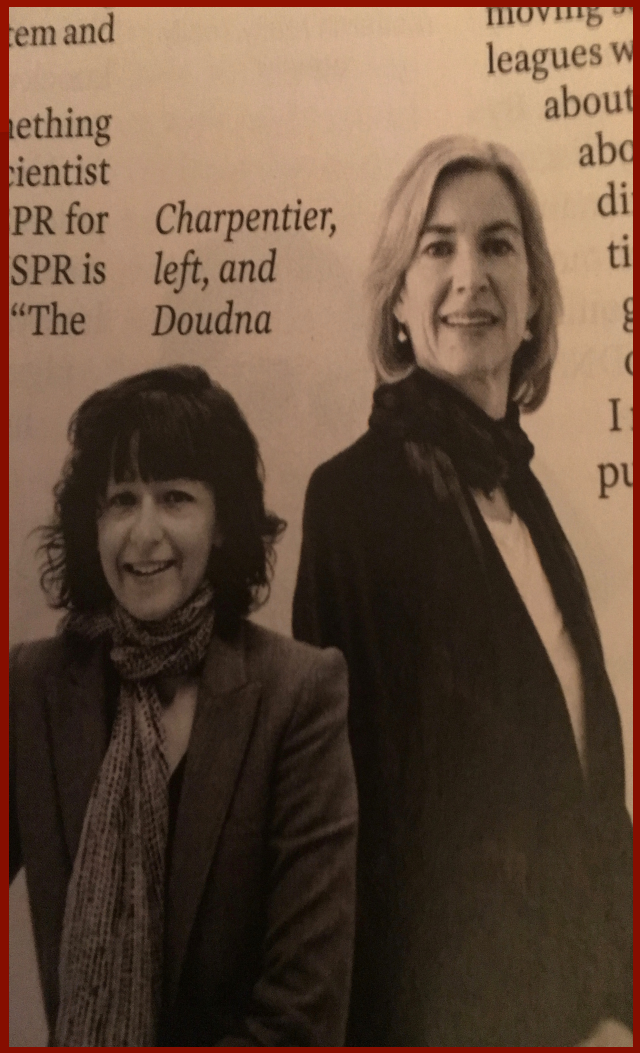
ENTER GENE EDITING AND UNDERSTANDING THE FUNCTIONS OF THE HUMAN BRAIN

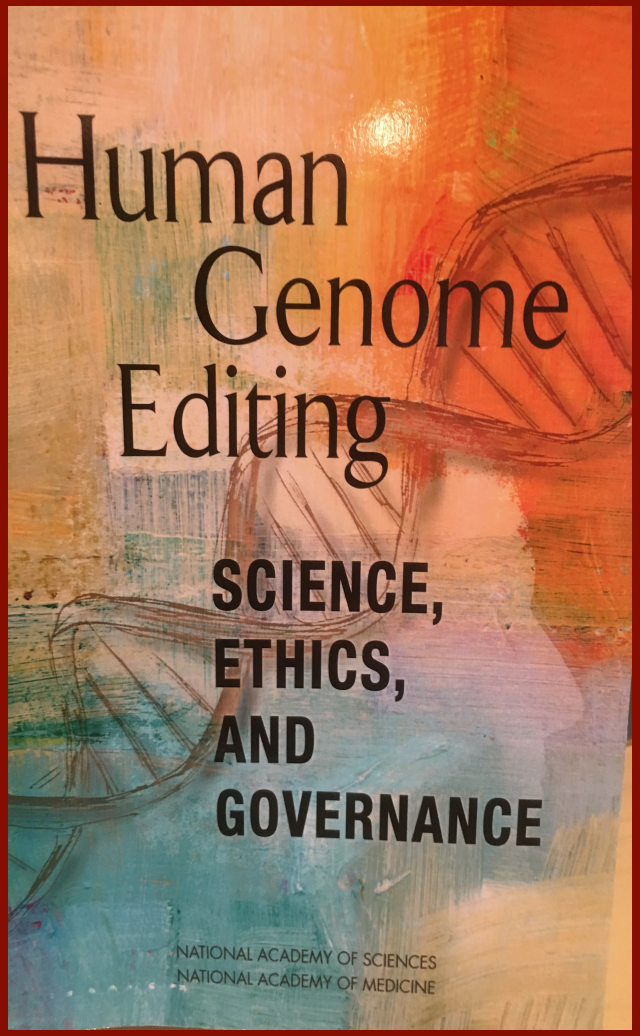




TWO WOMEN WHO CHANGED THE TRAJECTORY OF MODERN GENOMICS (2012-)



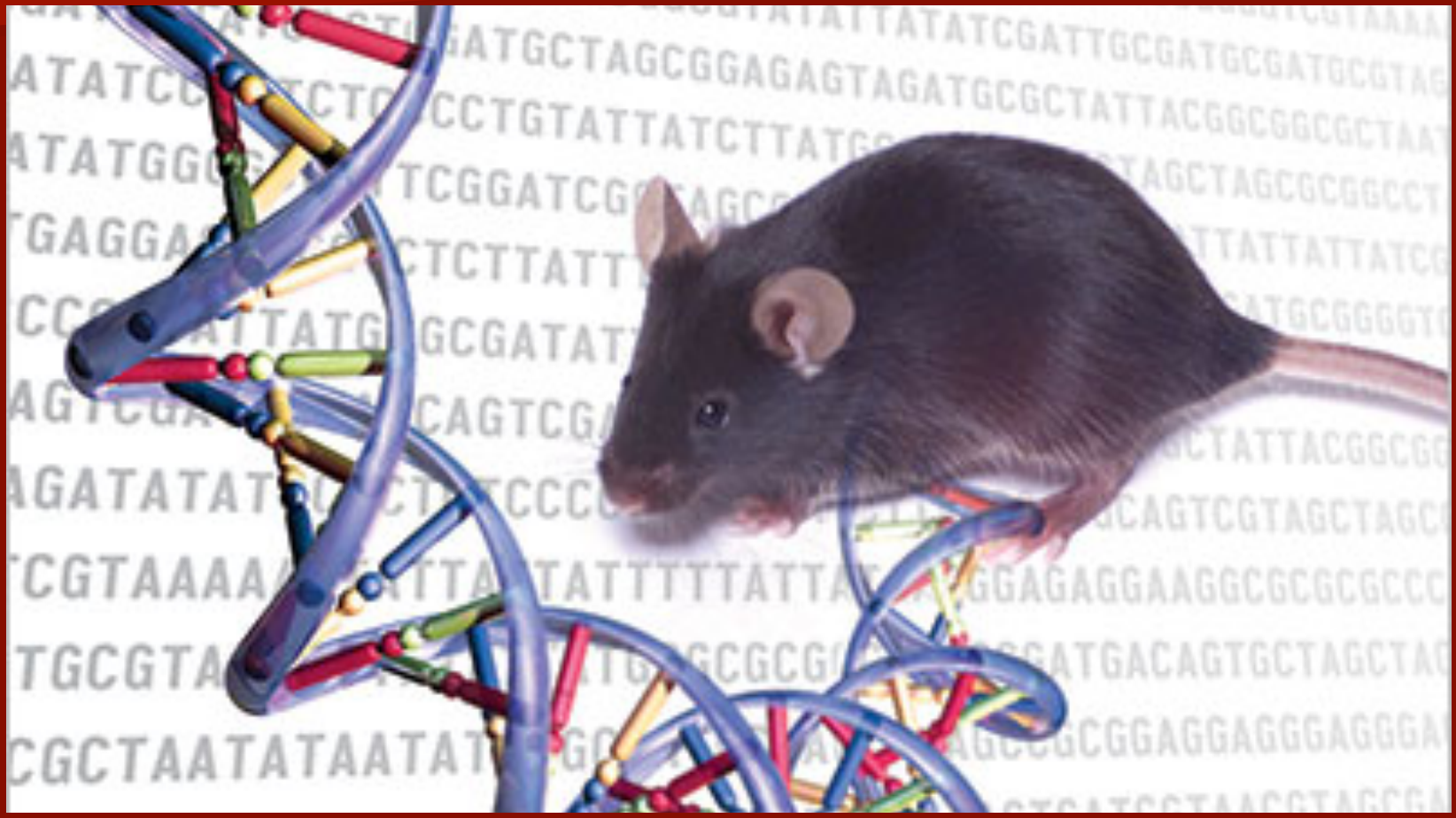




CRISPR: A Gene Editing Technique
(clustered regularly interspaced short palindromic repeats)

- Edit human embryonic germ cells
- Gene editing followed by *in vitro* fertilization can eliminate risk for many Mendelian (monogenic) diseases
- Shown to remove HIV and HPV-16 gene sequences from human cells (AIDS? Oral & Cervical Cancers)?
- Provide precise diagnoses for diseases and disorders
- Used to make plants and animals resistant to disease; create animal bioreactors; create mice strains with human gene mutations, eliminate insect-bearing infectious diseases (eg. Malaria, Zika virus, polio, Ebola, etc)

CRISPR/Cas9 system being used to correct many inherited single gene mutations such as sickle-cell anemia, thallasemia & deafness

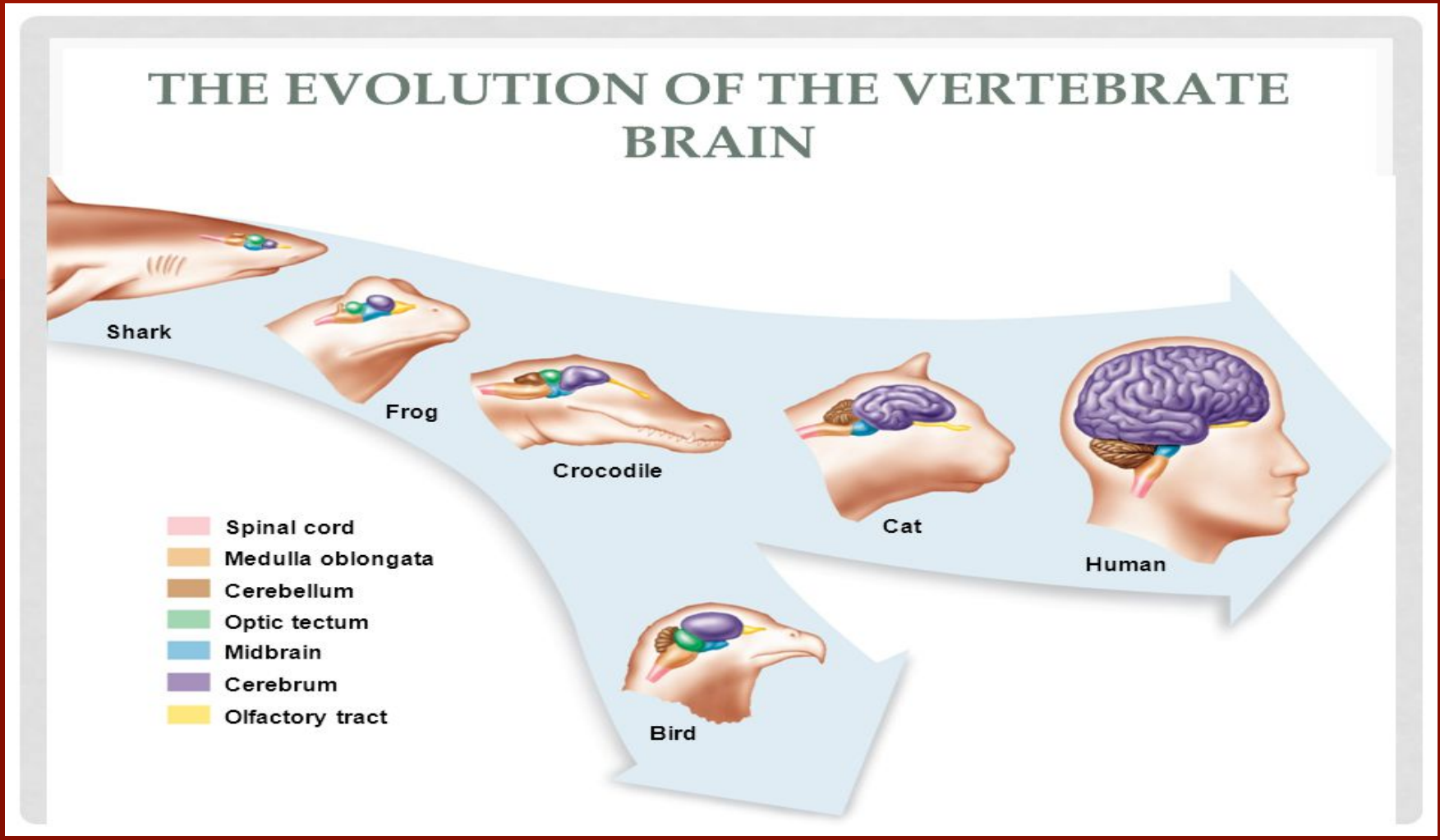


BRAIN INITIATIVE: A Public-Private Research Initiative With The Goal To Understand The Human Brain

NIH, NSF, DOD (DARPA)
Allen Institute of Brain Science
Howard Hughes Medical Institute
The Kavli Foundation

2016-2020: Technology Development (Genomics and Imaging)

2020-2025: Applications to Disease and Disorders (e.g. 5.5 million Alzheimer's patients in 2017)



Two greatest mysteries in all of nature are the mind and the universe! As to human brain, 170.6 billion brain cells (half neurons and half glial cells). Further, each neuron has tens of thousands of synaptic connections or brain has hundred trillion synapses.

Scale of Challenge? **Same #brain cells in children and adults**

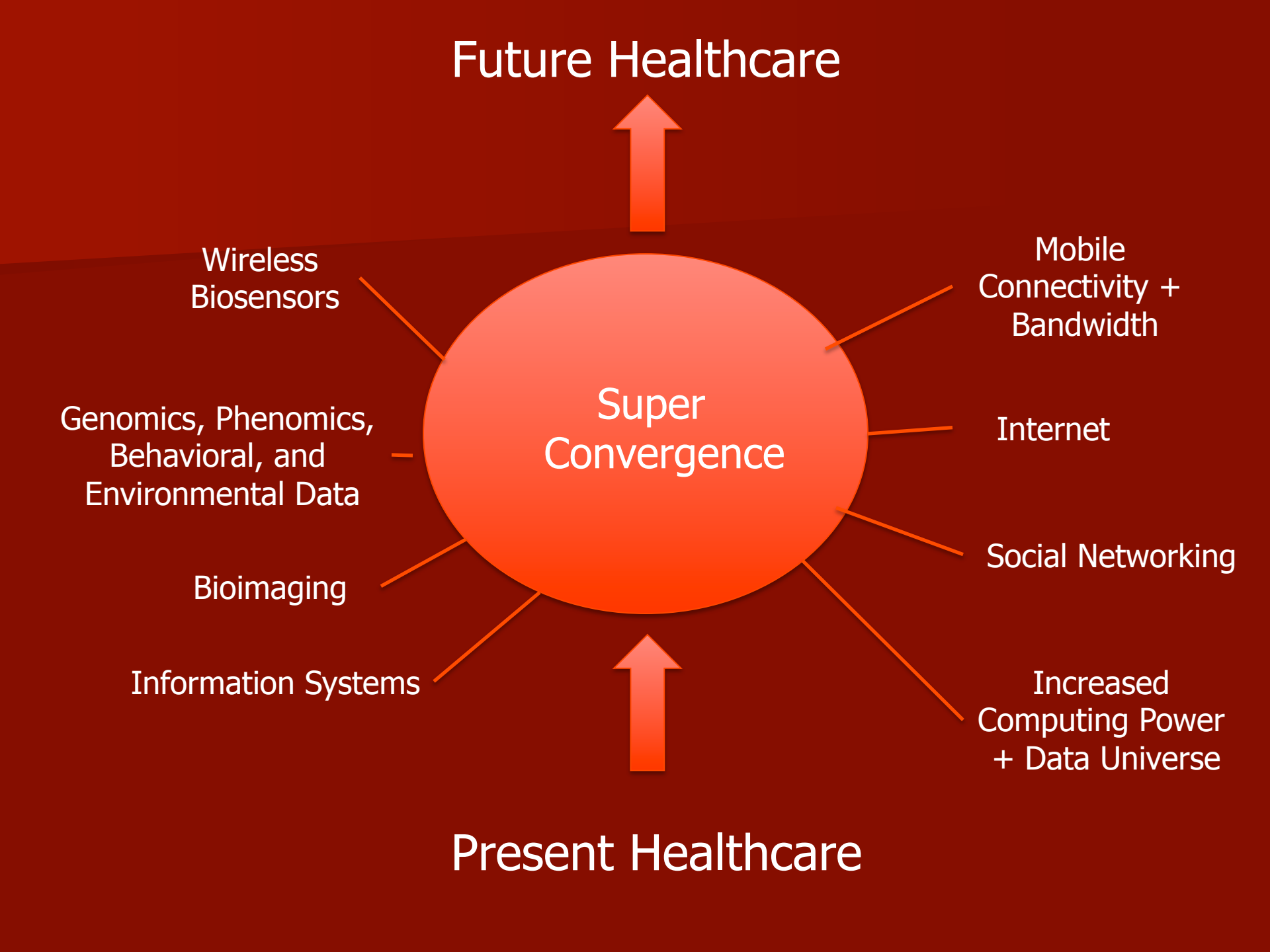
3 pound organ

- It takes 25 years to develop human brain
- Number brain cells same in children and adults (170 billion; half neurons and ½ glial cells)
- During first 2 years, neurons (brain cells) connect through synapses; two million synapses form every second in infant and by two years we have one hundred trillion synapses, 2x number found in the adult brain.
- Neural *"pruning"* reduces #synapses by 50%.
- Synapses respond to environmental stimulus (e.g. sounds, smells, visions, touch, perceptions, reflections, socioeconomic determinants) and form neuronal and glial cell synaptic patterns

Early 21st Century "Prosthetic" Brain

(Inquiry-Based Learning, search engine, Internet, AI)

Your Human Genome "In Your Hand" for $1,000/person by 2018


Future Healthcare
Wireless Biosensors
Genomics, Phenomics, Behavioral, and Environmental Data
Bioimaging
Information Systems
Super Convergence
Mobile Connectivity + Bandwidth
Internet
Social Networking
Increased Computing Power + Data Universe
Present Healthcare

What is Implementation Science?

- Explores barriers to successful interventions
- Evolved from failure to transfer evidence based interventions into real world contexts
- Focus on implementation fidelity instead of an outcome measure (Implementation fidelity refers to the degree to which an intervention or programme is delivered as intended)
- Major goal to reduce health disparities, homeless, and poverty (46.5 mill people in poverty including 20 million 50% below poverty line in USA)

EXAMPLES OF IMPLEMENTATION SCIENCE WORKSHOPS TO INTEGRATE GENOMICS INTO HEALTHCARE BY NATIONAL ACADEMY OF MEDICINE (2015-Present)

ENABLING PRECISION MEDICINE
The Role of Genetics in
Clinical Drug Development
PROCEEDINGS OF A WORKSHOP
Morgan L. Boname, Amanda Wagner Gee, Theresa Wizemann,
Siobhan Addie, and Sarah H. Beachy, *Rapporteurs*
Forum on Drug Discovery, Development, and Translation
Roundtable on Genomics and Precision Health
Board on Health Sciences Policy
Health and Medicine Division

THE NATIONAL ACADEMIES PRESS
Washington, DC
www.nap.edu

December 28th, 2017

JAMA Published Online doi:10.1001/jama.2017.19138

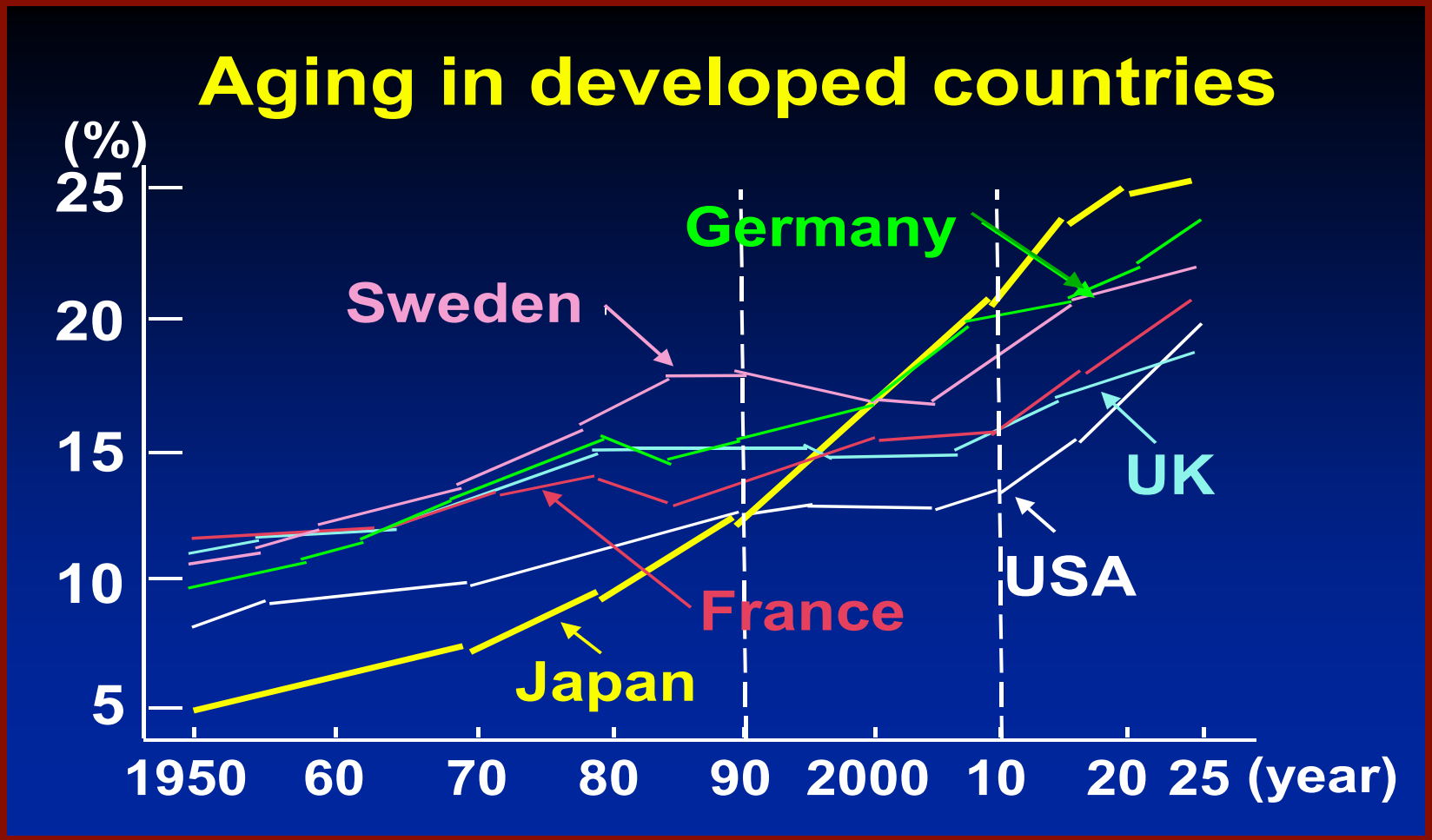
Improving Public Health Requires Inclusion of Underrepresented Populations in Research

Catherine Y. Spong and Diana W. Bianchi (NICHD/NIH)

- Genomics ushered in promising therapies for individuals
- Personalized medicine is being promoted and has already impacted precision cancer diagnosis and treatments
- Despite advances, children, older adults, pregnant and lactating women, and individuals with physical and intellectual disabilities experience limited evidence-based therapies
- Clinical Trials to include women introduced in 1990 at NIH
- Until "Best Pharmaceuticals for Children Act (2002)," pediatric dose based on extrapolation from adults.
- Implementation science serves as an advocate for inclusion of underrepresented populations in biomedical research

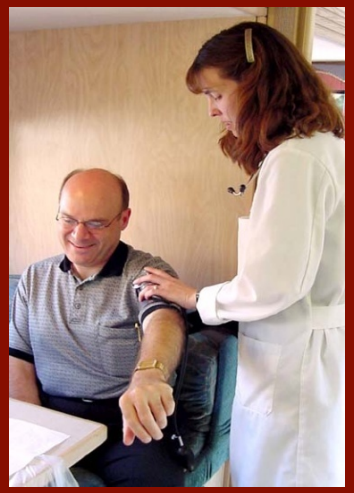
Comparison Between Industrial Nations

Health care for all seniors (>65yrs) including mental, vision, hearing and oral health…(72.8 million by 2030; 90 million by 2050 in USA; 1 in 5 Americans 65yrs+; >80yrs fastest growing)

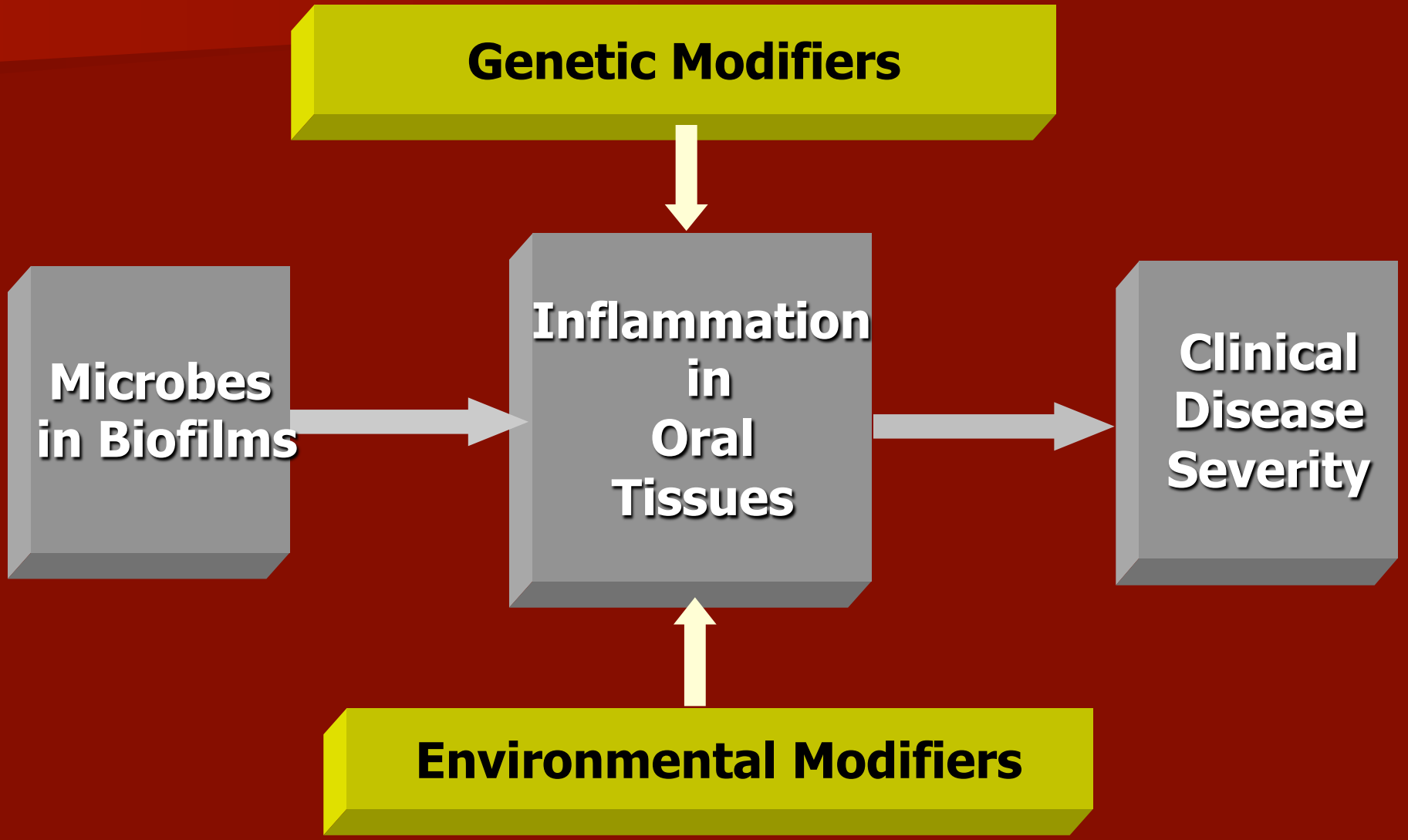


US Managing Chronic Diseases

- >133 million Americans have chronic diseases
- #1 chronic disease of children is tooth decay (4.5 million births per year)
- >50% of 65yrs+ have 5^{+} conditions (e.g. cancer, heart, arthritis, osteoporosis, type2 diabetes, pulmonary diseases, periodontal diseases, sclerosis, chronic depression, cerebral vascular diseases, chronic pain, etc.)
- *Chronic diseases cause 70% of deaths in USA*
- Consume 75% of health care costs (75% of 3 trillion dollars/ year)
- 40% of chronic patients *do not get* all recommended therapies
- In USA, majority of chronically ill patients spend >70% of lifetime health expenses in last 6 months of life
- Currently, Medicare *does not have* dental or hearing benefits, and negligible vision and mental health benefits

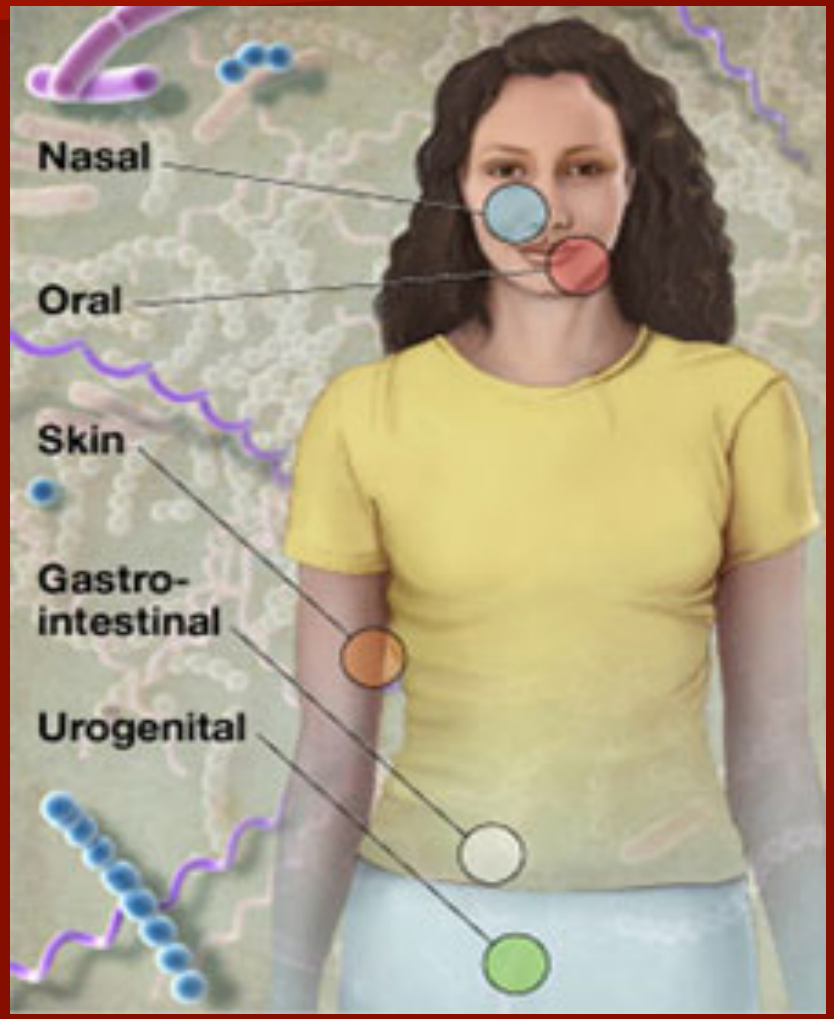


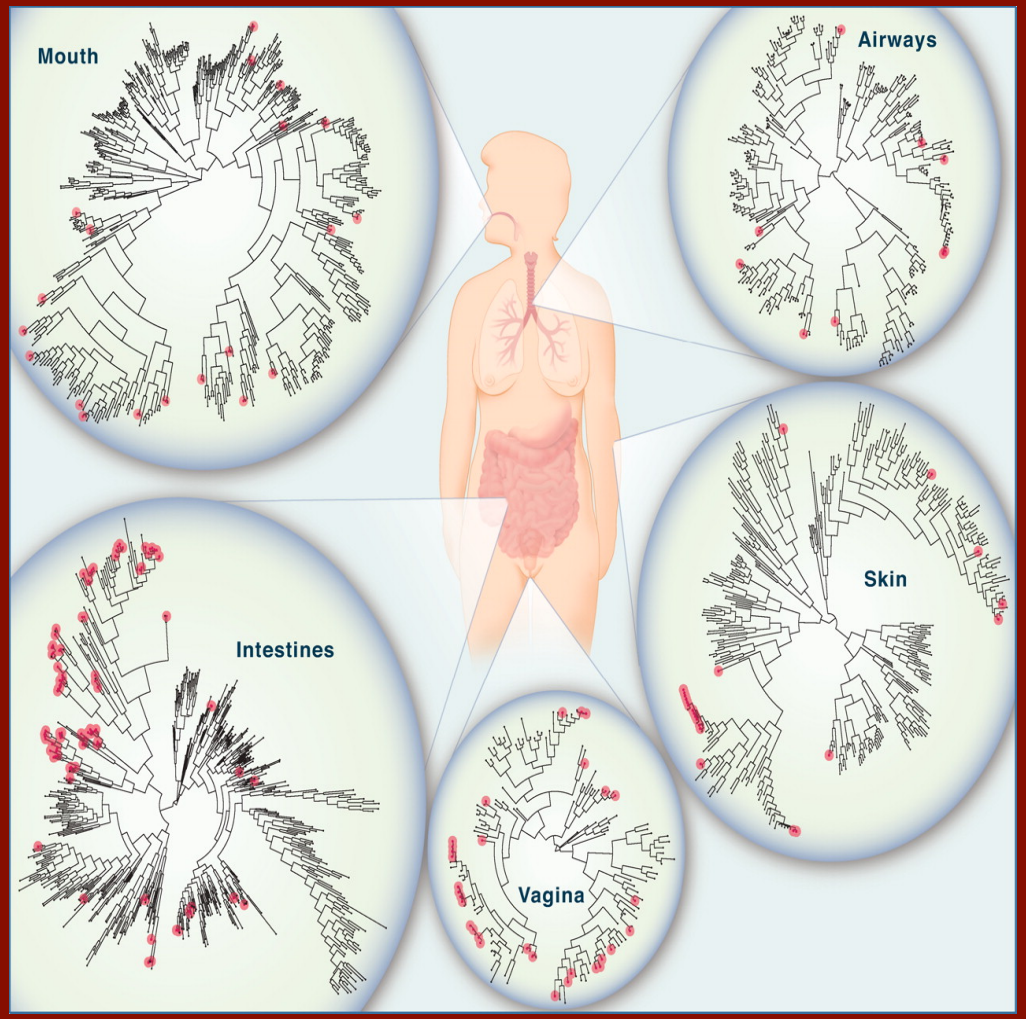
Genetic Factors in Oral Microbial Infections



MICROBIOME

75 to 200 trillion microorganisms; 50 trillion human somatic cells in adult (~3:1 ratio)





Next Frontier in Antimicrobials

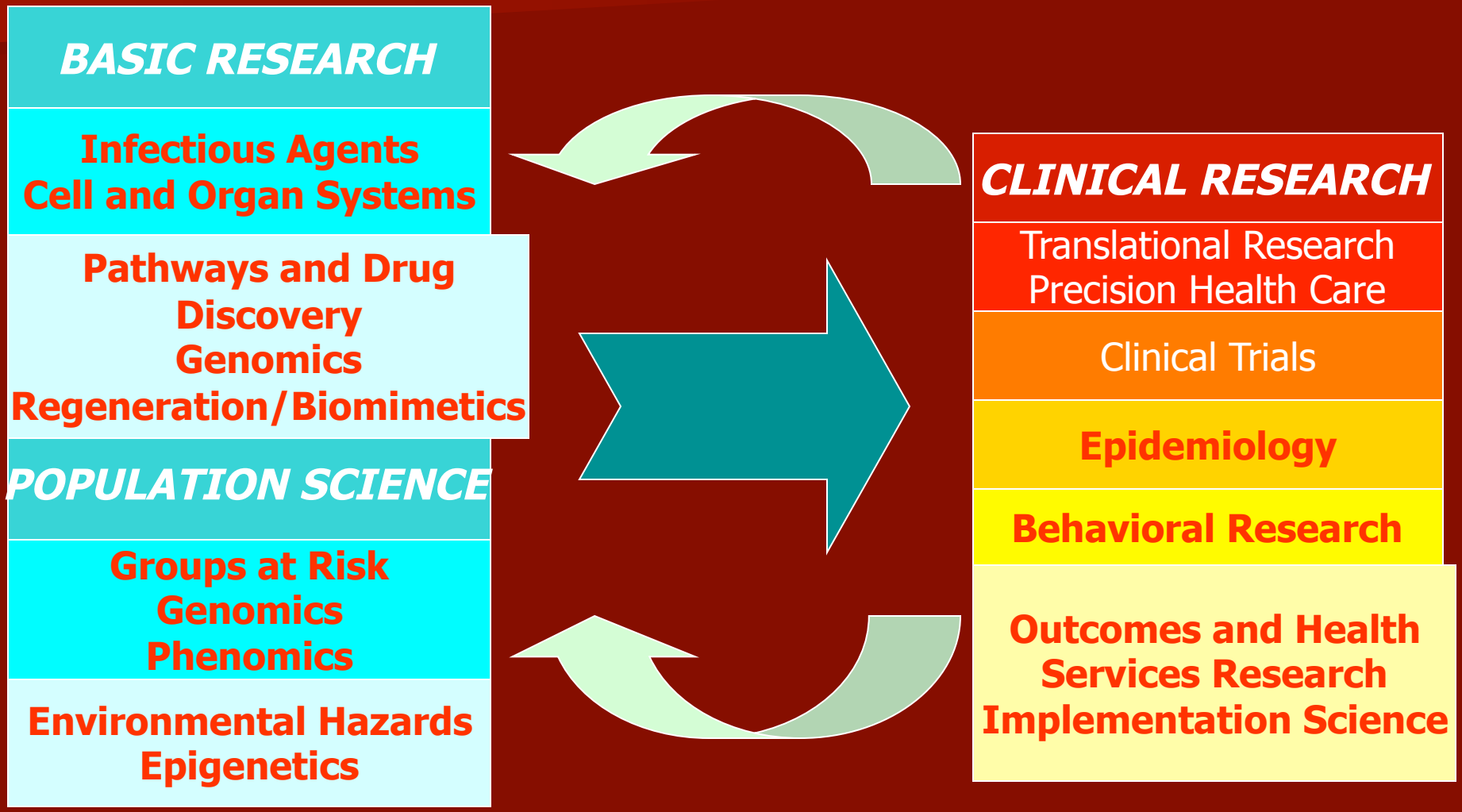
- **Targeted killing of *Streptoccocus mutans* by a phermone-guided "Smart" antimicrobial peptide**
- **Quarum sensing genes**
- **Microbial gene transfer, genetic variance, and antimicrobial resistance**
- **Chronic microbial infections (teeth, implants, ear, lung, and heart)**
- **Innovations for targeting viral and yeast infections ("smart, targeted molecules")**

Strategic Plan of NIDCR 2014-2019

"Enable Precise and Personalized Craniofacial-Oral-Dental Health Care"

- Martha Somerman DDS, PhD.
  Director, NIDCR, NIH

Today's Oral Health Research Agenda: *Basic, Clinical, Population, Behavioral*



Genetics, Genomics & Dental Public Health

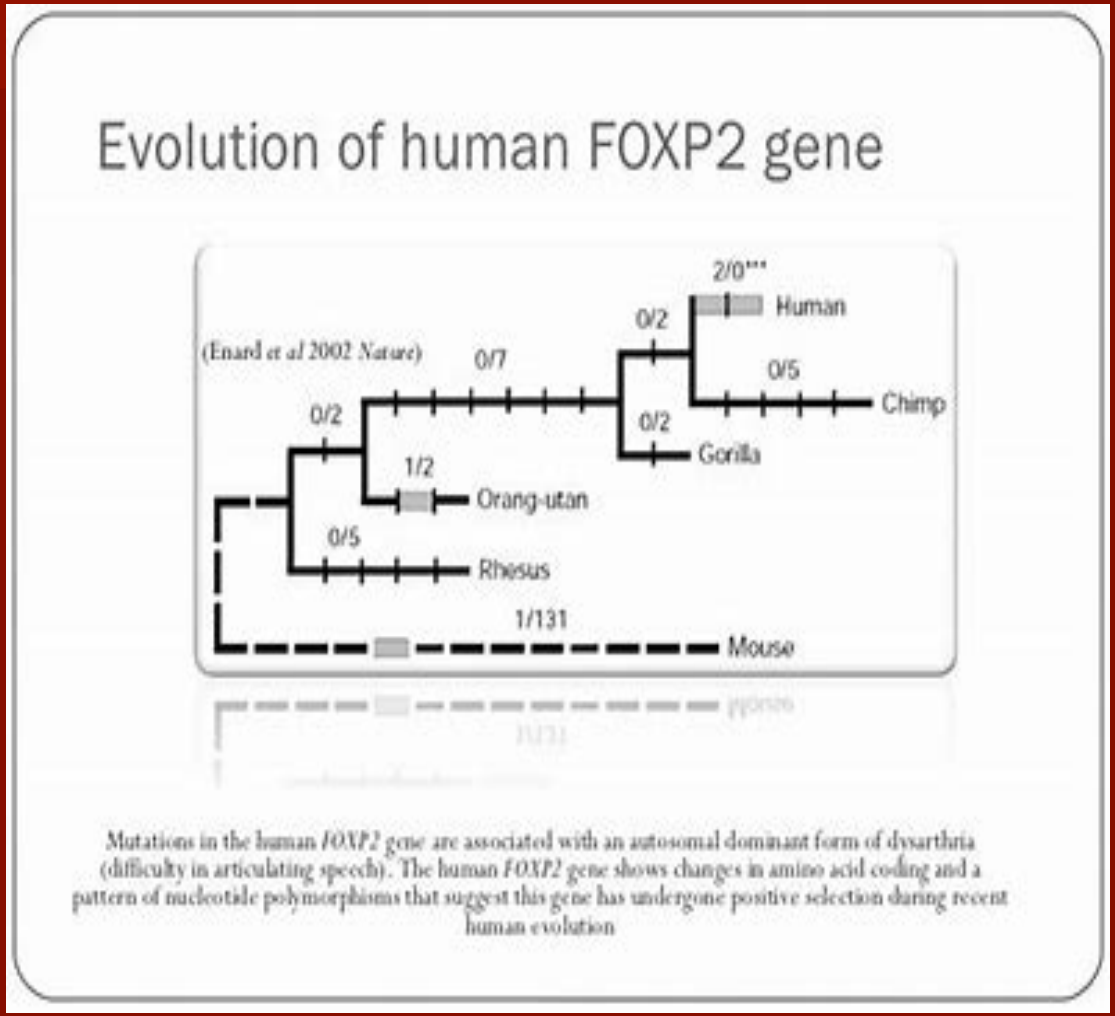
- Birth Defects
- Dental caries
- Periodontal Disease (s)
- Pain (Acute and Chronic)
- TMJ
- Genomic epidemiology of oral diseases (soft & hard tissues)
- Autoimmune diseases
- Stem cells & tissue engineering (biomaterials)
- Saliva (diagnostics)
- Oral/Systemic Diseases (e.g. cardiovascular, diabetes, cancers osteoporosis, osteoarthritis)
- Taste and smell
- Infectious diseases (e.g. viral, bacterial and yeast)
- Pharmacogenomics

HIGHLIGHTS SCIENTIFIC PROGRESS IN 2017

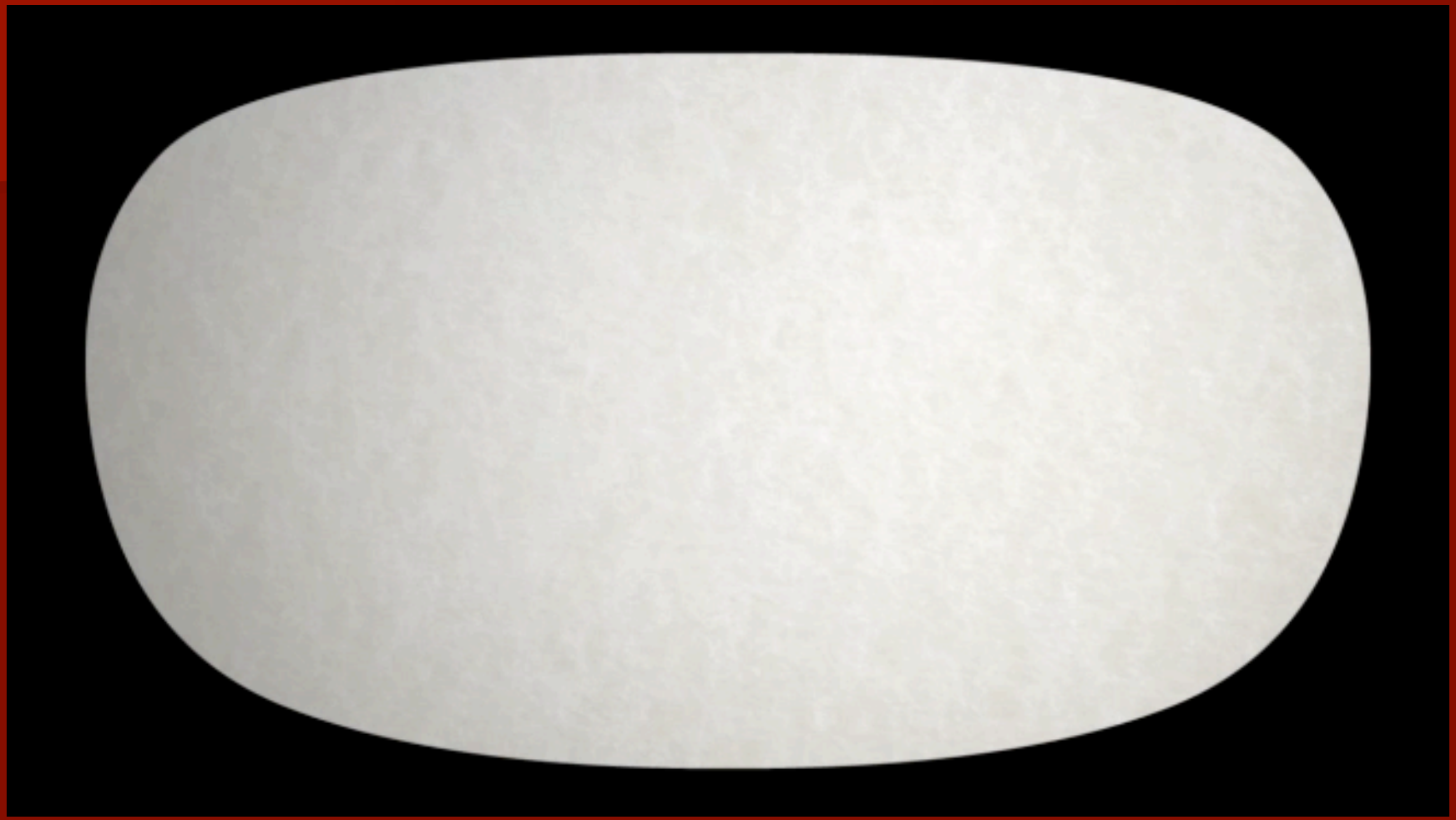
- Gene Therapy Success for Spinal Muscular Atrophy (SMA) caused by mutations in gene SMN1 and new drug *Nusineren*
- FDA approved first CAR-T cell immunotherapy for acute lymphoblastic leukemia (most common childhood cancer in USA)
- FDA approved second CAR-T cell immunotherapy for B-cell lymphoma
- FDA (December 2017) approved pioneering gene therapy to treat children and adults with degeneration of eye's retina
- Gene-editing studies in mice reversed a number of diseases such as Huntington's using CRISPR-Cas9; in China (early 2018) new human clinical trials to treat oral-esophageal cancers (HIV-16) and AIDS (HIV)
- Bioimaging of "living processes" using Cryo-EM (this technology won Nobel Prize in 2017 for three scientists)
- Human FOXP2 gene mutation causes deafness in mouse strain called "Beethoven strain" using CRISPR/Cas9 system

SELECT GENETIC ADVANCES OF 2017

- FDA endorses DNA-altering treatments (e.g. *Kymriah* for leukemia, *luxturnia* for inherited progressive blindness)
- Studies increase hearing in "Beethoven Mice"
- CART therapy for lymphoma



Is healthcare ready for large-scale DNA screening for hearing deficits? In addition to NIH's 1 million people goal, the Geisinger Medical Center and Health System (near Danville, PA) has already sequenced the DNA from 92,400 people in 2017 with goal of 3.3 million people by 2022. Screening primarily for cancer, cardiovascular and communication diseases and disorders risk and diagnostics



Major Global Accomplishments of 2017

- A smaller share of the world's people were hungry, impoverished or illiterate than any time before
- Everyday, 217,000 living in poverty were advanced (less than $2day)
- Everyday, 325,000 people gained access to electricity
- Everyday, 300,000 people gained access to clean drinking water
- A smaller proportion of children died than ever before
- The proportion of disfigured by leprosy, blinded by diseases like trachoma or suffering from other ailments declined
- Globally, today less than 15% of world's population are illiterate, and less than 10% now live in poverty
- Since 1990, more than 100 million children have been saved by vaccinations, diarrhea treatment, breast-feeding promotions and other simple public health measures

Data: Gates Foundation,
WHO, UN, and NY Times