GENOMIC DATA ANALYSIS

Irene Tiemann-Boege

Irene.tiemann@jku.at

LVA-Nr. 320.301 and 320.304

OUTLINE FOR TODAY

- Why is genomics important?
  - genetics perspective-find cause of diseases
  - synthetic biology: build your own genome
  - evolutionary biology; Where do we come from?
- Commercializing genomics
- Ethical aspects

GENETICS PERSPECTIVE

- My child is sick!
- Finding the gene/genes responsible for a disease
- Problem similar to finding a needle in a haystack-one single nucleotide change in $3x10^9$ bases is responsible
- An example from a child with progeria

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HUTCHINSON-GILFORD PROGERIA SYNDROME

- GENETIC CONDITION
- Caused by a change in the genetic information (DNA)
- Caused by a single *de novo* mutation
- affected child from normal parents (occurred in the germline)
- Dramatic, premature aging-- Early aging syndrome
- After 1 year: dramatically accelerated symptoms of aging
- Death usually at the age of 12

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FINDING THE CAUSE FOR PROGERIA?

- Doctor, my child is sick, please help!
- What gene is involved?
- **Then:** a task for gene hunters; use positional Cloning and years of work
- **Today:** a task for anybody who has access to NGS and interpret the data; a few weeks of work

- Work pipeline:
- Identification of mutation > functional validation > finding a cure

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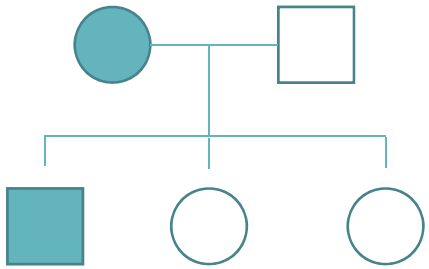
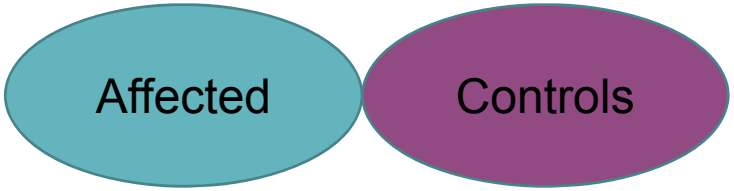
IDENTIFYING GENES CAUSING DISEASE

- Linkage
  - Pedigree analysis
  - Test markers distributed in the whole genome
  - Collect families with multiple affected members



- Association (GWAS)
  - Big cohorts
  - Samples for control and subjects
  - Compare polymorphisms (markers) in both groups



MENDELIAN (SINGLE TRAIT) GENETIC DISEASES CAN BE STUDIED IN PEDIGREES; MONOGENIC DISEASES

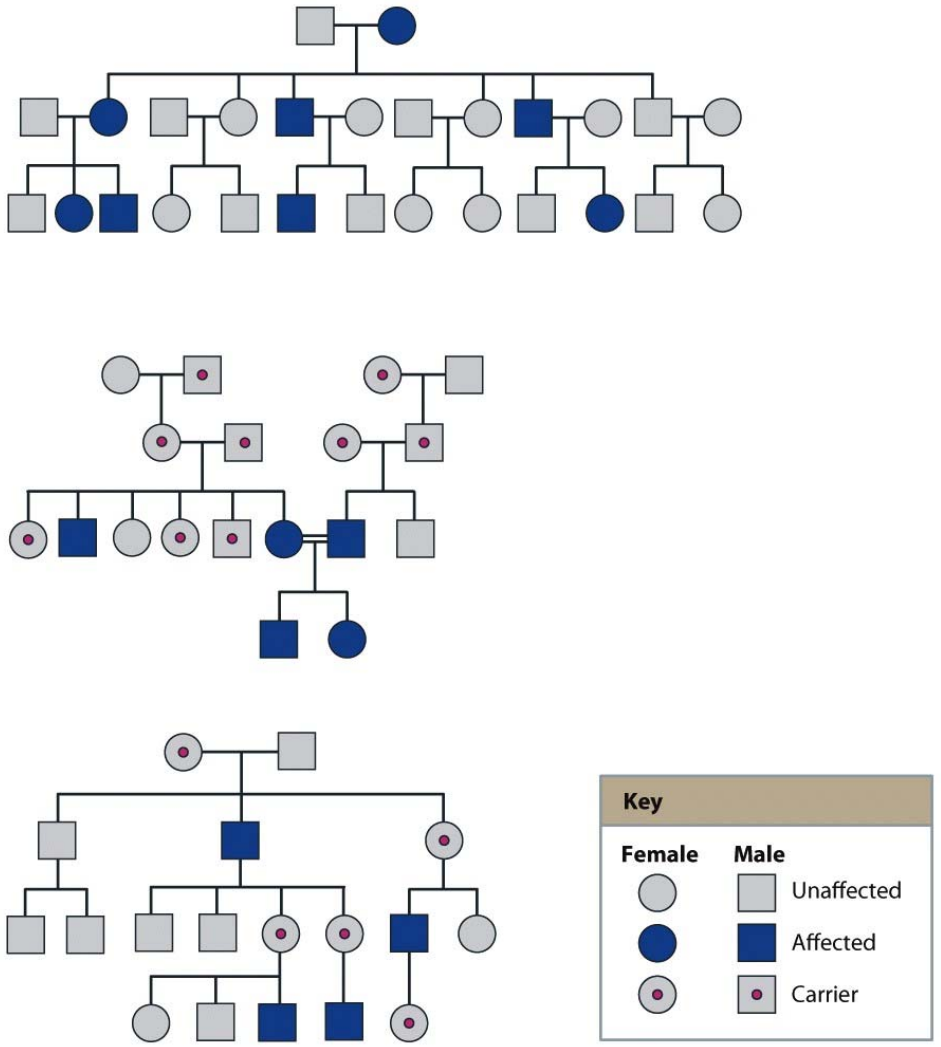
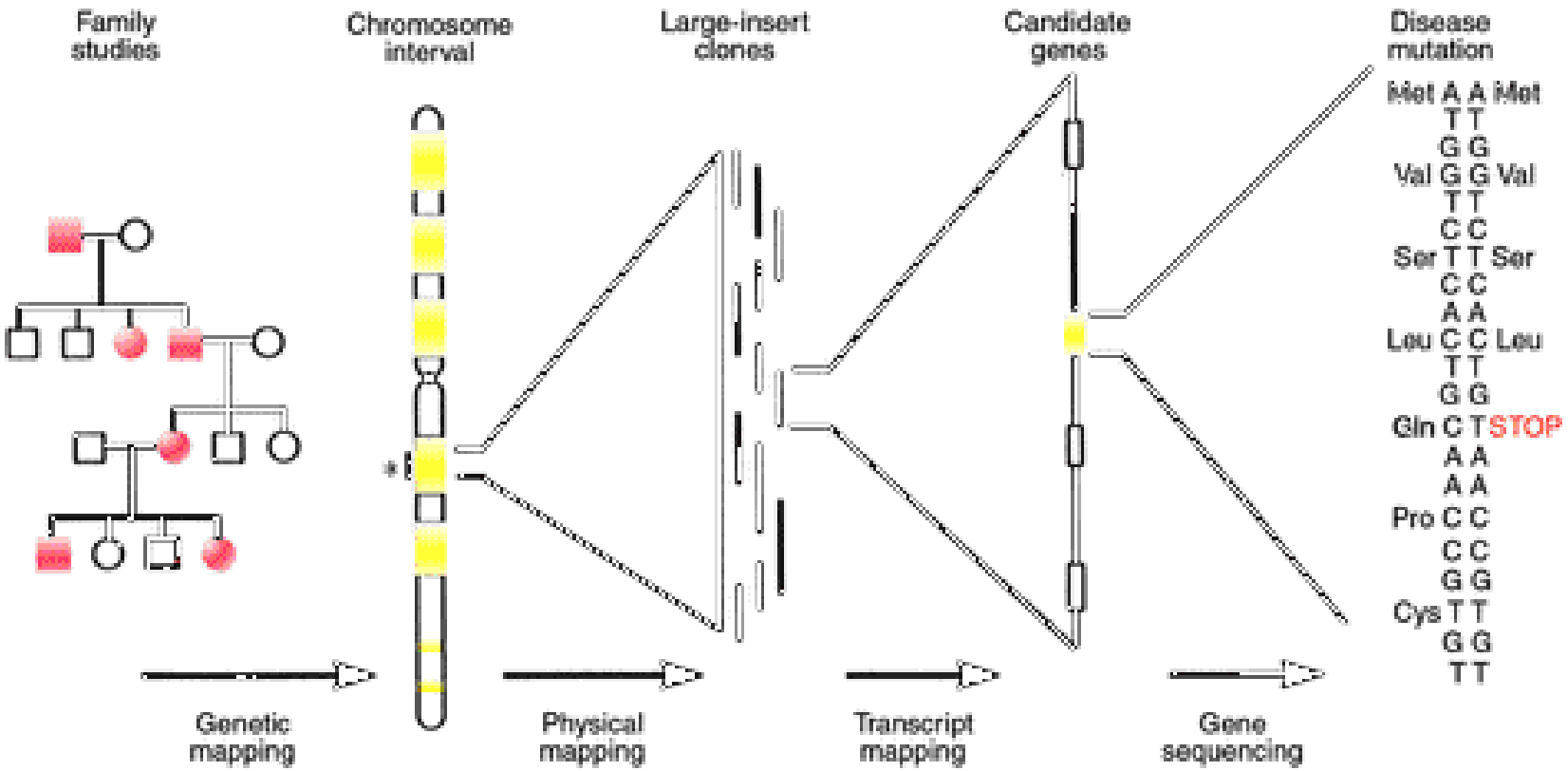


Figure 3.1 Human Evolutionary Genetics, 2nd ed. (© Garland Science 2014)

FINDING THE GENE MUTATED IN PROGERIA (20 YEARS AGO)

- Pedigree analysis followed by positional cloning or WES:



FINDING A SINGLE, HIGHLY PENETRANT CODING MUTATIONS TODAY

- WES:
- Whole Exome sequencing (WES)
- Large-scale genome and exome sequencing projects:
  - Finding loss of function variants
  - Finding healthy human knock-outs (explore gene function)
  - single, highly penetrant coding mutations
    - Lek M et al. Analysis of protein-coding genetic variation in 60,706 humans. Nature. 2016
    - Narasimhan et al. Health and population effects of rare gene knockouts in adult humans with related parents. Science (80-). 2016;8624:1–8.

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FINDING A SINGLE, HIGHLY PENETRANT CODING MUTATIONS TODAY

- Exome sequencing (inexpensive and fast)
- Quick access to the low hanging fruit:
- Family studies, case-control studies, and population cohorts pick up a signal everywhere
- Gene identification followed by numerous validation and in particular functional/mechanistic studies of the respective candidate genes.
- But: functional validation is still very hard
- Connect the mutation/variant in that gene to the observed phenotype

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USES OF GWAS

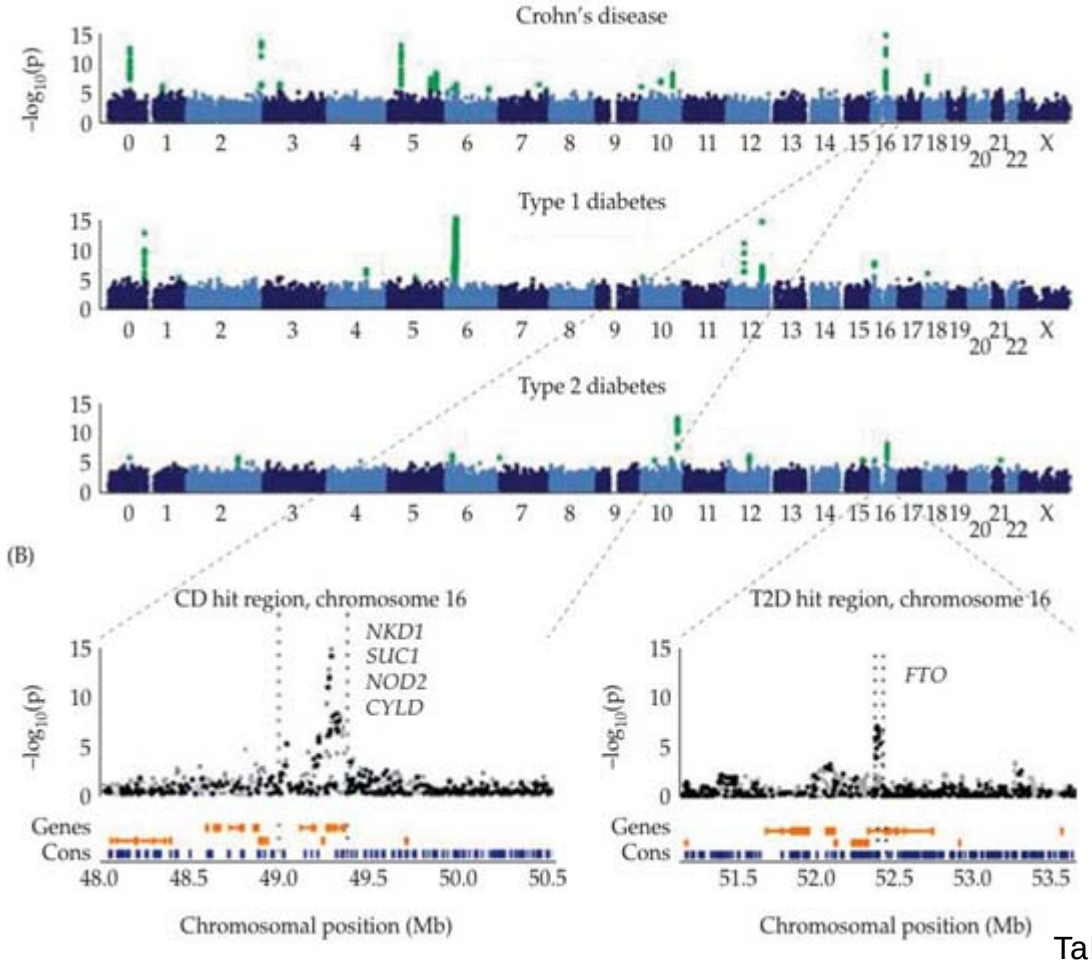
- identification of genetic risk factors that increase the susceptibility to the disease

  - Eg. complex nature of inflammatory bowel disease-ulcerative colitis (UC), Crohn's disease (CD)

  - common SNP alleles that are significantly more frequent in patients than in healthy controls

  - Read more:
    - Britt-Sabina et al. Opportunities and challenges of whole-genome and -exome sequencing. BMC Genetics. 2017

WHOLE GENOME ASSOCIATION STUDIES (GWAS)



Taken from Gibson. A Primer of Genome Science, 3rd ed.)

FUNCTIONAL VALIDATION

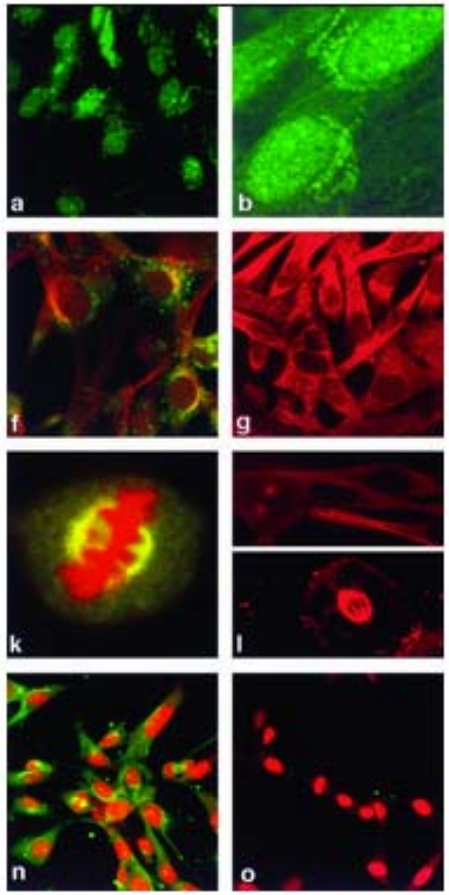
- Genomics is not enough! The work for molecular biologists
- Leave your fancy high-throughput machines, and bioinformatics and head back to the lab-a perishing skill?

  - ☐ Molecular assays

  - ☐ Biological assays

MOLECULAR ASSAYS

- Does the mutation cause the following changes?
  - ☐ mRNA expression (exon usage, alternative splicing)
  - ☐ Transcript/protein localization
  - ☐ Protein/DNA interaction
  - ☐ Protein/protein interaction with sophisticated biophysical techniques
  - ☐ Localization of where and when the protein is expressed

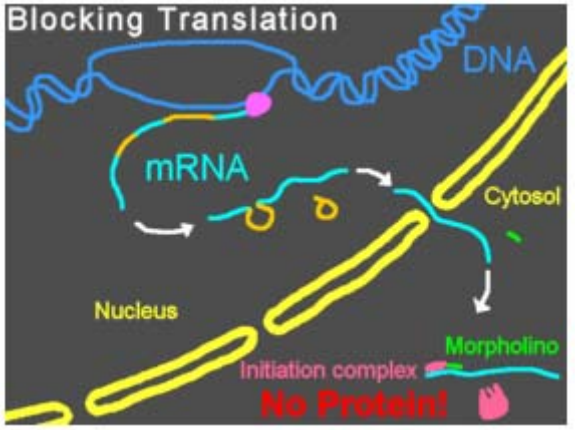


Subcellular localization
(Weiqiao, PNAS 1998)

BIOLOGICAL ASSAYS

- What is the effect of the candidate mutation in living cells or organisms (evidence of a causal relationship between genotype and phenotype)

- Human cell lines. Gene knockdown (by siRNA or transfection with a plasmid or virus overexpressing the mutant protein
- Animal models: complete or partial knock-outs, or substitution by the mutant protein
- See the effect on a complete organism



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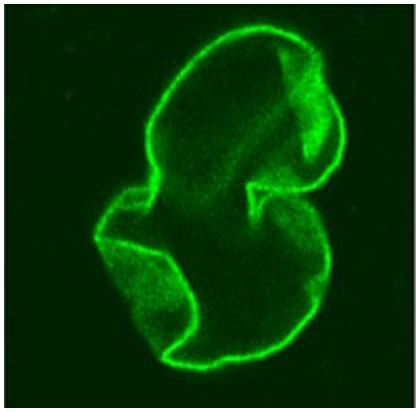
FUNCTIONAL VALIDATION: FROM SEQUENCE TO THE FUNCTION

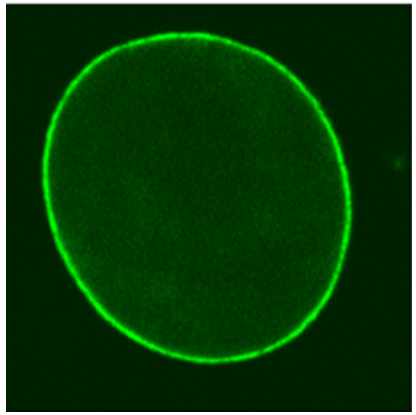
- Single base substitution in the lamin (LMNA) gene found in progeria patients in 2003.
- Lamin A is a protein of the membrane surrounding the nucleus
- Nonsense mutation: early truncation of the protein
- Truncated LMNA resulted in aberrant scaffolding of the nuclear membrane proteins
- Physical stress to cells with aberrant nuclear membranes causes an early aging an cell death

BIOLOGICAL ASSAYS FOR FUNCTIONAL VALIDATION

- Use human cell lines to demonstrate the effect of the mutation of the cell's phenotype
- Truncated lamin A fails to properly integrate in the scaffold of membrane proteins and creates disfigurement of the nucleus (lobular shape).



Progeria nucleus



Normal nucleus

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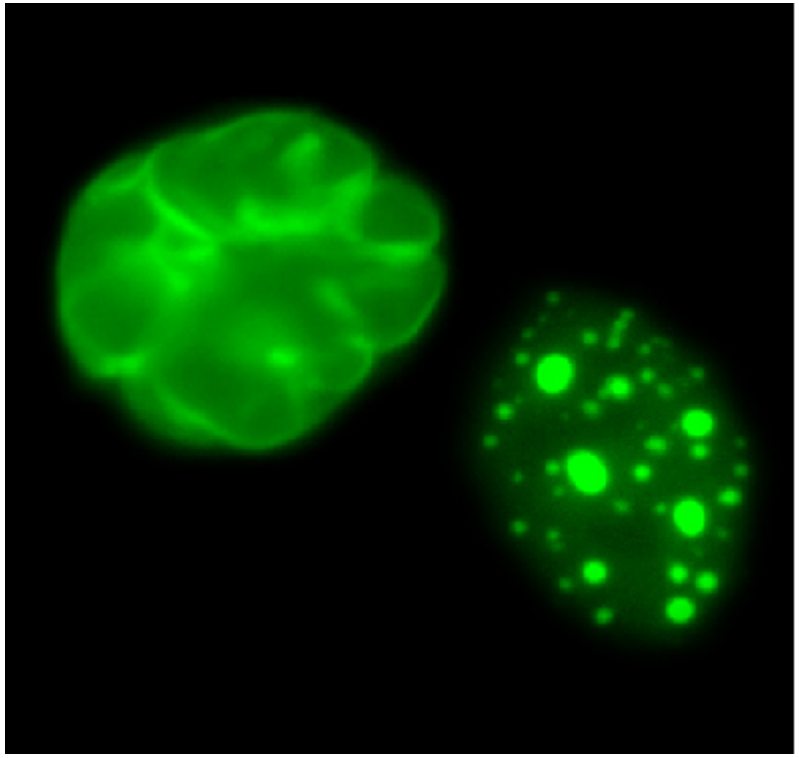
FUNCTIONAL VALIDATION (UNDERSTAND THE MOLECULAR BIOLOGY OF THE GENE)

- LMNA carries two tags (like ZIP codes) that direct the protein to the inner nuclear membrane
- Targeting of LMNA is accomplished via farnesylation
- The tag (farnesyl) is removed and LMNA can be integrated into the membrane
- The tag of Progeria LMNA cannot be removed and LMNA becomes permanently stuck to the inner nuclear membrane.
- Are there any drugs (farnesylation inhibitors) that can prevent progeria?

CURES FOR PROGERIA?

- Farnesyltransferase inhibitors (FTIs)—anticancer drug can slow down progeria by reversing the damage from the mutant protein



Untreated cells from progeria patients (left) compared to cells treated with farnesyltransferase inhibitors (right).

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CURES FOR PROGERIA?

- Gene editing?
- CRISP/Cas genome editing

Genetic Syndromes & Gene Therapy

Arancio et al., J Genet Syndr Gene Ther 2014, 6:1
http://dx.doi.org/10.4172/2157-7412.1000256

Review Article Open Access

Hutchinson Gilford Progeria Syndrome: A Therapeutic Approach via Adenoviral Delivery of CRISPR/cas Genome Editing System

Walter Arancio*, Swonild Ilenia Genovese, Giuseppe Pizzolanti and Carla Giordano

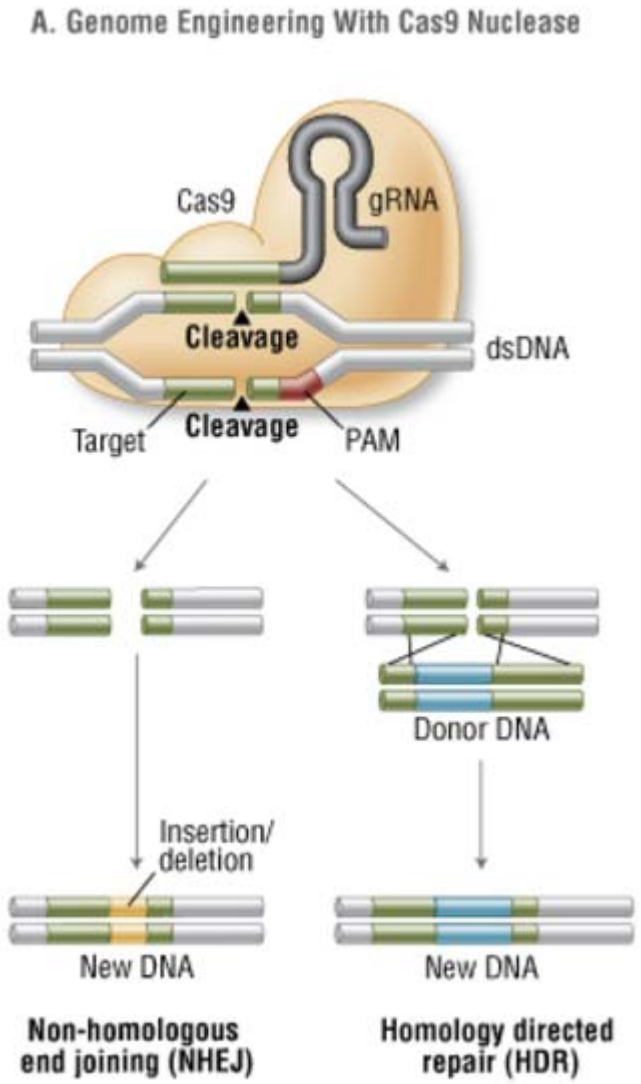
Section of Cardio-Respiratory and Endocrine-Metabolic Diseases, Biomedical Department of Internal and Specialist Medicine (Di.Bi.M.I.S.), University of Palermo, Piazza delle Cliniche 2, 90127 Palermo, Italy

Abstract

Hutchinson-Gilford Progeria Syndrome (HGPS) is a rare human genetic disease caused by mutations in the *LMNA* gene. *LMNA* codes for structural components of the nuclear lamina. Alterations of nuclear lamina lead to a very variable class of diseases known as laminopathies. In detail, HGPS manifests a severe premature ageing phenotype due to the accumulation of a dominant negative form of lamin-A called progerin. With current treatments, the life expectancy of HGPS patients does not exceed their second decade. Death is usually due to cardiovascular complications.

CRISPR/CAS9 AND TARGETED GENOME EDITING

- Jennifer Doudna and Emmanuelle Charpentier
- re-engineering of Cas9 endonuclease with a guide RNA (gRNA)
- Mixing the gRNA with Cas9 results in cutting the DNA target specified by the guide RNA
- The double strand break is repaired by homologous recombination OR NHEJ



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GENE THERAPY

- If genetically modified foods are not allowed in Austria; should gene editing in humans be allowed?
- Should it be allowed in the case of progeria?; imagine your child is sick!
- What considerations should be taken?
  - What are the risks of failure or modifying other genes? Do we fully understand the black box?
    - e.g. Gene modifications in somatic versus germline tissue
  - Treatment of a disease versus a condition
    - e.g. achondroplasia (short-limb stature); right of people being different

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IN VIVO TARGETED GENOME EDITING

- Was inefficient, feasible only in dividing cells (most adult tissues); off-target effects
- *Suzuki et al. Nature. Dec 2016.*
  - homology-independent targeted integration (HITI) strategy combined with CRISPR/Cas9
  - robust DNA knock-in in both dividing and non-dividing cells

OUTLINE FOR TODAY

- Why is genomics important?
  - genetics perspective-find cause of diseases
  - synthetic biology: build your own genome
  - evolutionary biology; Where do we come from?
- Commercializing genomics
- Ethical aspects

BUILD A MINIMAL GENOME

- What genes are necessary for life?
  - The minimal genome: Smallest set of genes an organism needs to live

- *Mycoplasma genitalium*
  - One of the first genomes to be sequenced
  - Smallest known genome
  - One circular chromosome
  - 580Mb, 482 genes

The minimal gene complement of Mycoplasma genitalium.

Fraser CM, Gocayne JD, White O, Adams MD, Clayton RA, Fleischmann RD, Bult CJ, Kerlavage AR, Sutton G, Kelley JM, Fritchman RD, Weidman JF, Small KV, Sandusky M, Fuhrmann J, Nguyen D, Utterback TR, Saudek DM, Phillips CA, Merrick JM, Tomb JF, Dougherty BA, Bott KF, Hu PC, Lucier TS, Peterson SN, Smith HO, Hutchison CA 3rd, Venter JC.
Institute for Genomic Research, Rockville, MD 20850, USA.

Science. 1995 Oct 20;270(5235):397-403.

MINIMAL GENOME: SET OF GENES FOR LIFE?

- Identify and test a set of genes necessary and sufficient for life
  - Based on conservation of genes…
  - Compare multiple bacterial genomes—206 genes are always present with function in:
    - translation
    - transcription
    - replication
    - cell membrane proteins
    - minimal transport systems

Cellular life forms are capable of importing metabolites and thus of the majority of metabolic enzymes are not essential for life

GENES NECESSARY FOR LIFE?

- These functions would be excluded
  - DNA repair machinery
  - molecular chaperones
  - metabolic pathways
  - signal transduction apparatus
- All genes necessary to respond to changes or stress in the environment

BUILD AN ARTIFICIAL GENOME WITH THE GENES DEFINED FOR LIFE

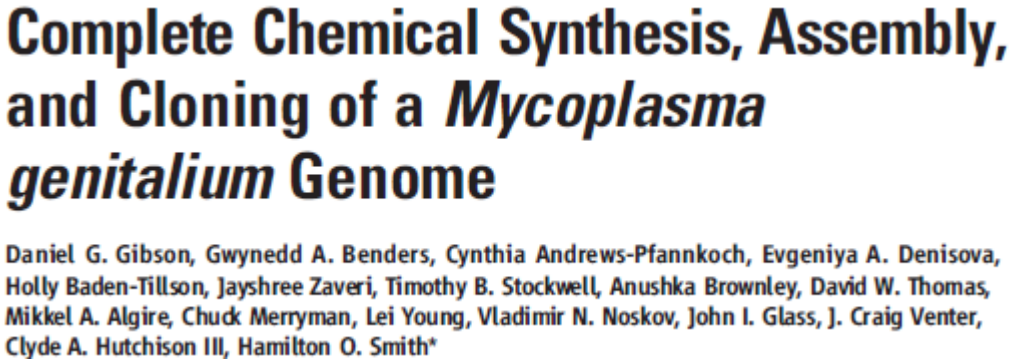
- Identify and test a set of genes necessary and sufficient for life
  - Compare multiple bacterial genomes—206 genes are always present
  - Randomly mutate candidate genes of M. genitalium without affecting viability –knock outs
  - Fuse candidate genes into an artificial genome

THE MINIMAL GENOME PROJECT

- Craig Venter and Hamilton Smith: create Mycoplasma laboratorium
- Synthetic species derived from M. genitalium
- First artificial genome build from a test tube
- Was built by combining 7kb fragments into larger fragments

MYCOPLASMA LABORATORIUM

- Gibson et al. 2008. Science



Complete Chemical Synthesis, Assembly, and Cloning of a *Mycoplasma genitalium* Genome

Daniel G. Gibson, Gwynedd A. Benders, Cynthia Andrews-Pfannkoch, Evgeniya A. Denisova, Holly Baden-Tillson, Jayshree Zaveri, Timothy B. Stockwell, Anushka Brownley, David W. Thomas, Mikkel A. Algire, Chuck Merryman, Lei Young, Vladimir N. Noskov, John I. Glass, J. Craig Venter, Clyde A. Hutchison III, Hamilton O. Smith*

- Combination of genome information and raw chemicals to construct a “living organism”
- Syntesis of long oligonucleotides and clones and joined into larger cassettes

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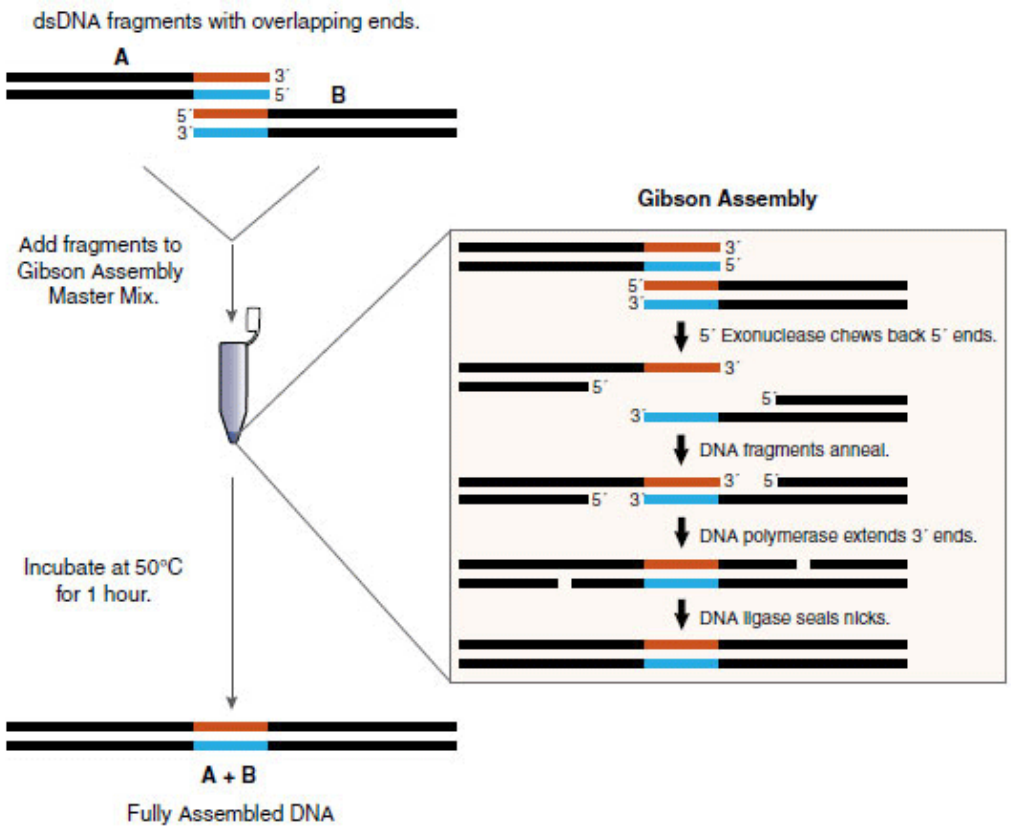
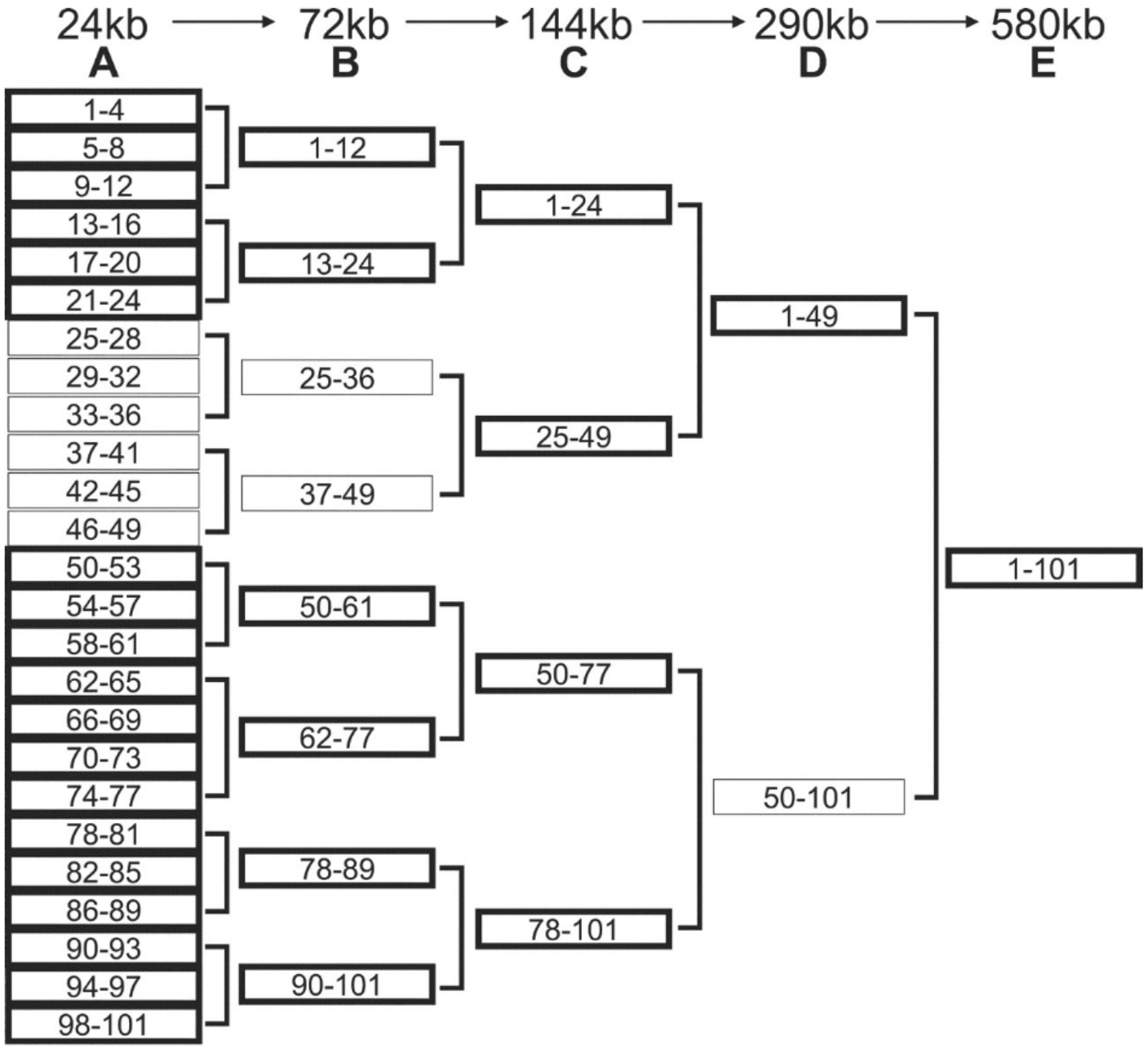
GIBSON ASSEMBLY

- Order synthetic fragments from a oligo production facility
- You give them the sequence and they send you a double stranded DNA fragment (~500bp)
- Fuse fragments together and create your own gene and then protein





Each cassette contains one or more genes; boundaries of cassettes at intergenic regions.

Set-up allows the future manipulation of genes in individual cassettes. The cassettes overlap 80-300bp for joining purposes

From: Gibson et al. 2008. Science.

MINIMAL GENOME PROJECT: TACKLED AN ENGINEERING CHALLENGE

- improved DNA construction technology
- Make organisms easier to engineer for a particular purpose
- Scary thought: “Gibson et al. demonstrates that it is now possible to construct the genomes for all known human viruses, including strictly regulated pathogens (such as smallpox), from publicly available DNA sequence data, methods, and materials” (Endy 2008. Science)
- Before this was possible only through highly skilled experts and considerable resources

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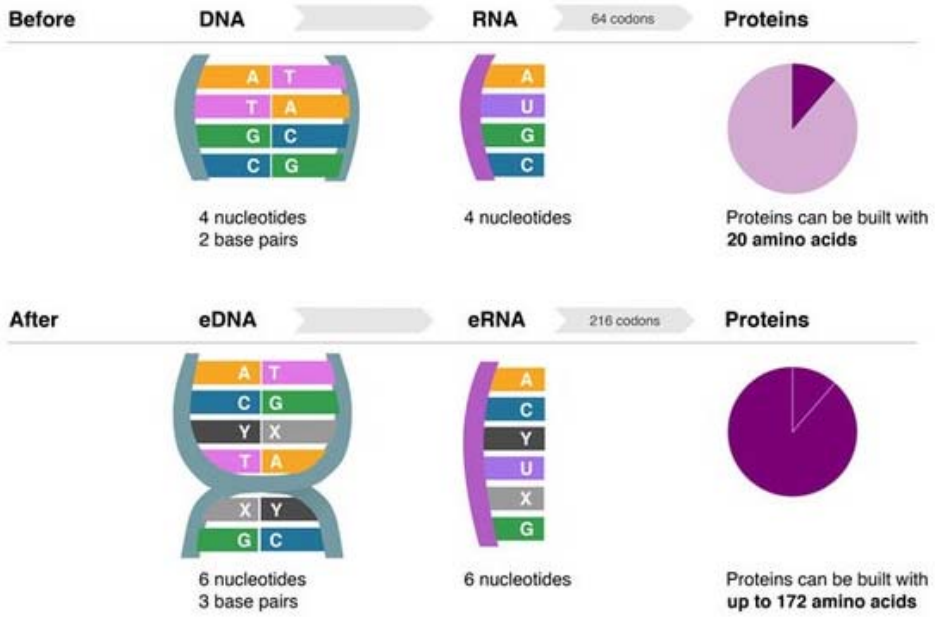
NEW DIRECTIONS OF SYNTHETIC BIOLOGY

- Creation of cells with 6 DNA letters (Romesberg, Scripps Institute)
- The biggest challenge was making sure the enzymes copy and transcribe the new DNA.



Cells with an expanded genetic alphabet could potentially make a wider range of proteins.

OUTLINE FOR TODAY

- Why is genomics important?
  - genetics perspective-find cause of diseases
  - synthetic biology: build your own genome
  - evolutionary biology; Where do we come from?
- Commercializing genomics
- Ethical aspects

WHICH NON-HUMAN ANIMALS ARE THE CLOSEST LIVING RELATIVES OF HUMANS?

- This question has been considered since Darwin wrote that “much light will be thrown on the origin of man and his history” in On The Origin of Species.

- Before the development of molecular techniques, morphological characters were the major source of evidence available to place
- humans in the tree of life
- morphology is the only tool we have for reconciling most fossils with living species.

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EXACT PHYLOGENIES CAN BE BUILD WITH MOLECULAR DATA

- Molecular data go back much further than fossils

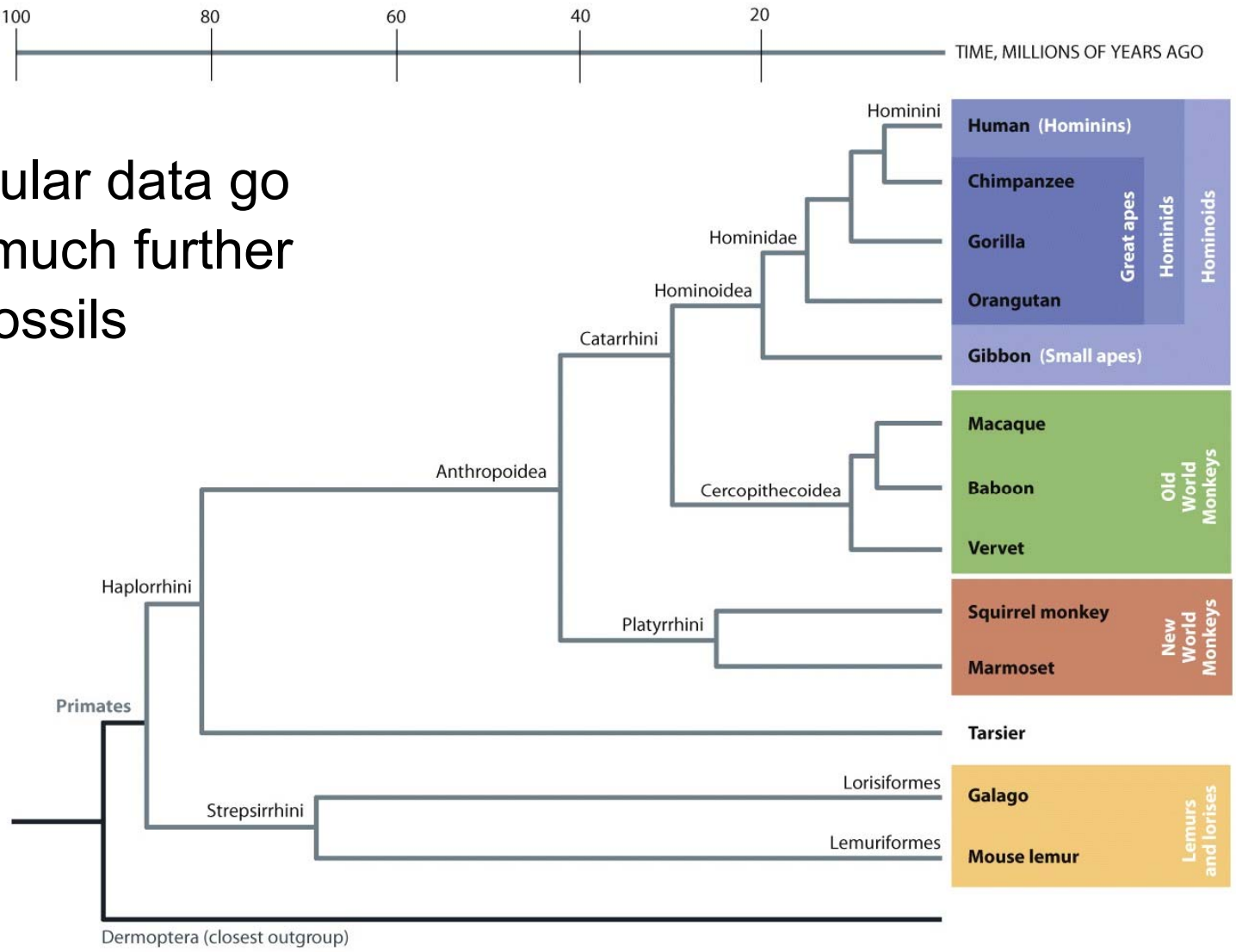


Figure 7.3 Human Evolutionary Genetics, 2nd ed. (© Garland Science 2014)

PRIMATE GENOME PROJECTS

- What makes us human?
  - Finding the genes that are unique to humans and confers our special characteristics
  - Sequencing the chimpanzee (our closest relative)—Chimpanzee Genome Project
  - Sequencing the Neanderthal (ancestral vs. derived)

WHAT GENETIC CHANGES HAVE MADE US HUMAN?

- human genes are 97% identical to chimpanzee
- Differences accumulated 7-5 MY.
- Differences in related to morphological, physiological, biochemical, and behavioral traits
- Following the publication of human and great ape genome sequences, more than 600 human-specific genes have been characterized.

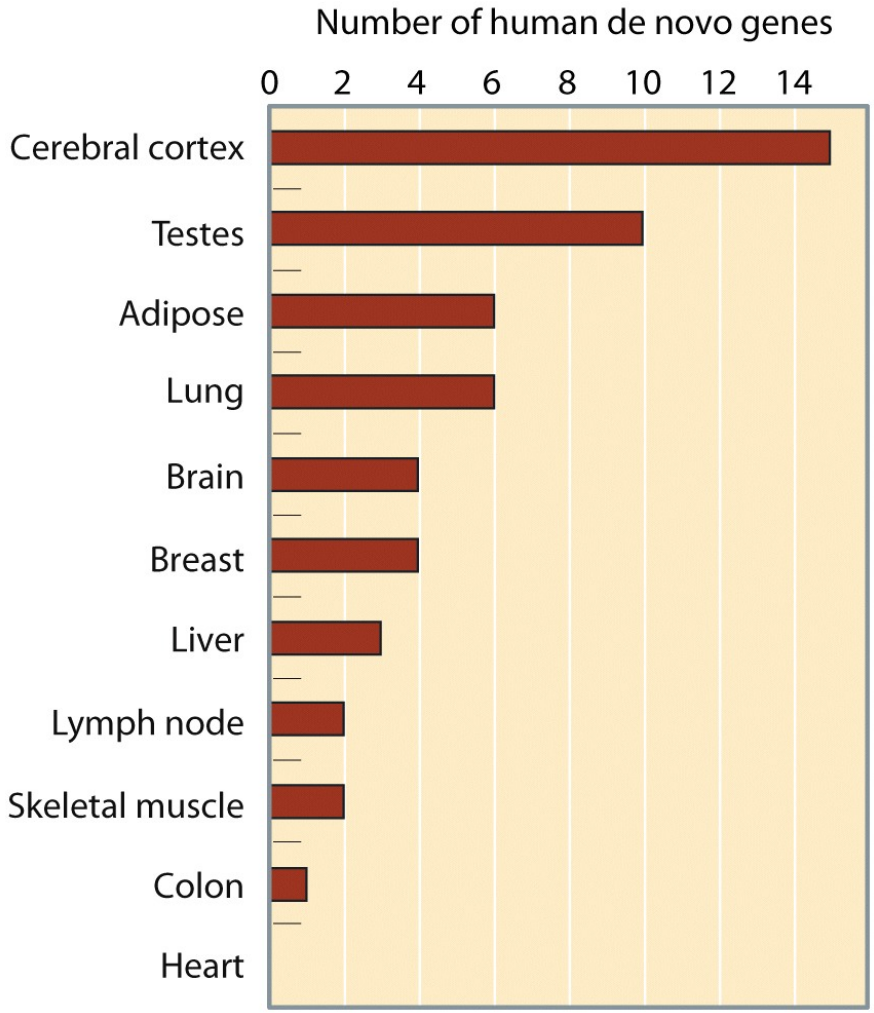


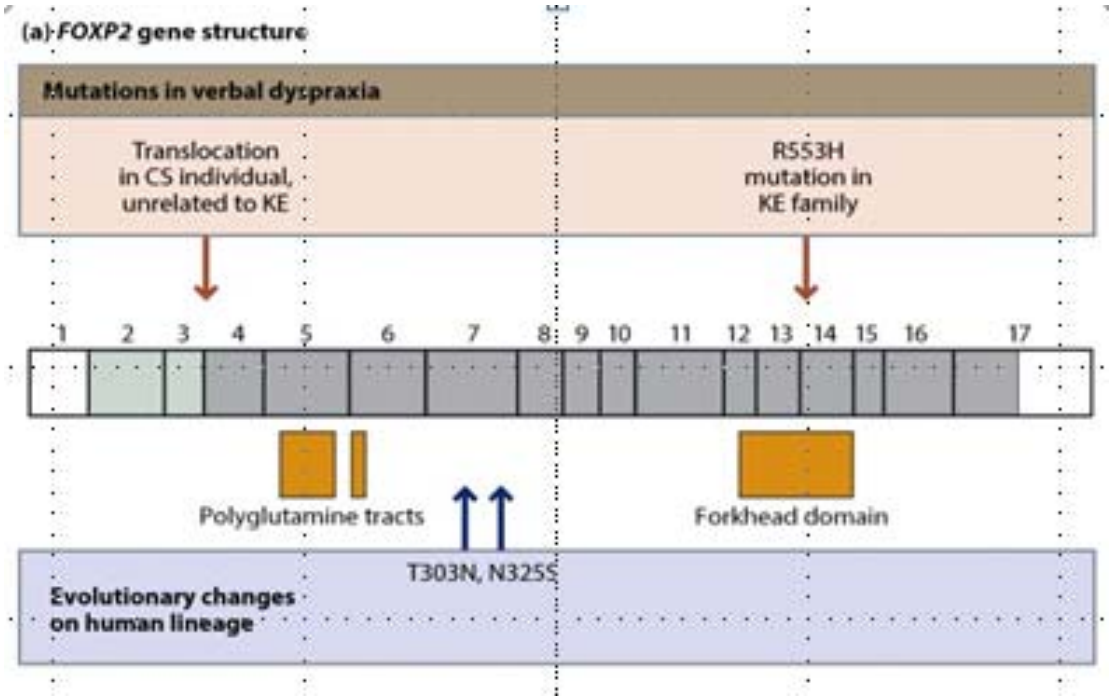
Figure 8.9 Human Evolutionary Genetics, 2nd ed. (© Garland Science 2014)

DIFFERENCES BETWEEN HUMAN AND CHIMP

- **600 genes identified unique to humans**
  - Most changes in genes:
    - language-related genes (FOXP2)—speech development,
    - hearing genes
    - immune system
    - brain development
  - 348 transcription factor genes evolve 50% faster in the human than in the chimp

STRUCTURE AND EVOLUTION OF THE FOXP2 GENE

- FOXP2
- 17 exons
- alternative splice variants
- Structural features shown in yellow boxes.
- Red arrows: inactivating mutations that lead to speech disorders



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STRUCTURE AND EVOLUTION OF THE FOXP2 GENE

b. Neuroimaging: group average activation in the unaffected and affected members of the KE family carrying out a language task

c. Amino acid changes during FOXP2 evolution within mammals are shown by arrows

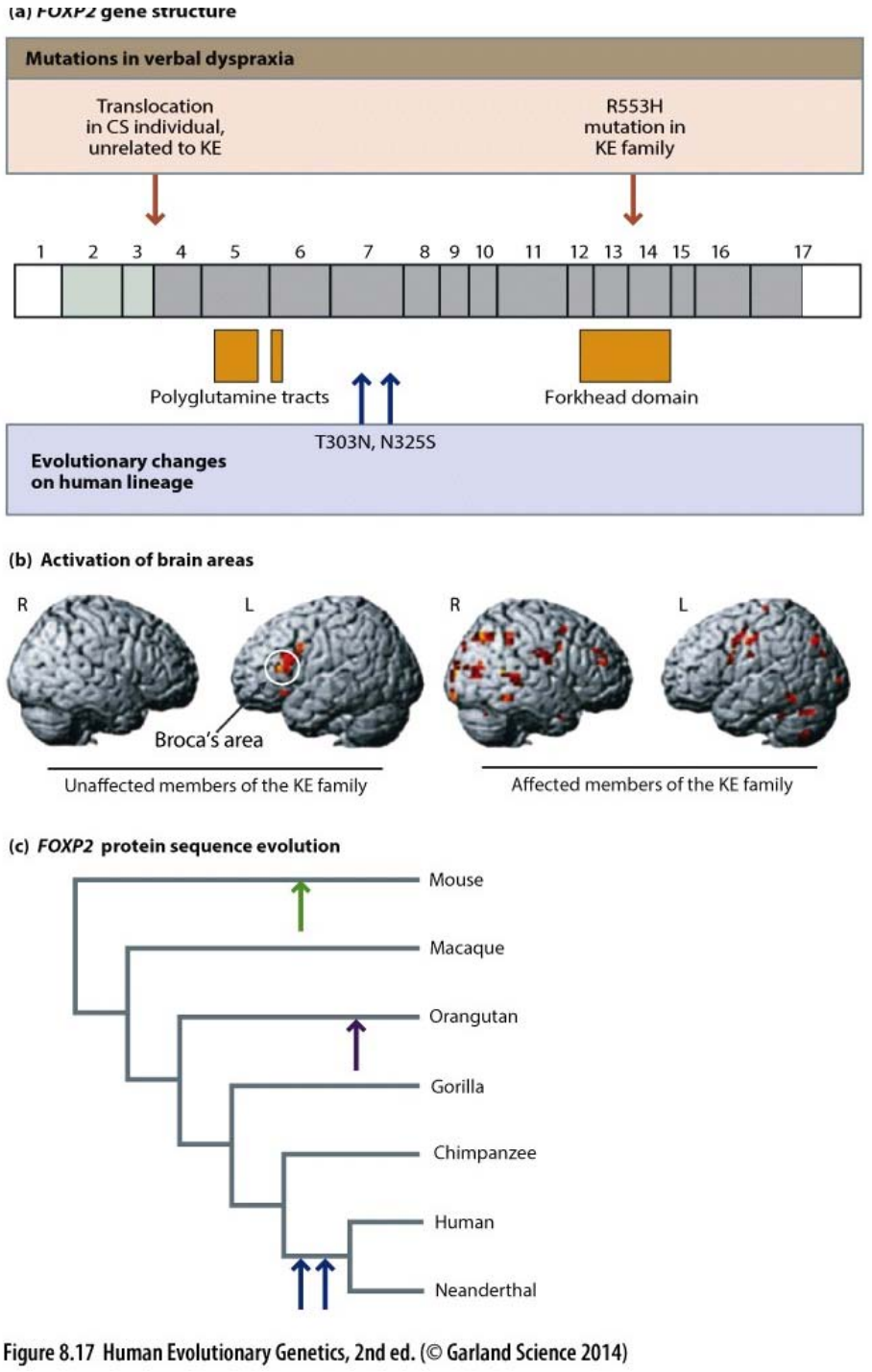

Figure 8.17 Human Evolutionary Genetics, 2nd ed. (© Garland Science 2014)

SEQUENCING THE NEANDERTHAL

- Reasons for sequencing Neanderthal
  - Identify changes in the modern human after leaving Africa (100,000yr ago)
  - Neanderthal has also the speech related gene FOXP2
  - Extracting, identifying and sequencing ancient DNA from fossils is a technically challenging task

PRIMATE GENOME PROJECTS

- Where do we come from?
- Sequencing ancestral DNA:
  - Neanderthal
  - Denisovans-What are Denisovans?
    - The first evidence of Denisovans comes from a small bone from Siberia

GROUP OF SVANTE PÄABO (MAX PLANK, DE) SEQUENCED WHOLE DENISOVAN GENOME

- Whole genome sequence from small bone
- DNA is 30,000-40,000 years old
- Information from DNA about the Denisovan fossil:
  - Girl
  - Denisovans were closer to Neanderthals than modern humans
  - Denisovans mixed with Neanderthals and our ancestors

INTERBREEDING BETWEEN HOMINOID GROUPS

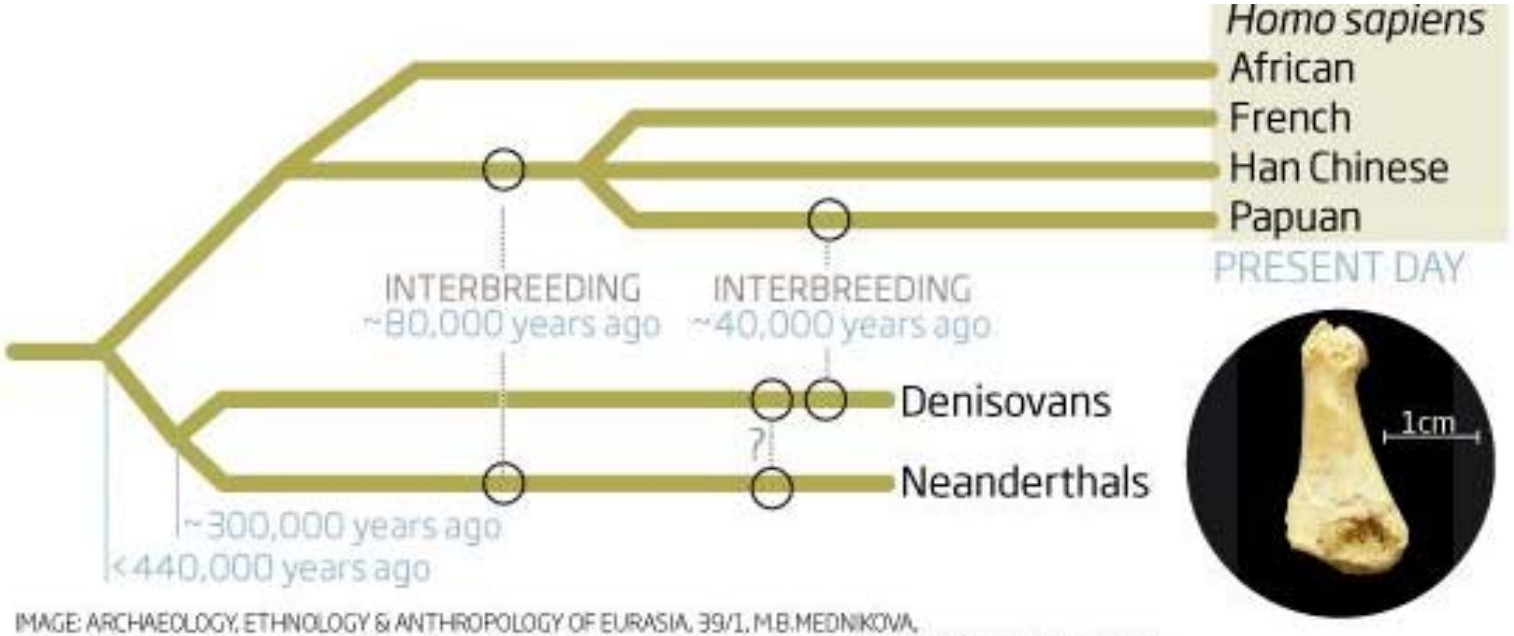

IMAGE: ARCHAEOLOGY, ETHNOLOGY & ANTHROPOLOGY OF EURASIA, 39/1, M.B.MEDNIKOVA,
A PROXIMAL PEDAL PHALANX OF A PALEOLITHIC HOMININ FROM DENISOVA CAVE, ALTAI, COPYRIGHT ELSEVIER, 2011

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OTHER ANCIENT DNA SEQUENCING

- 2013 Sequencing bones from the Neanderthals of the Altai mountains
  - Altai Neanderthal's parents were probably half-siblings
  - Insight into social patterns: rearing children between close relatives was not that uncommon in Neanderthal
  - Neanderthals and Denisovans mixed also with Homo erectus

ARE WE SO DIFFERENT?

- Comparison of genomes between Neanderthals, Denisovans and modern humans:
- 96 amino acid changes in 87 proteins in modern humans compared to Neanderthals
- 3 of 87 are expressed in the proliferative layers during mid-fetal brain development
- look for any functional differences in animal models with these 87 genes
  - Are these genes involved in the evolution of culture?
  - Social interactions—cooperativity?
  - Communication
  - Language, verbalization

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NEANDERTHAL FOOTPRINTS IN THE MODERN HUMAN BRAIN

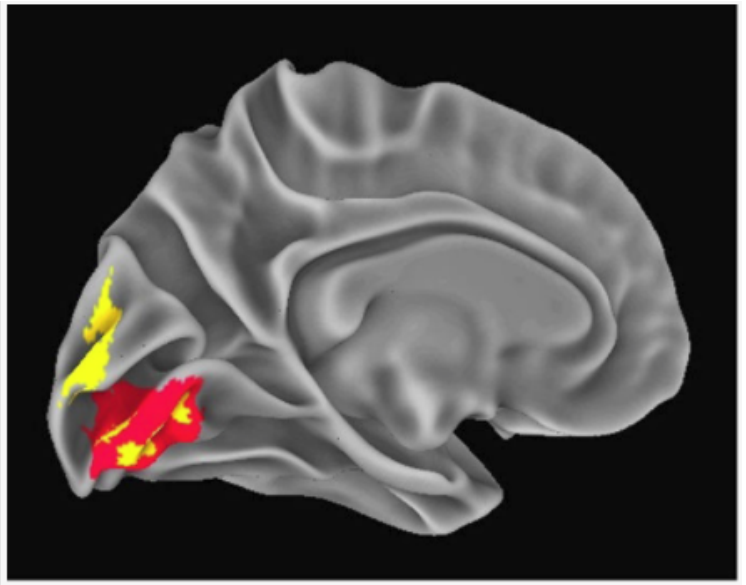
- By combining genetic and neuroimaging data genetic, it is possible to determine the effect of the Neanderthal inheritance in our brain
- Neanderthal alleles most likely entered the human genome in Eurasia as modern humans ventured out of Africa 47,000–65,000 years ago
- 2% of the ancestry of each non-African modern human traces to DNA from Neanderthals
- How do we know it is Neanderthal DNA? SNPs exclusive in the Neanderthal genome

NEANDERTHAL FOOTPRINTS IN THE MODERN HUMAN BRAIN

- Neanderthal alleles have been associated with a range of clinical traits, including depression and tobacco use.
- Neanderthal-derived genetic material (more than 100,000 SNPs determines the Neander-Score

It's been proposed that Neanderthals depended on visual-spatial abilities and toolmaking for survival—more so than on the social affiliation and group activities that typify the success of modern humans—and that Neanderthal brains evolved to preferentially support these visuospatial functions

Gregory MD et al. Neanderthal-Derived Genetic Variation Shapes Modern Human Cranium and Brain. Sci Rep. 2017



NeanderScore related brain changes in the primary visual cortex (1).

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- Why is genomics important?
  - genetics perspective-find cause of diseases
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AMBRY GENETICS

- Genetic counselling
- Search for mutations that cause observed phenotype
- Recommend test for genetic diseases
  - Usually requested by doctors or hospitals
  - Find genetic factors
  - Insurance issues
  - Implications of the results

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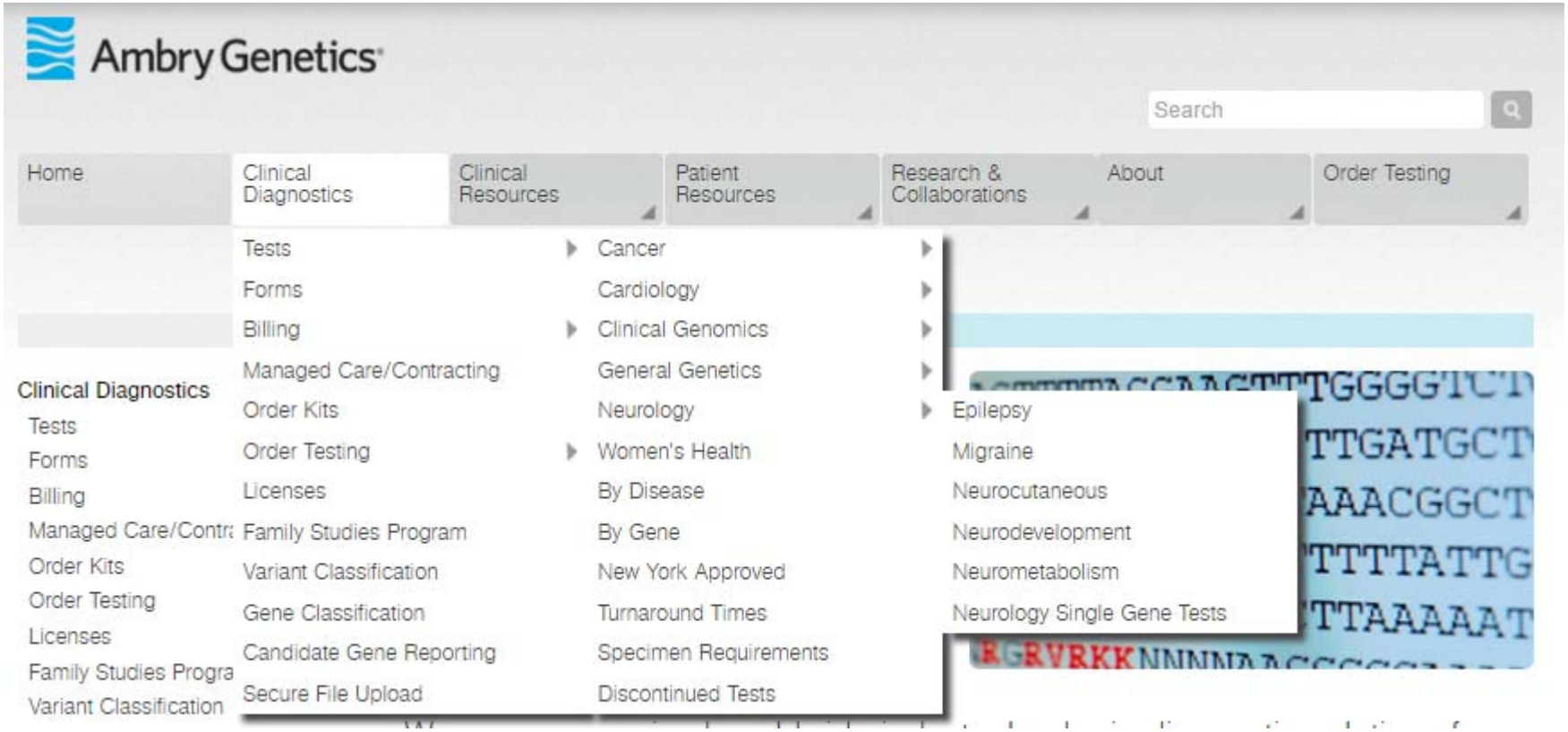
AMBRY GENETICS

- Exome sequencing for diagnostic purposes
- Have identified 45,000 mutations in ~500 different genes.



AMBRY GENETICS

- Cancer tests: BRCA1 and BRCA2
- BRCA1 and BRCA2 mutations are implicated in 25-50% of hereditary breast cancer cases
- Female BRCA1 mutation carriers have a 57-87% risk to develop breast cancer and a 39-40% risk to develop ovarian cancer by age 70

AMBRY GENETICS

- Testing Benefits & Indication
- If you have a family history of breast cancer or other cancer; testing should be considered
- Genetic testing is useful to:
  - Diagnose a personal and/or family history suggestive of hereditary breast and ovarian cancer
  - risk-reducing options for BRCA1 or BRCA2 mutation-positive patients and their relatives
  - Cancer is only dangerous once it has spread (time when it is usually detected)
  - Genetic testing allows detecting cancer earlier

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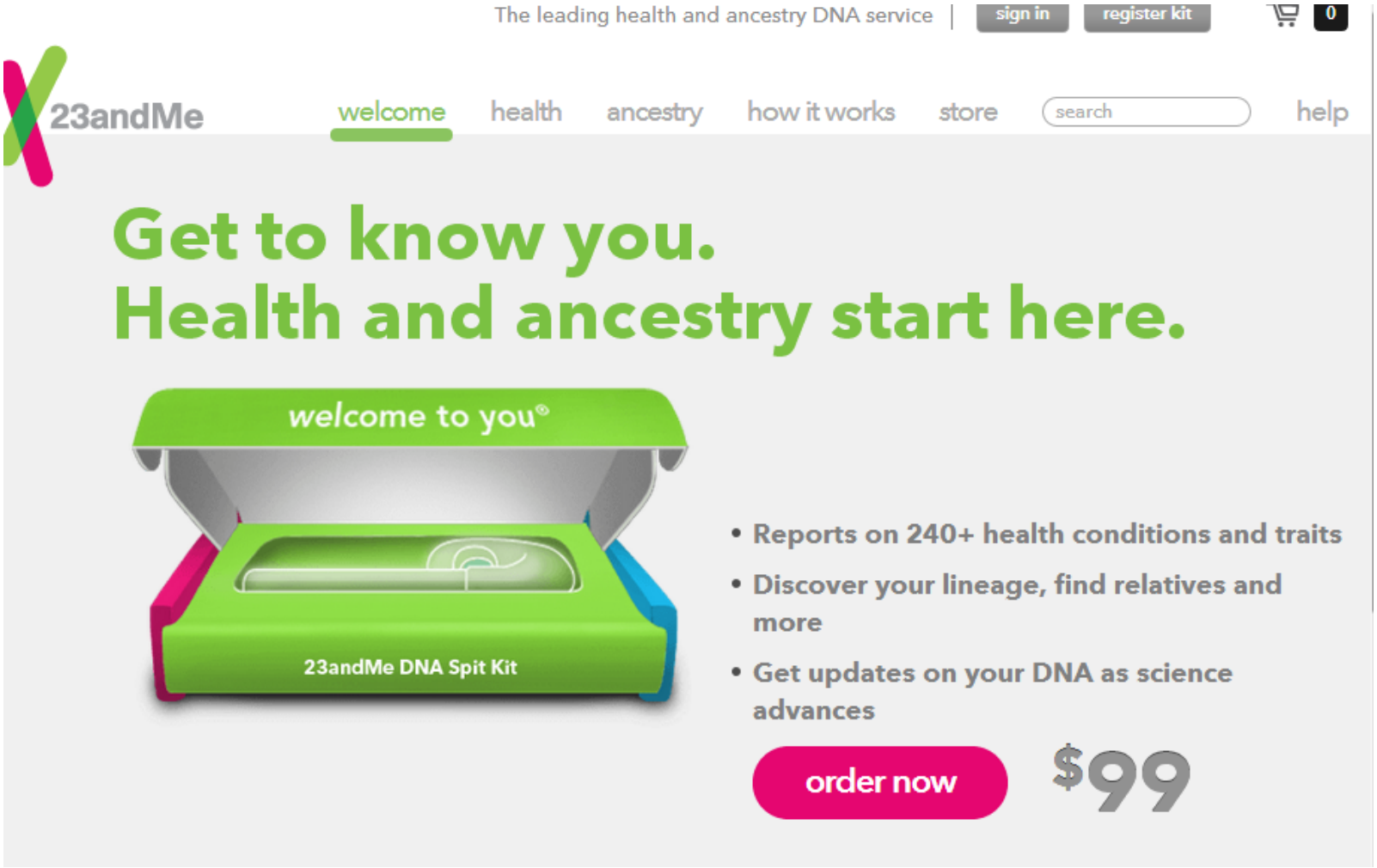
COMPANIES ANALYZING PERSONAL GENETIC INFORMATION ARE ON THE RISE!



23ANDME

What your DNA says about you.

Find out things like if your body metabolizes caffeine quickly, or if you're at a higher risk for diabetes. The more you know about your DNA, the more you know about yourself.

Carrier status

Find out if your children are at risk for inherited conditions, so you can plan for the health of your family.

Health risks

Understand your genetic health risks. Change what you can, manage what you can't.

Drug response

Arm your doctor with information on how you might respond to certain medications.

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- Send in your saliva
- Discover (6-8 weeks), your reports are ready in your online account. Log in and start discovering what your DNA says about you…and family; new increase price form 2014: $149.
- Learn what percent of your DNA is from populations around the world
- Contact your DNA relatives across continents or across the street
- Build your family tree and enhance your experience with relatives

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23ANDME—TERMS AND CONDITIONS

Which Personal Information We Collect

"Personal Information" is information that can be used to identify you, either alone or in combination with other information. 23andMe collects and stores the following types of Personal Information (see Terms of Service for a full list of related definitions):

- **"Registration Information"** is the information you provide about yourself when registering for and/or purchasing our Services (e.g. name, email, address, user ID and password, and payment information).
- **"Genetic Information"** is information regarding your genotype (e.g. the As, Ts, Cs, and Gs at particular locations in your genome), generated through processing of your saliva by 23andMe or by its contractors, successors, and assignees; or otherwise processed by and/or contributed to 23andMe.
- **"Self-Reported Information"** is all information about yourself, including your disease conditions, other health-related information, personal traits, ethnicity, family history, and other information that you enter into surveys, forms, or features while signed in to your 23andMe account. Self-Reported Information is included in 23andWe Research only if you have given consent as described in the applicable Consent Document.
- **"User Content"** is all information, data, text, software, music, audio, photographs, graphics, video, messages, or other materials - *other than* Genetic Information and Self-Reported Information - generated by users of 23andMe Services and transmitted, whether publicly or privately, to or through 23andMe.
- **"Web Behavior Information"** is information on how you use the 23andMe website (e.g. browser type, domains, page views) collected through log files, cookies, and web beacon technology.
- **"Referral Information"** is information that you provide when referring 23andMe Services to your friends and contacts as part of a 23andMe referral program.

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YOUR PRIVACY AND SECURITY

- At 23andMe, we're committed to maintaining the security and confidentiality of your personal information. We've put security measures in place to help protect against the loss, misuse or alteration of information under our control. We use procedural, physical and electronic security methods designed to prevent people who aren't authorized from getting access to this information.

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23ANDME

- The fate of 23andMe
- In 2013 the US Food and Drug Administration (FDA) ordered 23andMe to discontinue marketing its personal genome service (PGS) as the company had not obtained the legally required regulatory approval resulting in concerns about the potential consequences of customers receiving inaccurate health results
- The company still sells a personal genome test without health-related results in the United States.
- 23andMe has been selling a product with both ancestry and health-related components in Canada and UK since 2014
- 23andMe has typed over 750,000 individuals; selling the information to pharmaceutical companies

RESEARCH: 23ANDME AND AMBRY GENETICS

- provide important resources for researchers
- based on the massive amounts of data of customers who have consented to research and completed online surveys about depression (120,000-450,000 customers)
- Read more at https://blog.23andme.com/23andme-research/new-genetic-findings-on-depression/#sYkqrqALxVHtBH80.99

New Genetic Findings On Depression

August 1, 2016
Published by 23andMe under 23andMe Research

In a new study, scientists have found genetic markers associated with depression in people of European descent.

In what is by far the largest study of its kind focused on major depressive disorder, researchers from Pfizer, Massachusetts General Hospital and 23andMe identified 17 single nucleotide polymorphisms in 15 genetic loci significantly associated with depression among people of European ancestry. The study may lead to better understanding of the biology of the condition. Major depressive disorder is characterized by mood changes, sleep disruption, fatigue and loss of appetite, and is one of the leading causes of disability and is estimated to affect more than 350 million people worldwide.

OUTLINE FOR TODAY

- Why is genomics important?
  - genetics perspective-find cause of diseases
  - synthetic biology: build your own genome
  - evolutionary biology; Where do we come from?
- Commercializing genomics
- Ethical aspects

CAN GENETIC INFORMATION HARM YOU?

- Do you want to learn about unwanted family-status
  - Paternity testing?
- Do you want to learn about carrier status?
  - When having children?
  - Match-making based on genetic compatibility?
  - predisposition to disease (Huntington)?
  - breast cancer?

  - Can knowledge of your genetic information harm you?
    - E.g insurance costs?

GROUP ASSESSMENT—A FEW EXAMPLES ON HOW GENETIC INFORMATION CAN HAVE AN IMPACT

- Should blood tests maybe required in addition to drug tests for evaluation purposes (fitness for the job)?
  - If you are in a high-performance sport
  - Restrict individuals with a genetic predisposition to depression to stressful jobs

Use genetic test for pre-screening students for acceptance into high-demand careers?

GROUP ASSESSMENT—A FEW EXAMPLES ON HOW GENETIC INFORMATION CAN HAVE AN IMPACT

- Should parents be allowed to test their unborn for genetic disorders in order to make proper decisions on whether to continue the pregnancy? **Non-invasive prenatal screening:**

- Where should the limit be?
  - Should parents be allowed to test and preselect fertilized eggs to be implanted by in vitro fertilization?

ETHICS AND PRIVACY

- How has genomics impacted society and law?
  - Blood tests are available for various fatal diseases such as Huntington's Disease, Cystic Fibrosis, and Colon Cancer
  - Identification of genes that enhance physical performance; candidate genes for reaction speed, etc.
  - Should your genetic information be disclosed?
    - Protection against the misuse of genetic information

ETHICS AND PRIVACY

- ELSI—the world's largest bioethics program
  - ELSI –Ethical, legal, and social issues
  - Fairness in the use of genetic information,
  - Handling of the privacy and confidentiality genetic information
  - Should testing for untreatable diseases be allowed?
  - Should parents have their minor children tested?
  - Are the tests are reliable enough?
  - Should parents be allowed to test their unborn for diseases in order to make proper decisions on whether to continue the pregnancy?
- ELSI's ultimate goal is to fully understand all of the ethnic, cultural, social, and psychological issues that are in standing and be able to spread greater acceptance of for the Human Genome Project.

ELSI RESEARCH PROGRAM PRIORITIES

- “Grand challenges” for the future of genomic research.
- * Intellectual Property Issues Surrounding Access to and Use of Genetic Information--Laws, regulations, and practices of “genomic”commercialization Eg. Gene patents
- * Ethical, Legal and Social Factors that use Genetic Information to Improve Health –
- * Conduct of Genetic Research. Approval by ethics committee for protocols that involves humans.

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ELSI RESEARCH PROGRAM PRIORITIES

- “Grand challenges” for the future of genomic research.
- Genetic Information and Technologies in non-Health Care Settings
  - eg. employment, insurance, education, adoption, criminal justice, or civil litigation.
- Genomics on Concepts of Race, Ethnicity, Kinship and Individual and Group Identity
  - Do races exist; is one race smarter than another?
- Impact of knowledge about genomic information about Human Traits and Behaviors
  - are there genes for better learning, aging, athletic performance?

Different Individuals, Cultures and Religious Traditions View have different Ethical Boundaries

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REAL LIFE CASES

- Maternity testing for aneuploidies—mom was identified to have cancer, or even worse, have chromosomal anomalies herself (eg. sex chromosomes).
- DNA law tested
  A US company is the first to face penalties under the Genetic Information Nondiscrimination Act,

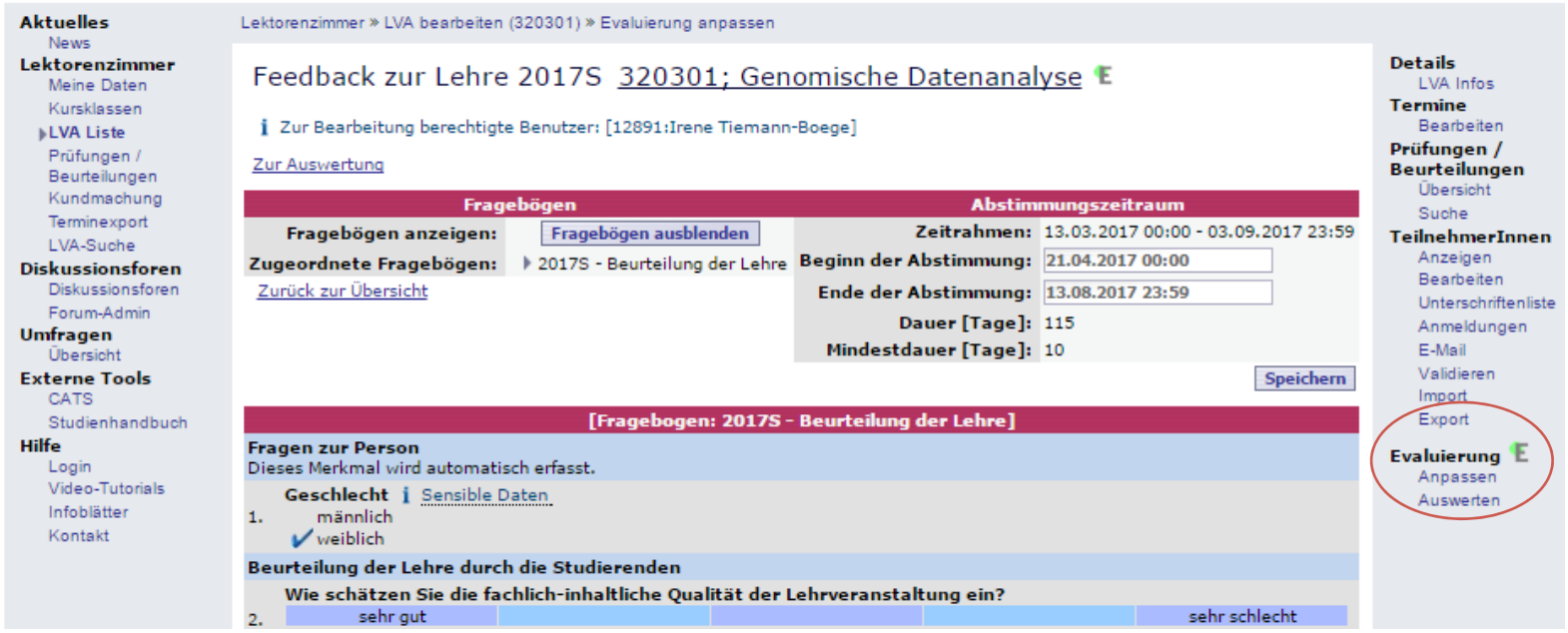
  - In June 2015, a federal court in Georgia awarded US$2.25 million to Jack Lowe and Dennis Reynolds, whose employer, Atlas Logistics Group Retail Services in Atlanta, Georgia, tested their DNA in a bid to identify who had left feaces on its premises. Neither man was the ‘devious defecator’. See go.nature.com/wtsvn3 for more.

WHAT DOES THE FUTURE DEPARE?

- http://www.sciencemag.org/news/2018/02/q-george-church-and-company-genomic-sequencing-blockchain-and-better-drugs?utm_campaign=news_daily_2018-02-08&et_rid=299548847&et_cid=1839488

DEADLINES

- Final exam: Thursday: 07.06.2018 from 9:15-11:15
  - You have to pass the exam, in order to pass the course
- Assay: Due date Thursday 22.05.2018 at 23:55
- Student evaluation in KUSSS
- Feedback zur Lehre 2018SS Genomische Datenanalyse



JOHANNES KEPLER
UNIVERSITÄT LINZ

QUESTIONS?

JOHANNES KEPLER
UNIVERSITÄT LINZ
Altenberger Straße 69
4040 Linz, Österreich
www.jku.at