

Introduction to Genomics

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The Wellcome Trust Centre for Human Genetics

University of Oxford

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Bioinformatics and Genomics 35

Course Overview

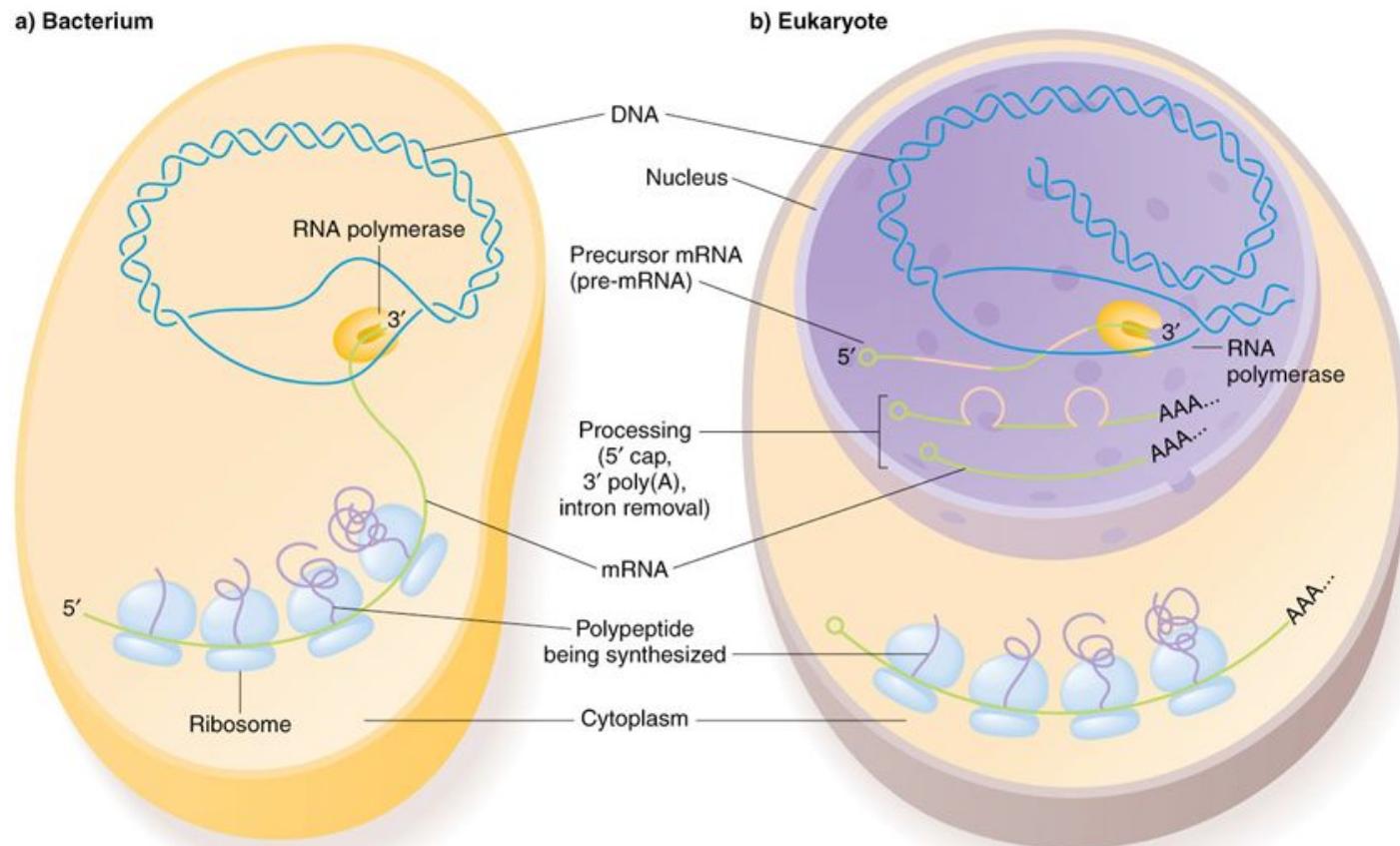
- Use current course overview

Genomics vs Genetics

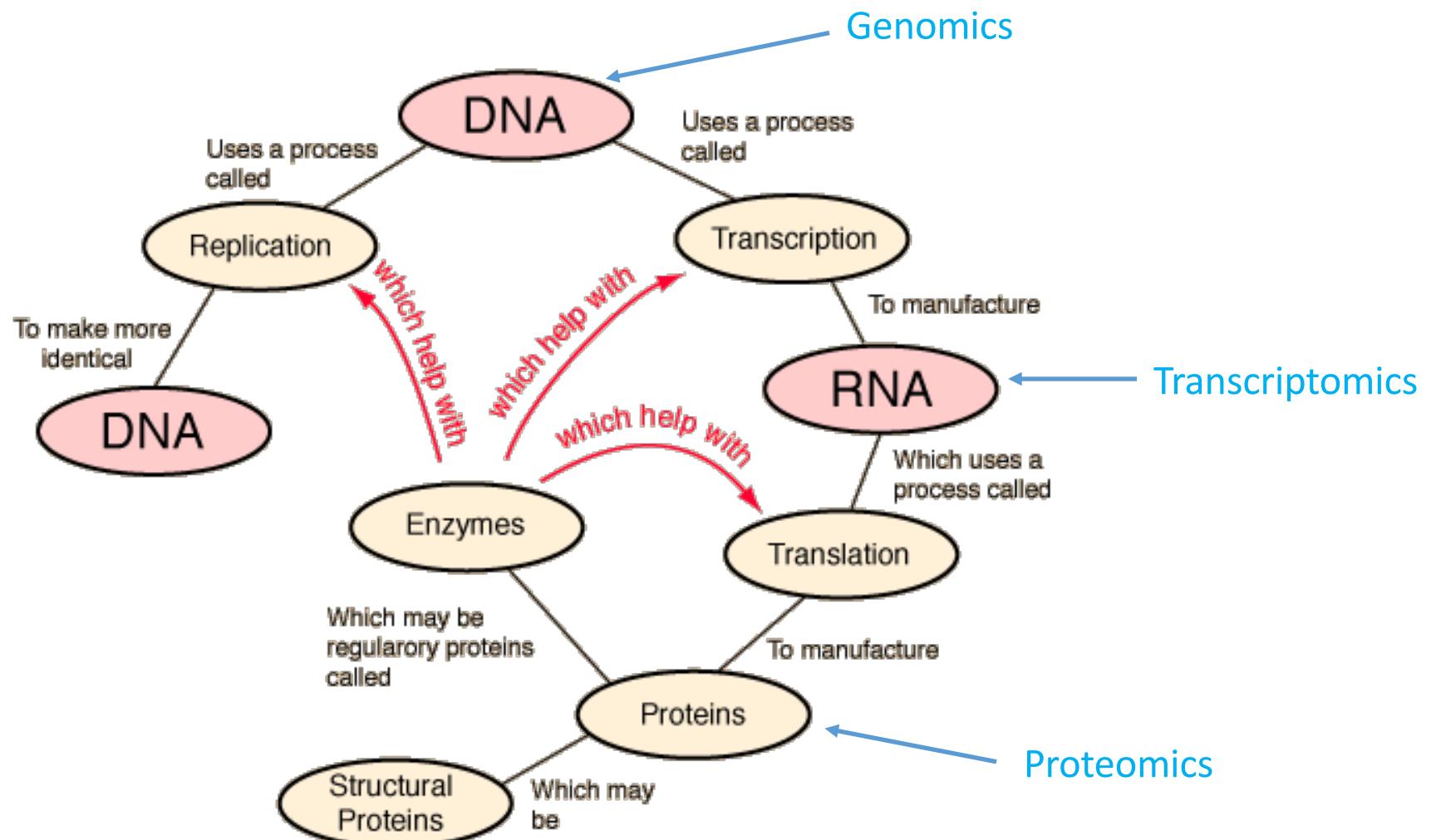
- What do they both mean?
- Genomics: The study of all DNA in a cell (a genome) and relationships between genes.
- Genetics : The study of a specific gene in a cell.

Why are genetics and genomics important?

Central Dogma of Biology



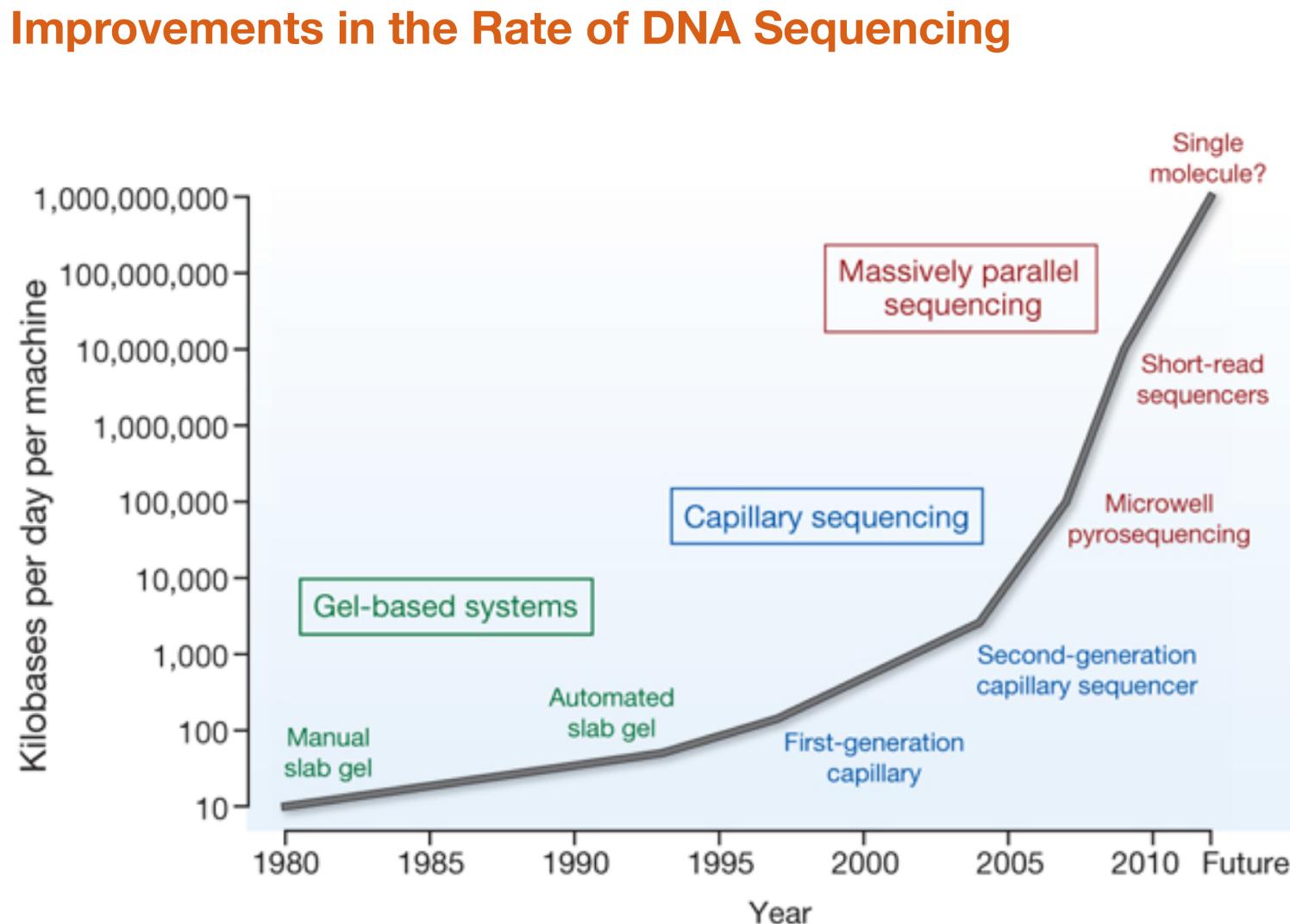
Central Dogma of Biology



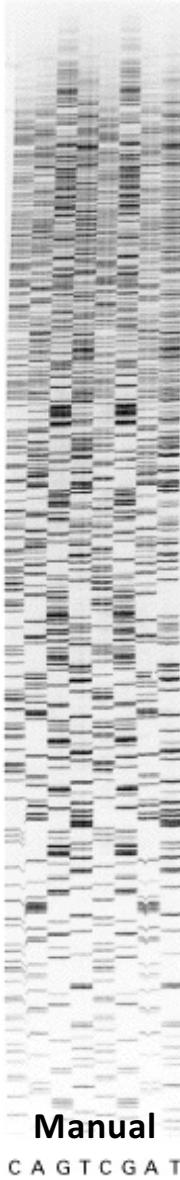
Sequencing the Human Genome

- The first human genome draft was completed in 2001.
- It cost \$2.7bil over 13 years
- International effort:
 - universities and research groups across the United States, the United Kingdom, France, Germany, Japan and China participated.
- Now, one person can achieve this in less than 1 month for ~USD\$1,000.

Timeline genome sequencing



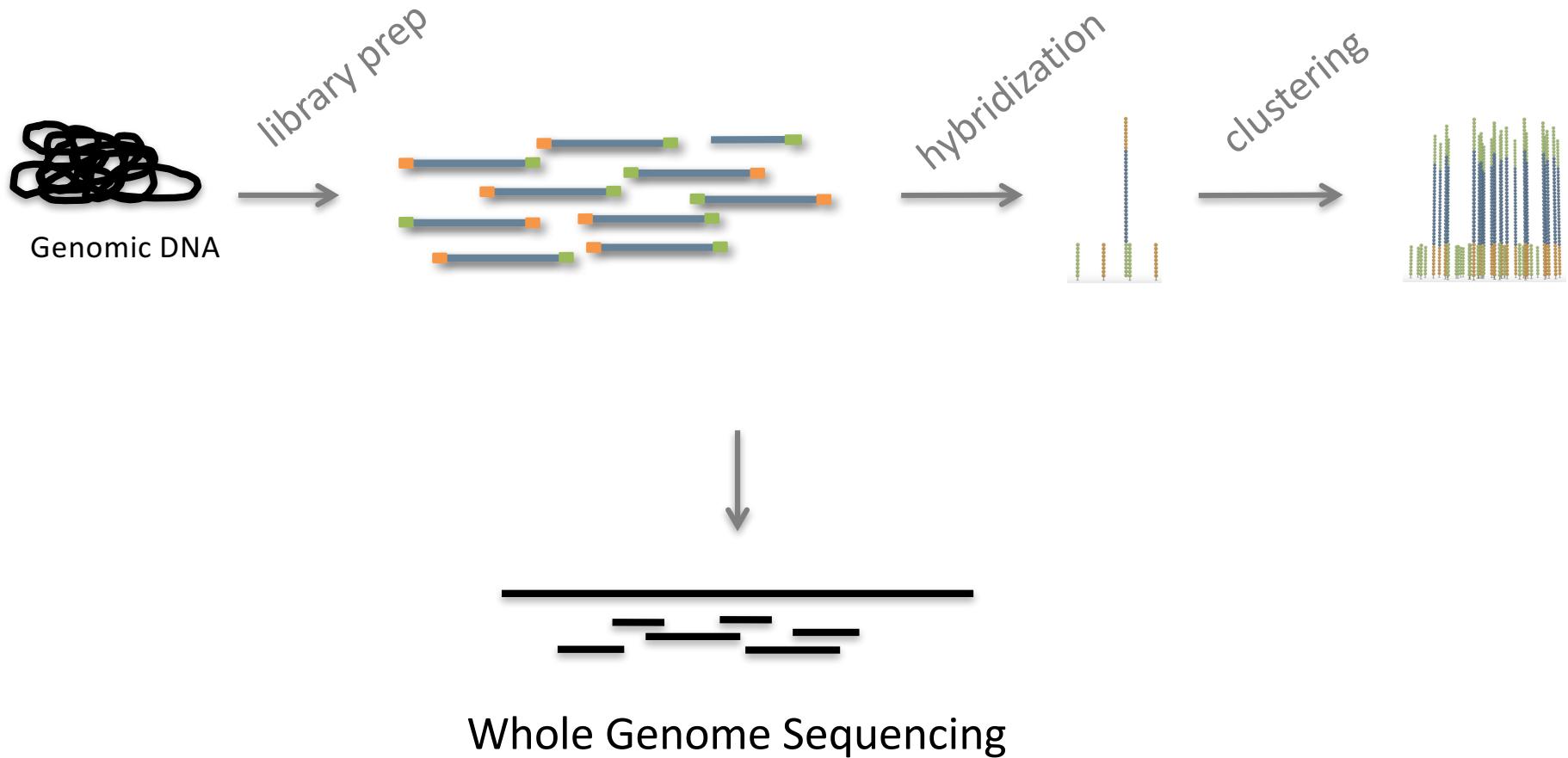
How is it achieved?



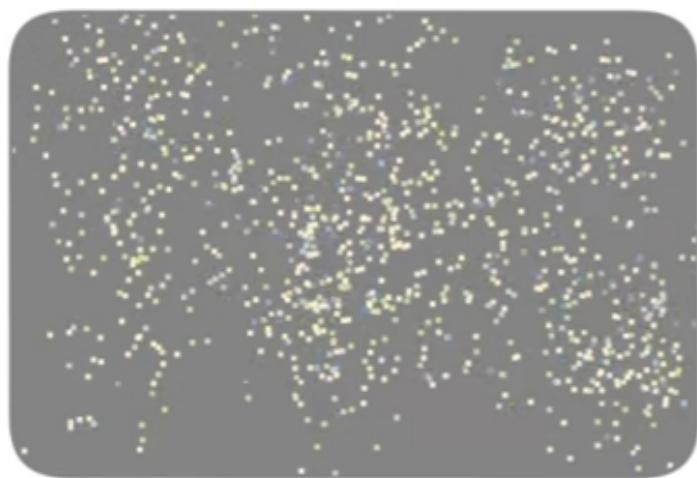
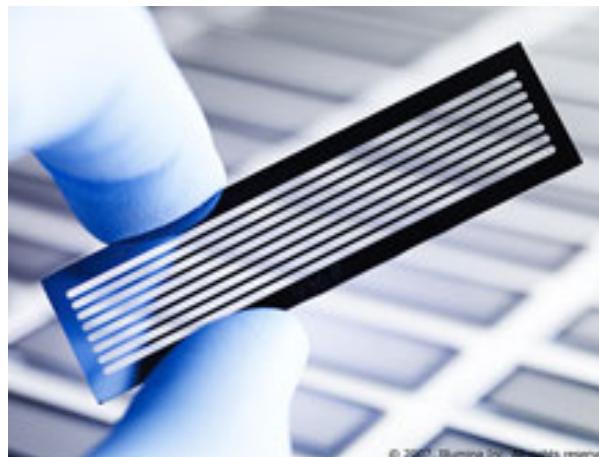
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Next generation sequencing (NGS)



Illumina Sequencing



Flow cell

AA TGGCTAAGGCTTACGCC
AAAAC GCCGTACTACCTCAI
TCTT GCAGTAGTAAGAAAC
ACAAA TGGCTAAGGCTTAC
ACTACCTCAGCAGTAGTAAI
AAA GGCTAAGGCTTACGCC
CTTACGCCGTACTACCTCAI
TCTAGCAGTAGTAAGAAAC
ATCAAATGGCTAAGGCTTAC
CTTACCTCAGCAGTAGTAAI
AAAGC CTAAGGCTTACGCC

What next?

Now we have...

Billions of small chunks of DNA sequenced
in a computer file...

But what does it mean?

Bioinformatics comes next!

The full tale

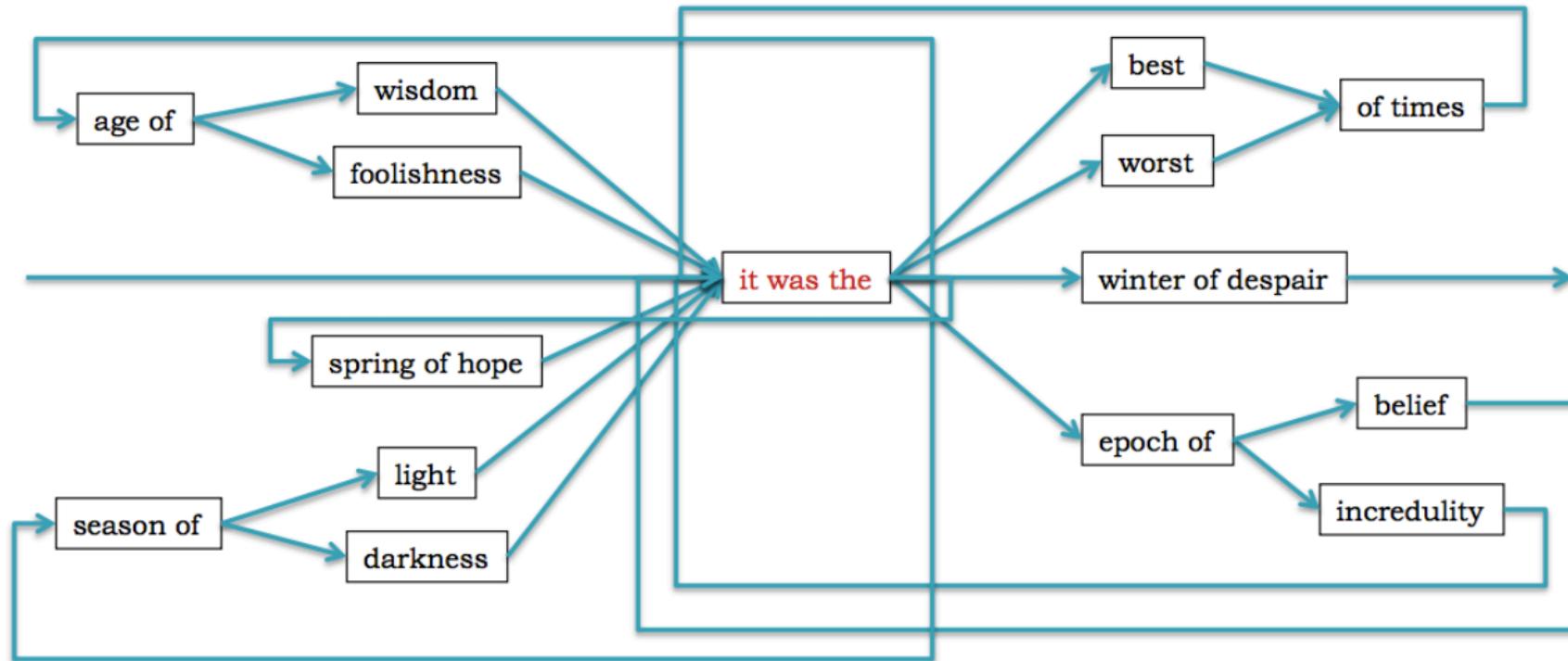
... it was the best of times it was the worst of times ...

... it was the age of wisdom it was the age of foolishness ...

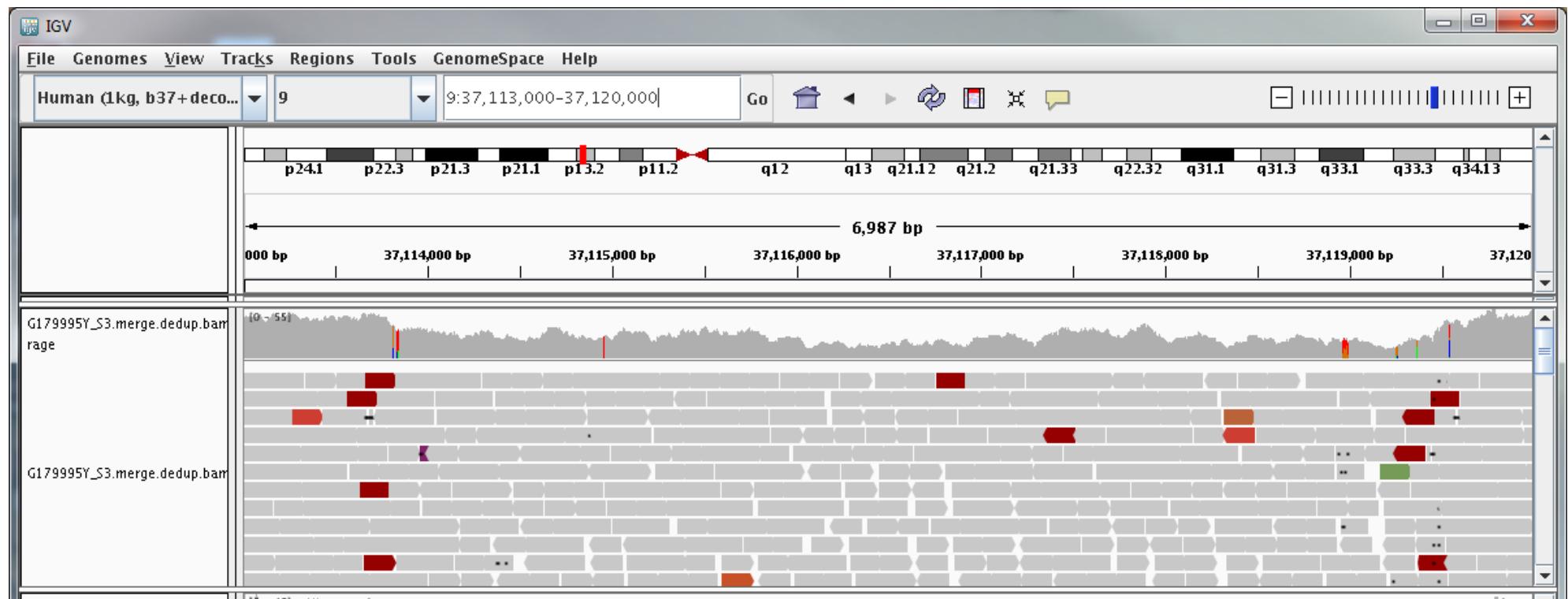
... it was the epoch of belief it was the epoch of incredulity ...

... it was the season of light it was the season of darkness ...

... it was the spring of hope it was the winter of despair ...



Integrated Genome Viewer (IGV)



How does genomics impact our lives?

(Precision) Medicine

Flu transmission
HCV and HIV treatment

Ebola – quarantine and treatment

Cancer – diagnosis and targeted treatment

Diabetes – nature vs nurture

Nutri-genomics

Heritable diseases:
Alzheimers

Parkinsons

Fertility:
Diagnosis
Improved IVF Processes

Crime

Identify suspects and victims

Old and new evidence

Good and bad quality samples (old DNA)

Space Travel

Impact on DNA from being in space

Heritable diseases:
Muscular Dystrophy
Degenerative Myelopathy

Models for human disease

Crops and Farming

Adaptability and resilience (weather, pesticides, fungicides)

Improved product quality e.g. cotton, Golden rice

Disease resistance genes e.g. Ash dieback

Animals

Heritable traits:
coat colour



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Health

First 'three person baby' born using new method

By Michelle Roberts

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'Three-parent baby' born ahead in historic

inheriting deadly genetic diseases

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Reproduction

First UK baby with DNA from three people could be born next year

Clinics set to apply to offer treatment to help women with mitochondrial mutations after regulator gives green light



This article is 3 months old

1,546

Ian Sample Science editor



@iansample

Thursday 15 December 2016 11.55 GMT



The Human Fertilisation and Embryology Authority has said clinics can seek licences for the procedure.
Photograph: Christopher Furlong/Getty Images

Most popular



Middlesbrough 1-3
Manchester United:
Premier League - as it
happened



Don't tell me you weren't
warned about Corbyn |
Nick Cohen



Tottenham Hotspur v
Southampton: Premier
League - live!



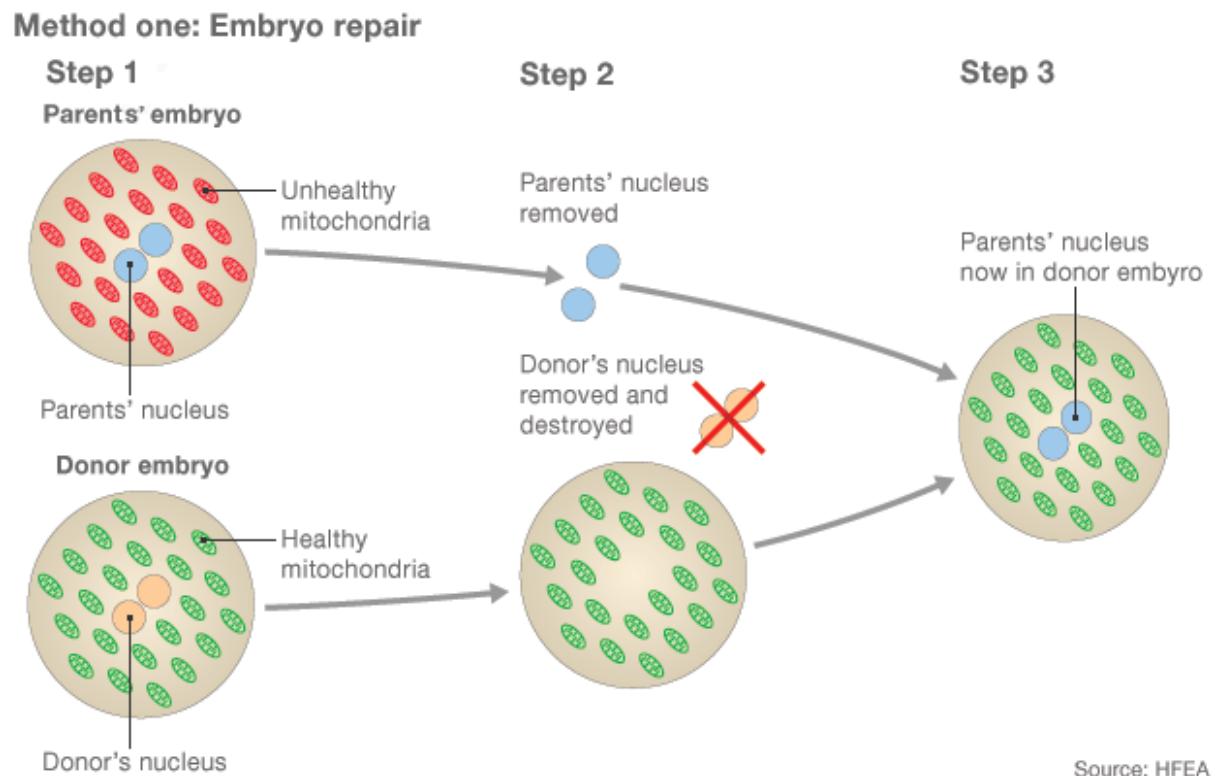
Police seek 33-year-old
man in connection with

Precision Medicine

- Transition into first example –
 - More relatable example first
 - Talk about applications cancer, rare disease
 - Then into mitochondria == prevention not just diagnosis/therapy

Sex

- Mitochondrial replacement therapy (MRT)
- Prevent inheritance of mitochondrial disorders
- Legalized Britain 2015
- Dec 15, 2016 approved by UK's Human Fertilisation and Embryology Authority



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NATURE | NEWS

Neanderthal tooth plaque hints at meals — and kisses

Analysis paints picture of diets, medicine and possible intimacy with humans.

Ewen Callaway

08 March 2017

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A painting of a Neanderthal sitting by a campfire, eating from a bowl. Two other Neanderthals are visible in the background near the fire.

Palm up



A photograph showing a person's legs and feet as they walk through a field of oil palm trees, harvesting fruit.

A makeover for the world's most hated crop

Oil palm has a reputation as an environmental menace. Can the latest genetic research change that?

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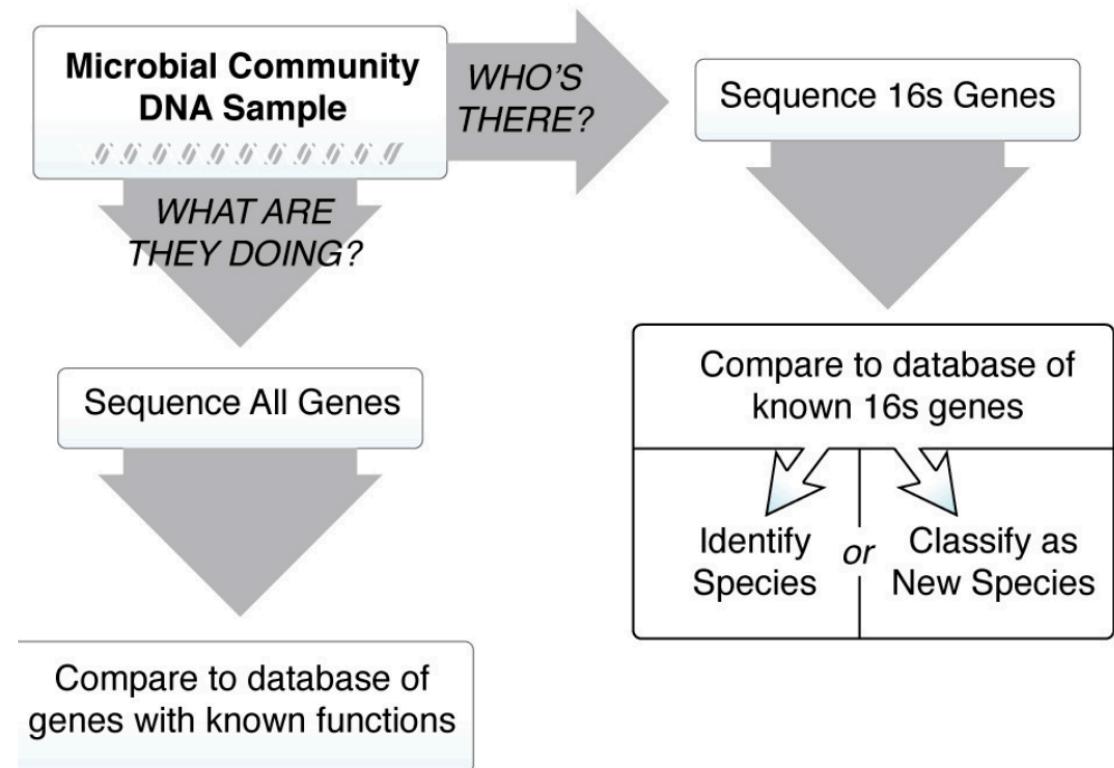
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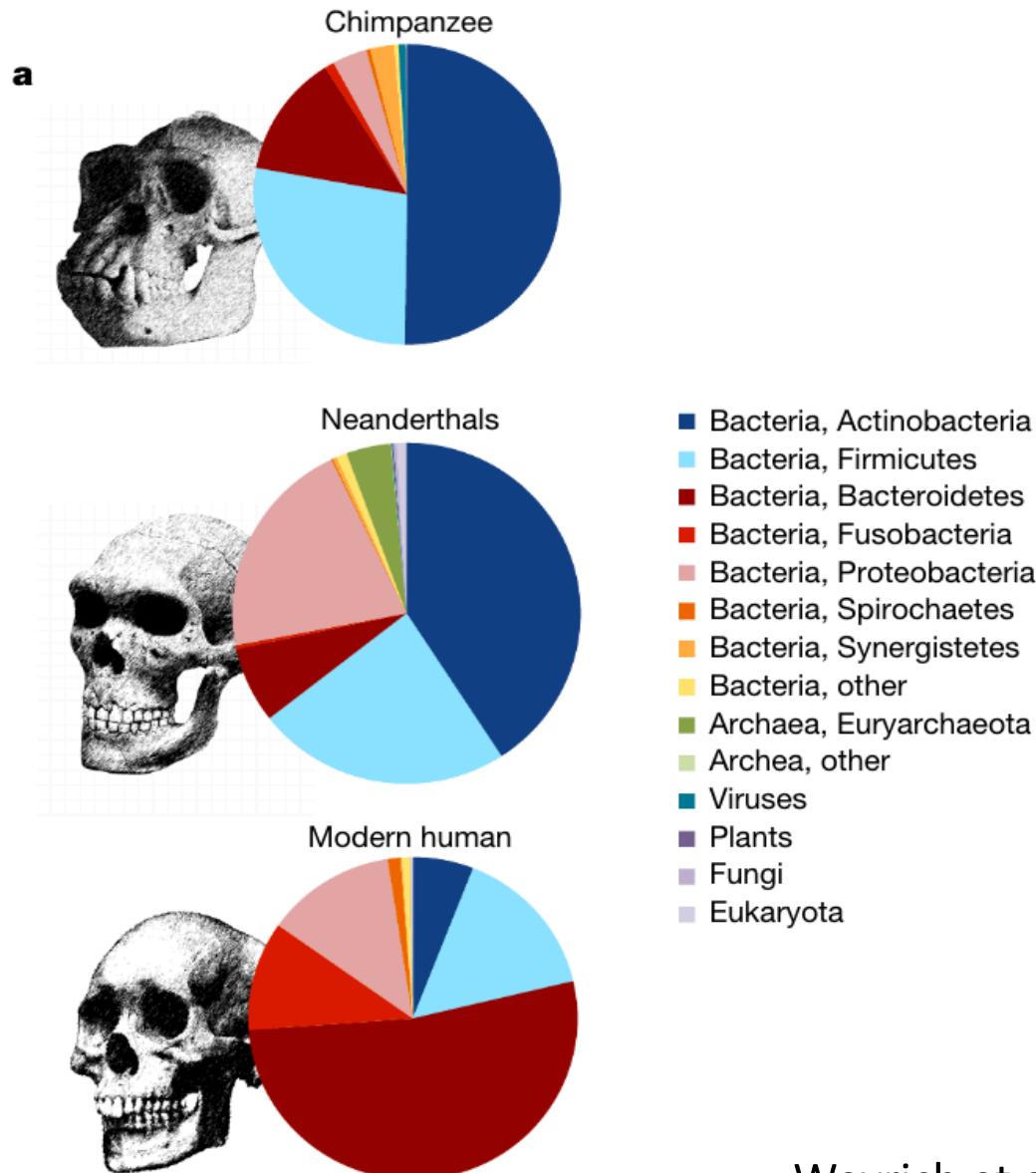
- Fossilized ancient DNA
- Teeth microbiome



<http://learn.genetics.utah.edu/content/microbiome/ecosystem/>

Metagenomics

- Bacterial composition
- Diet
- Sex



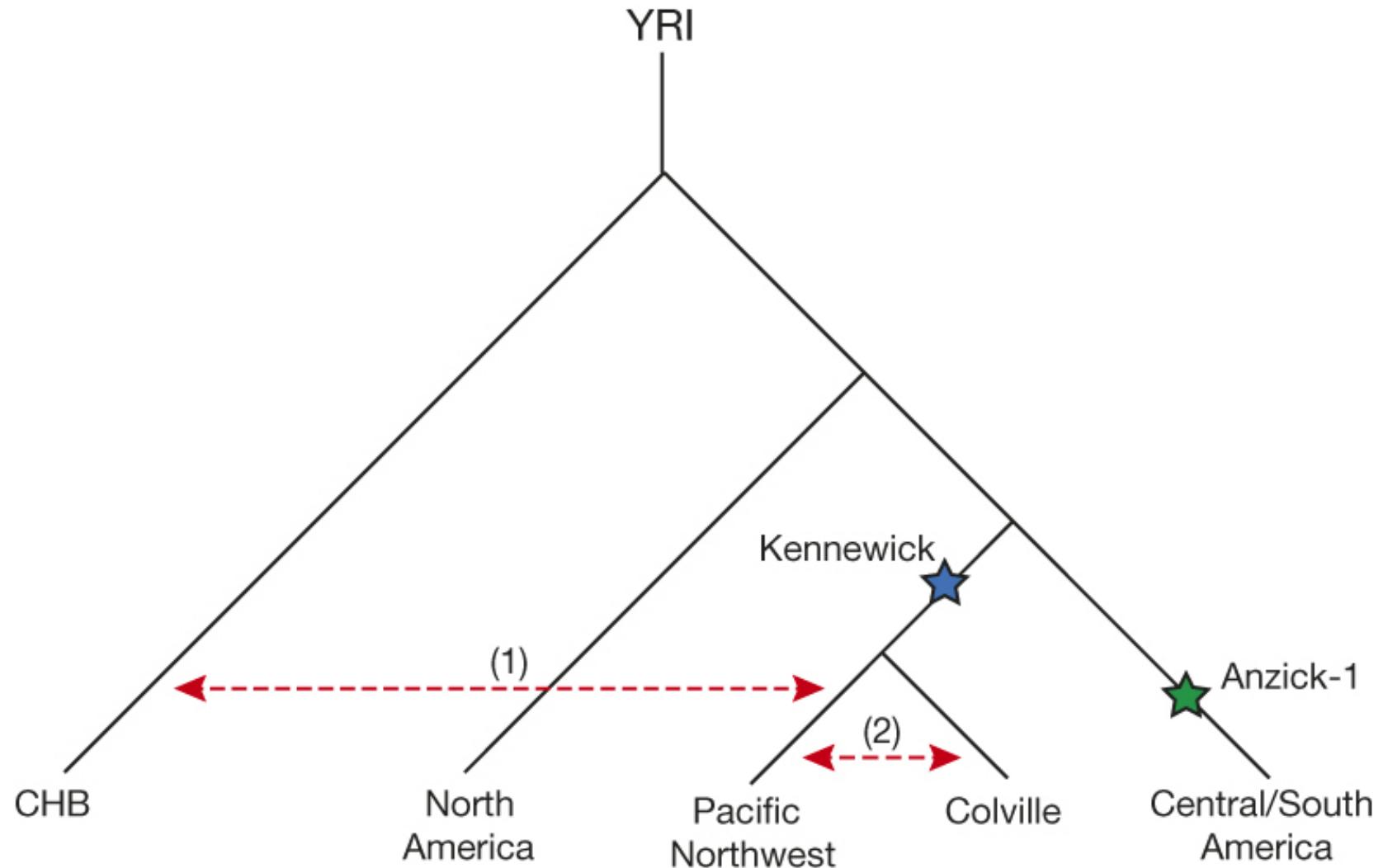
Forensics, ancestry

- Kennewick Man, the “Ancient One”
 - Discovered 1996
 - Columbia Riverbed, Kennewick, Washington
 - Dated to ~9,000 years ago
- Cranial morphology was used to initially reject ancestry
 - 5 tribes claim ancestry
 - Confederated Tribes of the Colville Reservation (Colville)



Chip Clark
Smithsonian's National Museum of Natural History

Comparative genomics to infer relationships among individuals

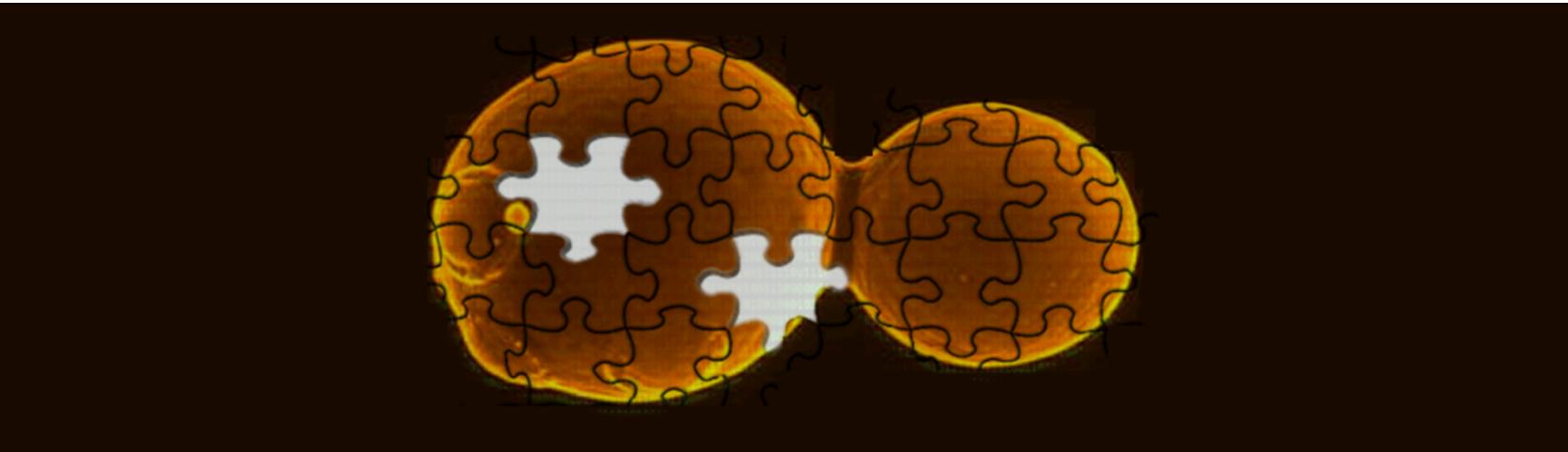


Toy exercise ?
Alignment of 3 sequences
count number positions “informative”
infer sequence similarity A closer to B or C

Synthetic biology



Synthetic Yeast 2.0
Building the world's first synthetic eukaryotic genome together

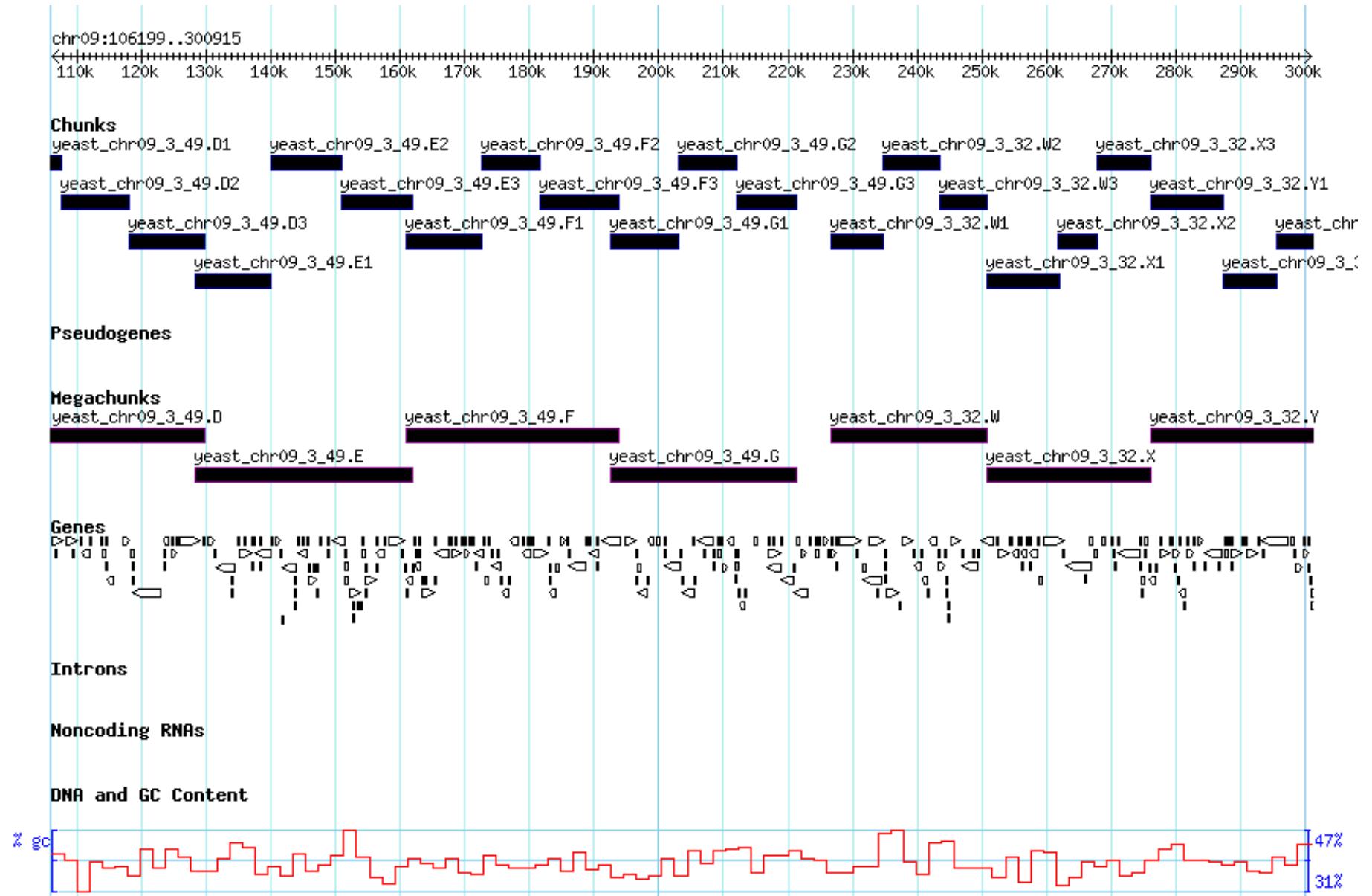


Home **Sc2.0** Build-A-Genome Collaborators Design Software Team FAQ Sponsors SAVI

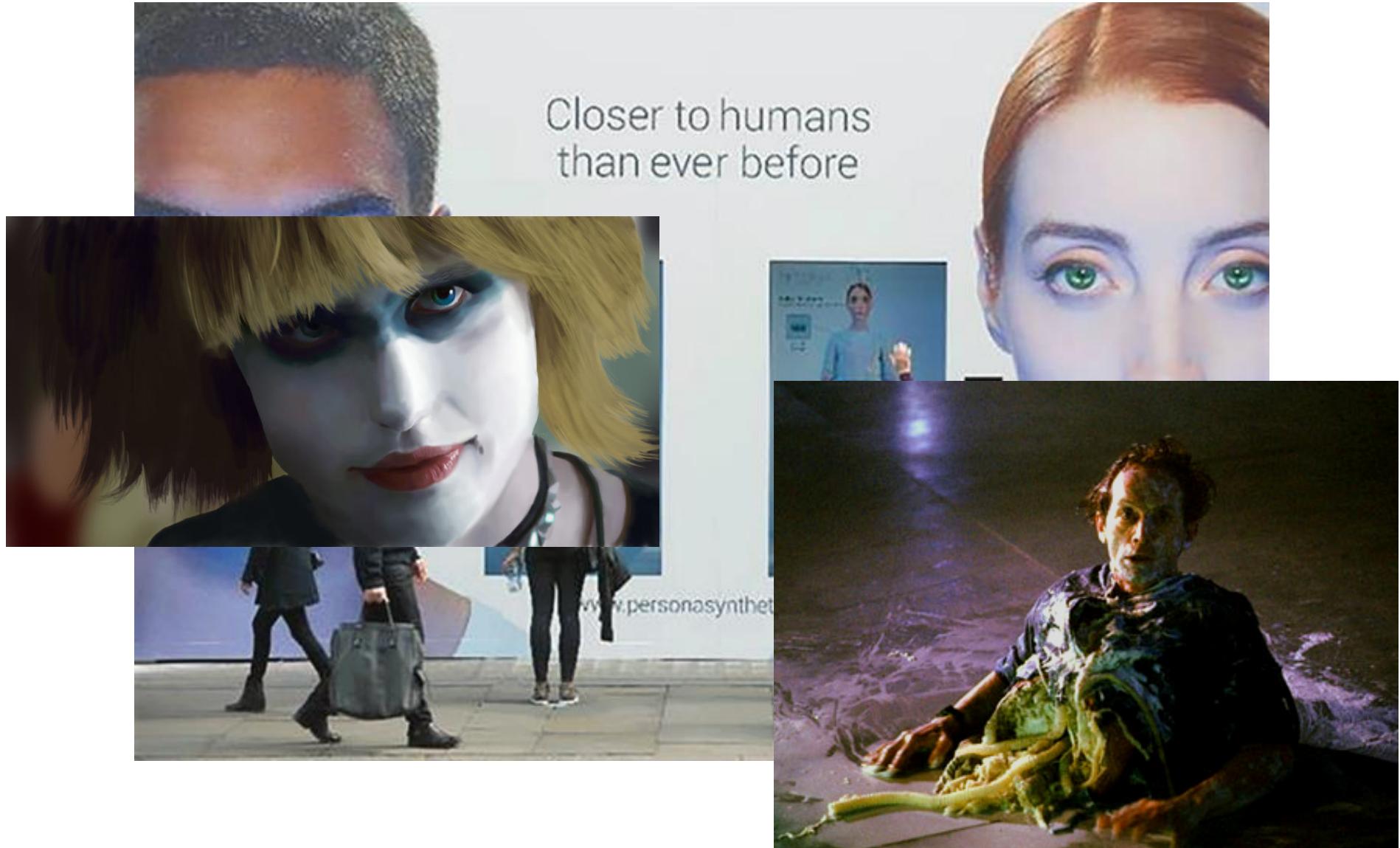
[sc2-0 home](#)

[Sc2.0 gbrowser](#)

SC2.0 Genome Browser



Why synthetic genomes?





<http://www.ex-astris-scientia.org/inconsistencies/refguide/tricorder-thesquireofgothos.jpg>

The future of sequencing...

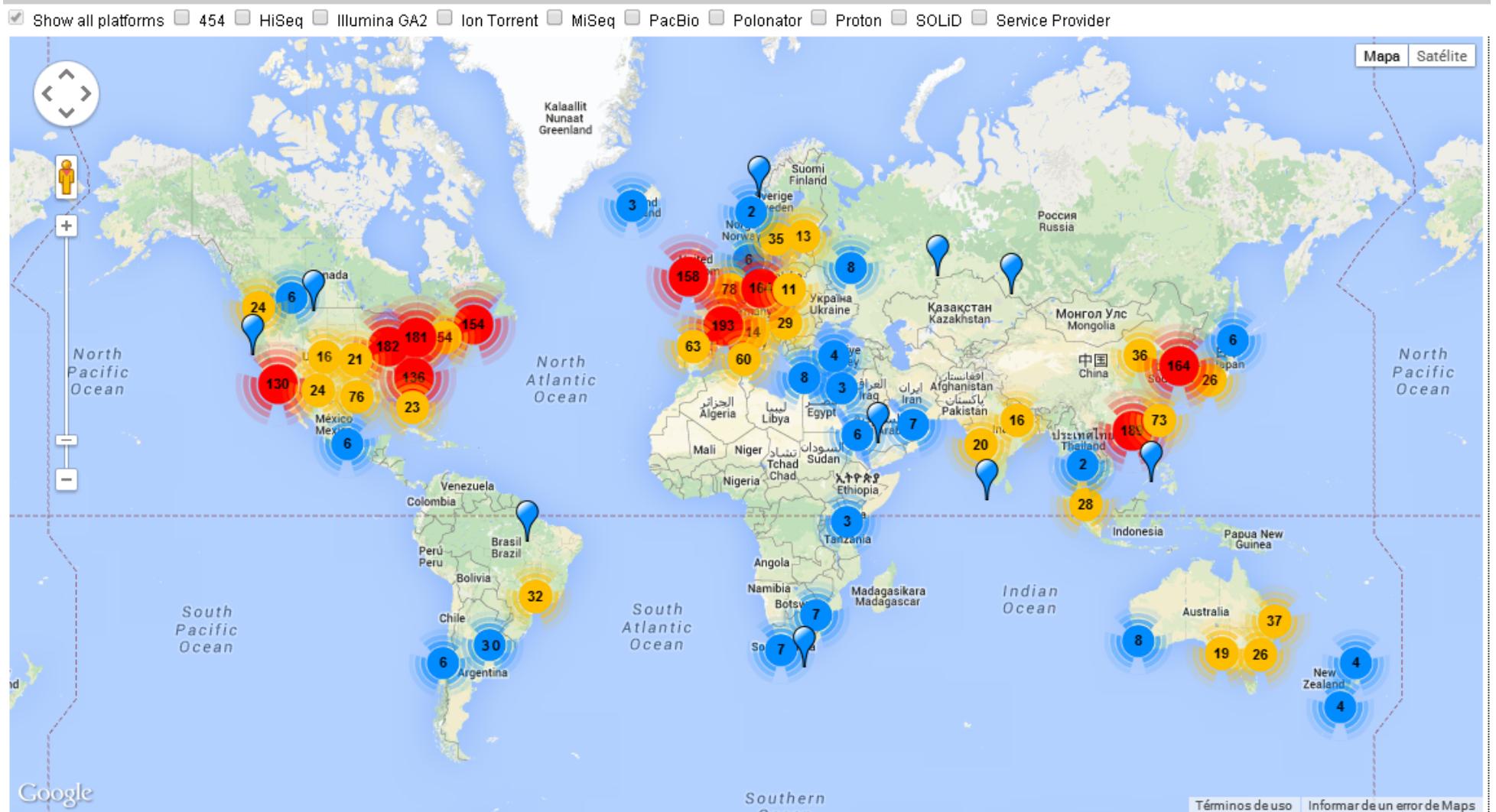


Tiny SmidgION is currently in early-stage development

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Sequencing across the world

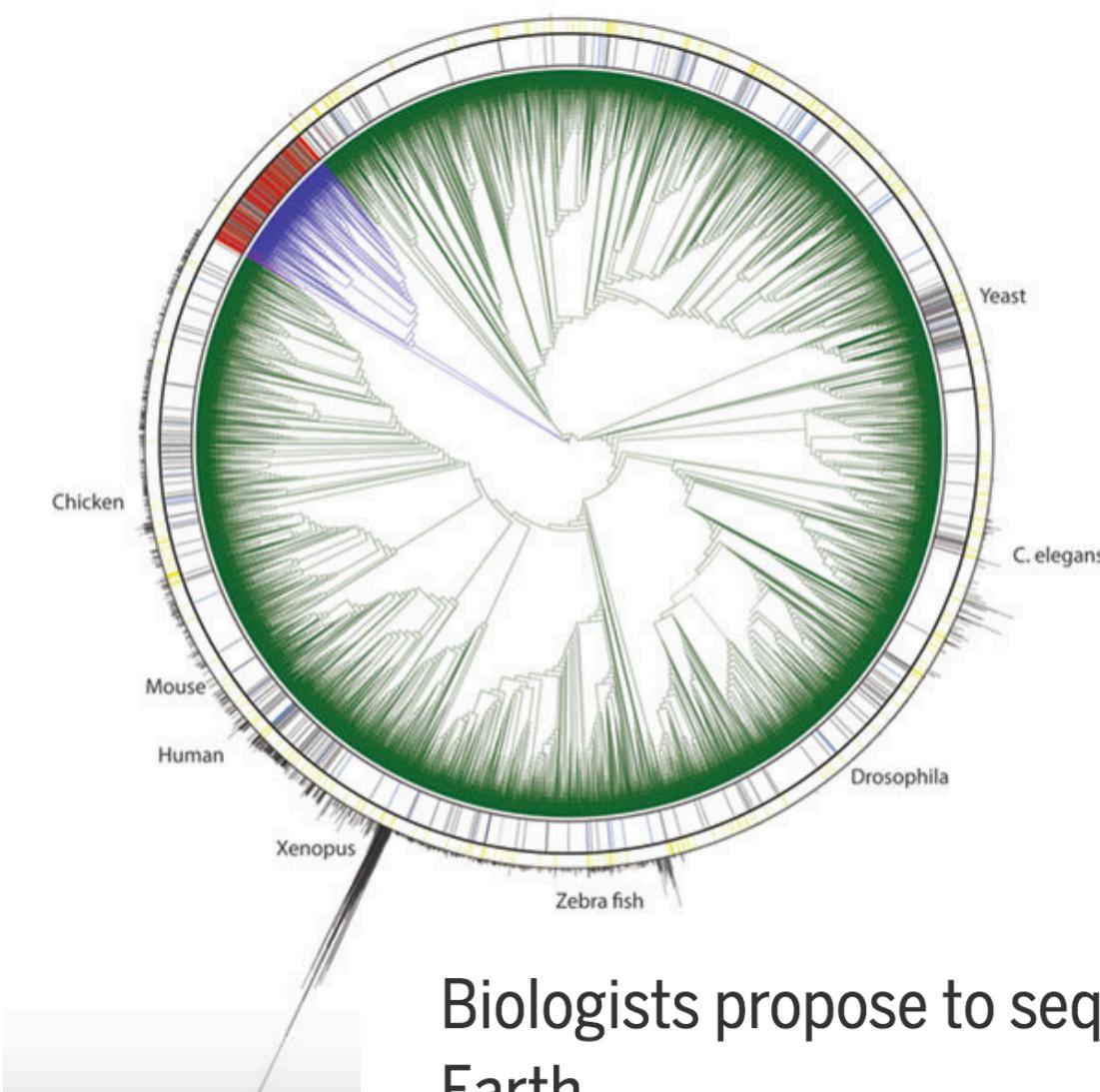


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Earth Biogenome Project



green = eukaryotes
blue = bacteria
purple = archaea
red = sequenced genomes

Biologists propose to sequence the DNA of all life on Earth

How d?

The screenshot shows the Galaxy web interface at <https://usegalaxy.org>. The top navigation bar includes links for Analyze Data, Workflow, Shared Data, Visualization, Help, User, and a search bar. The left sidebar, titled "Tools", lists various categories: Get Data, Send Data, Lift-Over, Collection Operations, Text Manipulation, Datamash, Convert Formats, Filter and Sort, Join, Subtract and Group, Fetch Alignments/Sequences, NGS: QC and manipulation, NGS: DeepTools, NGS: Mapping, NGS: RNA Analysis, NGS: SAMtools, NGS: BamTools, and NGS: Picard. A central banner says "Try Galaxy on the Cloud" with the subtext "Now you can have a personal Galaxy within the infinite Universe". The right panel, titled "History", shows a list of imported datasets, each with a preview icon, edit button, and delete button. The datasets listed are:

- imported: Galaxy 101 NGS Variant (21 shown)
- 313.43 MB
- 10: Filter SAM on data 6
- 9: Filter SAM on data 7
- 8: Map with BWA for Illumina on data 4 and data 3: mapped reads
- 7: Map with BWA for Illumina on data 2 and data 1: mapped reads
- 6: FastQC_raw_child-ds-2.fq.html
- 5: FastQC_raw_child-ds-1.fq.html
- 4: raw_mother-ds-2.fq

Summary and take-home messages

- Goals for today
 - Understand the difference genetics V genomics
 - Survey specific applications of genomics in biology
 - Introduce tools and concepts of genomic analysis
- Next class – in lab tutorial
- Moving forward
 - Genomics technologies
 - Theory: from strings to assemblies
 - Practical applications of tools for bioinformatics

Terminology

- Genetics
- Genomics
- Bioinformatics
- Alignment
- Ploidy
- Homology
- Orthology
- Phylogeny
- Parsimony
- Microbiome
- Metagenomics
- CLI
- GUI

Further reading