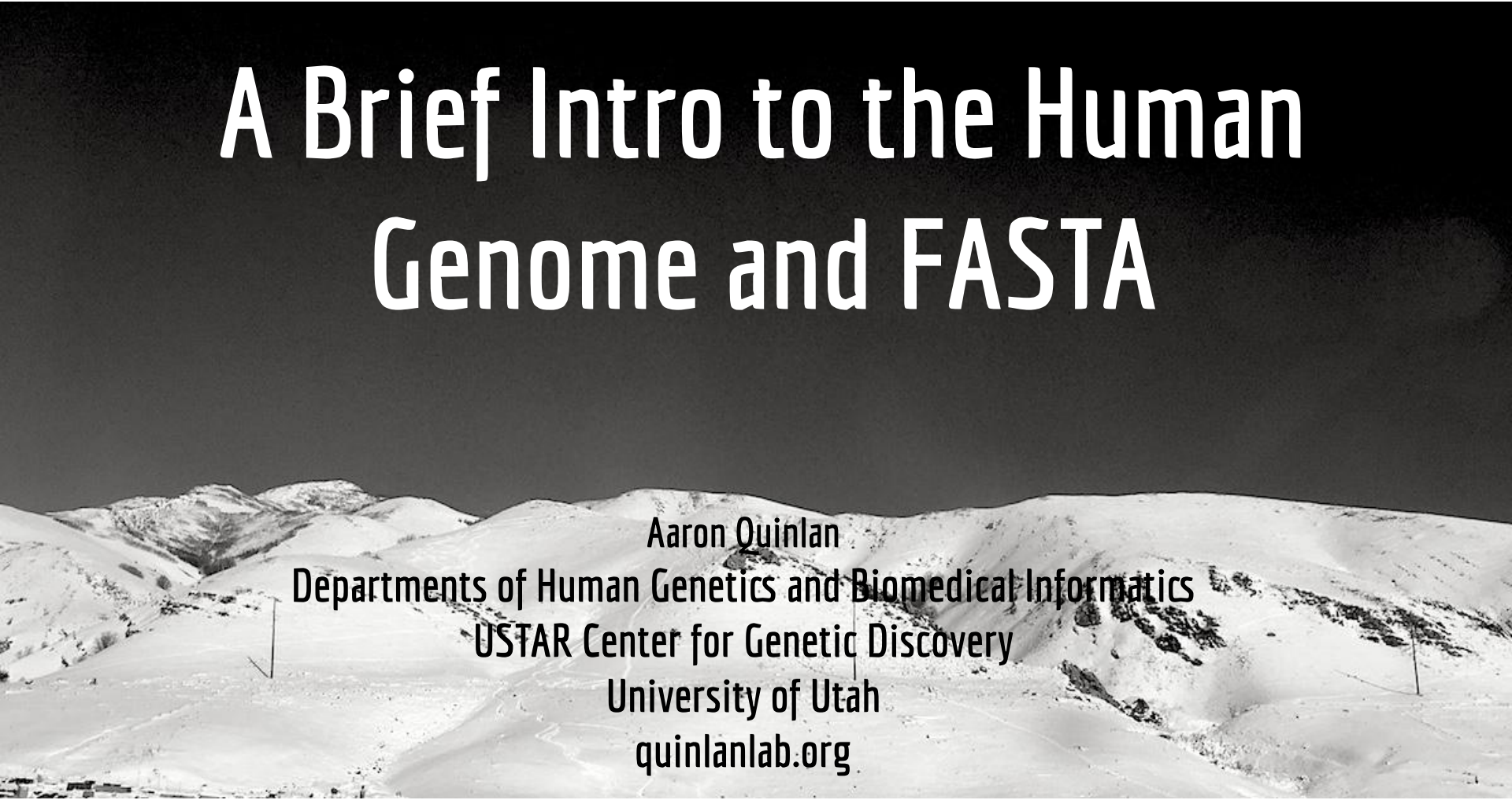
A Brief Intro to the Human Genome and FASTA



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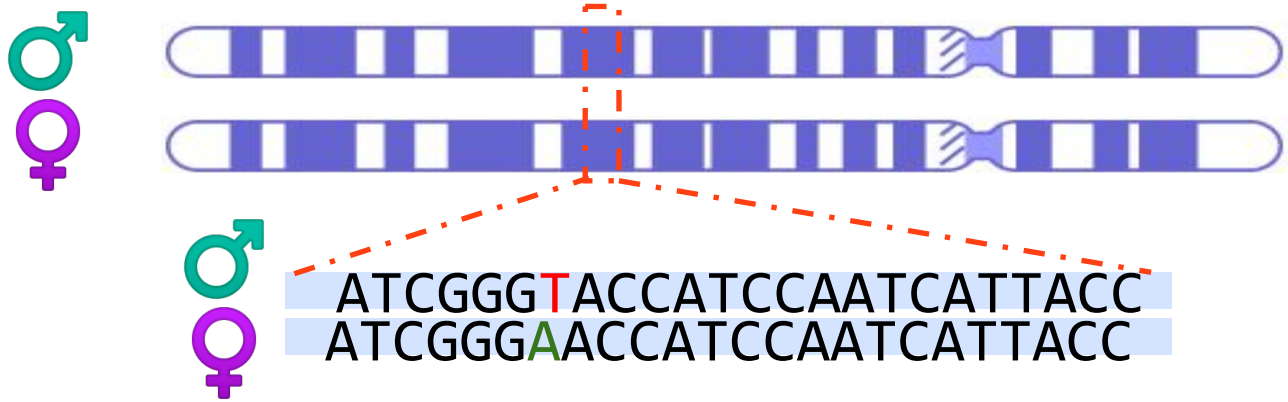
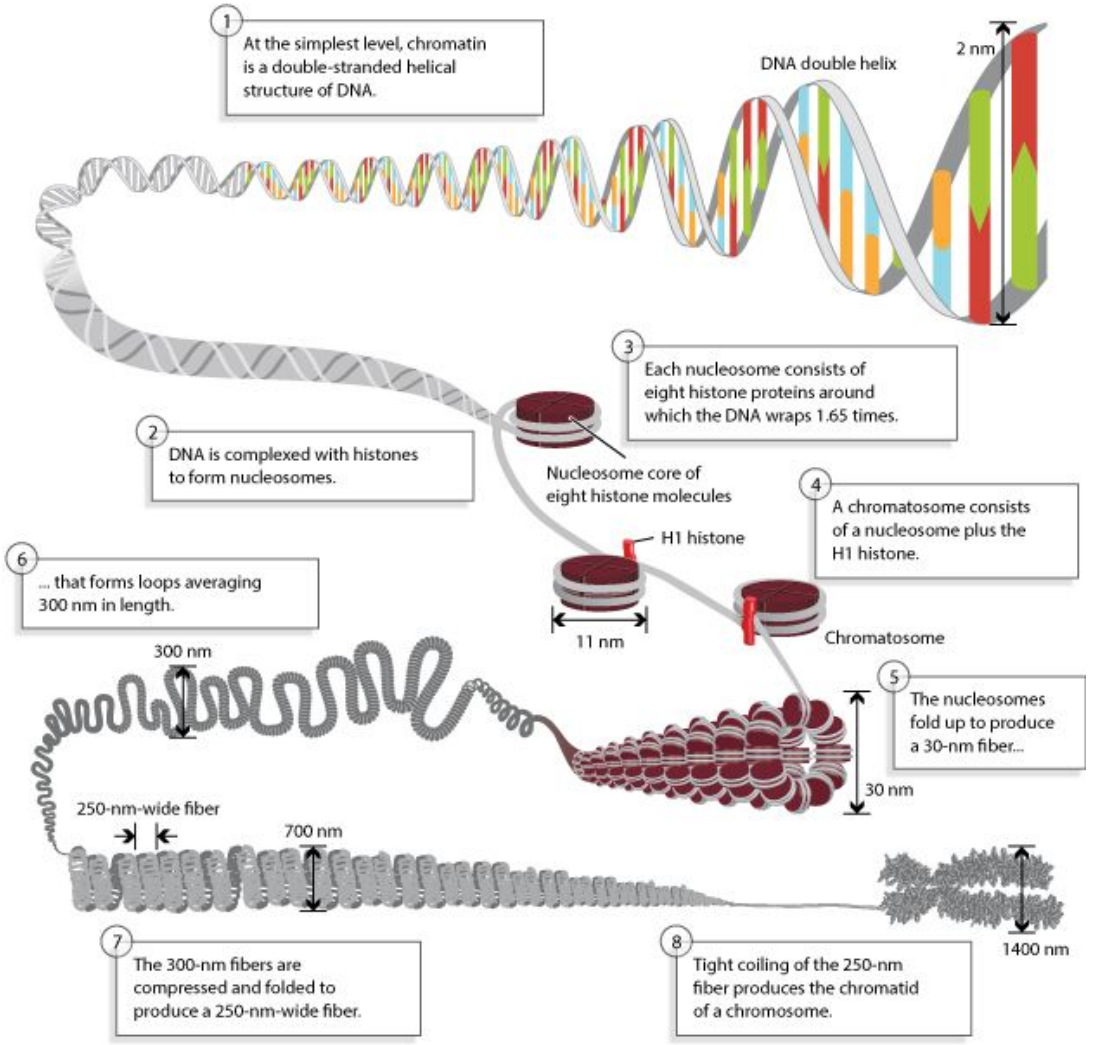
Humans are diploid.



Our genome is comprised of a paternal and a maternal "haplotype". Together, they form our "genotype"

The human genome from a macro to micro scale



Our genome: mini quiz

How many *distinct* chromosomes in the nuclear human genome?

24: the autosomes (chromosome 1-22), sex chromosomes (X, Y)

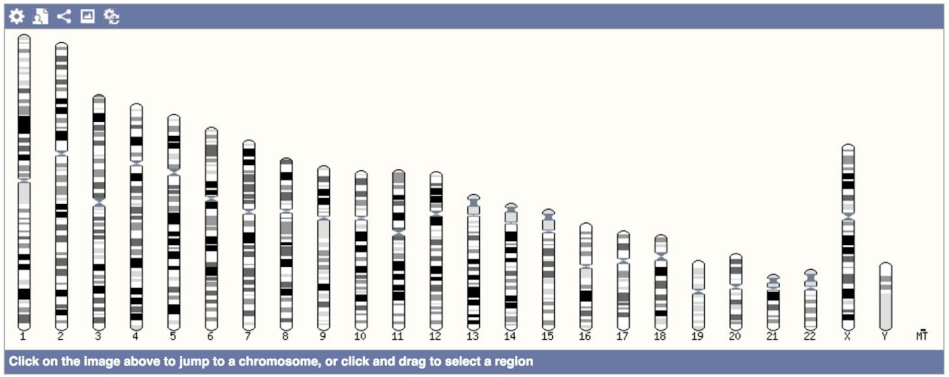
How many chromosomes exist in a (typical) haploid human genome ?

23: the autosomes (chromosome 1-22) and one sex chromosomes (X or Y)

How many chromosomes exist in a (typical) diploid human genome ?

46: two haploid genomes - one from mother and one from father

The human genome - basic stats



- 3.096 billion base pairs (haploid)
- 20,441 protein coding genes
- 198,002 coding transcripts (isoforms of a gene that each encode a distinct protein product)

Summary

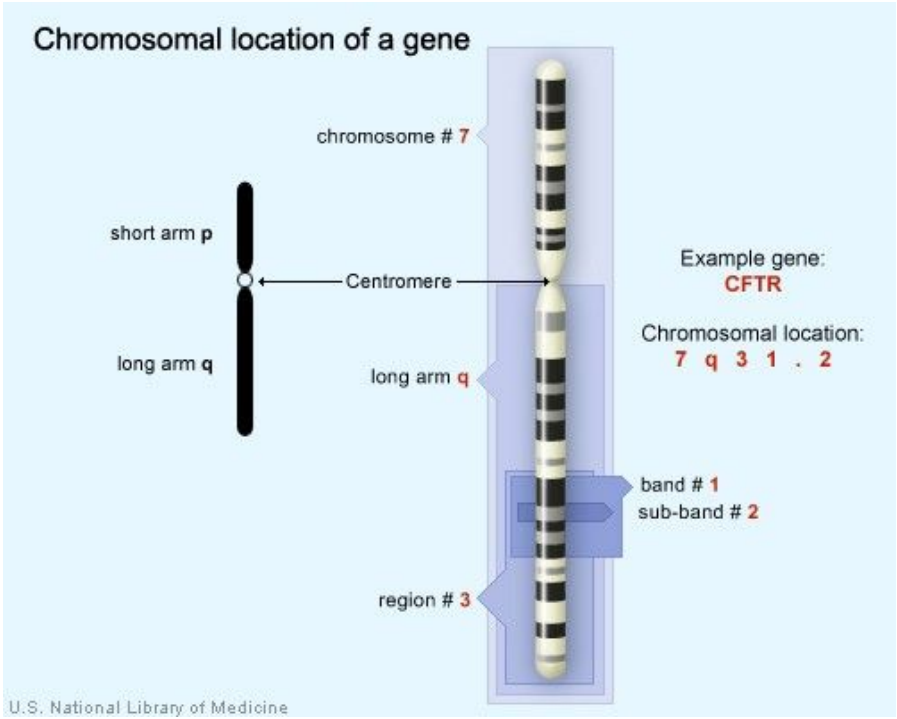
Assembly	GRCh38.p7 (Genome Reference Consortium Human Build 38), INSDC Assembly GCA_000001405.22, Dec 2013
Database version	87.38
Base Pairs	3,547,762,741
Golden Path Length	3,096,649,726
Genebuild by	Ensembl
Genebuild method	Full genebuild
Genebuild started	Jan 2014
Genebuild released	Jul 2014
Genebuild last updated/patched	Jun 2016
Gencode version	GENCODE 25

Gene counts (Primary assembly)

Coding genes	20,441 (incl 526 readthrough)
Non coding genes	22,219
Small non coding genes	5,052
Long non coding genes	14,727 (incl 214 readthrough)
Misc non coding genes	2,222
Pseudogenes	14,606 (incl 5 readthrough)
Gene transcripts	198,002

http://uswest.ensembl.org/Homo_sapiens/Location/Genome

Chromosome Giemsa banding (G-banding)



- Heterochromatic regions, which tend to be rich with adenine and thymine (AT-rich) DNA and relatively gene-poor, **stain more darkly** with Giemsa and result in G-banding
- Less condensed ("open") chromatin, which tends to be (GC-rich) and more transcriptionally active, incorporates less Giemsa stain, resulting in **light bands in G-banding**.
- Cytogenetic bands are labeled p1, p2, p3, q1, q2, q3, etc., **counting from the centromere out toward the telomeres**. At higher resolutions, sub-bands can be seen within the bands.
- For example, the locus for the CFTR (cystic fibrosis) gene is **7q31.2**, which indicates it is on **chromosome 7**, **q arm**, **region 3, band 1, and sub-band 2. (Say 7,q,3,1 dot 2)**

https://en.wikipedia.org/wiki/G_banding, https://ghr.nlm.nih.gov/chromosome/1#ideogram

A first map of the human genome

articles

Initial sequencing and analysis of the human genome

International Human Genome Sequencing Consortium*

* *A partial list of authors appears on the opposite page. Affiliations are listed at the end of the paper.*

The human genome holds an extraordinary trove of information about human development, physiology, medicine and evolution. Here we report the results of an international collaboration to produce and make freely available a draft sequence of the human genome. We also present an initial analysis of the data, describing some of the insights that can be gleaned from the sequence.

http://www.nature.com/nature/journal/v409/n6822/full/409860a0.html

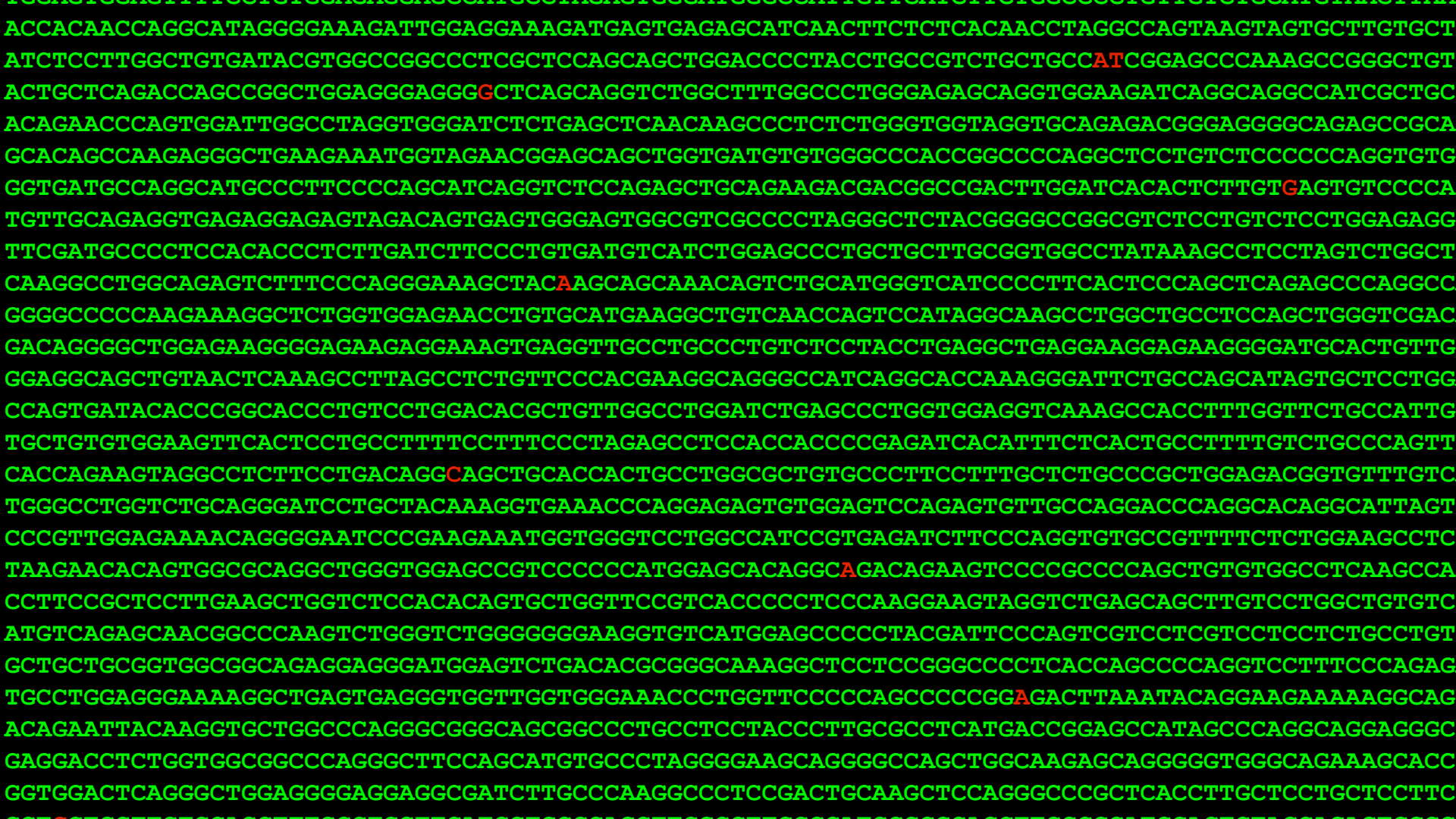
A first map of the human genome ("build 1")

table 8 1 of 4

Table 8 Chromosome size estimates

Chromosome*	Sequenced bases† (Mb)	FCC gaps‡		SCC gaps‖		Sequence gaps#		Heterochromatin and short arm adjustments**(Mb)	Total estimated chromosome size (including artefactual duplication in draft genome sequence)†† (Mb)	Previously estimated chromosome size‡‡ (Mb)
		Number	Total bases in gaps§ (Mb)	Number	Total bases in gaps¶ (Mb)	Number	Total bases in gaps☆ (Mb)			
All	2,692.9	897	152.0	4,076	142.7	145,514	80.6	212	3,289	3,286
1	212.2	104	17.7	347	12.1	11,803	6.5	30	279	263
2	221.6	50	8.5	296	10.4	12,880	7.1	3	251	255
3	186.2	71	12.1	336	11.8	14,689	8.1	3	221	214
4	168.1	39	6.6	343	12.0	12,768	7.1	3	197	203
5	169.7	46	7.8	337	11.8	10,304	5.7	3	198	194
6	158.1	15	2.6	275	9.6	5,225	2.9	3	176	183
7	146.2	27	4.6	195	6.8	4,338	2.4	3	163	171
8	124.3	41	7.0	249	8.7	8,692	4.8	3	148	155
9	106.9	19	3.2	122	4.3	6,083	3.4	22	140	145
10	127.1	14	2.4	163	5.7	8,947	5.0	3	143	144
11	128.6	29	4.9	193	6.8	8,279	4.6	3	148	144
12	124.5	26	4.4	168	5.9	8,226	4.6	3	142	143
13	92.9	12	2.0	115	4.0	5,065	2.8	16	118	114
14	86.9	13	2.2	40	1.4	775	0.4	16	107	109
15	73.4	18	3.1	104	3.6	5,717	3.2	17	100	106
16	73.1	55	9.4	102	3.6	4,757	2.6	15	104	98
17	72.8	41	7.0	95	3.3	4,261	2.4	3	88	92
18	72.9	22	3.7	113	4.0	4,324	2.4	3	86	85
19	55.4	49	8.3	108	3.8	2,344	1.3	3	72	67
20	60.5	7	1.2	33	1.2	469	0.3	3	66	72
21	33.8	4	0.1	0	0.0	0	0.0	11	45	50
22	33.8	10	1.0	0	0.0	0	0.0	13	48	56
X	127.7	141	24.0	182	6.4	4,282	2.4	3	163	164
Y	21.8	6	1.0	19	0.7	113	0.1	27	51	59
NA	5.1	0	0	134	0.0	577	0.3	0	0	0
UL	9.3	38	0	7	0.0	566	0.3	0	0	0

http://www.nature.com/nature/journal/v409/n6822/full/409860a0.html

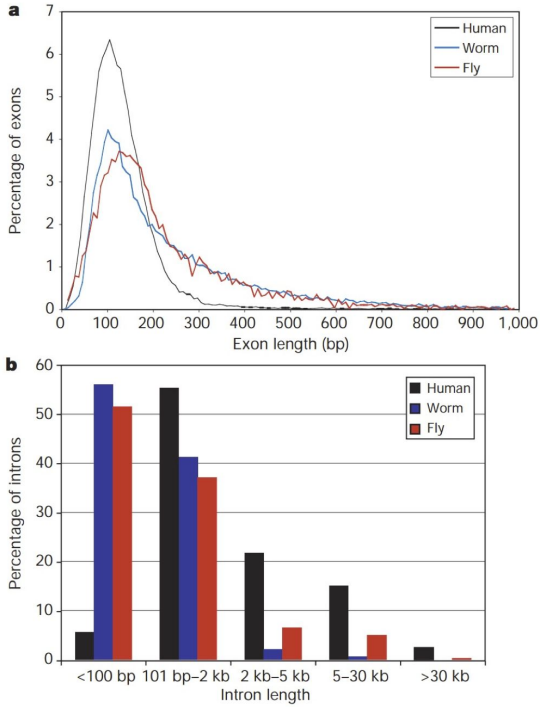


Gene content

"There appear to be about 30,000-40,000 protein-coding genes in the human genome -- only about twice as many as in worm or fly. However, the genes are more complex, with more alternative splicing generating a larger number of protein products." (Over time this has evolved to an estimate of approximately 20,000 protein coding genes, which reflects roughly the number of genes in fly and worm)

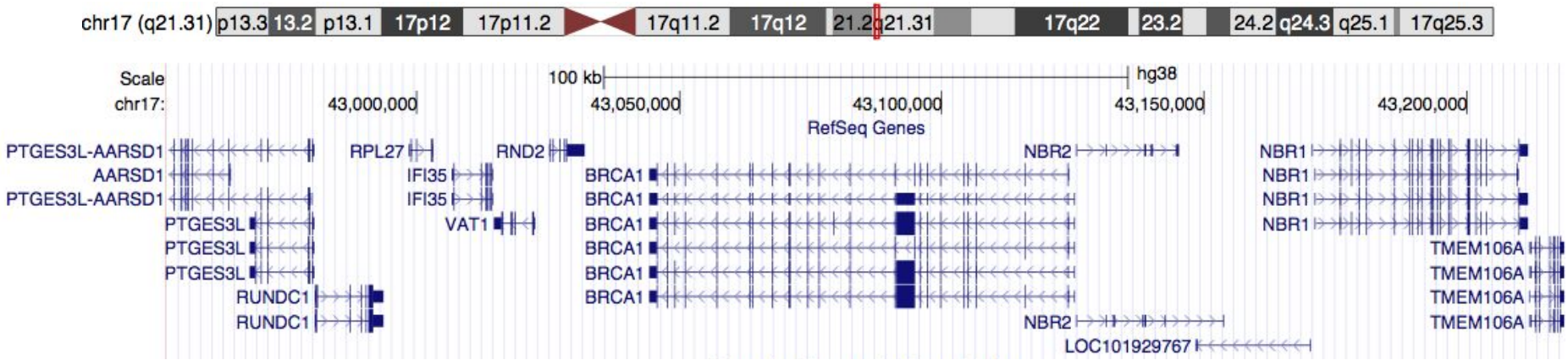
Table 21 Characteristics of human genes

	Median	Mean
Internal exon	122 bp	145 bp
Exon number	7	8.8
Introns	1,023 bp	3,365 bp
3′ UTR	400 bp	770 bp
5′ UTR	240 bp	300 bp
Coding sequence (CDS)	1,100 bp 367 aa	1,340 bp 447 aa
Genomic extent	14 kb	27 kb



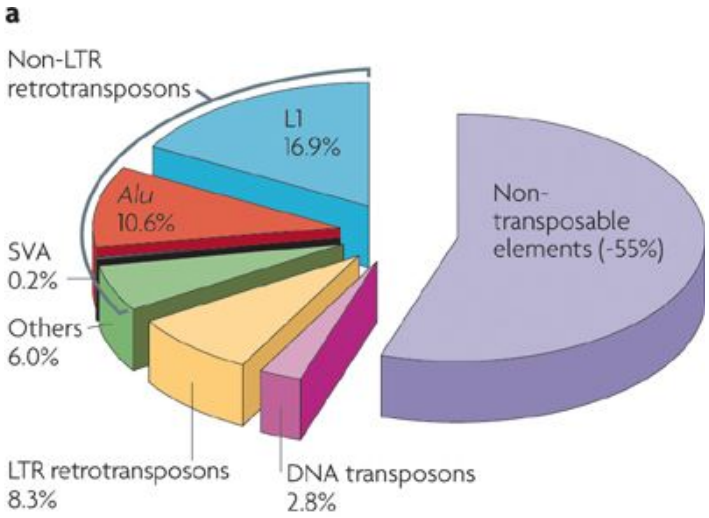
http://www.nature.com/nature/journal/v409/n6822/full/409860a0.html

Solely 2% of the human genome encodes proteins.

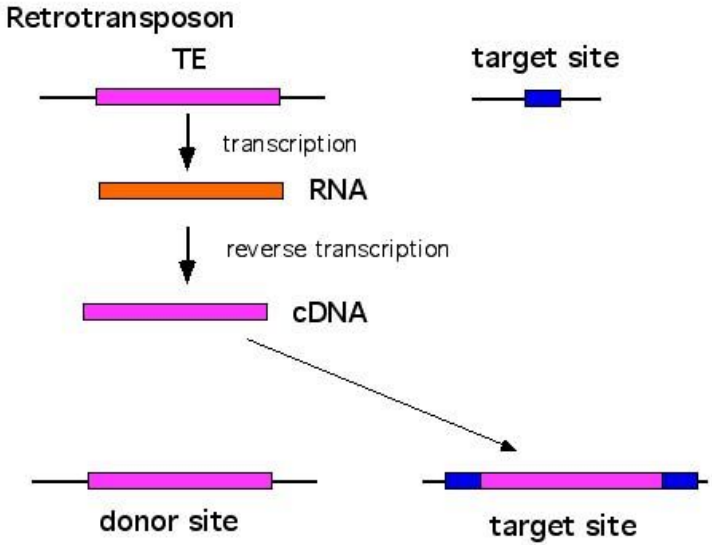


https://genome.ucsc.edu

Half of the human genome is comprised of repeats



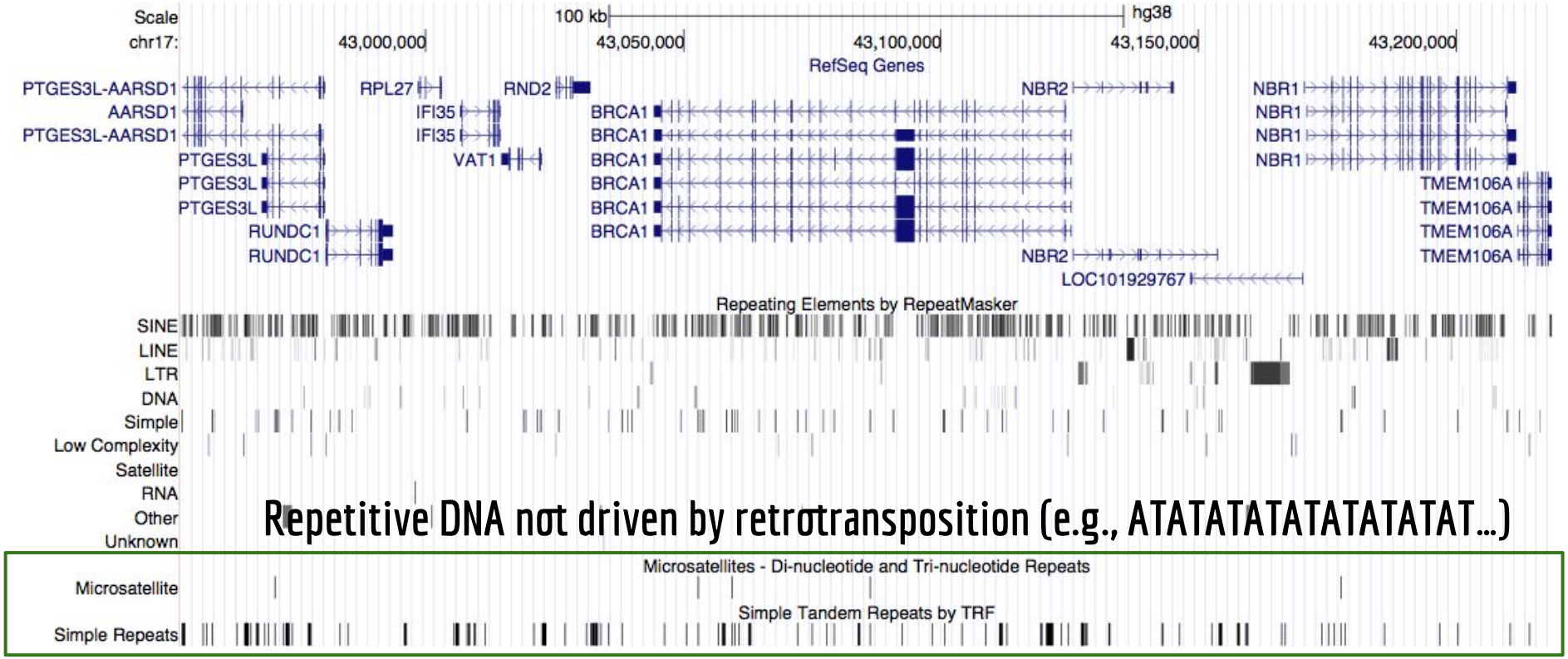
McClintock's "jumping genes" in maize



Retrotransposons use a "copy/paste" mechanism
DNA transposons use a "cut/paste" mechanism

http://www.nature.com/nrg/journal/v10/n10/pdf/nrg2640.pdf

Half of the human genome is comprised of repeats



Repetitive DNA not driven by retrotransposition (e.g., ATATATATATATATATAT…)

http://www.nature.com/nrg/journal/v10/n10/pdf/nrg2640.pdf

The human reference genome continues to change.

- Ongoing efforts to fill "gaps" and properly/thoroughly represent complex structures and loci in the genome (e.g., Major Histocompatibility Complex)
- Each improvement leads to a new genome "build". Currently on build 38.
- Experimental and computational methods provide new genome annotations
  - New gene models, transcription factor binding sites, and loci where human individuals differ (i.e., polymorphisms)
- Therefore, the human reference genome is by no means "complete"!
- How does the same genome yield such phenotypic diversity across tissue types?
- How does the genome evolve within an individual (tissues) and among a population?

Searching for and counting patterns in genomes with `grep`

```
~/workspace/dnaseq/references/all_sequences.fa
```

What will this command do?

```
grep ">" ~/workspace/dnaseq/references/all_sequences.fa
```

How many adenosines are there?

```
grep -v ">"
~/workspace/dnaseq/references/all_sequences.fa | grep
-c "A"
```