

To fight race science, double down on the genome

Ed Hagen, Washington State University

The problem

Genetics testing & online discourse

“And We Will Fight for Our Race!”

A Measurement Study of Genetic Testing Conversations on Reddit and 4chan

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Take-aways. Overall, we find that genetic testing is a rather popular topic of discussion in 4chan’s /pol/, often appearing in long/active threads. Also, genetic testing topics are often accompanied by images and memes with clear racial or hateful connotations. While the presence of highly toxic content in /pol/ is unsurprising, the specific content which accompanies threads related to genetic testing is very worrying. We find imagery with prominent figures of the alt-right movement (e.g., Lauren Southern, Richard Spencer), antisemitic memes (e.g., Happy Merchant), and topics of discussion using words with racial/hateful meaning (e.g., jewish, nigger), which may be an indicator that groups adjacent to the alt-right are using genetic testing to bolster their ideology.

The Buffalo shooter manifesto

**Posted two days before
murdering 10 black people
(180 pages)**

Was there a particular event or reason you decided to commit to a violent attack?

Before I begin I will say that I was not born racist nor grew up to be racist. I simply became racist after I learned the truth.

I started browsing 4chan in May 2020 after extreme boredom, remember this was during the outbreak of covid. I would normally browse /k/ because I'm a gun nut and /out/ because I love the outdoors and I eventually wound up on /pol/. There I learned through infographics, shitposts, and memes that the White race is dying out, that blacks are disproportionately killing Whites, that the average black takes \$700,000 from tax-payers in their lifetime, and that the Jews and the elite were behind this. From there, I also found other sites, like worldtruthvideos.website, dailyarchives.org, and dailystormer.cn where through data and exposure to real information I learned the truth. We are doomed by low birth rates and high rates of immigration. I never even



The truth is my personal life and experiences are of no value. I am simply a White man seeking to protect and serve my community, my people, my culture, and my race.

The Buffalo shooter manifesto

Copious citations of genetic ancestry literature

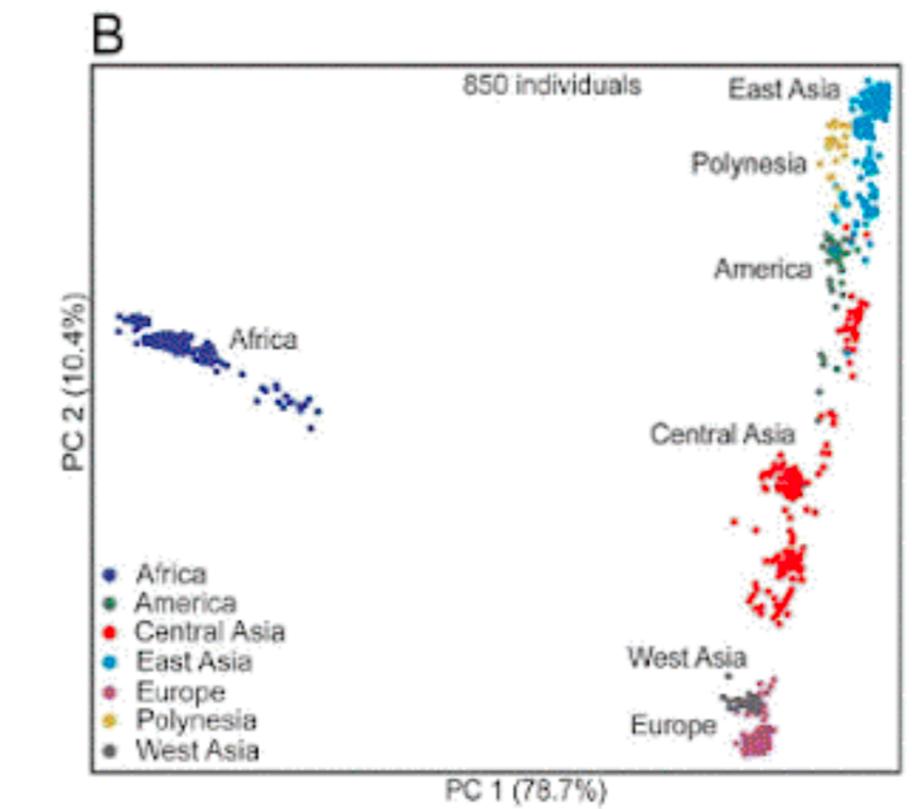
Myth #6: "There isn't significant genetic distance between races"

Fact: If we used the same standards of taxonomic classification we use for animals, *Homo sapiens* would have a number of subspecies.

Africans are cleanly separated from the rest of mankind and the genetic distance between Eurasians and Africans is higher than the distance between many subspecies of animals.

Species	Genetic diversity (^)	Recognized subspecies
Humans	~0.7	0
Jaguars	~0.7	9
Chimpanzees	~0.7	4
Leopards	~0.6	8
Pumas	~0.5	6
Elk	~0.4	7

Woodley, Michael. "Is *Homo sapiens* polytypic? Human taxonomic diversity and its implications." School of Biological Sciences, University of London. *Medical Hypotheses* 74 (2010) 195–201.



Xing J, Watkins WS, Shlien A, et al. Toward a more Uniform Sampling of Human Genetic Diversity: A Survey of Worldwide Populations by High-density Genotyping. *Genomics*.

"Whites and Blacks are separated by tens of thousands of years of evolution, and our genetic material is obviously very different." (p. 14)

"We must remove blacks from our western civilizations." (p. 24)

"...the Jews are the biggest problem the Western world has ever had. They must be called out and killed..." (p. 24)

"Ethnic Jews can be found by having a dominant mitochondrial haplogroup 'J'." (p. 25)



Bphm ✅ @BlkPHomo · 8h

I legitimately believe people like this should be shot.

...

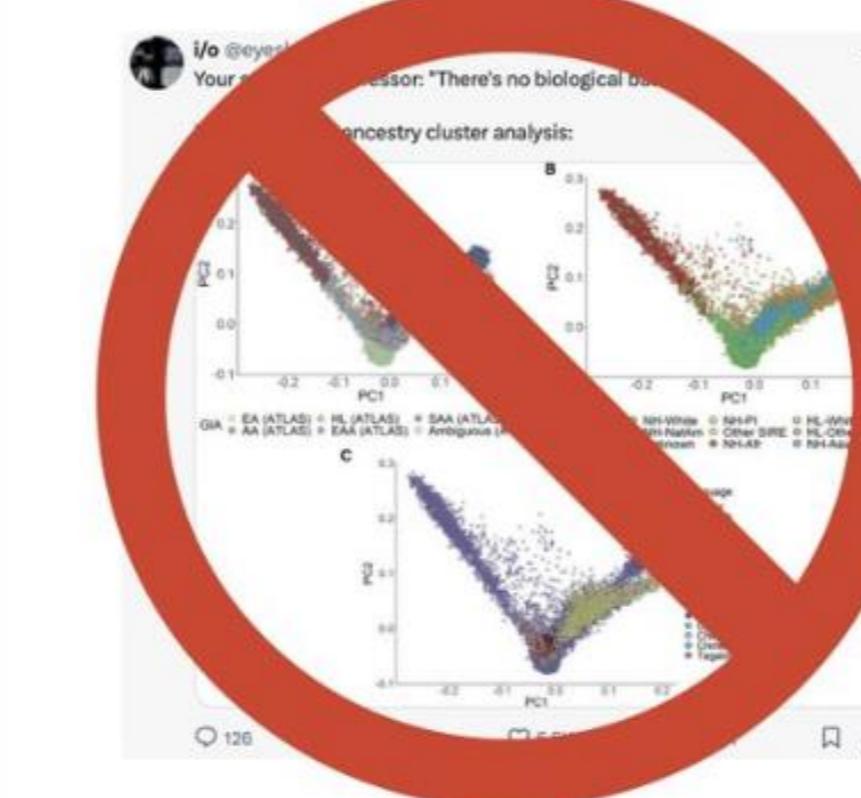


Ed Hagen @ed_hagen · Mar 19

7. My solution: we need a new cultural model of the genome based on the highly conserved (universal) interactions *within* the genome, whose biological significance VASTLY outweighs the biological significance of differences between genomes.

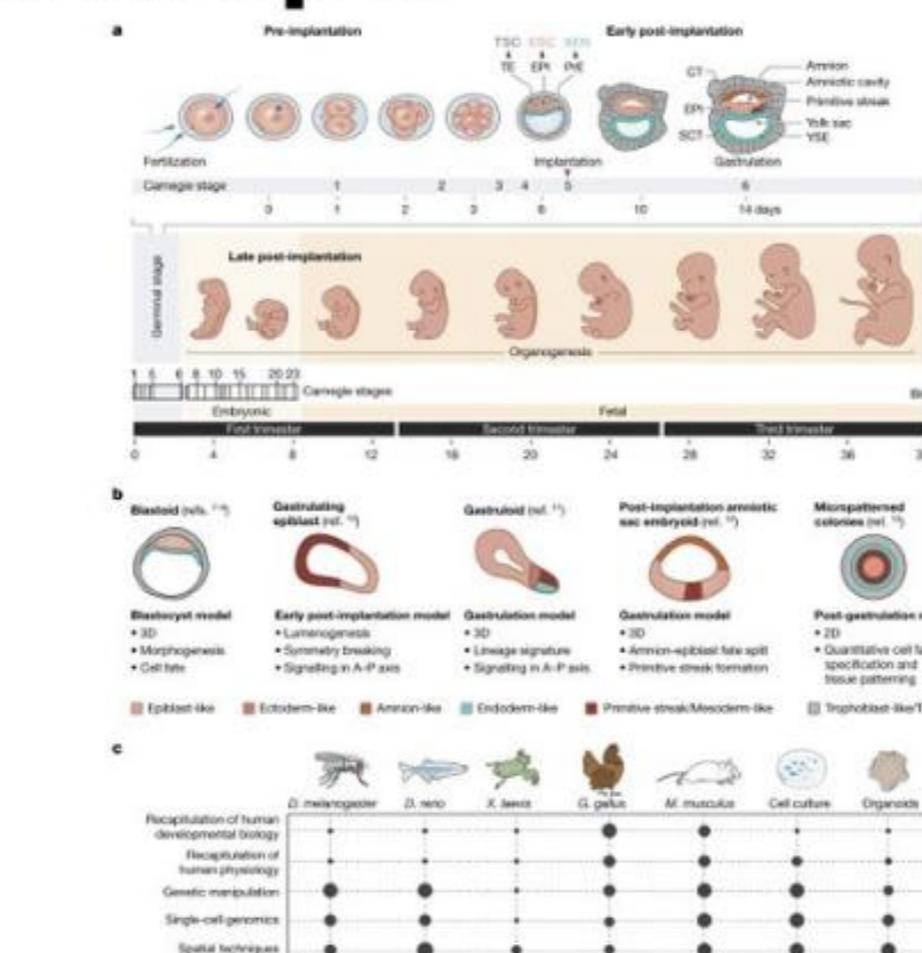
[Show this thread](#)

“It’s genetic”: Genome concepts

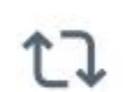


ALT

Difference



Regulatory (highly conserved)



The root problem

**Our cultural model of
“genetic” as **genetic**
difference corresponds
too closely to our **ethnic**
difference psychology**



“...in the history of the human species and in the early history of the human species but still true, there is a kind of if I may call it **nationalism or localism or villagism or tribalism**, whatever you wanna call it. That is to say, a group that has solidarity living together which deals with other groups that have their own solidarity often in a **hostile and contradictory way...**”

Lewontin (reluctantly) concedes there could be genetic population differences in psychology and behavior



The Concept of Race with Richard Lewontin

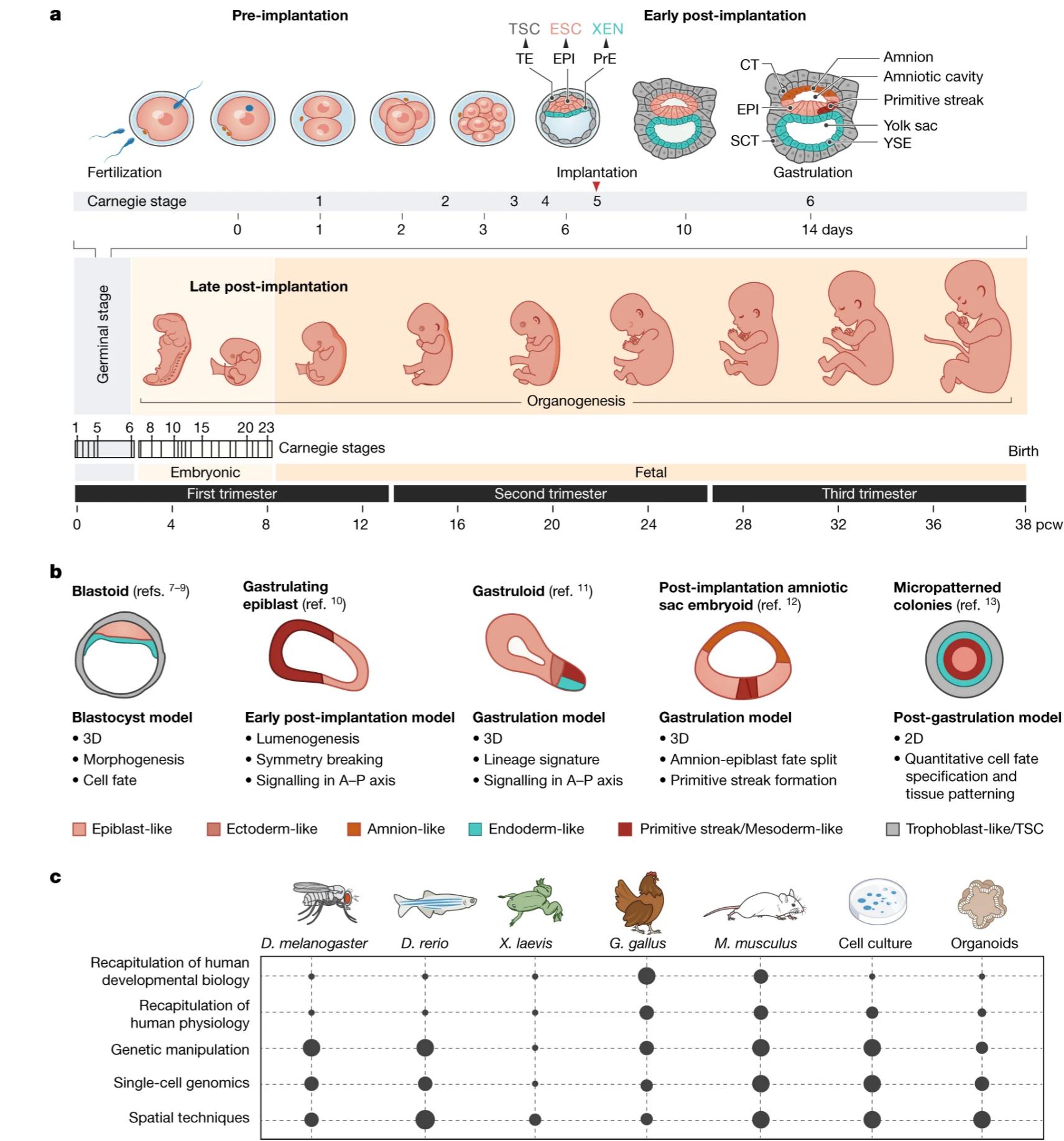
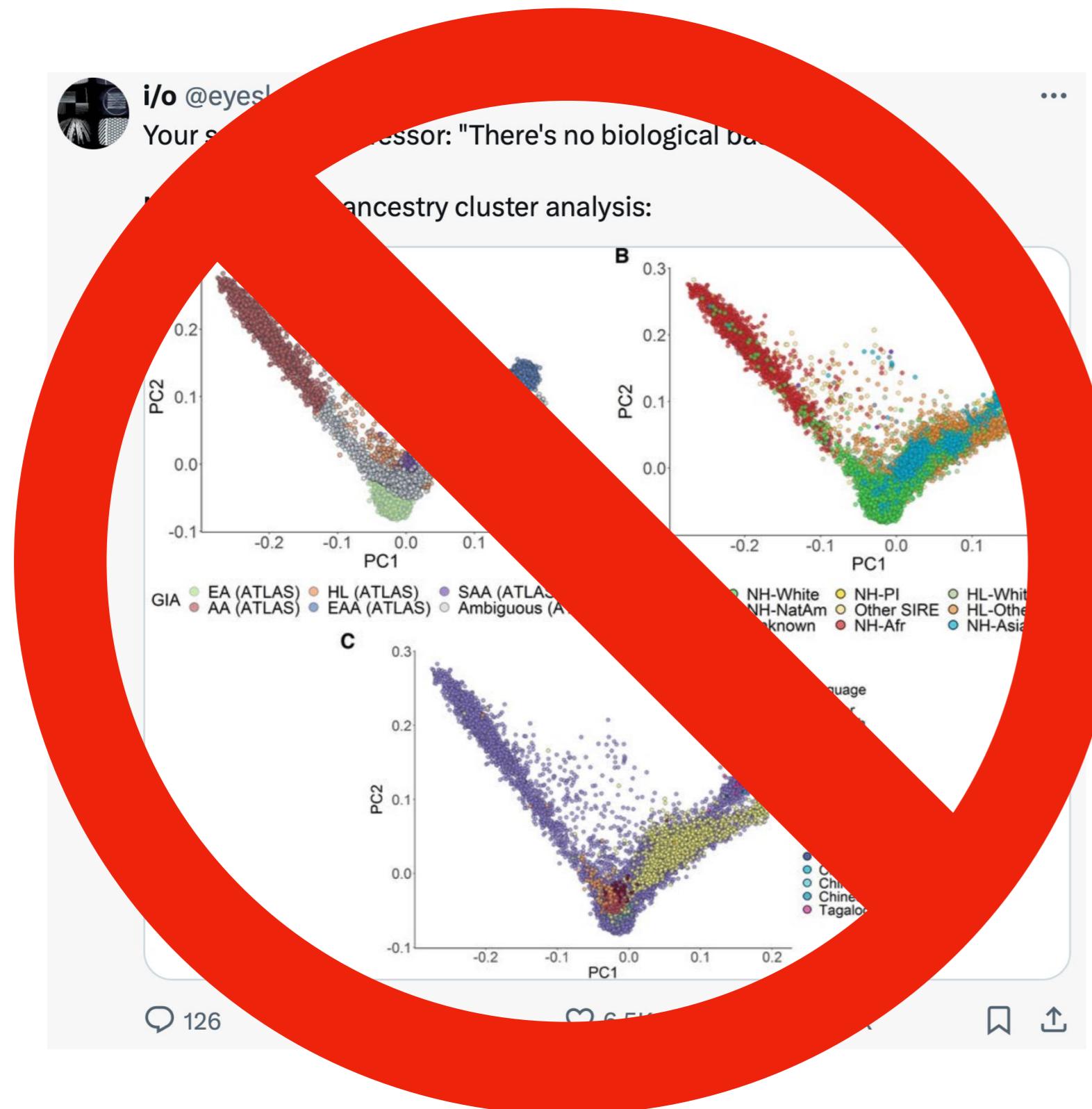
“...that doesn't prove that there isn't a gene someplace, nobody's ever found it, **that might influence your charitable instincts, and that maybe people in Africa have a much higher frequency of that gene than people in England.** That could be, but nobody's ever found it and there's no reason to think that such things exist.”

Fragile solutions

- Ancestry ≠ race
- Admixture
- Epigenetics (the genome as a “blank slate”)
- Non-genetic variation

All implicitly endorse the residual biological importance of genetic variance and ignore the profound biological importance of the parts of the genome that don't vary

Cultural models of “genetic”



Difference

Regulatory (highly conserved)

Line	POS	REF	ALT			
1	34	q	Q	16	42	um ume
1	42	,	:	17	15	e i
2	14	n	N	17	16	fpr fpr
3	5	s	S	17	23	l L
3	16	a	A	17	33	l L
3	37	f	F	18	18	o O
4	13	rm	rme	18	34	f S
4	27	s	S	19	16	rr r
5	15	g,	g	19	27	'v u
5	26	,	:	20	28	q Q
5	32	i	y	20	33	a u
5	31	ie	ye,	21	13	b B
6	8	,	;	21	19	;
7	5	h	H	21	21	w W
7	12	ch	k	21	31	f these F
7	29	s	f	21	34	de d
7	34	n	N	21	40	el dle
7	37	ra	ral	21	43	e, e
7	42	s	f	22	32	ie y
7	45	ck	cke	24	15	' e
8	6	f	F	24	18	c C
8	17	i	y	24	22	tr tre
8	17	ir	yre	24	35	s f
8	23	;	?	24	38	b B
8	25	t	'T	25	4	t T
8	36	su	sum	25	8	i el
9	3	v	u	25	23	p P
9	18	s	f	25	24	uz u
9	20	'd	'd.	26	30	f s
9	23	t	T	26	34	ll lle
9	27	i	y	27	8	i y
9	37	ep	epe	27	19	s s that
10	12	er	erc	28	6	c C
10	23	d	D	28	17	do d
10	28	,	;	28	28	c C
10	30	ay	I	28	32	ds of vs all

Second Quarto (1604) vs First Folio (1623)

Line	POS	REF	ALT			
1	34	q	Q	16	42	um
1	42	,	:	17	15	i
2	14	n	N	17	16	fpr
3	5	s	S	17	23	L
3	16	a	A	17	33	L
3	37	f	F	18	18	O
4	13	r̄m	rme	18	34	S
4	27	s	S	19	16	r
5	15	g,	g	19	27	'v
5	26	,	:	20	28	Q
5	32	i	y	20	33	u
5	31	ie	ye,	21	13	B
6	8	,	;	21	19	?
7	5	h	H	21	21	W
7	12	ch	k	21	31	these F
7	29	s	f	21	34	d
7	34	n	N	21	40	dle
7	37	ra	ral	21	43	e,
7	42	s	f	22	32	y
7	45	ck	cke	24	15	e
8	6	f	F	24	18	C
8	17	i	y	24	22	tre
8	17	ir	yre	24	35	f
8	23	;	?	24	38	B
8	25	t	'T	25	4	T
8	36	su	sum	25	8	el
9	3	v	u	25	23	P
9	18	s	f	25	24	uz
9	20	'd	'd.	26	30	s
9	23	t	T	26	34	ll
9	27	i	y	27	8	y
9	37	ep	epe	27	19	s that
10	12	er	erc	28	6	C
10	23	d	D	28	17	d
10	28	,	;	28	28	C
10	30	ay	I	28	32	ds of vs all

1 To be, or not to be, that is the qQuestion,:
 2 Whether 'tis nNobler in the mind to suffer
 3 The sSlings and aArrows of outragious fFortune,
 4 Or to take Armes against a sSea of troubles,
 5 And by opposing, end them,: to diye, to sleep
 6 No more,; and by a sleep, to say we end
 7 The hHeart-achke, and the thouſtand nNaturall sfhockes
 8 That fFlesh is heiyre too;? t'Tis a consummation
 9 Devuoutly to be wiſh'd. tTo diye to sleepe,
 10 To sleep, perchance to dDream,; ayI, there's the rub,
 11 For in that sleep of death, what dreams may come,
 12 When we haue sfhufflel'd off this mortall coile,
 13 Muft giue vus paufe,. tThere's the refspect
 14 That makes cCalamitiey of fo long life:
 15 For who would beare the wWhips and fScornes of time,
 16 Th'oe Oppreffors wrong, the proudore mans cContumely,
 17 The pangs of deifpriz'd lLoue, the lLawes delay,
 18 The infolence of oOffice, and the fSpurnes
 19 That patient merrit of the'v unworthy takes,
 20 When he himfelfe might his qQuietaus make
 21 With a bare bBodkin;? wWho would ftheſe Fardeles beare,
 22 To grunt and fweat vnder a weariey life,
 23 But that the dread of fomething after death,
 24 The vndifcouer'ed cCountrey, from whosfe bBorne
 25 No tTrauieller returns, pPuzzels the will,
 26 And makes vs rather beare thofse illes we haue,
 27 Then fliye to others that we know not of.
 28 Thus cConfciencie dooes make cCowards of vs all,
 29 And thus the nNatvie hiew of rRefolution
 30 Is ficklied o're, with the pale caſt of tThought,
 31 And enterprifzes of great pitch and moment,
 32 With this regard theyir cCurreants turne awray,
 33 And loosfe the name of aAction. Soft you now,
 34 The faire Ophelia,? Nymph, in thy oOrizons
 35 Be all my finnes remembred.

The “between genome” difference concept

The “within genome” regulatory concept

The **sequence** matters, and
sequence is inherently a
within-genome property

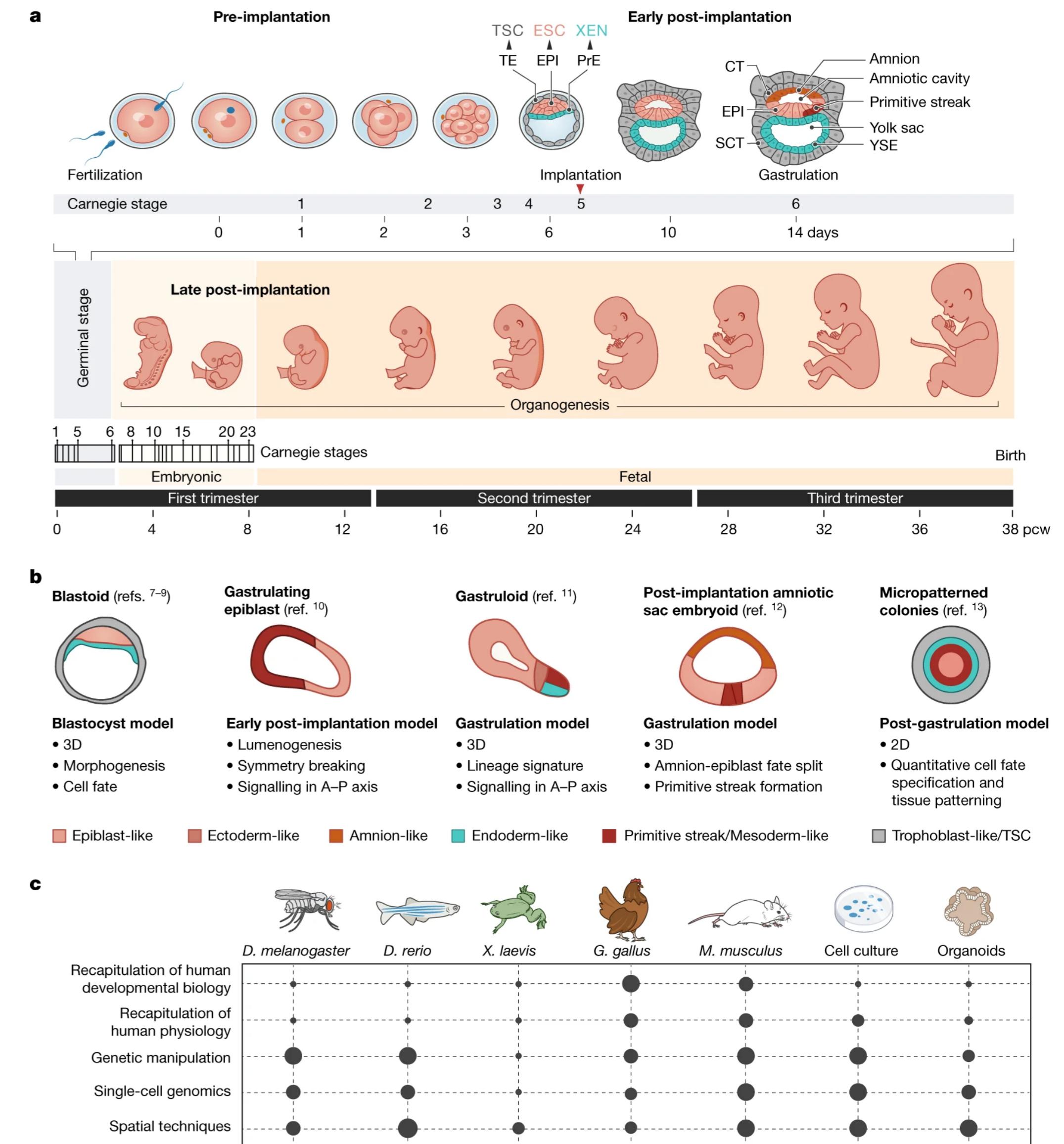
gtgtgagggaaaggagtgactcaggcaaggc
tttcatagagaaagagtctctgccagctt

The big question



Single fertilized cell → 30 trillion cell adult

15
The big answer:
gene regulatory networks



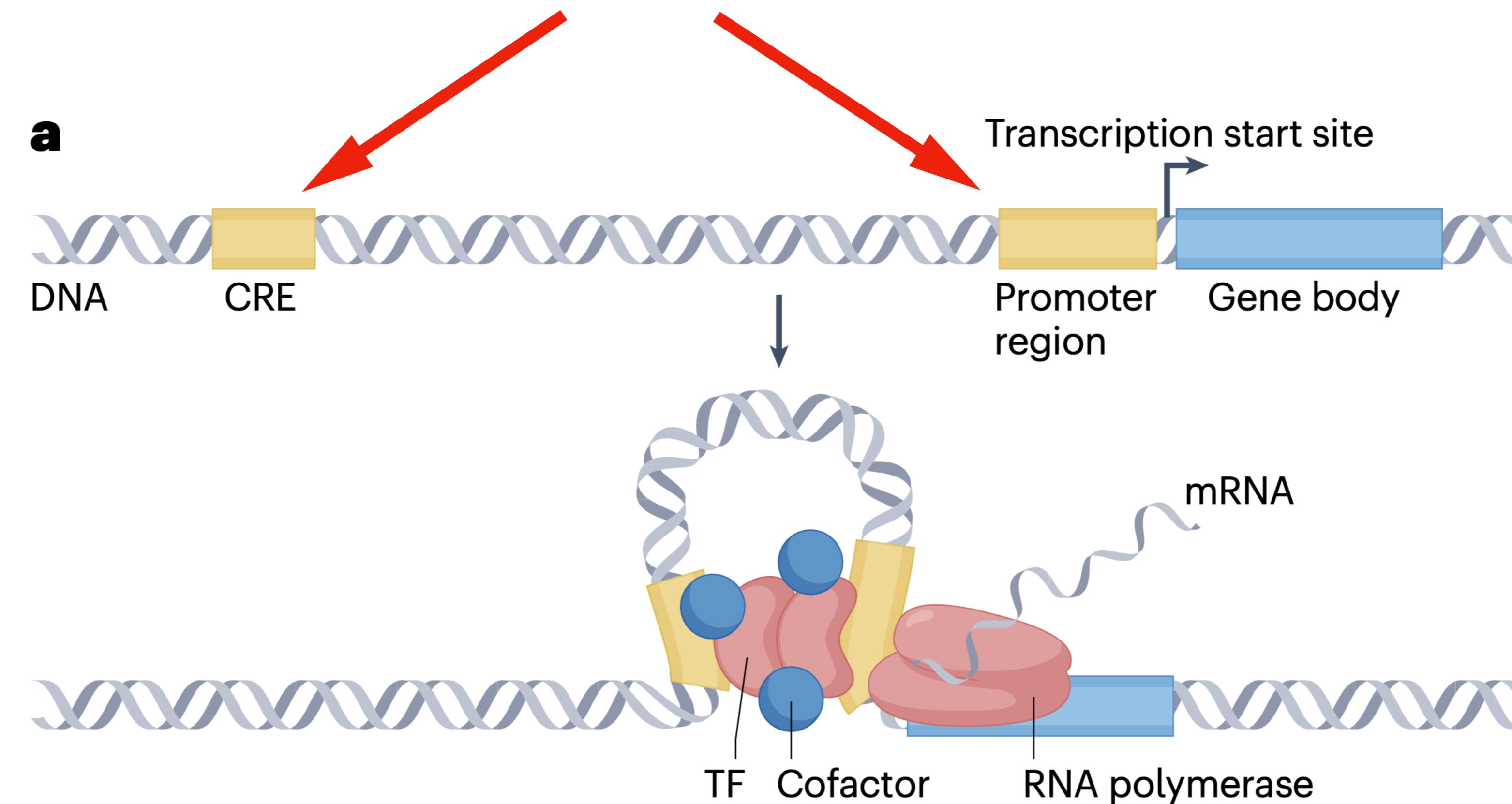
A better cultural model of “genetic”: The universal **regulatory** genome

Sequence-specific, within-genome interactions

- Nucleotide-nucleotide (RNA-coding, protein-coding, binding sites)
- DNA-binding proteins (transcription factors)
- RNA-binding proteins (splicing factors)
- RNA-binding RNA (miRNA, siRNA)
- Protein-protein interactions

Gene regulatory networks

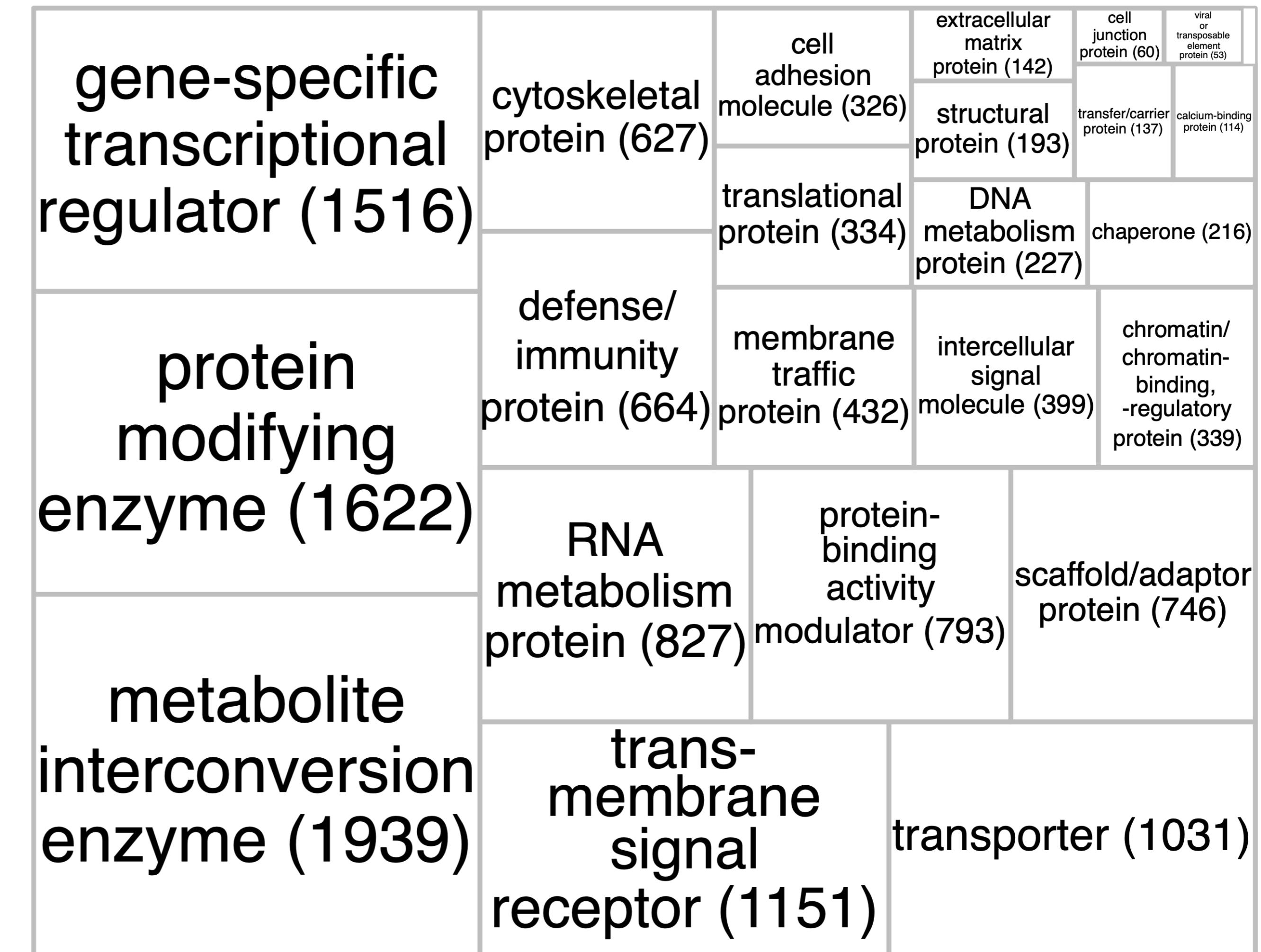
cis-regulatory elements (150-350 bps)
Each contains multiple transcription factor binding sites (7-20 bps) (Andrews et al. 2023)



Human protein coding genes are highly conserved

- ~20K human coding genes; 1.5% of the genome
- 25-39% are essential to life (a homozygous knockout is lethal; Cacheiro & Smedley, 2023)
- 69% under strong or extremely strong constraint (Zeng et al. 2023)
- 9% evolving neutrally (Zeng et al. 2023)
- Since the divergence of the human lineage from orangutans c. 16.5 mya, only 36 new genes have appeared, 14 of which are present in all extant African apes, 5 of which are present in chimpanzees and humans, one of which is present in gorillas and humans, and 16 of which are unique to humans (Guerzoni & McLysaght, 2016)
- 1 new gene every 500K years (Guerzoni & McLysaght, 2016)
- Many essential yeast genes (47% of 414) successfully replaced with human orthologs (genes retain functionality over 1 billion years) (Kachroo et al. 2015)

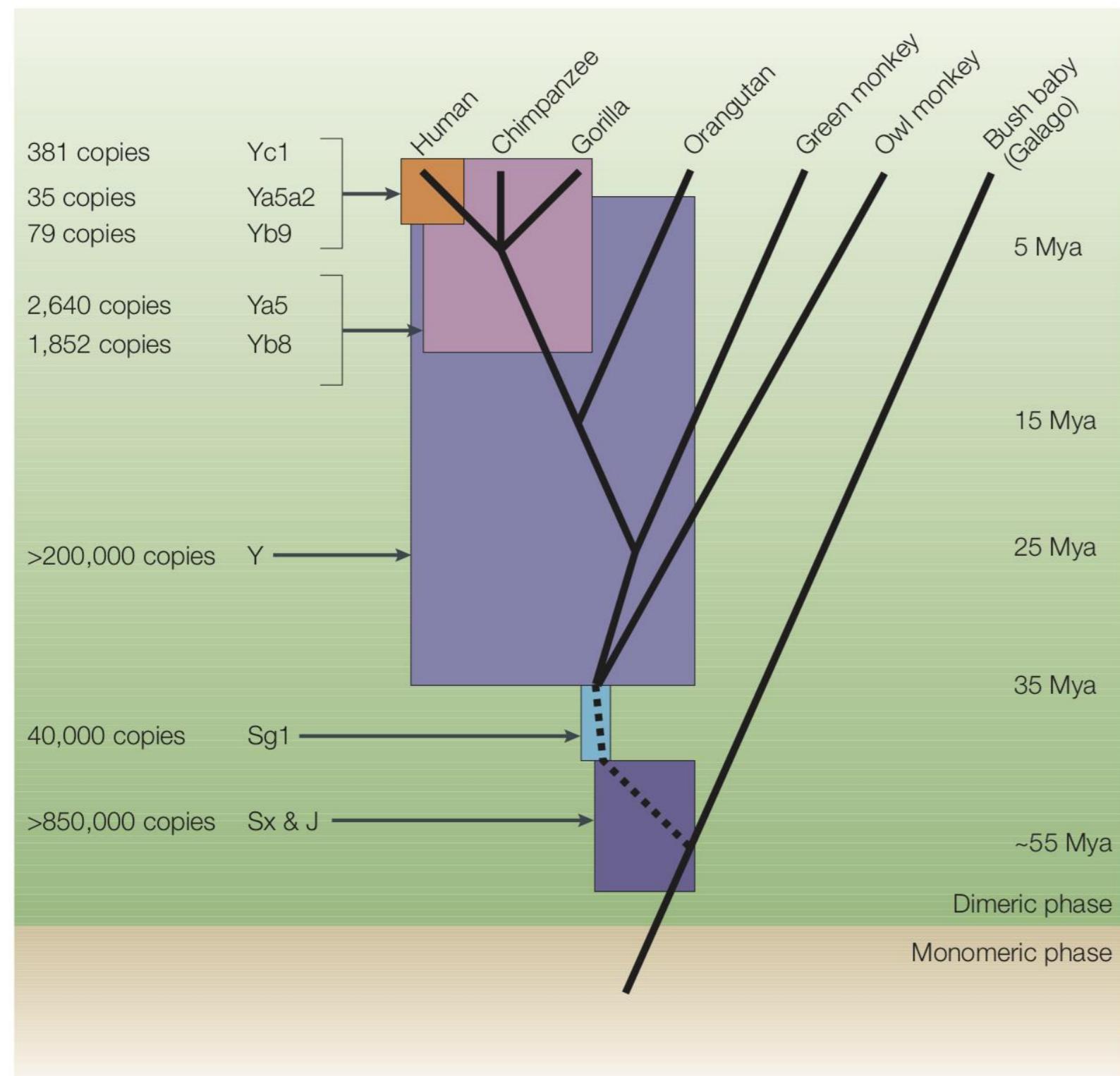
Human proteins are complex molecular machines that perform critical functions



Human protein-coding genes by class. Areas are proportional to the number of genes in each protein class (specified in parentheses). Not displayed: unclassified genes (N=6695). Data from PANTHER 17.0 ([Thomas et al., 2022](#)).

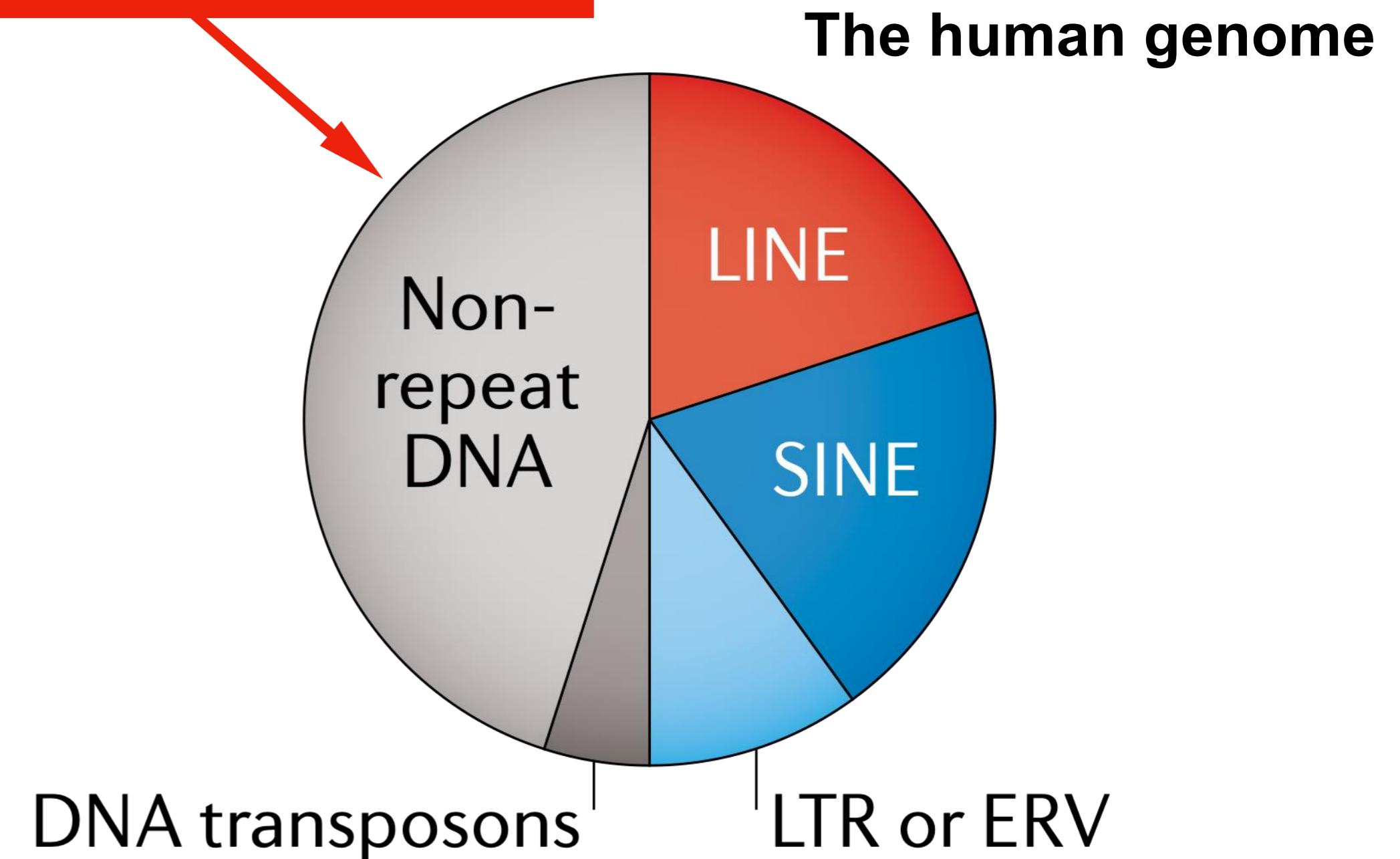
The human genome

A quick introduction



The expansion of Alu elements in primates. Batzer and Deininger 2002.

Protein-coding: 1.5%
Noncoding/regulatory: 8-15%?



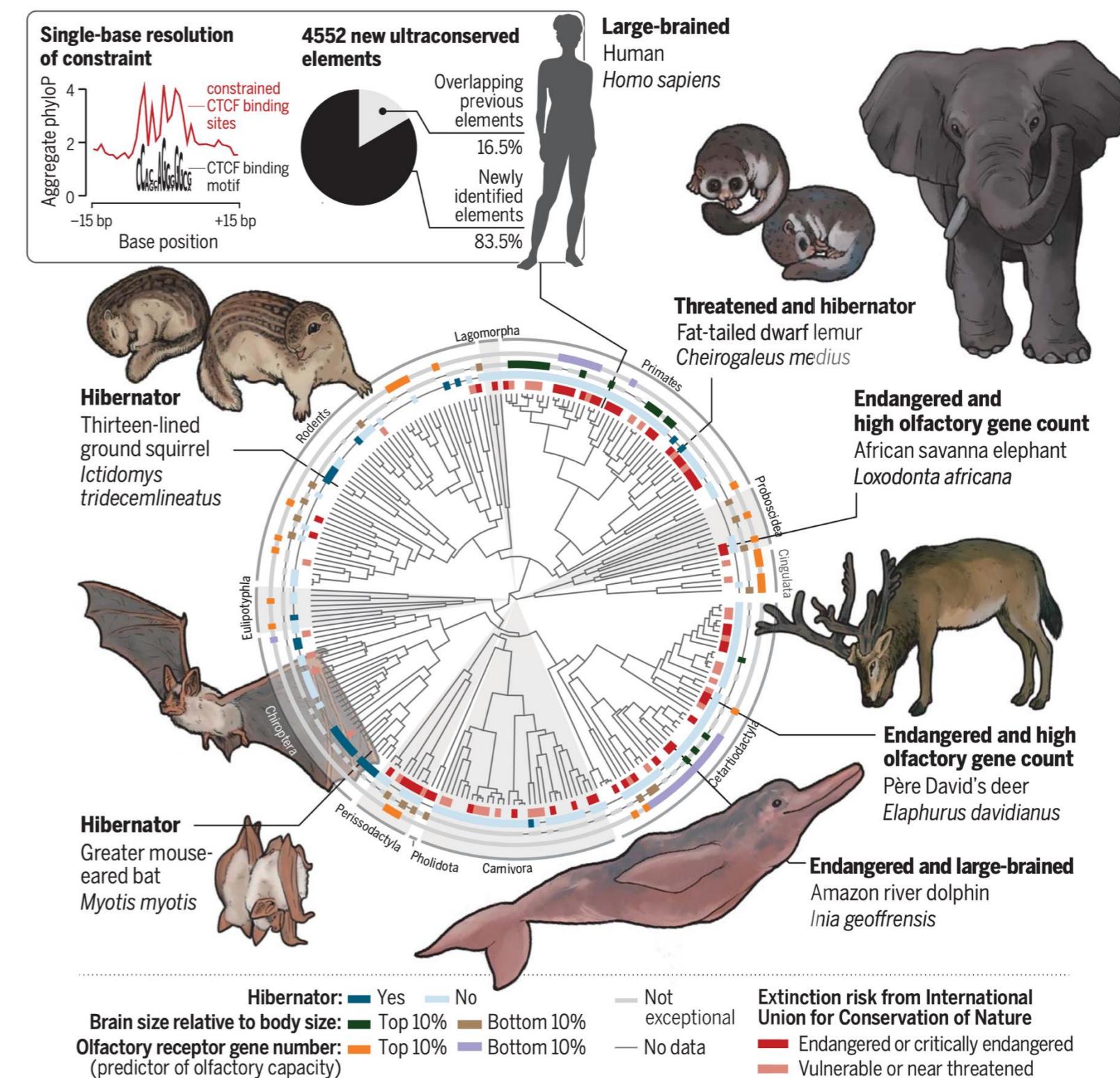
Payer and Burns 2019

LINE/SINE: long/short interspersed elements
LTR: long terminal repeats; ERV: endogenous retroviruses

Unlike coding sequences, functional noncoding sequences are **difficult to identify**

Evolutionary constraint and innovation across hundreds of placental mammals

Matthew J. Christmas^{1†}, Irene M. Kaplow^{2,3†}, Diane P. Genereux⁴, Michael X. Dong¹, Graham M. Hughes⁵, Xue Li^{4,6,7}, Patrick F. Sullivan^{8,9}, Allyson G. Hindle¹⁰, Gregory Andrews⁷, Joel C. Armstrong¹¹, Matteo Bianchi¹, Ana M. Breit¹², Mark Diekhans¹¹, Cornelia Fanter¹⁰, Nicole M. Foley¹³, Daniel B. Goodman¹⁴, Linda Goodman¹⁵, Kathleen C. Keough^{15,16,17}, Bogdan Kirilenko^{18,19,20}, Amanda Kowalczyk^{2,3}, Colleen Lawless⁵, Abigail L. Lind^{16,17}, Jennifer R. S. Meadows¹, Lucas R. Moreira^{4,7}, Ruby W. Redlich²¹, Louise Ryan⁵, Ross Swofford⁴, Alejandro Valenzuela²², Franziska Wagner²³, Ola Wallerman¹, Ashley R. Brown^{2,3}, Joana Damas²⁴, Kaili Fan⁷, John Gatesy²⁵, Jenna Grimshaw²⁶, Jeremy Johnson⁴, Sergey V. Kozyrev¹, Alyssa J. Lawler^{3,4,21}, Voichita D. Marinescu¹, Kathleen M. Morrill^{4,6,7}, Austin Osmanski²⁷, Nicole S. Paulat²⁶, BaDoi N. Phan^{2,3,27}, Steven K. Reilly²⁸, Daniel E. Schäffer², Cynthia Steiner²⁹, Megan A. Supple³⁰, Aryn P. Wilder²⁹, Morgan E. Wirthlin^{2,3,31}, James R. Xue^{4,32}, Zoonomia Consortium§, Bruce W. Birren⁴, Steven Gazal³³, Robert M. Hubley³⁴, Klaus-Peter Koepfli^{35,36,37}, Tomas Marques-Bonet^{38,39,40,41}, Wynn K. Meyer⁴², Martin Nweeia^{43,44,45,46}, Pardis C. Sabeti^{4,32,47}, Beth Shapiro^{30,48}, Arian F. A. Smit³⁴, Mark S. Springer⁴⁹, Emma C. Teeling⁵, Zhiping Weng⁷, Michael Hiller^{18,19,20}, Danielle L. Levesque¹², Harris A. Lewin^{24,50,51}, William J. Murphy¹³, Arcadi Navarro^{38,40,52,53}, Benedict Paten¹¹, Katherine S. Pollard^{16,17,54}, David A. Ray²⁶, Irina Ruf⁵⁵, Oliver A. Ryder^{29,56}, Andreas R. Pfenning^{2,3}, Kerstin Lindblad-Toh^{1,4*}‡, Elinor K. Karlsson^{4,7,57*}‡

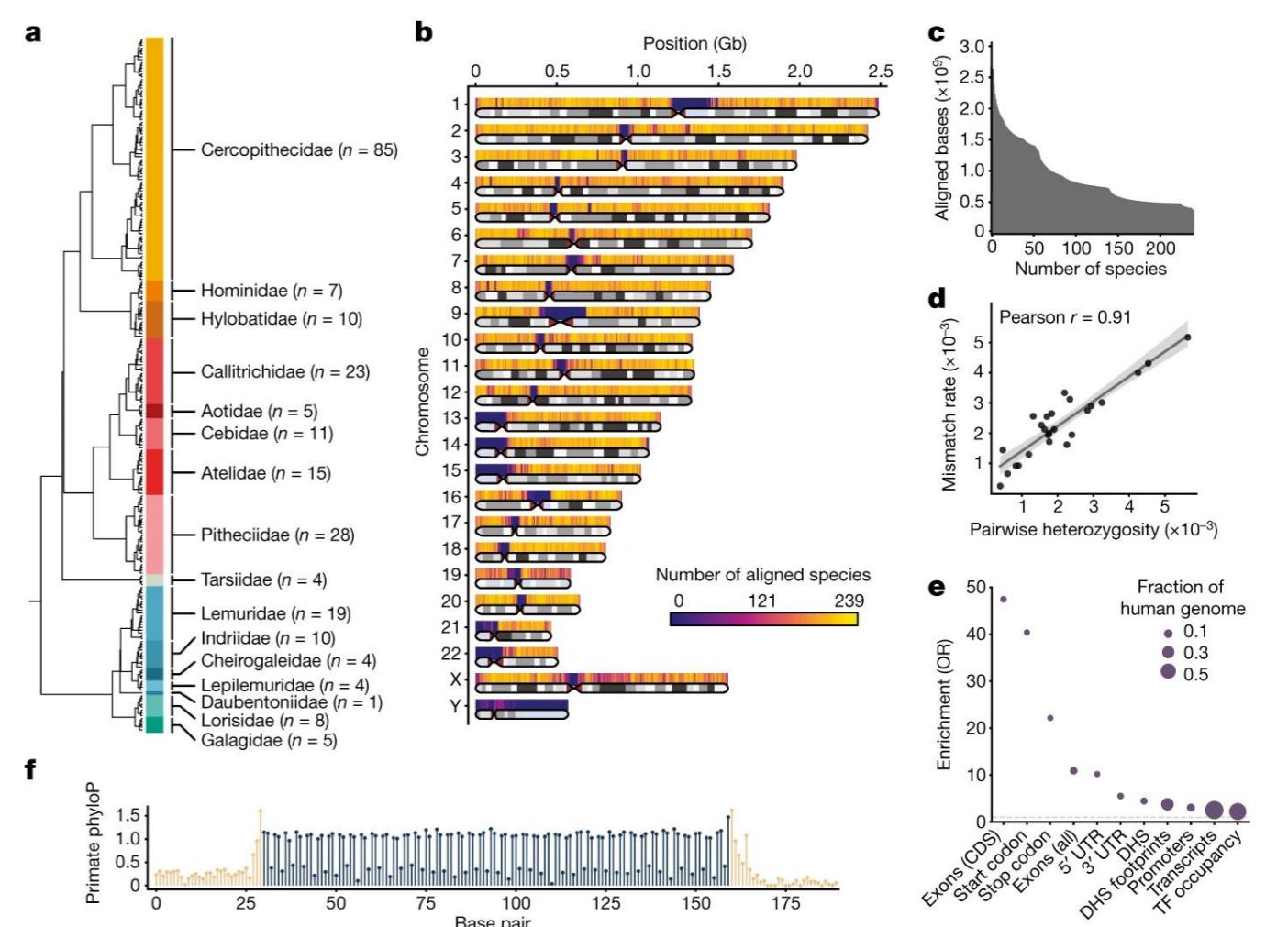


Article | Open access | Published: 29 November 2023

Identification of constrained sequence elements across 239 primate genomes

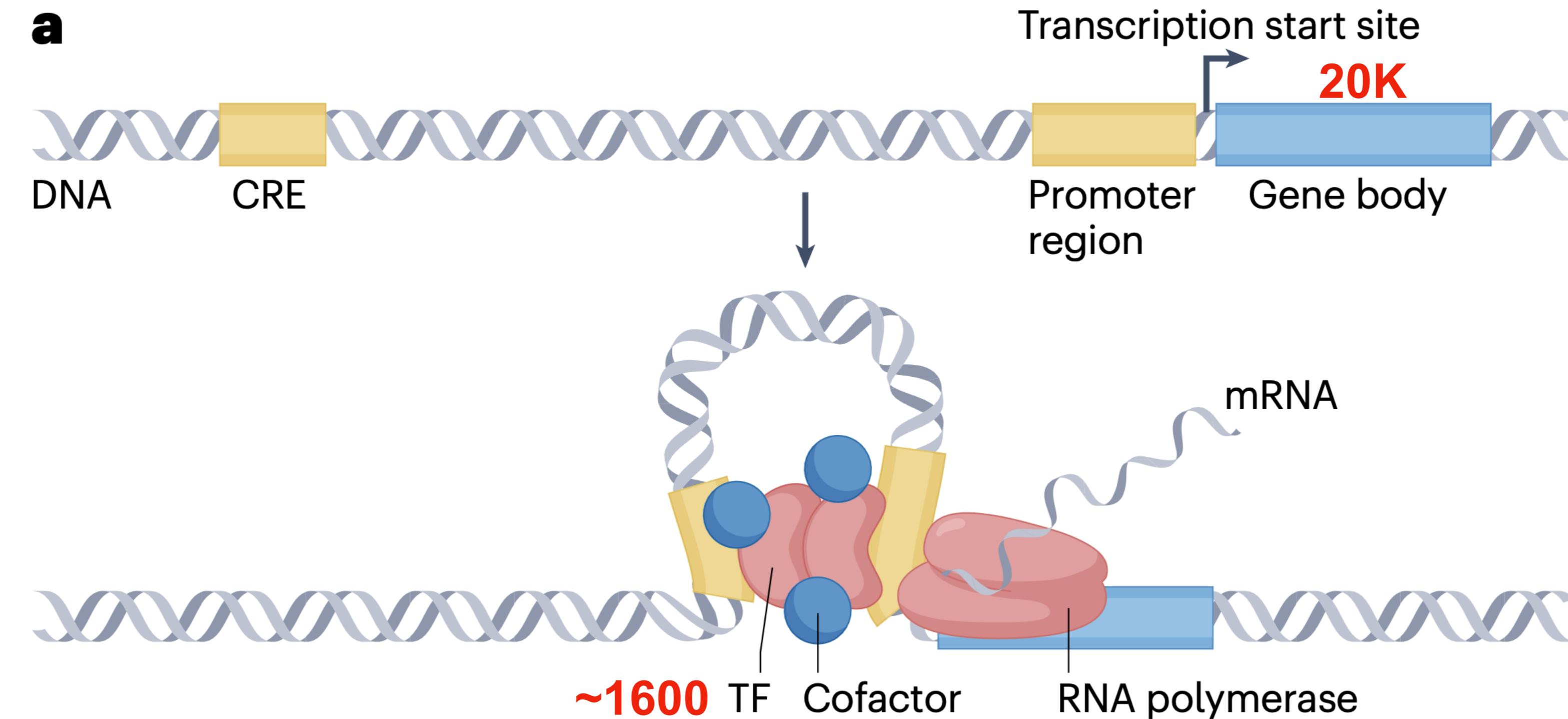
Lukas F. K. Kuderna, Jacob C. Ullrich, Sabrina Rashid, Mohamed Ameen, Lakshman Sundaram, Glenn Hickey, Anthony J. Cox, Hong Gao, Arvind Kumar, Francois Aguet, Matthew J. Christmas, Hiram Clawson, Maximilian Haeussler, Mareike C. Janiak, Martin Kuhlwilm, Joseph D. Orkin, Thomas Bataillon, Shivakumara Manu, Alejandro Valenzuela, Juraj Bergman, Marjolaine Rouselle, Felipe Ennes Silva, Lidia Agueda, Julie Blanc, ... Kyle Kai-How Farh + Show authors

Nature 625, 735–742 (2024) | Cite this article



Gene regulatory networks

Of ~1 million candidate human CREs, ~50% (42%) conserved across mammals, 10% conserved across all primates & some mammals, and 10% (11%) conserved only in primates (Andrews et al. 2023; Kuderna et al. 2024)



Of ~15 million human TFBS, 32% highly conserved, 25% primate specific (Andrews et al. 2023)

New **high-throughput** technologies

Investigate gene regulatory networks in single cells at scale

- DNA and RNA sequencing
- Tissue-specific RNA sequencing
- Single-cell sequencing
- Chromatin modifications (ChIP-seq, DNase-seq, ATAC-seq)
- Methylation
- Reporter assays
- Mass spec (Protein expression)
- CRISPR perturbation
- Organoids
- Spatial-omics
- 3D genome, chromatin
- Machine learning
- Consortia

Article

A human embryonic limb cell atlas resolved in space and time

<https://doi.org/10.1038/s41586-023-06806-x>

Received: 15 April 2022

Accepted: 31 October 2023

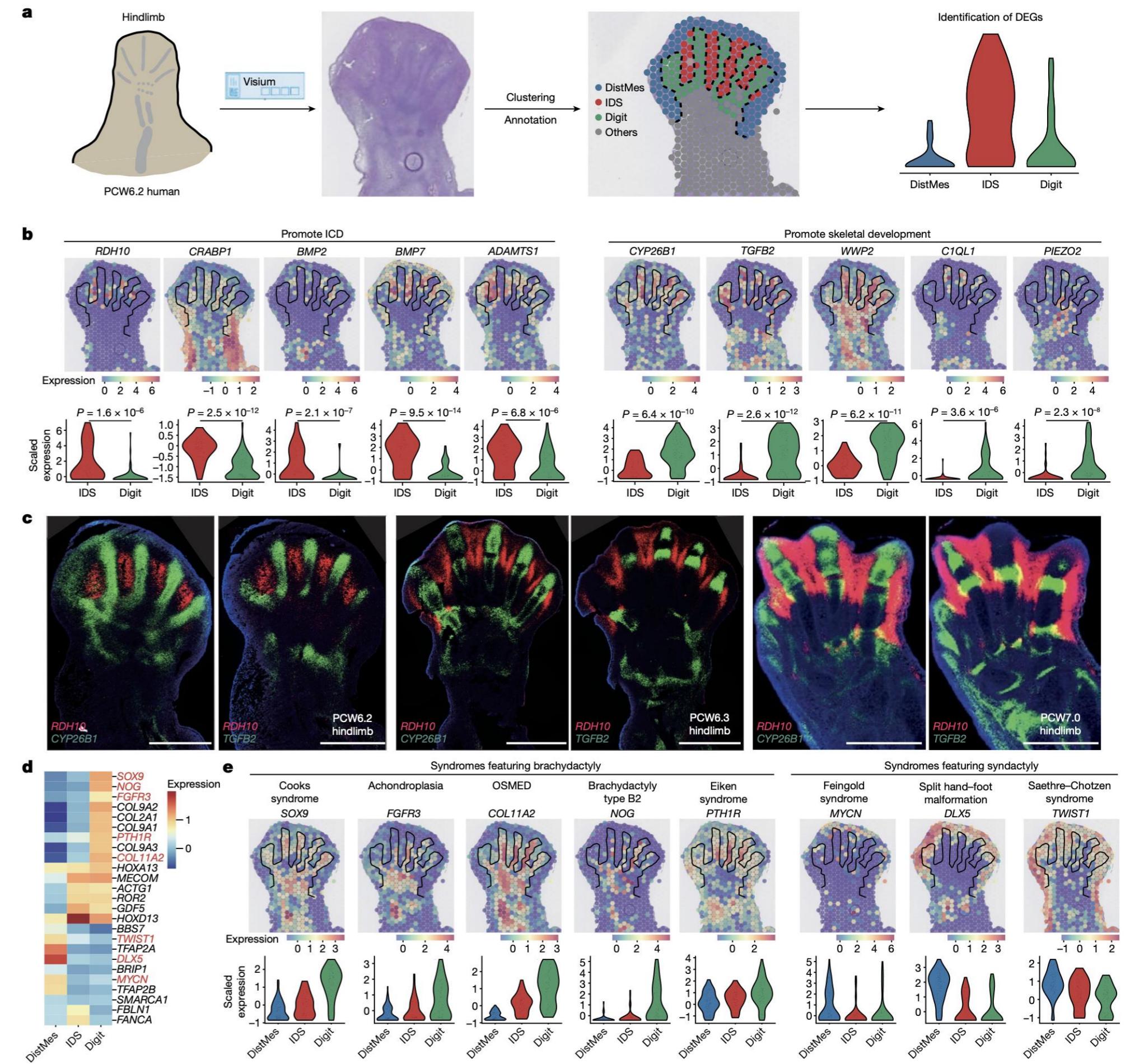
Published online: 06 December 2023

Open access

Bao Zhang^{1,21}, Peng He^{2,3,21}, John E. G. Lawrence^{3,4,21}, Shuaiyu Wang^{1,5,21}, Elizabeth Tuck³, Brian A. Williams⁶, Kenny Roberts³, Vitalii Kleshchevnikov³, Lira Mamanova^{3,18}, Liam Bolt^{3,19}, Krzysztof Polanski³, Tong Li³, Rasa Elmentaitė³, Eirini S. Fasouli^{3,20}, Martin Prete³, Xiaoling He^{7,8}, Nadav Yaron^{2,3}, Yixi Fu¹, Hao Yang¹, Chen Liang¹, Hui Zhang⁹, Raphael Blain¹⁰, Alain Chedotal^{10,11,12}, David R. FitzPatrick¹³, Helen Firth³, Andrew Dean¹⁴, Omer Ali Bayraktar³, John C. Marioni^{2,3}, Roger A. Barker^{7,8}, Mekayla A. Storer⁸, Barbara J. Wold⁶, Hongbo Zhang^{1,15,16} & Sarah A. Teichmann^{3,17}

A concrete example: This study identifies the gene regulatory networks that guide the development of the human limb from a few cells to a complete limb, and “the resulting integrated atlas showed highly conserved cell composition between humans and mice...”

Spatial expression pattern of genes involved in digit formation and phenotype



nature

Inferring and perturbing cell fate regulomes in human brain organoids

<https://doi.org/10.1038/s41586-022-05279-8>

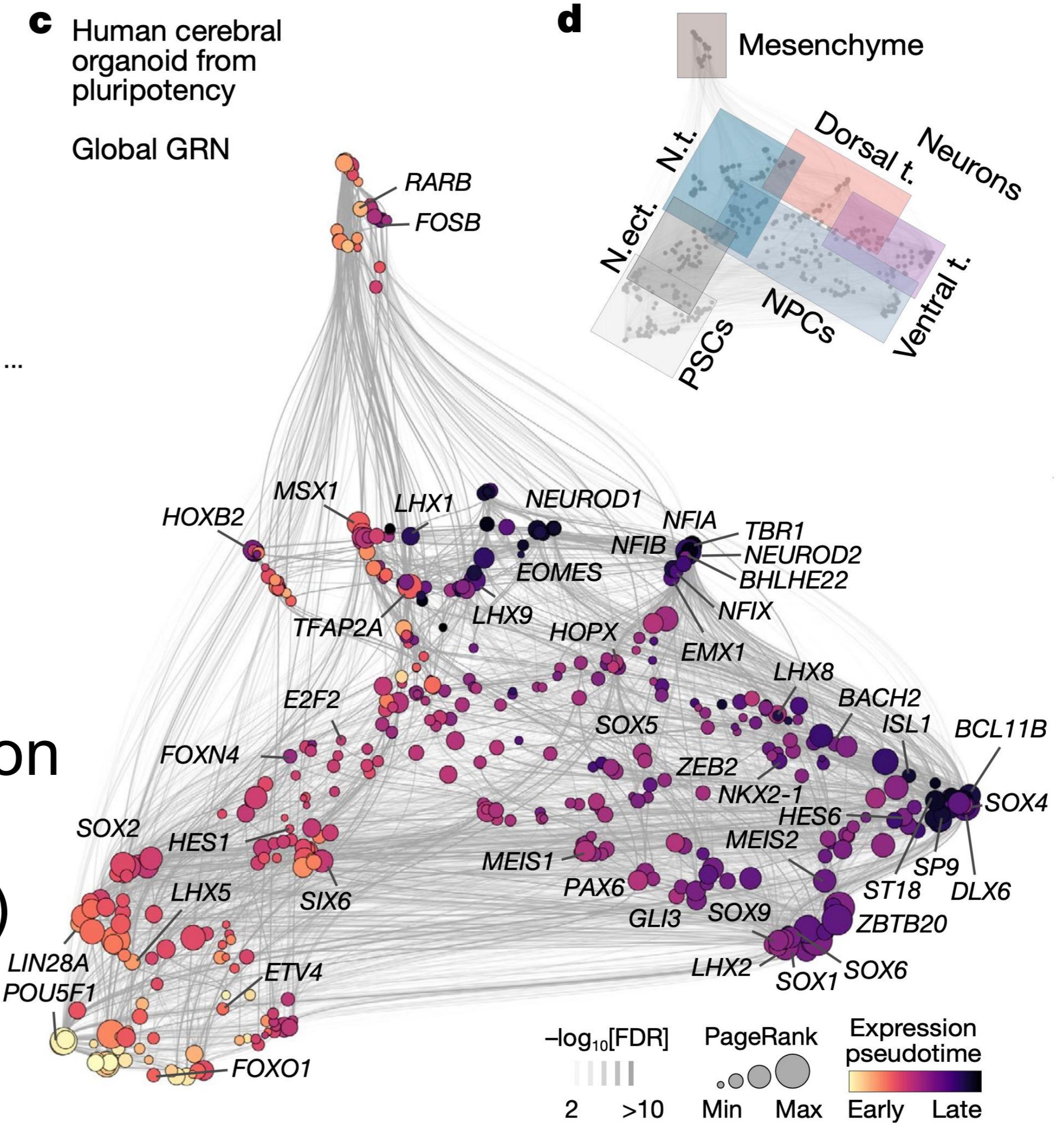
Received: 6 October 2021

Accepted: 25 August 2022

Jonas Simon Fleck^{1,6}, Sophie Martina Johanna Jansen^{1,6}, Damian Wollny², Fides Zenk¹, Makiko Seimiya¹, Akanksha Jain¹, Ryoko Okamoto¹, Małgorzata Santel¹, Zhisong He¹✉, J. Gray Camp^{3,4,5}✉ & Barbara Treutlein¹✉

Limb development: correlation, not causation

Here: experimental manipulation (CRISPR)
showing causation

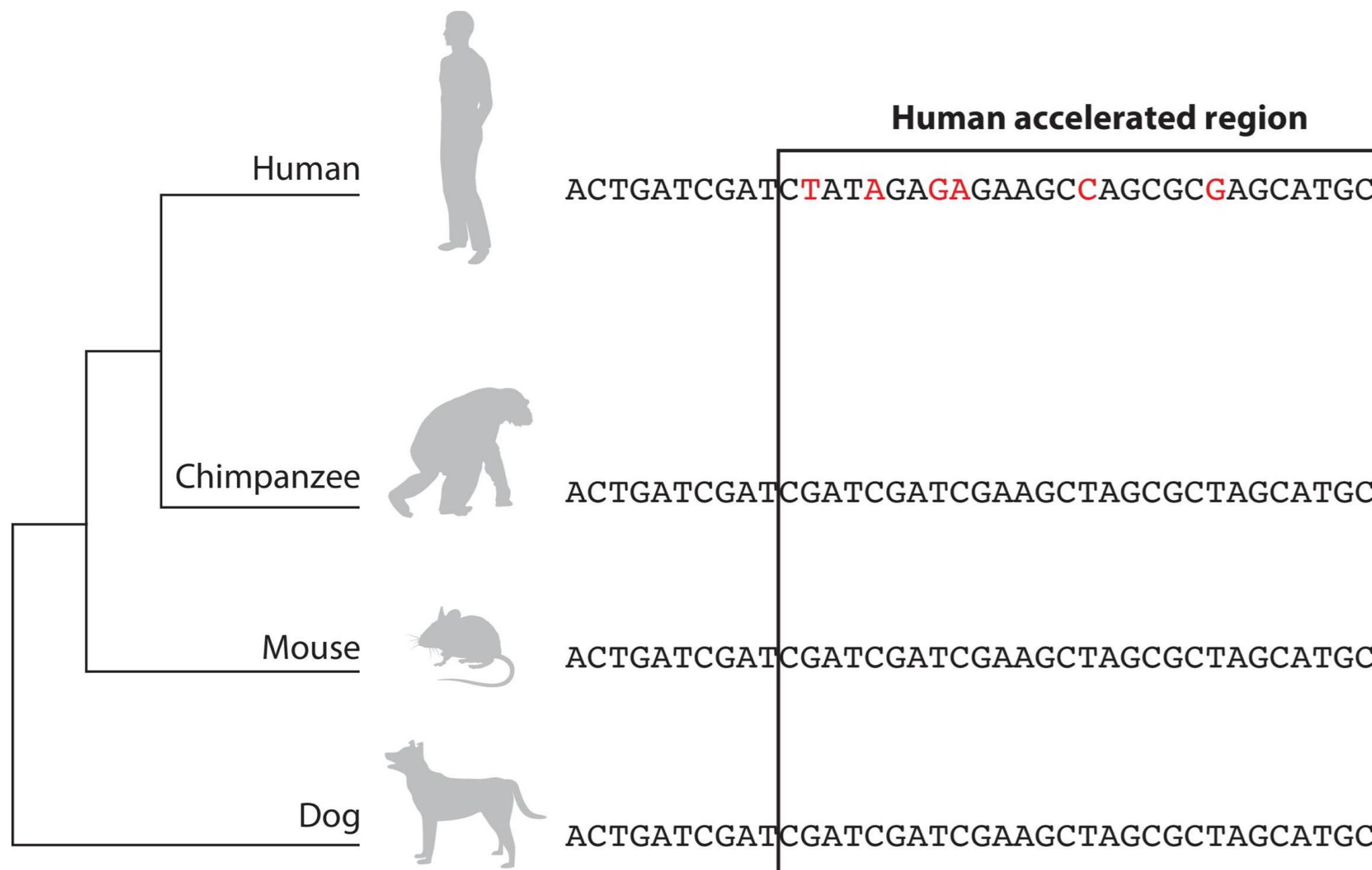


Concluding remarks

- Our current cultural model of “genetic” as genetic differences corresponds too closely to our “tribal” psychology
- As in versions of Hamlet’s soliloquy, genetic differences are often meaningless without understanding the underlying gene regulatory networks
- Gene regulatory networks determine cell fates (and thus development), **and are now being identified “at scale”**
- Transcription factors and other proteins are extremely highly conserved, and cis-regulatory elements are highly conserved
- A new cultural model of “genetic” as the universal regulatory genome might help undercut the use of genetics to justify ethnic conflict

Human accelerated regions (HARs)

Conserved sequences in nonhuman primates/mammals/vertebrates but high substitution rate in humans. Most are in enhancers (Whalen and Pollard 2022).



Analysis of Human Accelerated DNA Regions Using Archaic Hominin Genomes

Hernán A. Burbano , Richard E. Green, Tomislav Maricic, Carles Lalueza-Fox, Marco de la Rasilla, Antonio Rosas, Janet Kelso, Katherine S. Pollard, Michael Lachmann, Svante Pääbo

Published: March 7, 2012 • <https://doi.org/10.1371/journal.pone.0032877>

8.3% of substitutions in HARs are “recent”, i.e., post Neanderthal/Denisovan divergence (vs. 12.4% genome wide)

Human vs chimp embryoid gene expression

The relationship between regulatory changes in *cis* and *trans* and the evolution of gene expression in humans and chimpanzees

[Kenneth A. Barr](#), [Katherine L. Rhodes](#) & [Yoav Gilad](#) 

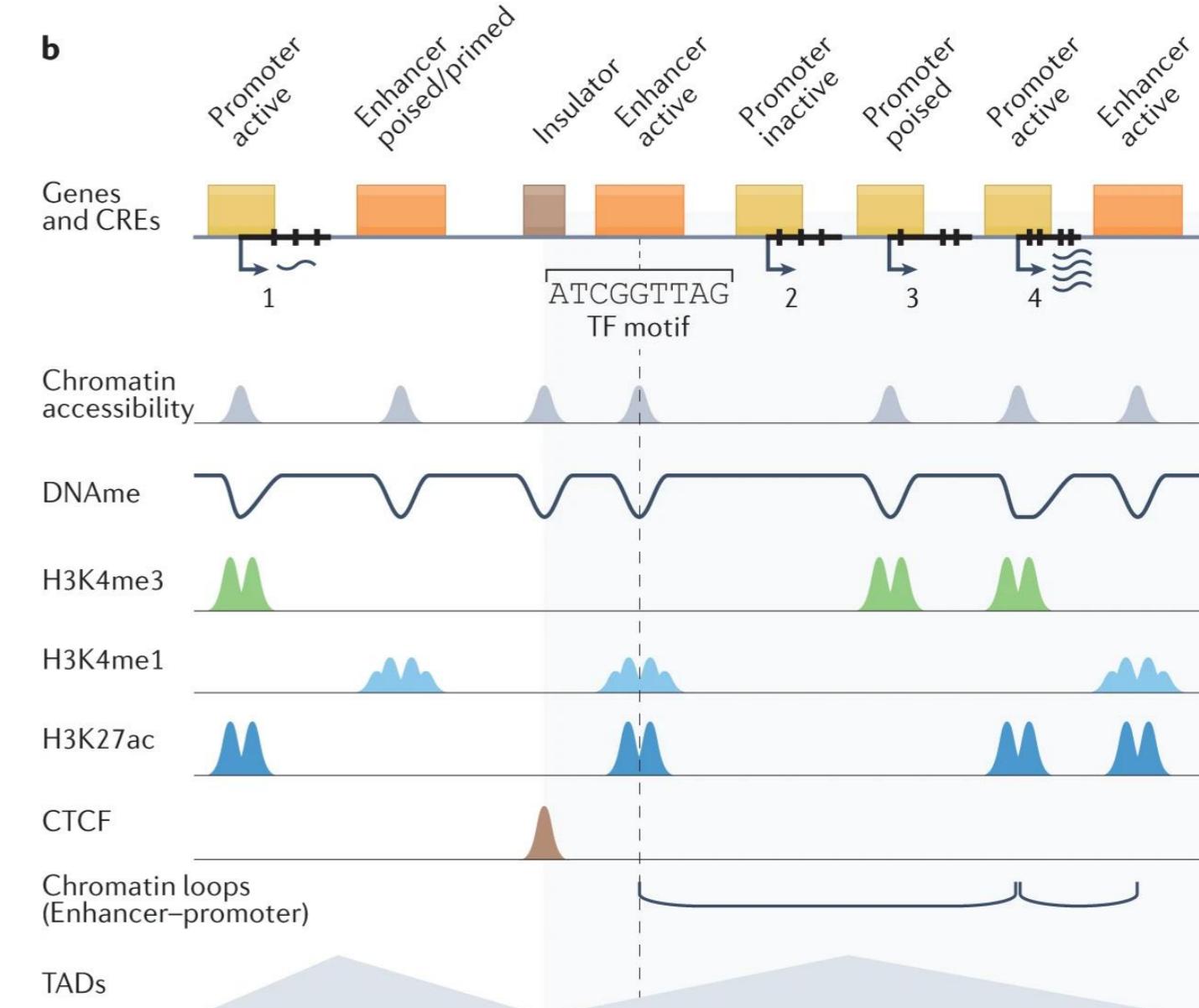
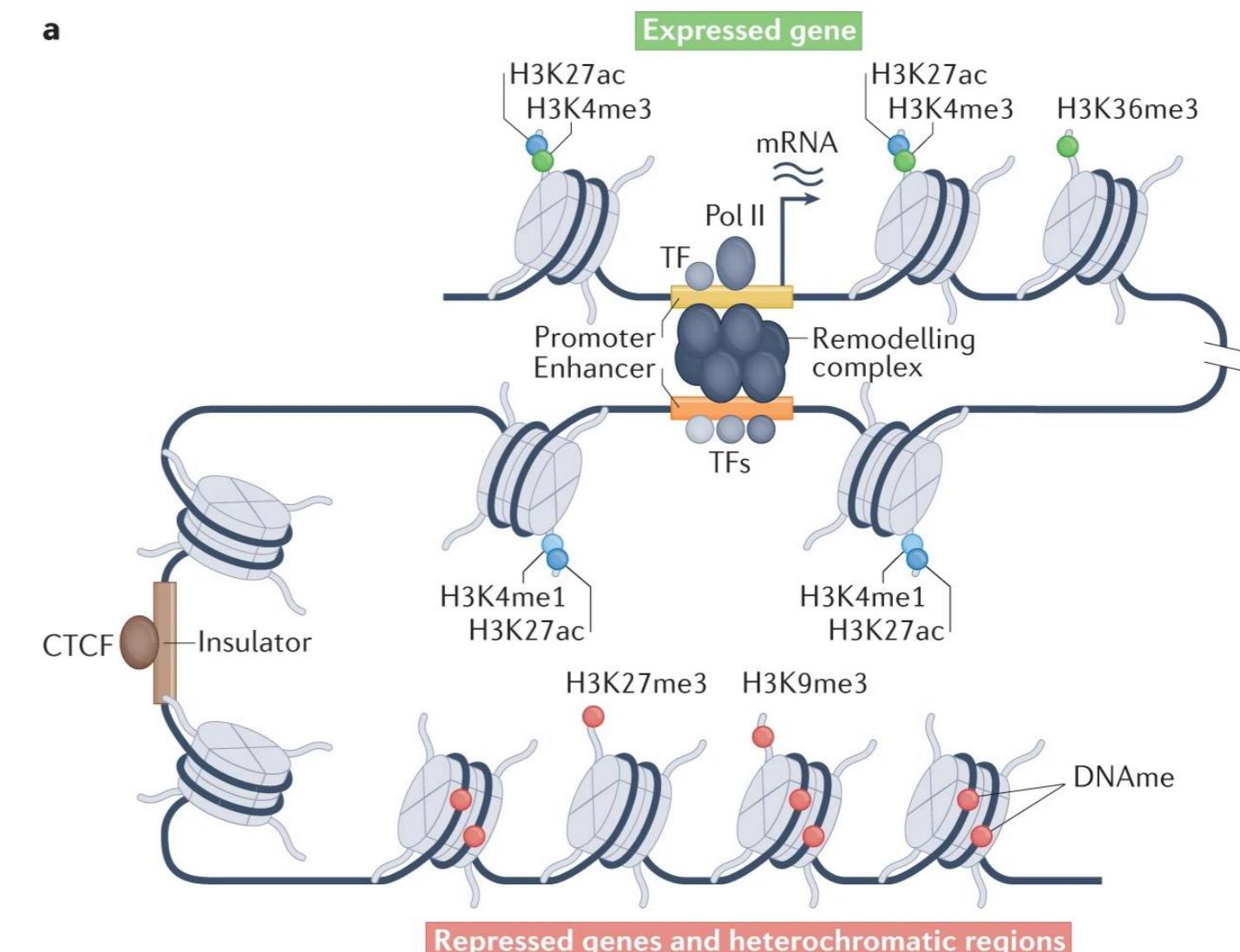
[Genome Biology](#) **24**, Article number: 207 (2023) | [Cite this article](#)

“We were somewhat surprised to find a large subset of genes whose expression is conserved in all of the cell types we were able to study. We did not expect such a large fraction of genes to be regulated in a similar way in humans and chimpanzees in over 70 different cell types, as this requires that the regulation of these genes is of sufficient functional importance in all of these cell types to evolve under relatively strong constraints.”

Characterizing *cis*-regulatory elements using single-cell epigenomics

Sebastian Preissl , Kyle J. Gaulton  & Bing Ren 

[Nature Reviews Genetics](#) 24, 21–43 (2023) | [Cite this article](#)



Deep learning of cross-species single-cell landscapes identifies conserved regulatory programs underlying cell types

Received: 18 July 2021

Accepted: 31 August 2022

Published online: 13 October 2022

 Check for updates

Jiaqi Li^{1,2,10}, Jingjing Wang  , Peijing Zhang^{1,2,10}, Renying Wang^{1,10}, Yuqing Mei¹, Zhongyi Sun¹, Lijiang Fei¹, Mengmeng Jiang^{1,2}, Lifeng Ma¹, Weigao E¹, Haide Chen^{1,2}, Xinru Wang¹, Yuting Fu¹, Hanyu Wu¹, Daiyuan Liu¹, Xueyi Wang¹, Jingyu Li  , Qile Guo³, Yuan Liao^{1,4}, Chengxuan Yu¹, Danmei Jia¹, Jian Wu⁵, Shibo He  , Huanju Liu  , Jun Ma  , Kai Lei⁸, Jiming Chen  , Xiaoping Han   and Guoji Guo  

Within-genome sequence spaces are **vast**

c^n

Upper bound

Element	c	n	Space
Alphabet	26	5	$\sim 10^7$
TFBS	4	7-20	$10^4 - 10^{12}$
CREs	4	150-350	$10^{90} - 10^{210}$
Amino acids	20	500	Inf
Transcription factors	1600	1-6	$\sim 10^{19}$

Conservation of human regulatory elements

- ~1600 transcription factors (Lambert et al. 2018)
- Candidate cis-regulatory elements (cCREs): 9.7% of the genome (ENCODE 2020)
- Mammals: 3.6 million sites perfectly conserved (compared to 191 expected under neutral evolution, Christmas et al. 2023)
- cCREs: 50% conserved in all mammals, a further 10% conserved in all primates and some mammals, a further 10% conserved only in primates (Andrews et al. 2023)
- Of 15.6 million transcription factor binding sites of 367 TFs (5.7% of the genome), 1/3 are highly conserved across mammals, and a further 1/4 conserved in primates (Andrews et al. 2023)

A single-cell time-lapse of mouse prenatal development from gastrula to birth

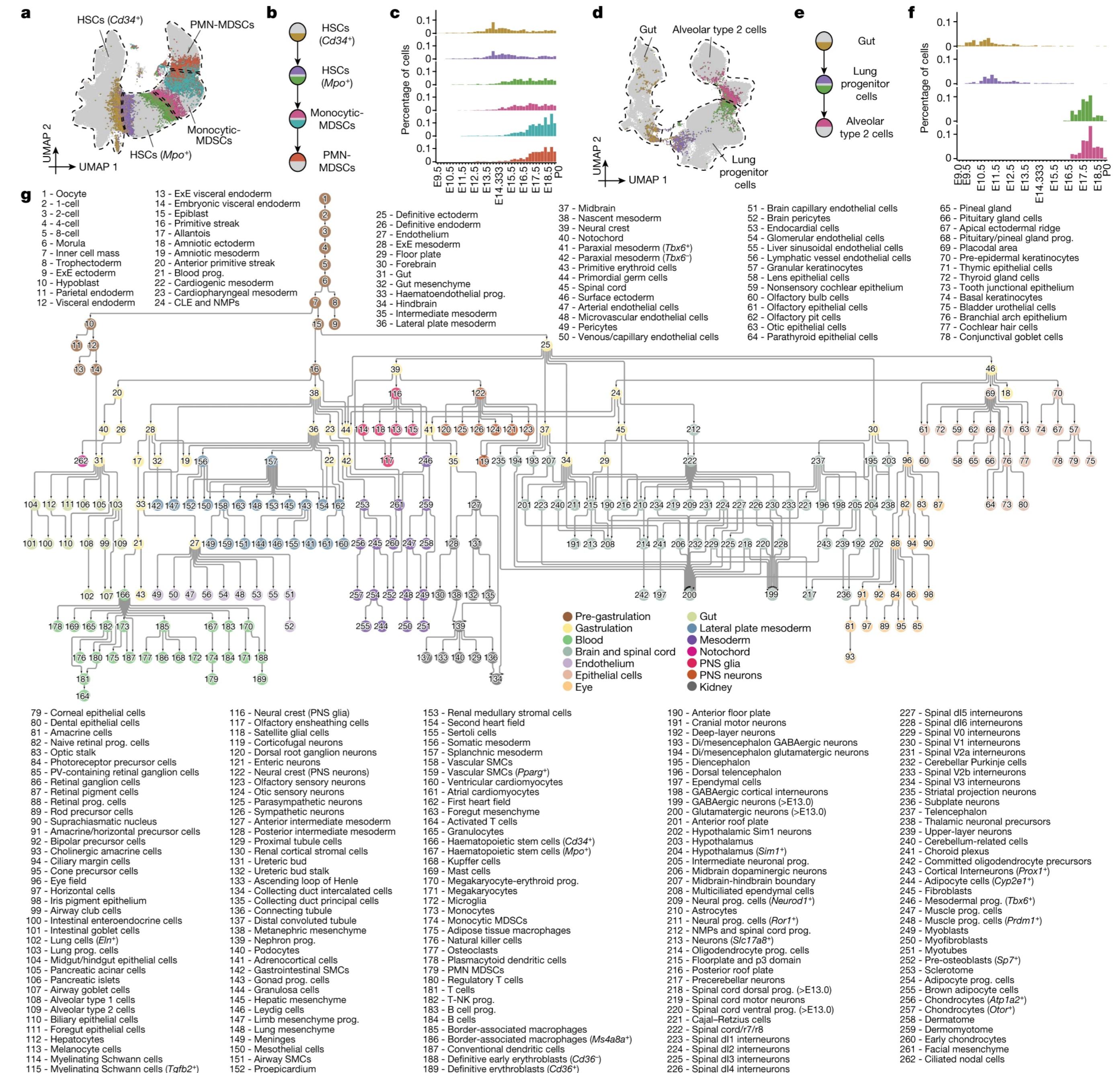
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An encyclopedia of enhancer-gene regulatory interactions in the human genome

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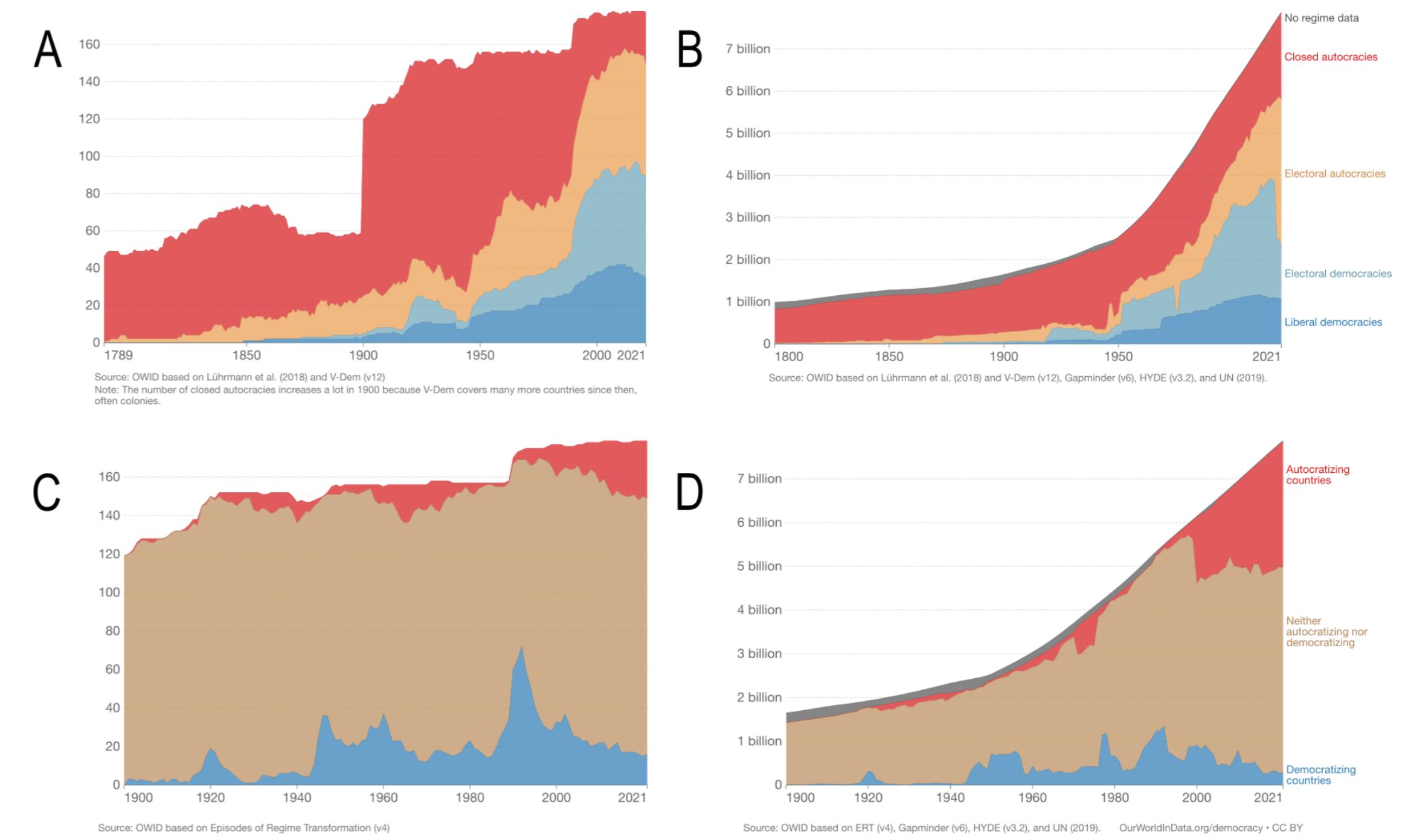
Hold out the genome: a roadmap to solving the *cis*-regulatory code

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Global democratic backsliding

Driven by **ethnic** and
religious conflict



A: Number of countries that are autocracies and democracies over time. **B:** Number of people living in autocracies and democracies over time. **C:** Number of autocratizing and democratizing countries over time. **D:** Number of people living in autocratizing and democratizing countries over time. Political regimes based on the criteria of the classification by Episodes of Regime Transformation (v4) and the assessment of V-Dem's experts. Note differences in the x-axes. Figures from Herre et al. (2013).

Gene regulatory networks

