Genomic solutions to sustainable development

Week 8 — Agrigenomics

8 April 2025

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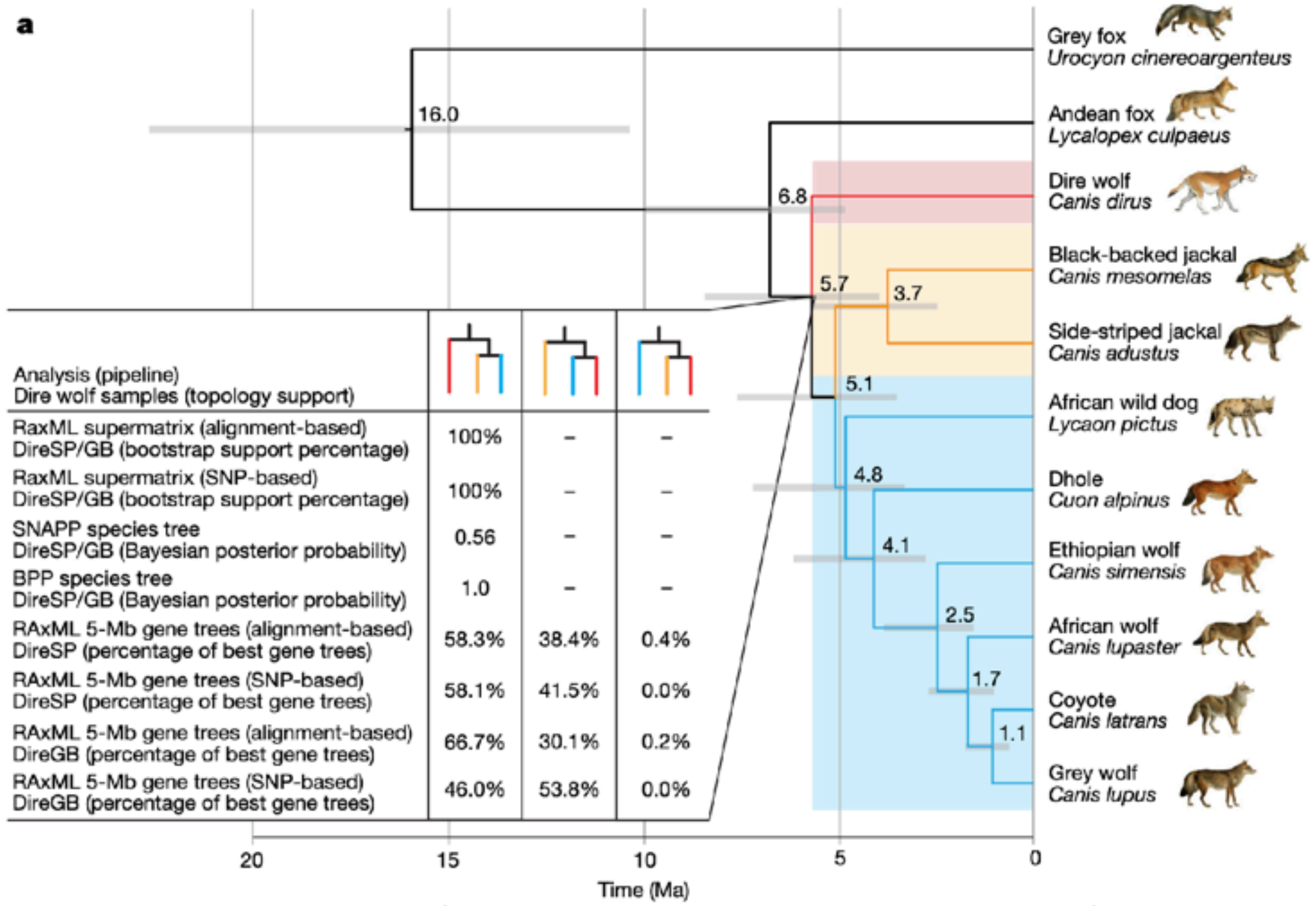
Add-on to ancient genomics lecture

Add-on to ancient genomics lecture

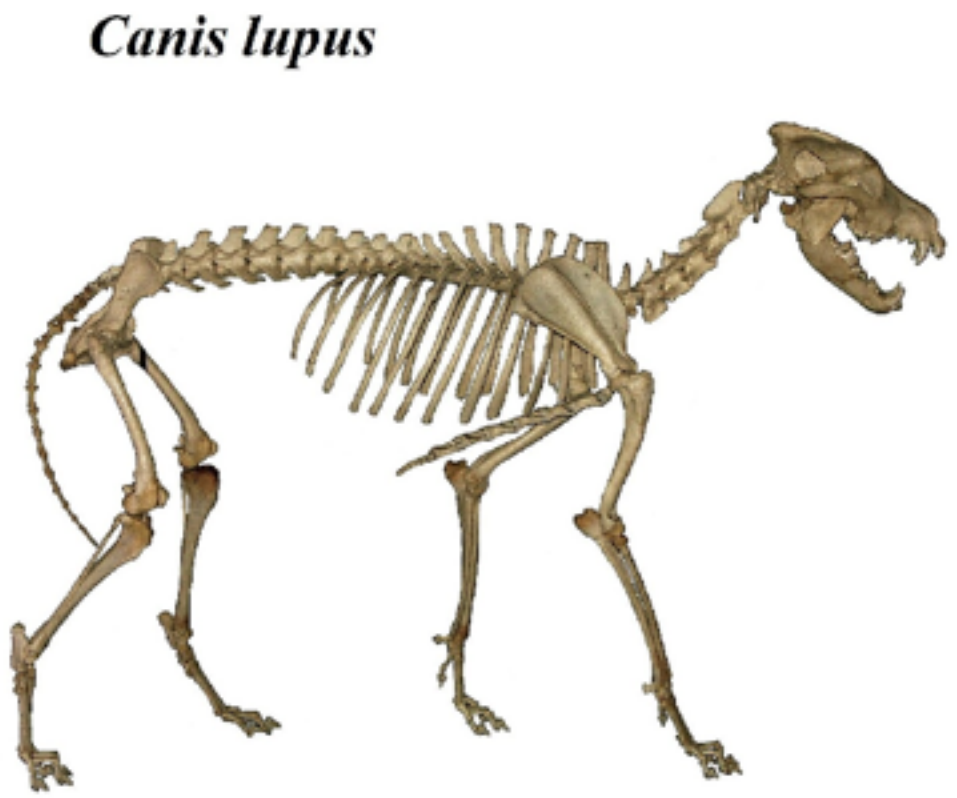
Dire wolf — an ancient species home to America



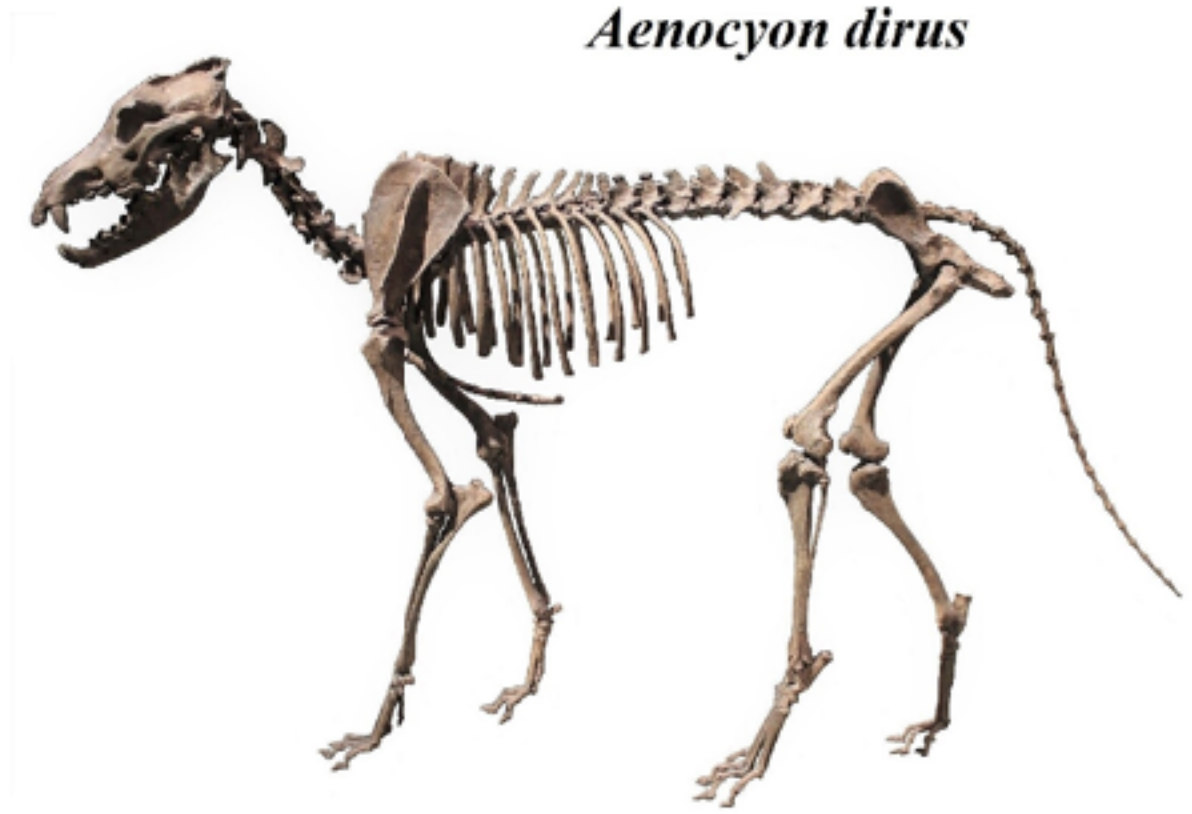
Analysis (pipeline) Dire wolf samples (topology support)			
RaxML supermatrix (alignment-based) DireSP/GB (bootstrap support percentage)	100%	–	–
RaxML supermatrix (SNP-based) DireSP/GB (bootstrap support percentage)	100%	–	–
SNAPP species tree DireSP/GB (Bayesian posterior probability)	0.56	–	–
BPP species tree DireSP/GB (Bayesian posterior probability)	1.0	–	–
RAxML 5-Mb gene trees (alignment-based) DireSP (percentage of best gene trees)	58.3%	38.4%	0.4%
RAxML 5-Mb gene trees (SNP-based) DireSP (percentage of best gene trees)	58.1%	41.5%	0.0%
RAxML 5-Mb gene trees (alignment-based) DireGB (percentage of best gene trees)	66.7%	30.1%	0.2%
RAxML 5-Mb gene trees (SNP-based) DireGB (percentage of best gene trees)	46.0%	53.8%	0.0%

Nature **591**, 87–91 (2021)

Grey wolf



Dire wolf



Wikipedia

Add-on to ancient genomics lecture

Dire wolf — an ancient and now *partially resurrected* species

Colossal Biosciences

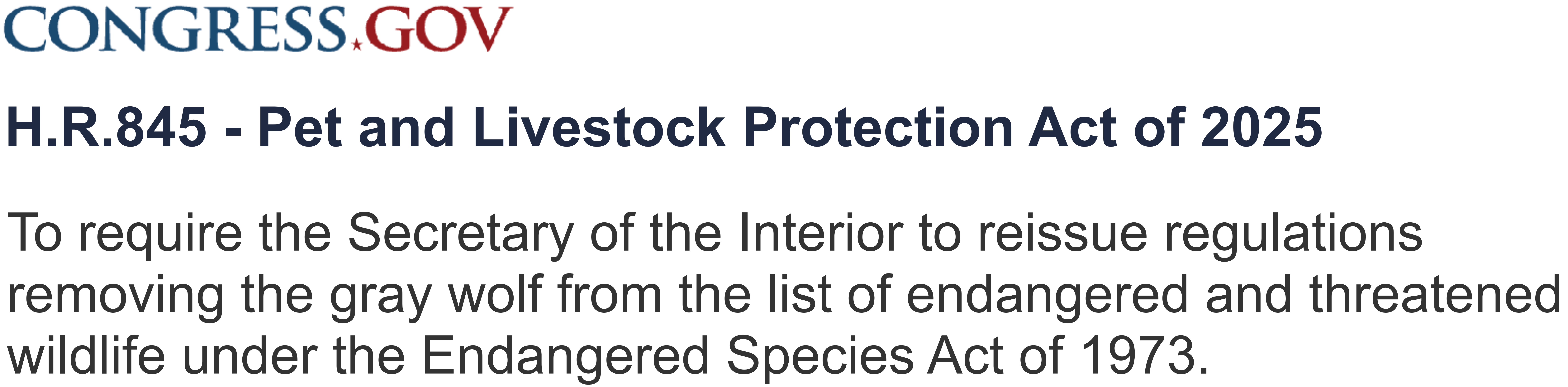
Colossal Biosciences

- Editing of 15 genes into grey wolf genomes and implantation of edited embryos into surrogate mothers
- Three healthy wolves are born (2 males and 1 female) with distinct traits: 20% bigger, white and thick fur, busy tail, and mane-like growth of hair around neck

https://www.nytimes.com/2025/04/07/science/colossal-dire-wolf-deextinction.html

Add-on to ancient genomics lecture

Future human-driven *re-extinction* of Dire-like wolves?



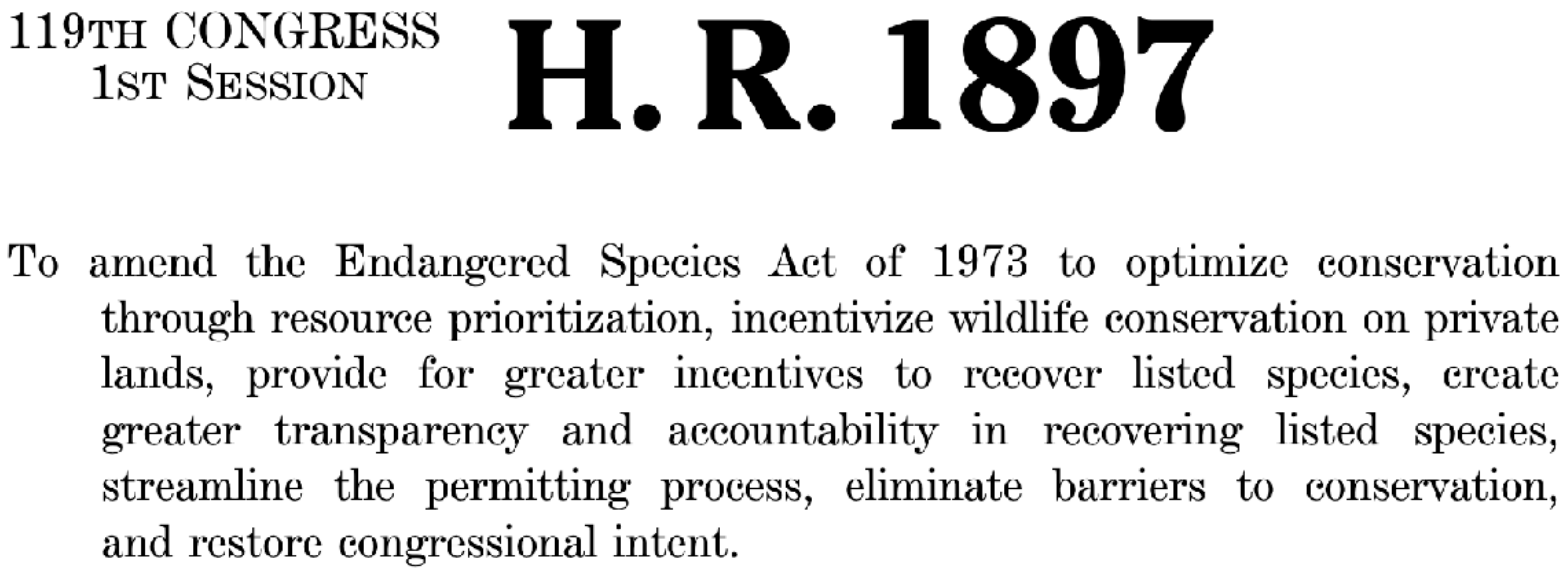
CONGRESS.GOV

H.R.845 - Pet and Livestock Protection Act of 2025

To require the Secretary of the Interior to reissue regulations removing the gray wolf from the list of endangered and threatened wildlife under the Endangered Species Act of 1973.

Add-on to ancient genomics lecture

Future human-driven *extinction* of endangered species?



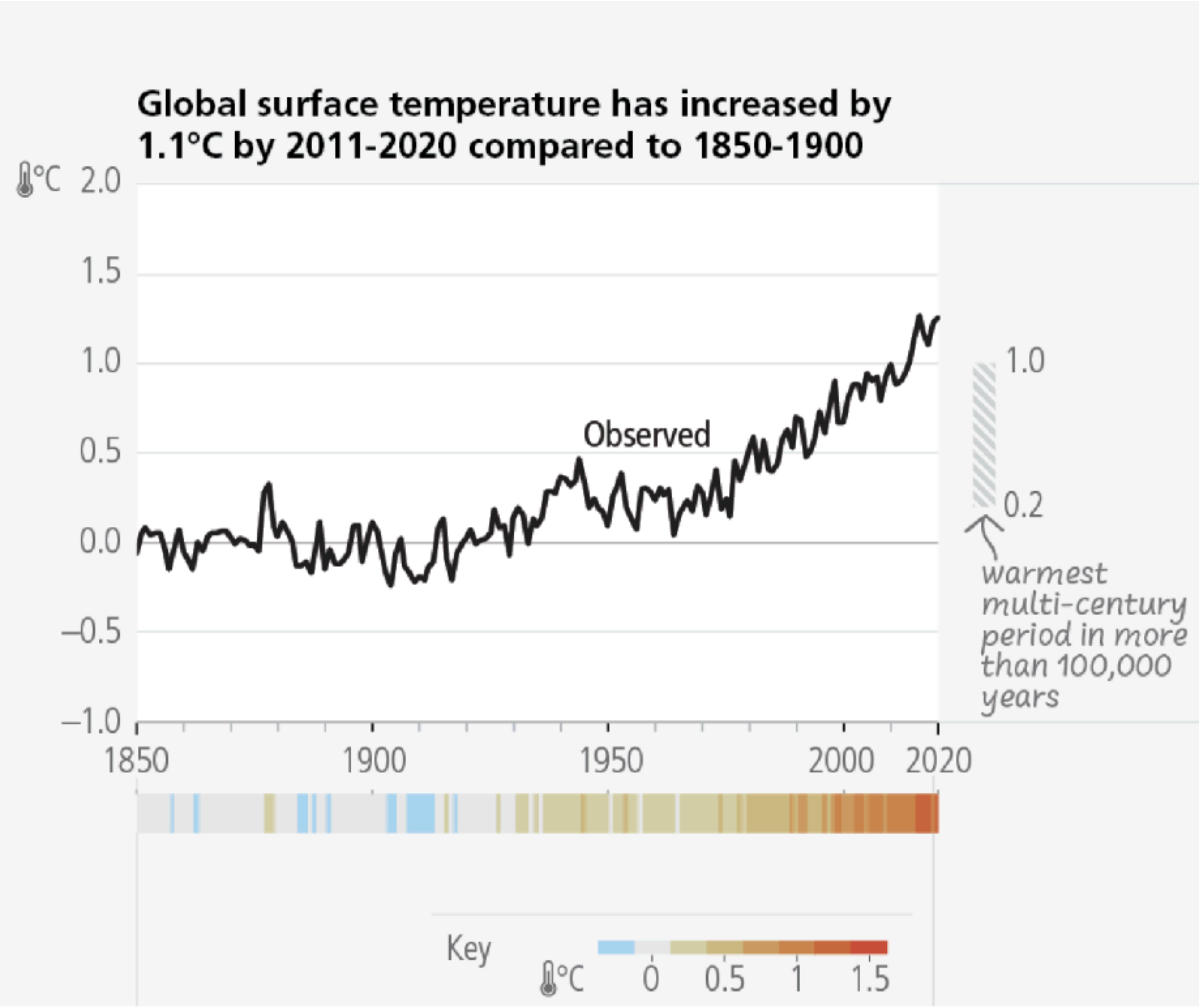
119TH CONGRESS
1ST SESSION

H. R. 1897

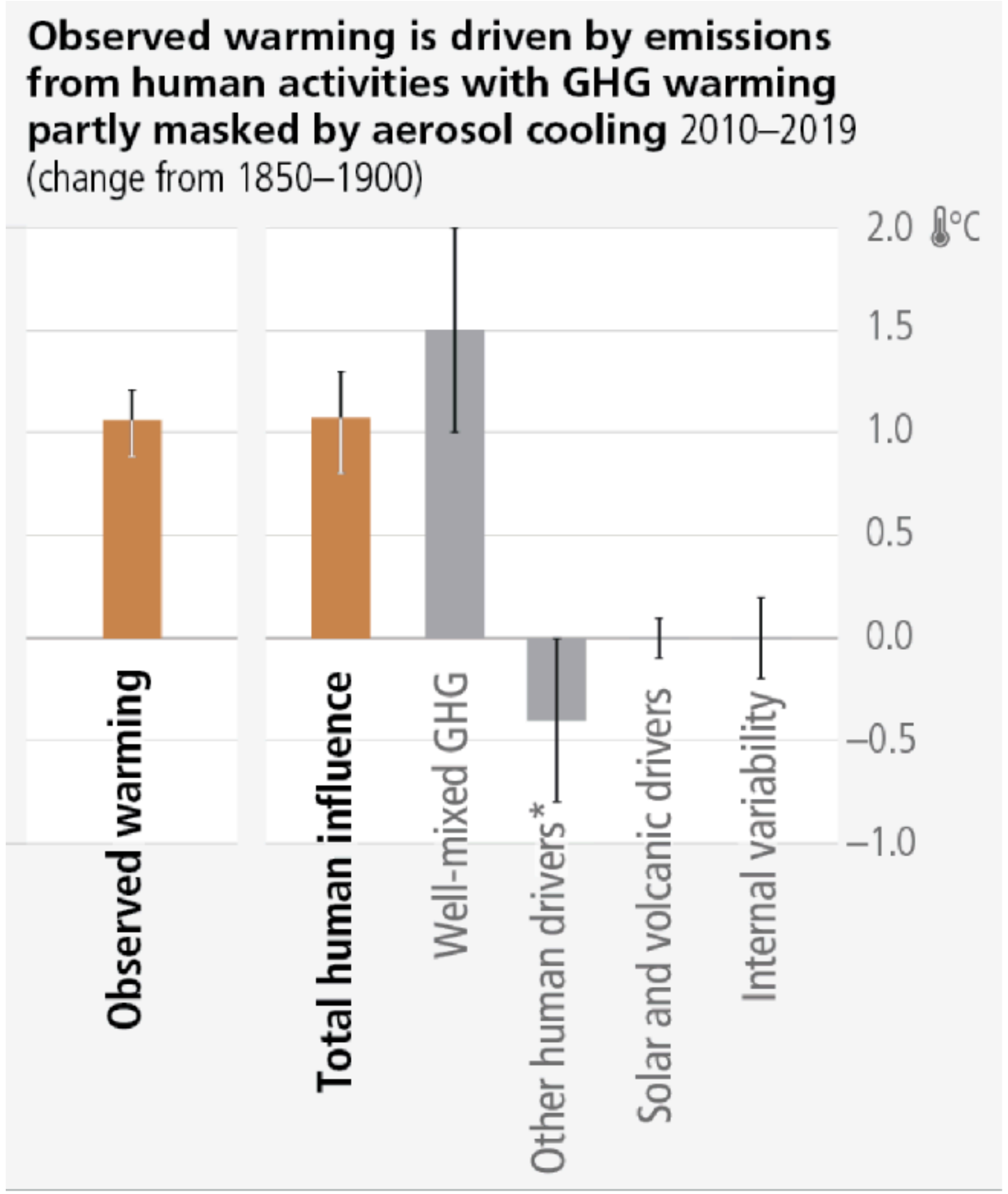
To amend the Endangered Species Act of 1973 to optimize conservation through resource prioritization, incentivize wildlife conservation on private lands, provide for greater incentives to recover listed species, create greater transparency and accountability in recovering listed species, streamline the permitting process, eliminate barriers to conservation, and restore congressional intent.

- Weakened safeguarding of habitats
- Less protection of endangered species
- Increase of private land control
- Limited scientific review

Global warming



Global surface temperature has increased by 1.1°C by 2011-2020 compared to 1850-1900



Observed warming is driven by emissions from human activities with GHG warming partly masked by aerosol cooling 2010–2019 (change from 1850–1900)

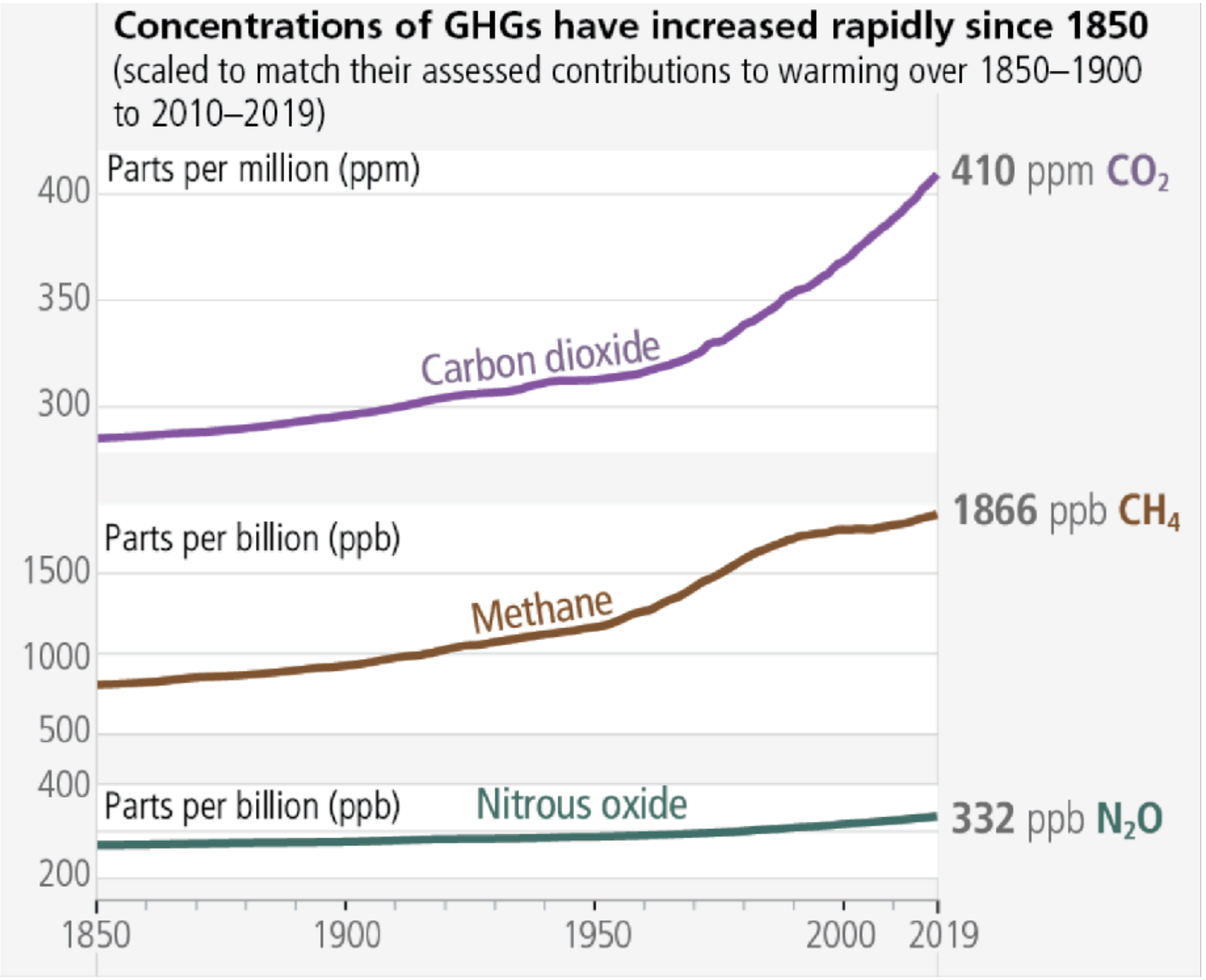
IPCC AR6 Synthesis Report

Greenhouse gases

Greenhouse gases (GHG):
Gaseous constituents of the atmosphere, both natural and anthropogenic, that absorb and emit radiation at specific wavelengths within the spectrum of radiation emitted by the Earth's surface, by the atmosphere itself, and by clouds. This property causes the greenhouse effect.

Water vapour (H2O), carbon dioxide (CO2), nitrous oxide (N2O), methane (CH4) and ozone (O3) are the primary GHGs in the Earth's atmosphere.

Human-made GHGs include sulphur hexafluoride (SF6), hydrofluorocarbons (HFCs), chlorofluorocarbons (CFCs) and perfluorocarbons (PFCs) and are found in refrigerators, air cons, insulating foams, aerosol sprays, fire protection systems, and electronics



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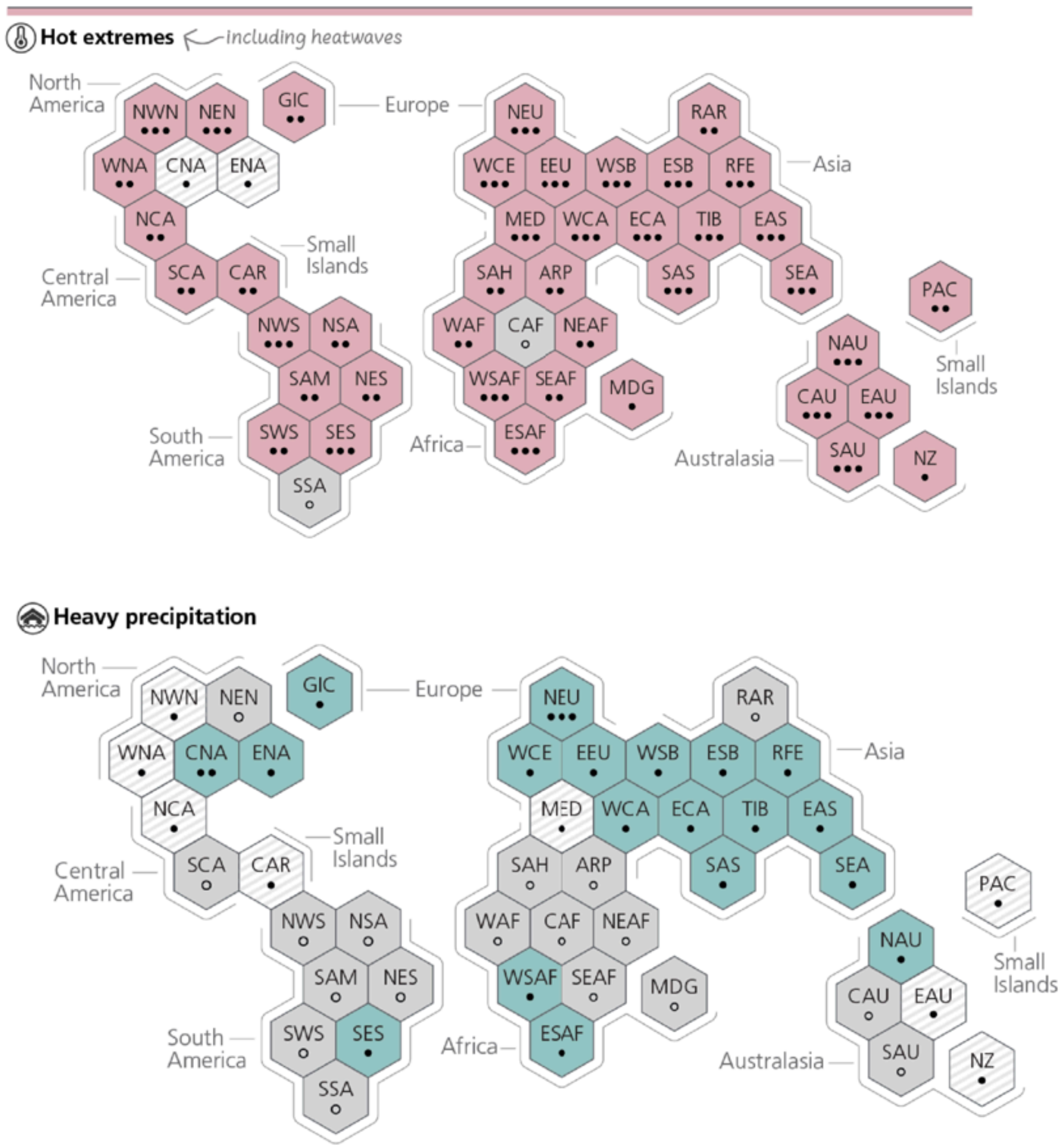
Global and local effects of climate change



Each hexagon corresponds to a region

NWN North-Western North America

IPCC AR6 WGI reference regions:
North America: NWN (North-Western North America, **NEN** (North-Eastern North America), **WNA** (Western North America), **CNA** (Central North America), **ENA** (Eastern North America), **Central America: NCA** (Northern Central America), **SCA** (Southern Central America), **CAR** (Caribbean), **South America: NWS** (North-Western South America), **NSA** (Northern South America), **NES** (North-Eastern South America), **SAM** (South American Monsoon), **SWS** (South-Western South America), **SES** (South-Eastern South America), **SSA** (Southern South America), **Europe: GIC** (Greenland/Iceland), **NEU** (Northern Europe), **WCE** (Western and Central Europe), **EEU** (Eastern Europe), **MED** (Mediterranean), **Africa: MED** (Mediterranean), **SAH** (Sahara), **WAF** (Western Africa), **CAF** (Central Africa), **NEAF** (North Eastern Africa), **SEAF** (South Eastern Africa), **WSAF** (West Southern Africa), **ESAF** (East Southern Africa), **MDG** (Madagascar), **Asia: RAR** (Russian Arctic), **WSB** (West Siberia), **ESB** (East Siberia), **RFE** (Russian Far East), **WCA** (West Central Asia), **ECA** (East Central Asia), **TIB** (Tibetan Plateau), **EAS** (East Asia), **ARP** (Arabian Peninsula), **SAS** (South Asia), **SEA** (South East Asia), **Australasia: NAU** (Northern Australia), **CAU** (Central Australia), **EAU** (Eastern Australia), **SAU** (Southern Australia), **NZ** (New Zealand), **Small Islands: CAR** (Caribbean), **PAC** (Pacific Small Islands)

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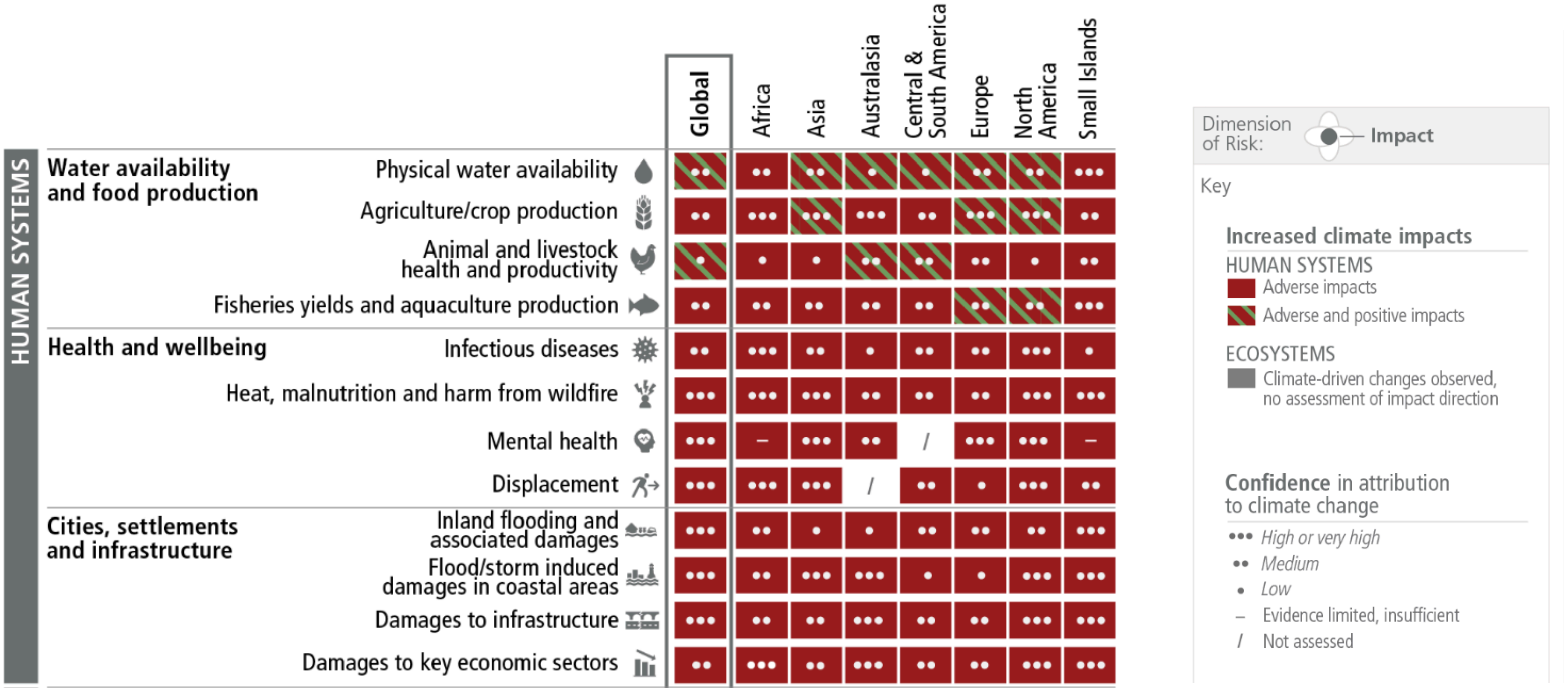
Climate change and food security



HUMAN SYSTEMS		Global	Africa	Asia	Australasia	Central & South America	Europe	North America	Small Islands
Water availability and food production	Physical water availability	▨ ••	🟥 ••	▨ ••	▨ •	▨ •	▨ ••	▨ ••	🟥 •••
	Agriculture/crop production	🟥 ••	🟥 •••	▨ •••	🟥 •••	🟥 ••	▨ •••	▨ •••	🟥 ••
	Animal and livestock health and productivity	▨ •	🟥 •	🟥 •	▨ ••	▨ ••	🟥 ••	🟥 •	🟥 ••
	Fisheries yields and aquaculture production	🟥 ••	🟥 ••	🟥 ••	🟥 ••	🟥 ••	▨ ••	▨ ••	🟥 •••
Health and wellbeing	Infectious diseases	🟥 ••	🟥 •••	🟥 ••	🟥 •	🟥 ••	🟥 ••	🟥 •••	🟥 •
	Heat, malnutrition and harm from wildfire	🟥 •••	🟥 •••	🟥 •••	🟥 ••	🟥 ••	🟥 ••	🟥 •••	🟥 •••
	Mental health	🟥 •••	🟥 –	🟥 •••	🟥 ••	/	🟥 •••	🟥 •••	🟥 –
	Displacement	🟥 •••	🟥 •••	🟥 •••	/	🟥 ••	🟥 •	🟥 •••	🟥 ••
Cities, settlements and infrastructure	Inland flooding and associated damages	🟥 •••	🟥 ••	🟥 •	🟥 •	🟥 ••	🟥 ••	🟥 ••	🟥 •••
	Flood/storm induced damages in coastal areas	🟥 •••	🟥 ••	🟥 •••	🟥 •••	🟥 •	🟥 •	🟥 •••	🟥 •••
	Damages to infrastructure	🟥 •••	🟥 ••	🟥 ••	🟥 •••	🟥 ••	🟥 ••	🟥 •••	🟥 •••
	Damages to key economic sectors	🟥 ••	🟥 •••	🟥 ••	🟥 •••	🟥 ••	🟥 ••	🟥 •••	🟥 •••

Dimension of Risk: Impact

Key

Increased climate impacts

HUMAN SYSTEMS
- 🟥 Adverse impacts
- ▨ Adverse and positive impacts

ECOSYSTEMS
- ■ Climate-driven changes observed, no assessment of impact direction

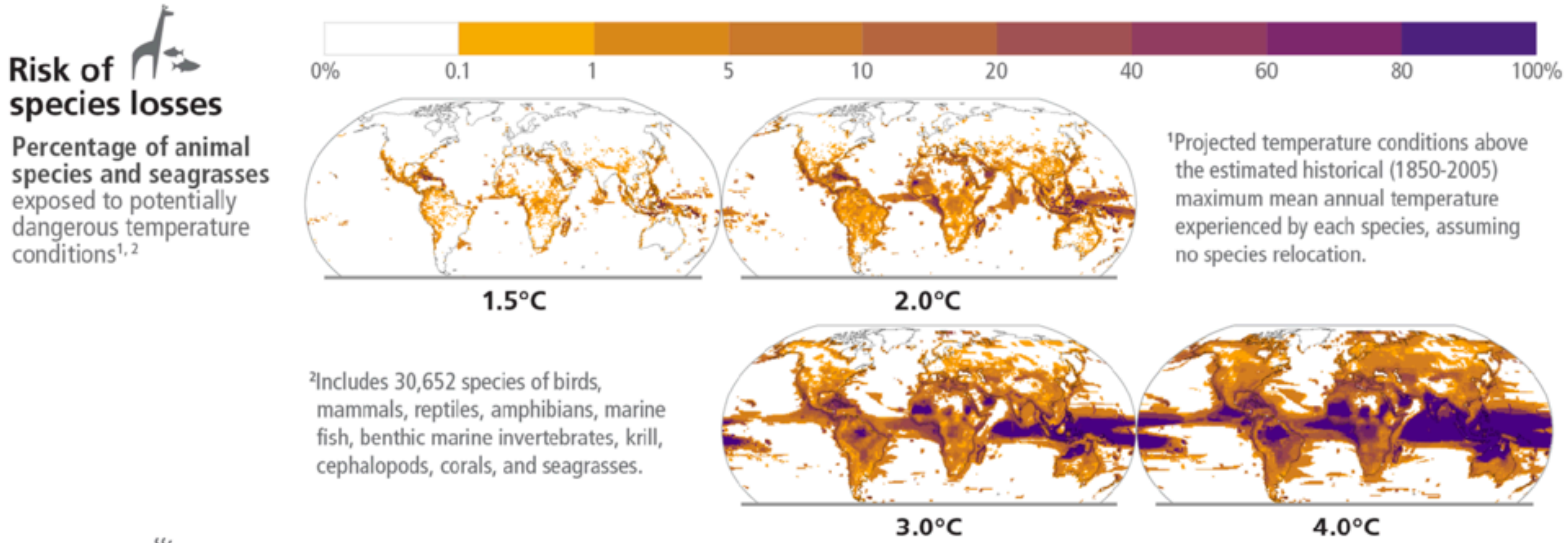
Confidence in attribution to climate change
- ••• *High or very high*
- •• *Medium*
- • *Low*
- – Evidence limited, insufficient
- / Not assessed

“Overall agricultural productivity has increased, climate change has slowed this growth in agricultural productivity over the past 50 years globally (medium confidence), with related negative crop yield impacts mainly recorded in mid- and low latitude regions, and some positive impacts in some high latitude regions (high confidence).”

IPCC AR6 Synthesis Report

Future impact of climate change on natural systems

at different global warming levels relative to 1850-1900 levels



Risks of species losses as indicated by the percentage of assessed species exposed to potentially dangerous temperature conditions

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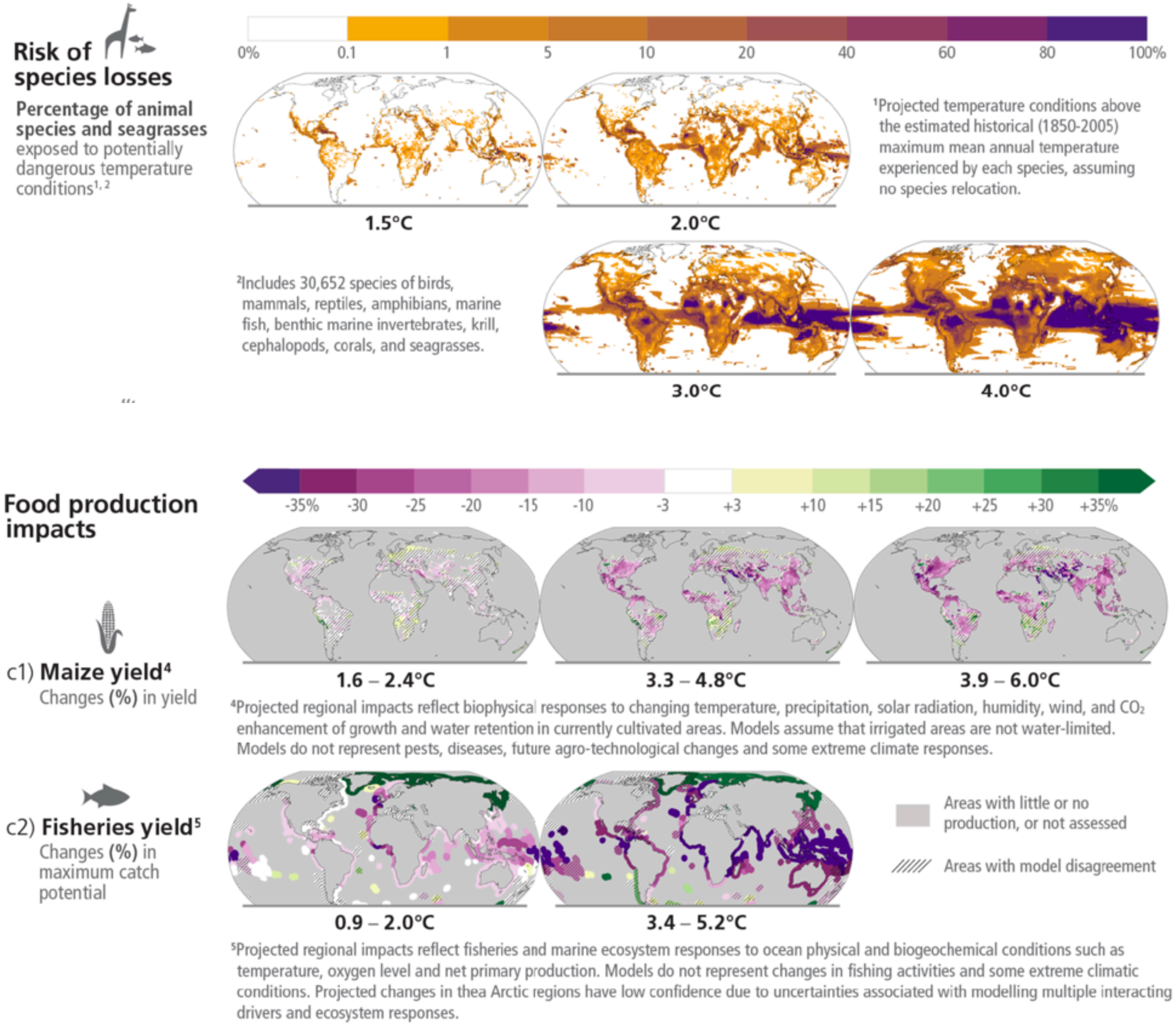
Future impact of climate change on natural systems

at different global warming levels relative to 1850-1900 levels



[1] Projected temperature conditions above the estimated historical (1850-2005) maximum mean annual temperature experienced by each species, assuming no species relocation.

[2] Includes 30,652 species of birds, mammals, reptiles, amphibians, marine fish, benthic marine invertebrates, krill, cephalopods, corals, and seagrasses.

[4] Projected regional impacts reflect biophysical responses to changing temperature, precipitation, solar radiation, humidity, wind, and CO_2 enhancement of growth and water retention in currently cultivated areas. Models assume that irrigated areas are not water-limited. Models do not represent pests, diseases, future agro-technological changes and some extreme climate responses.

[5] Projected regional impacts reflect fisheries and marine ecosystem responses to ocean physical and biogeochemical conditions such as temperature, oxygen level and net primary production. Models do not represent changes in fishing activities and some extreme climatic conditions. Projected changes in thea Arctic regions have low confidence due to uncertainties associated with modelling multiple interacting drivers and ecosystem responses.

Risks of species losses as indicated by the percentage of assessed species exposed to potentially dangerous temperature conditions

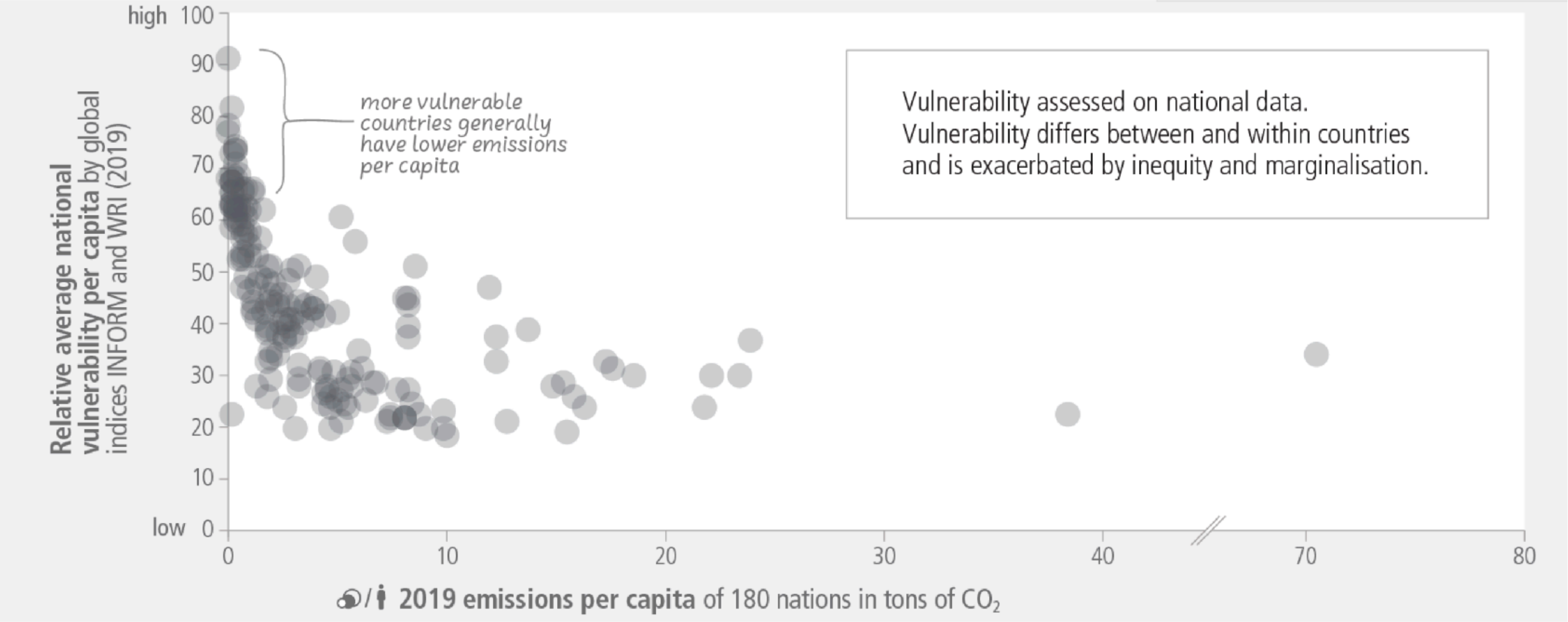
Changes in maize yield by 2080–2099 relative to 1986–2005 at projected global warming levels

Change in maximum fisheries catch potential by 2081–2099 relative to 1986–2005 at projected global warming levels

IPCC AR6 Synthesis Report

EPFL

Countries that have least contributed to climate change are more vulnerable



IPCC AR6 Synthesis Report

Methane (CH4), a powerful greenhouse gas

- **Short lifespan in the atmosphere:** 7-12 years for CH4 *vs* centuries to thousands of years for CO2

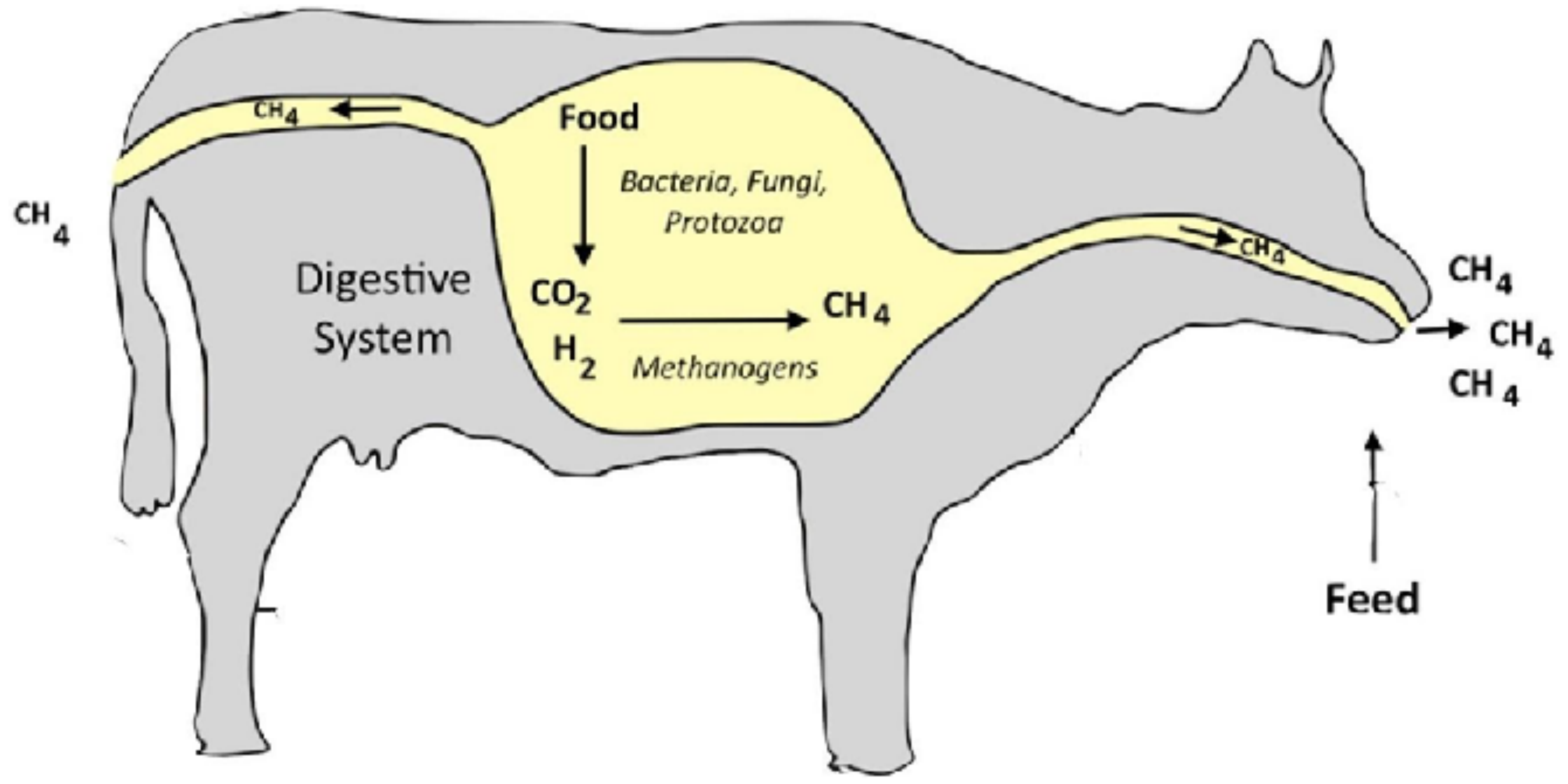
- **Methane is more potent to trap heat:** the global warming potential (GWP) — a measure how much heat a greenhouse gas traps in the atmosphere over a specific period relative to CO2 — of 1 kg of methane is 80-fold higher compared to 1 kg of CO2 over 20 years (IPCC 2021).

- **Methane** is responsible for 20-30% of the current global warming effect

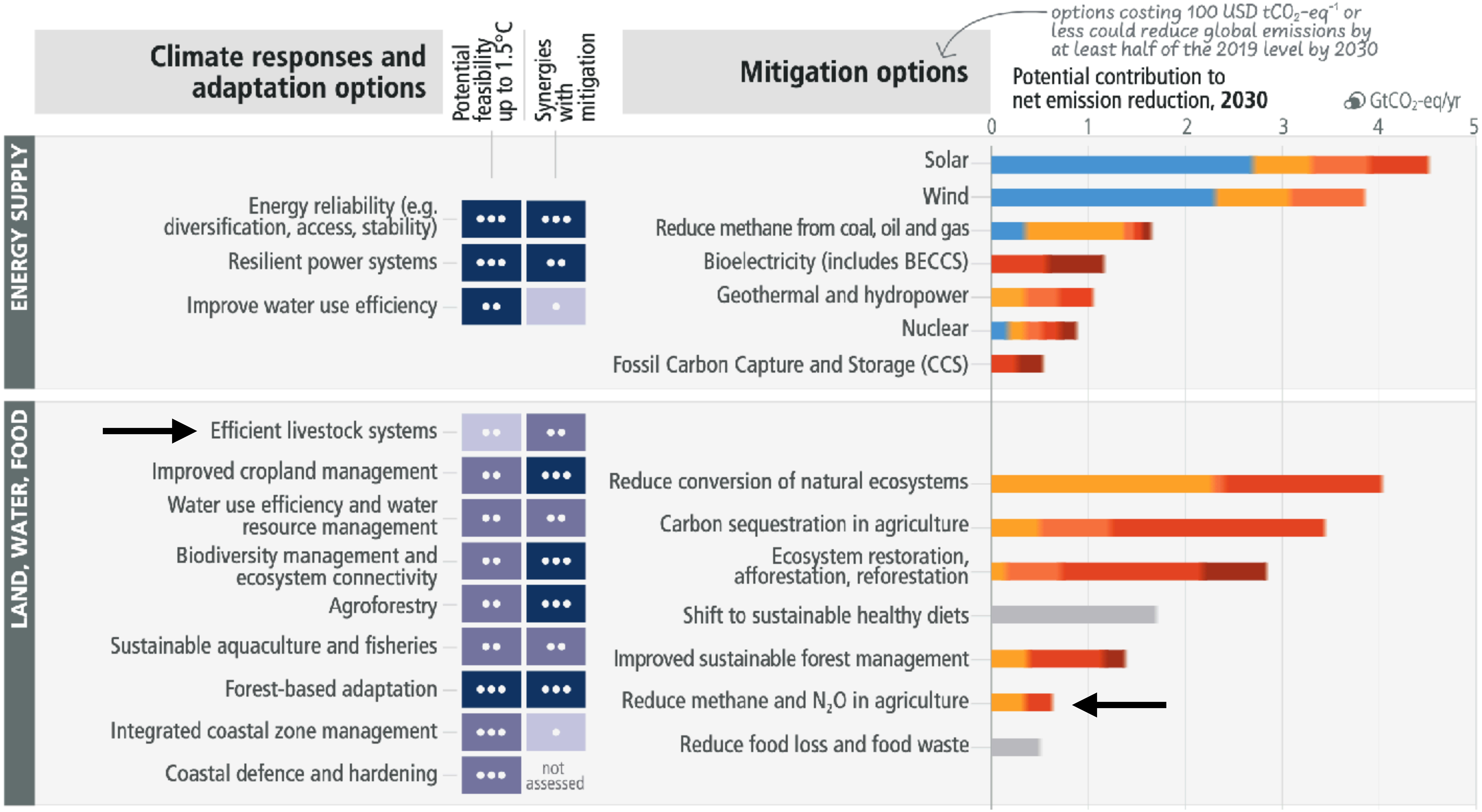
- **Cutting methane emissions** by 45% by 2030 could enable reaching climate goals

Cows and global warming

- **Cows in numbers:** 1.5B cows on earth with largest numbers in India (300M), Brazil (200M), China (100M), US (40M)
- **Methane emissions:** cows produce methane during digestion (enteric fermentation)
- **Enteric fermentation:** plant-based sugars are broken down by bacterial digestion, anaerobic archea (methanogens) produce methane as a byproduct of their metabolism, and cows burp methane.
- **Manure management**: decomposing cow dung emits methane
- **Land use:** raising cattle requires large areas of land, which leads to loss of forests (reduced carbon absorption)
- **Feed production:** feed for cattle (eg, corn, soy) uses fossil fuels and fertilizers, which release greenhouse gases during production/transport.
- **In Switzerland:** 80% of methane emissions due to livestock (1M cows)
- **Global greenhouse gas emissions due to livestock:** 10-20%
- **Reduction in livestock?** Likely not a viable option due to dietary (milk, meat, cheese), cultural, economic, and political reasons



Climate responses and adaptation options for the near future



Strategies to reduce methane emissions from cows

- **Chemical or biological food additives**
  - **Red seaweed (*Asparagopsis*)** can encapsulate methane analogous within specialized glands as a natural defense mechanism.
  - ***A. Taxiformis, a* red algae home to tropical waters,** can reduce at a algae biomass of 2-5% methane emissions by 99% *in vitro*
  - ***A. taxiformis*** as a diet supplement (0.2-0.5%) reduces methane emissions by 70-90% in cattle
  - **Bromoform** is the organic compound in seaweed that inhibits methanogenesis
  - **Potential toxicity of bromoform** for humans, cows, and the environment (detected in milk and urine) and classified as a potential carcinogen

Strategies to reduce methane emissions from cows

Bioengineering: cow bag pack to capture methane

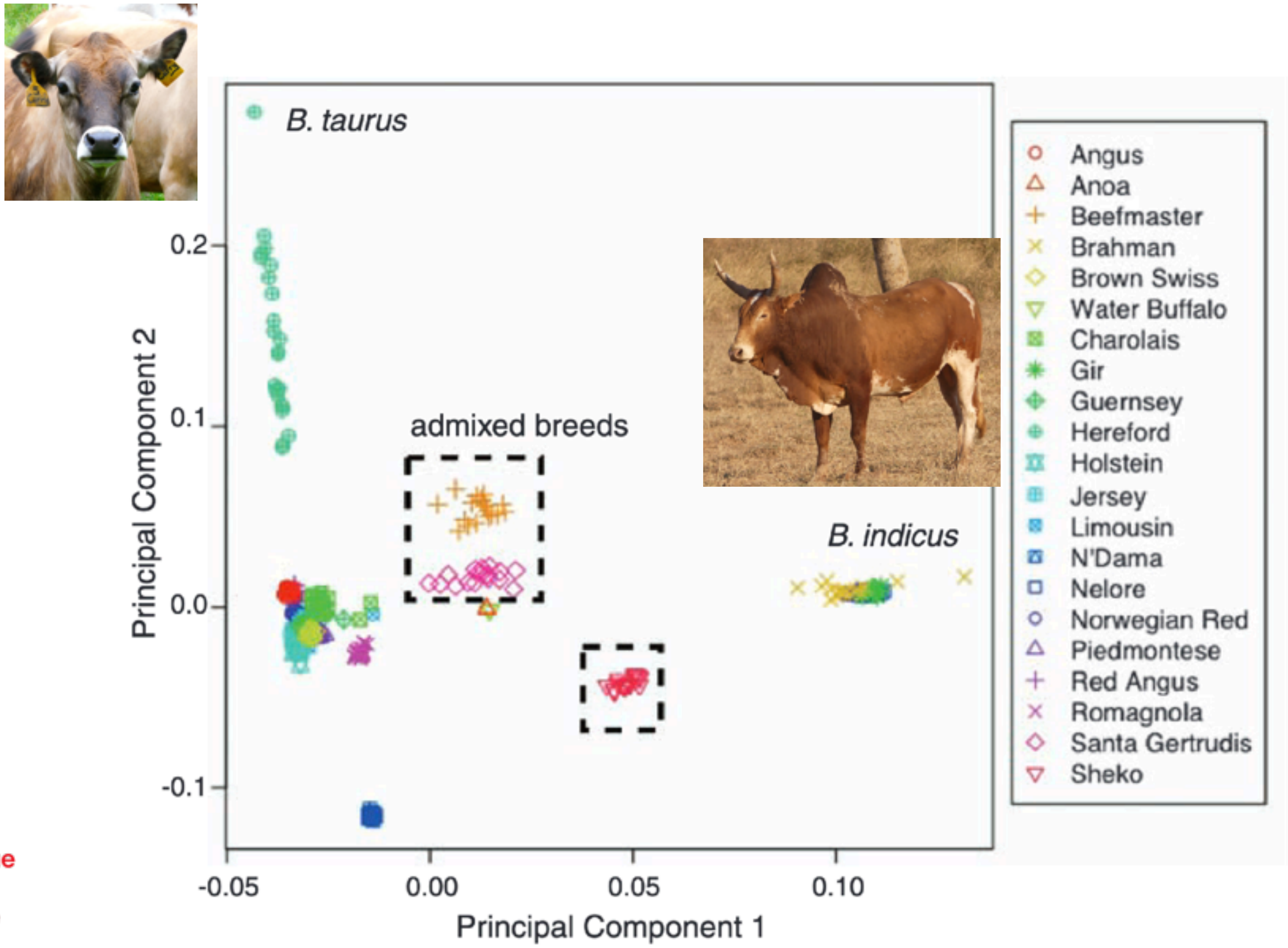
Argentina's National Institute for Agricultural Technology

Strategies to reduce methane emissions from cows

- **New diets:** potential of quick adaptation of rumen microbiota to new food source
- **Breeding and genetic engineering:** potentially more effective and a sustainable long-term strategy
    - Use genetic approaches to study methane emissions within and between bovine populations and map key methane-associated loci for breeding programs
    - Direct genetic selection of methane-low-emission cows should not affect cow’s health and economic performance
    - Essential to understand methane emission in lactating animals (during and between lactation cycles)

The bovine genome

- Domestication of cattle occurred about 8,000-10,000 years ago and now over 800 cattle breeds are established
- Bovine genome and genetic variation between cattle helps to understand complex traits (milk, meat, leather)
- Enhanced selective breeding and change characteristics

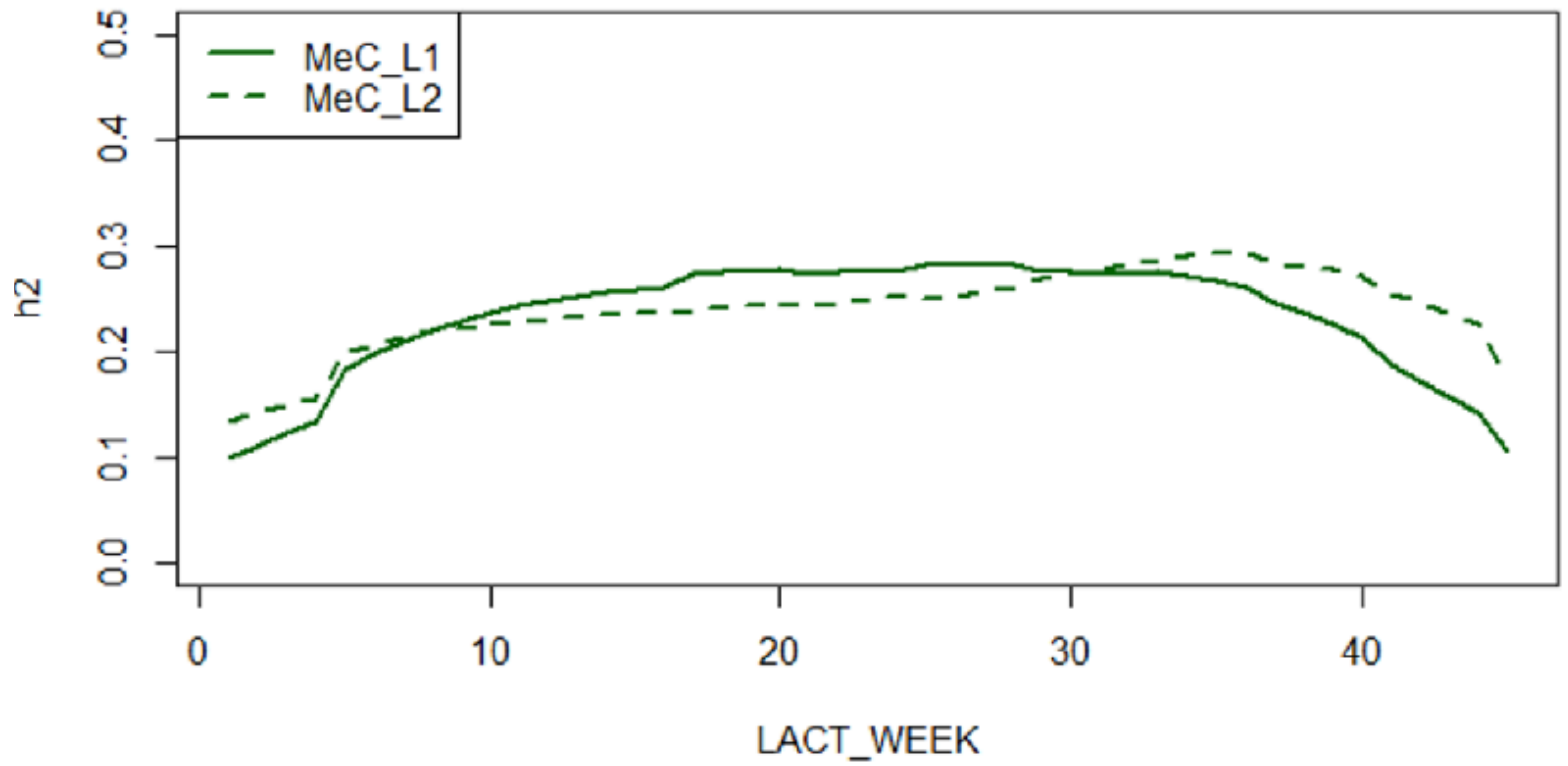


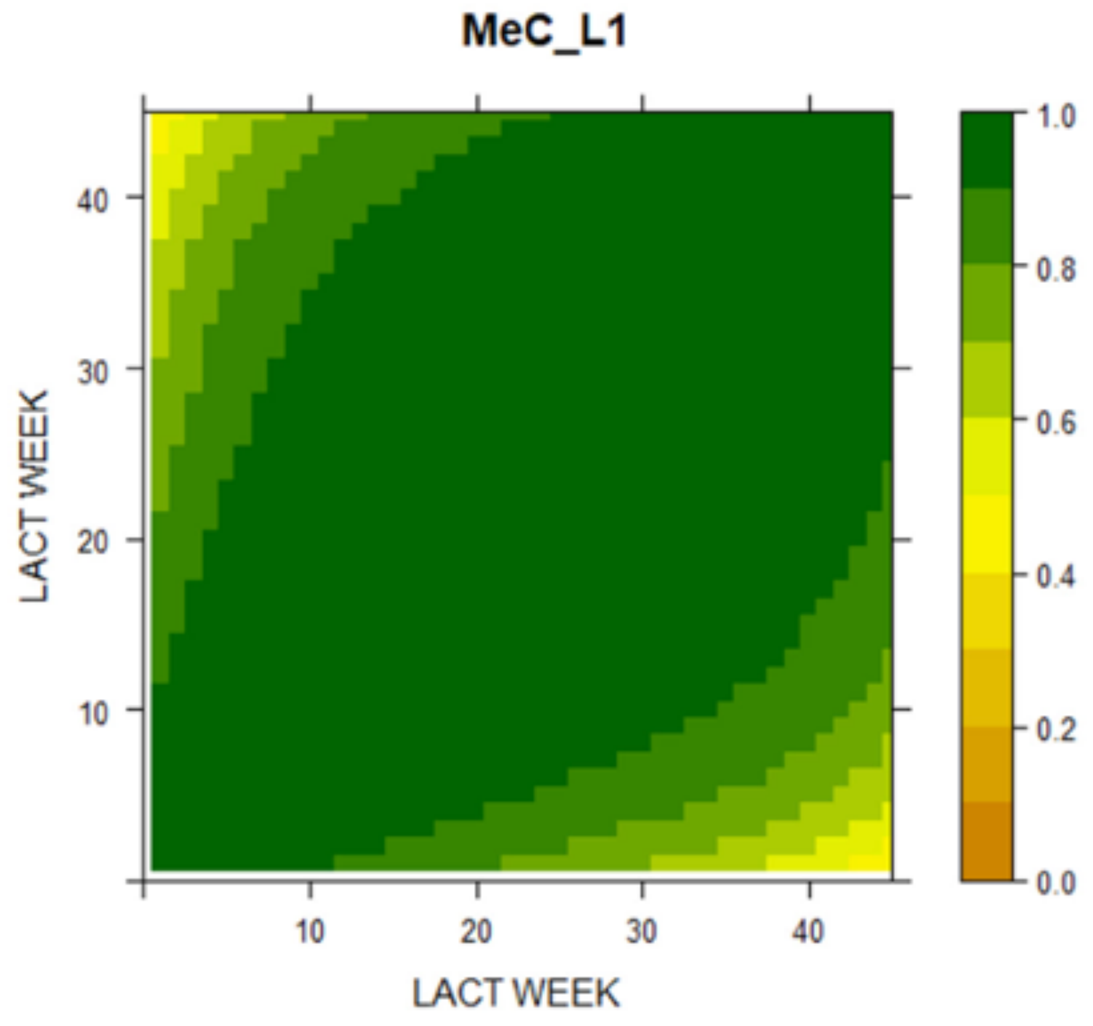
Genetics of methane emissions

- **Genetic heritability:** methane emissions were measured in 575 Danish Holstein cows over an 8 year time period and revealed a genetic heritability of 14% to 25% at the beginning of lactation, 28% to 47% in the middle of lactation, and 11-29% at the end of lactation

- **Genetic correlations** between different lactation weeks are overall high

- **Methane emission**: a novel environmental breeding trait





Journal of Dairy Science Vol. 105 No. 12, 2022

Methane emissions *vs* milk production

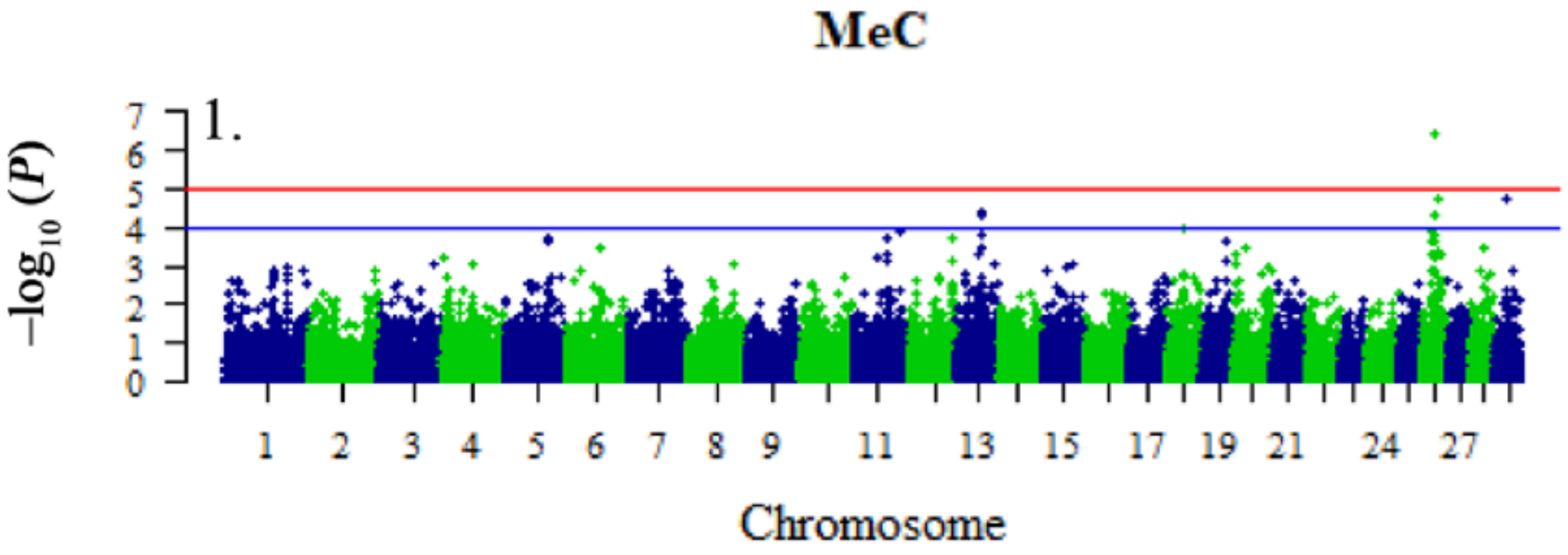
- Methane emission is genetically correlated with milk production (29%), feed intake (41%), and body weight (65%)

- Genetic selection strategies for reduced methane emission need to identify genetic loci that are independent of economically important traits (—> residual methane emission variants)

Journal of Dairy Science Vol. 104 No. 8, 2021

Genetic architecture of methane emission traits

- Discovery of genetic loci for targeted breeding programs, gene editing, and microbiome-driven breeding programs
- Genome-wide association studies for methane emission traits are currently underpowered and in an early stage to fully map the genetic architecture of methane emission (most studies based on 300 to 2,000 animals)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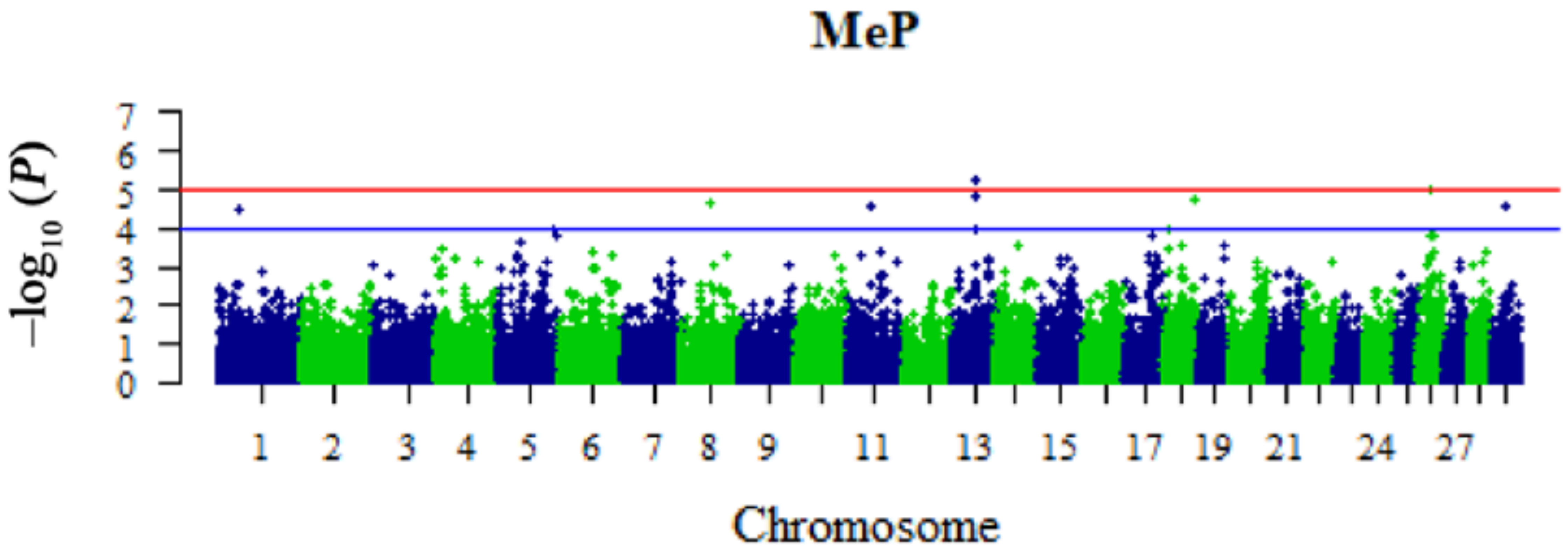
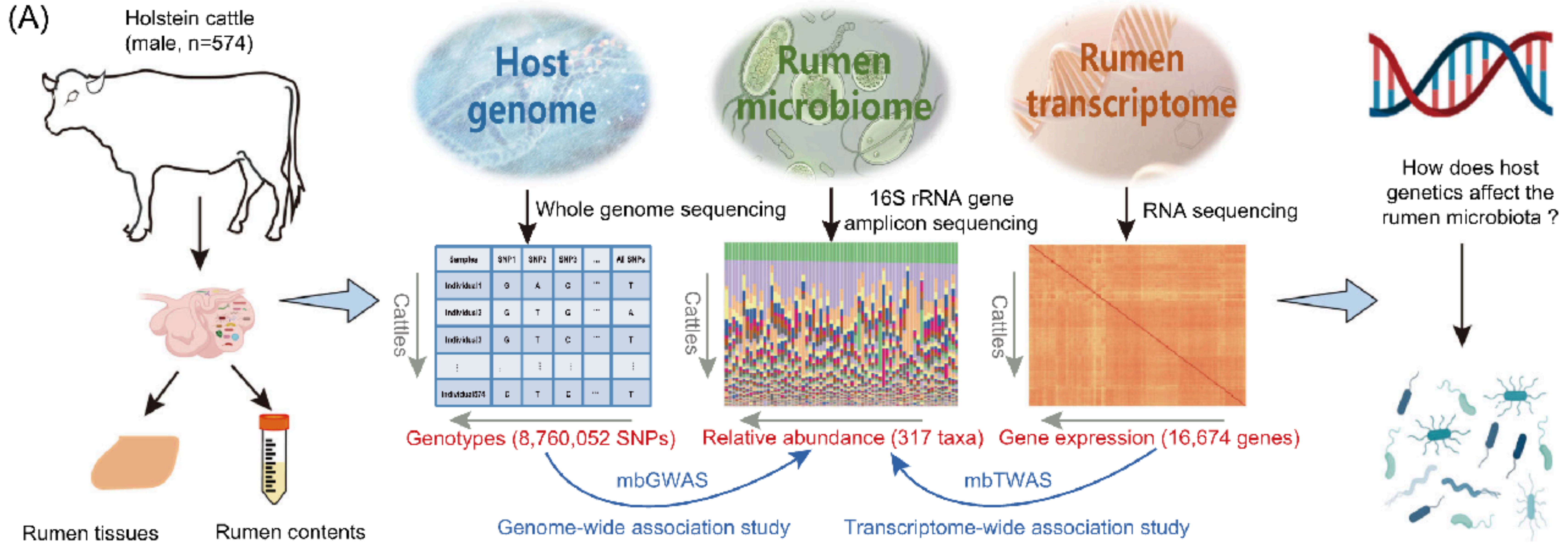
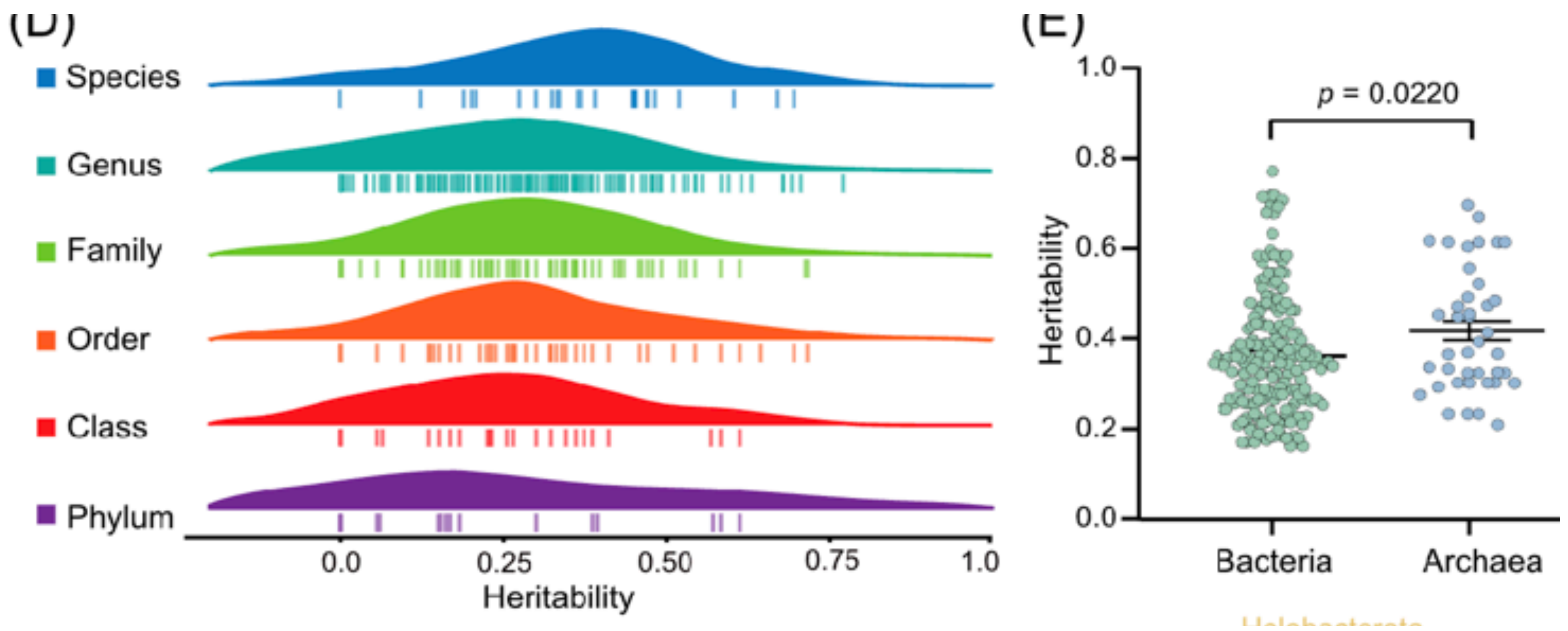

MeP

Journal of Dairy Science Vol. 104 No. 8, 2021

Impact of host genetics on the rumen microbiome

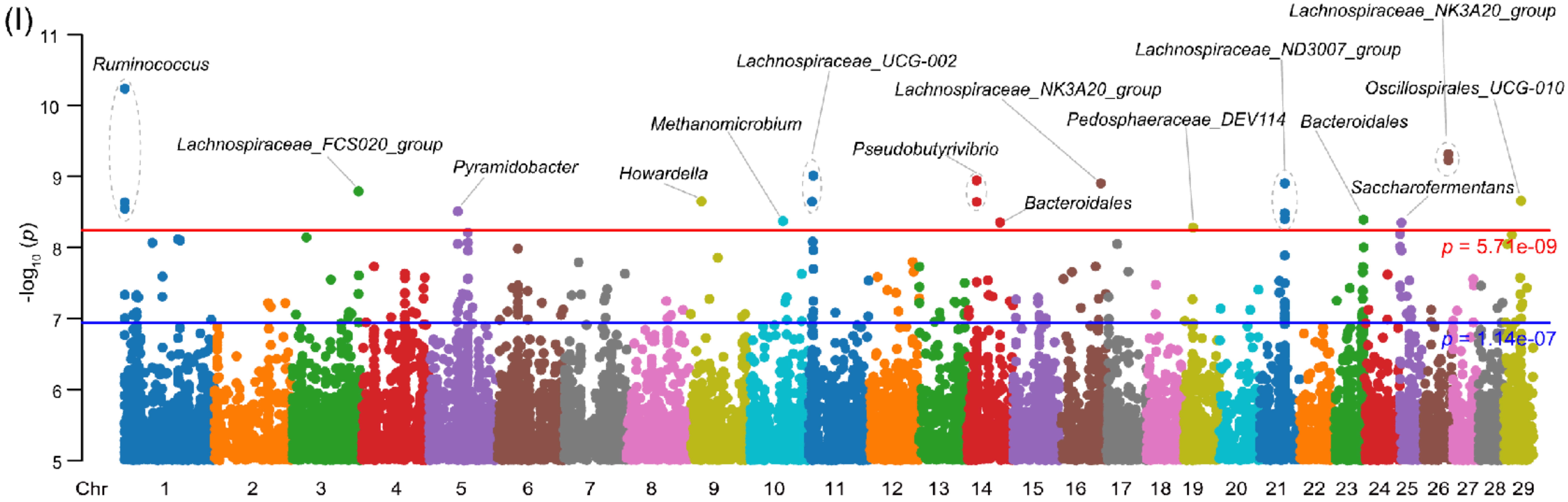




- 36% of rumen bacteria abundance explained by host genetics
- 41% of rumen archea abundance explained by host genetics

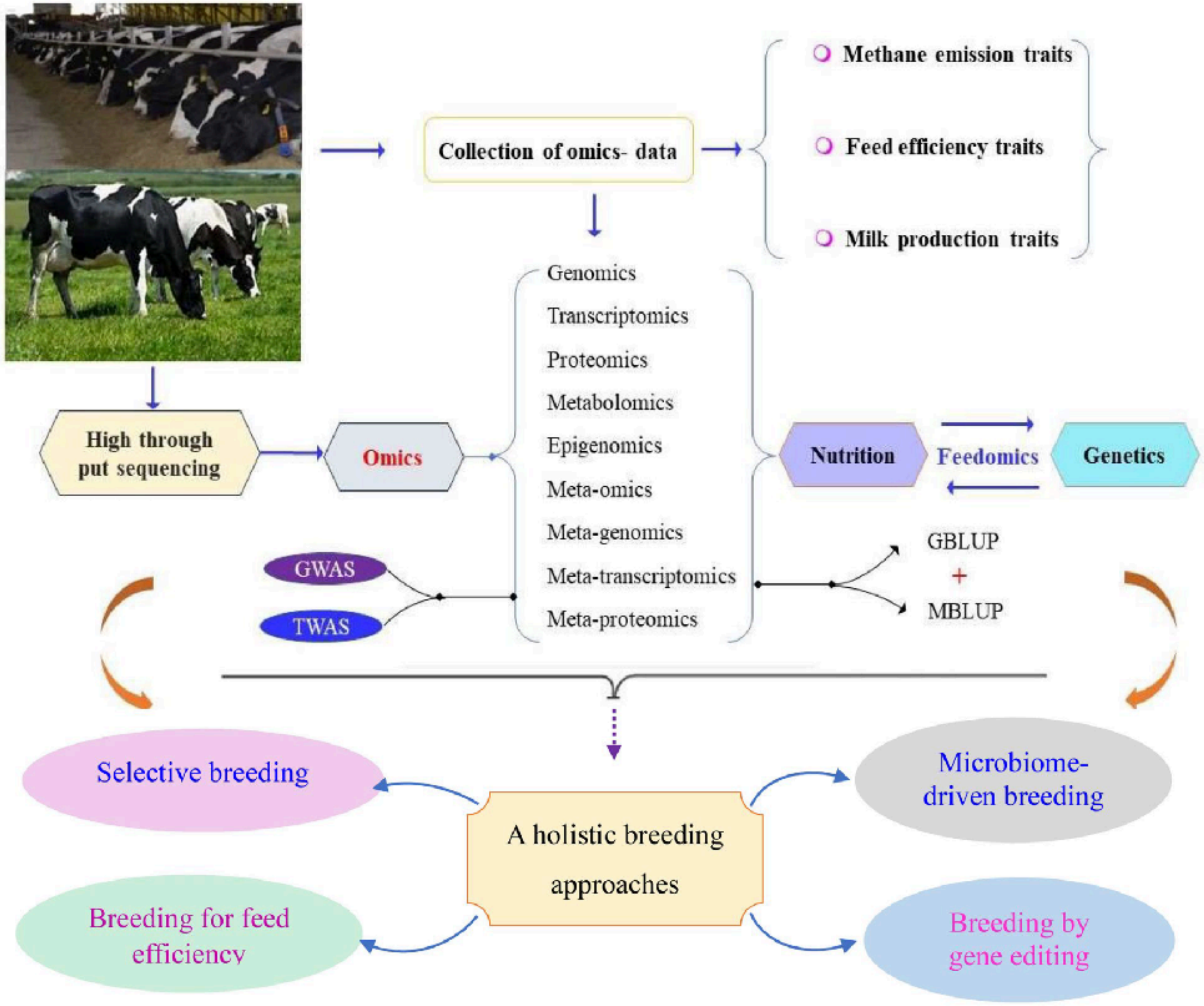
Imeta. 2024 Sep 3;3(5):e234.

Widespread association between host genetics and rumen microbiomes



Imeta. 2024 Sep 3;3(5):e234.

A holistic breeding approach



Animal Biotechnology 2024, Vol. 35, no. 1, 2362677

Cattle health, genomics, and sustainable farming

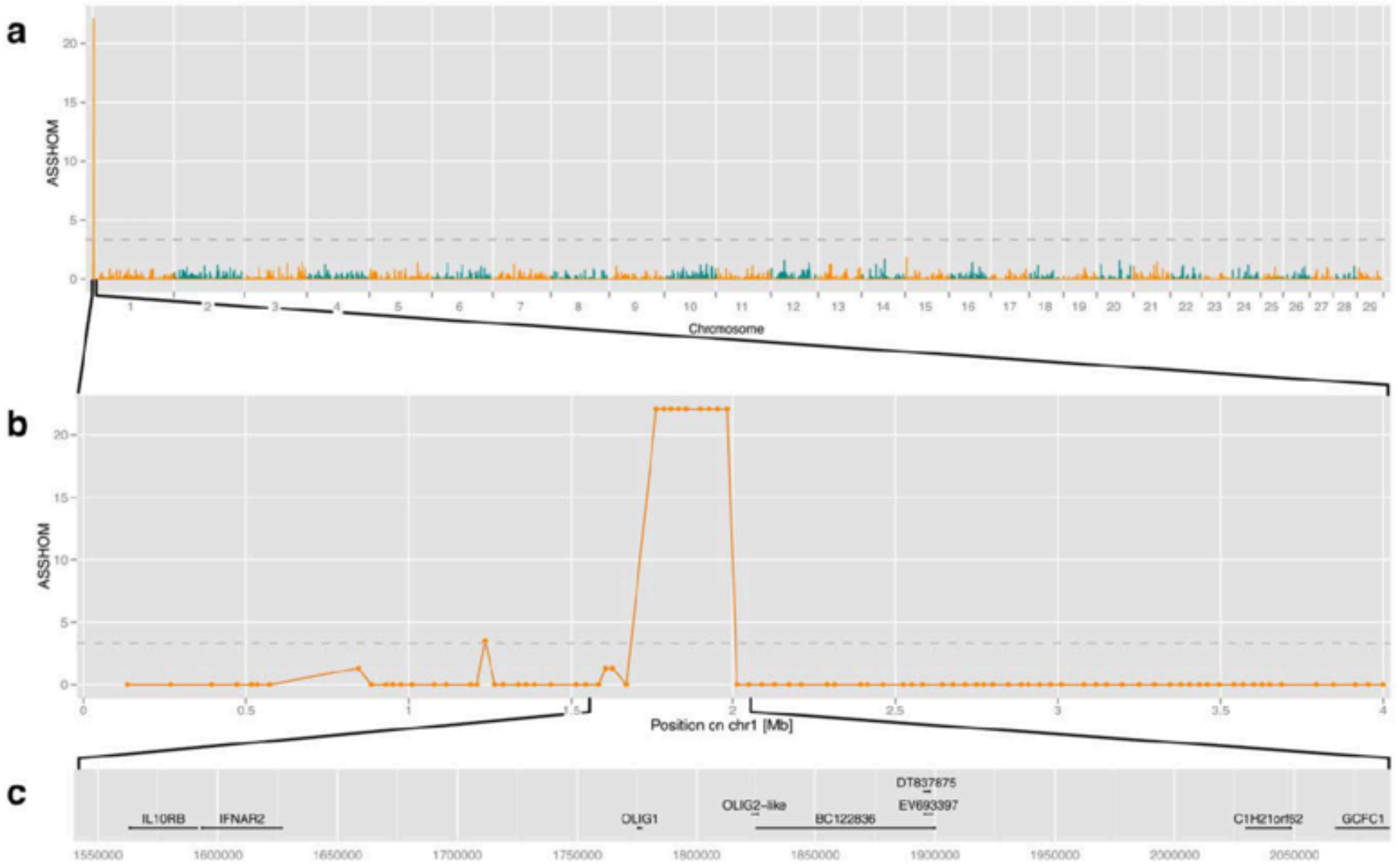
- **Disease resistance:** discovery of genetic markers and pathways linked to resistance against common diseases (eg, mastitis)
- **Heat & climate resilience:** new breeds that can cope with climate change
- **Selective breeding:** breeds animals with multiple traits
- **Traceability:** genomic data to support certification

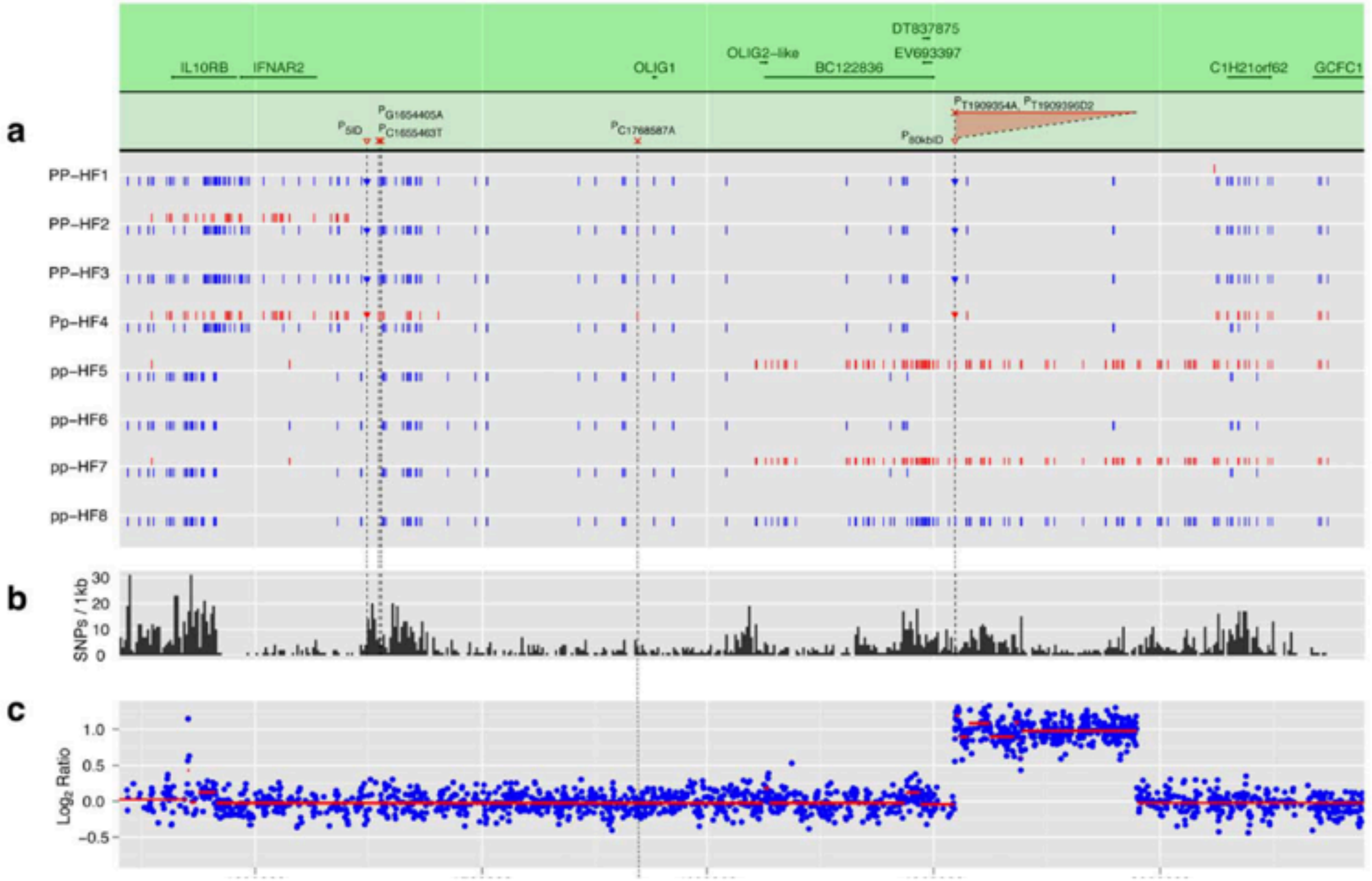
Livestock dehorning and disbudding

- Cattle are dehorned or disbudded for economic and safety reasons (eg, other cows)
- Dehorning should occur with local anesthesia and sedation, yet only 10% of dairy farmers follow guidelines
- In Switzerland, 75-90% of livestock are dehorned. In 2018, a referendum was held to provide subsidies to farmers that did not dehorn their livestock yet this was rejected

The *POLLED* locus

- Hornlessness (aka polled) is a dominant trait and common in beef breeds yet rare in dairy breeds
- Polled phenotype has been a target of selection since 1936 and the *POLLED* locus has been mapped in 1993
- In 2012, a GWAS of polled and horned cattle and genome sequencing revealed two independent non-coding structural variants at the *POLLED* locus (a 80 kb duplication and a 202 bp duplication)
- The target gene(s) of the non-coding causal *POLLED* mutations are still unknown (likely gene regulation)

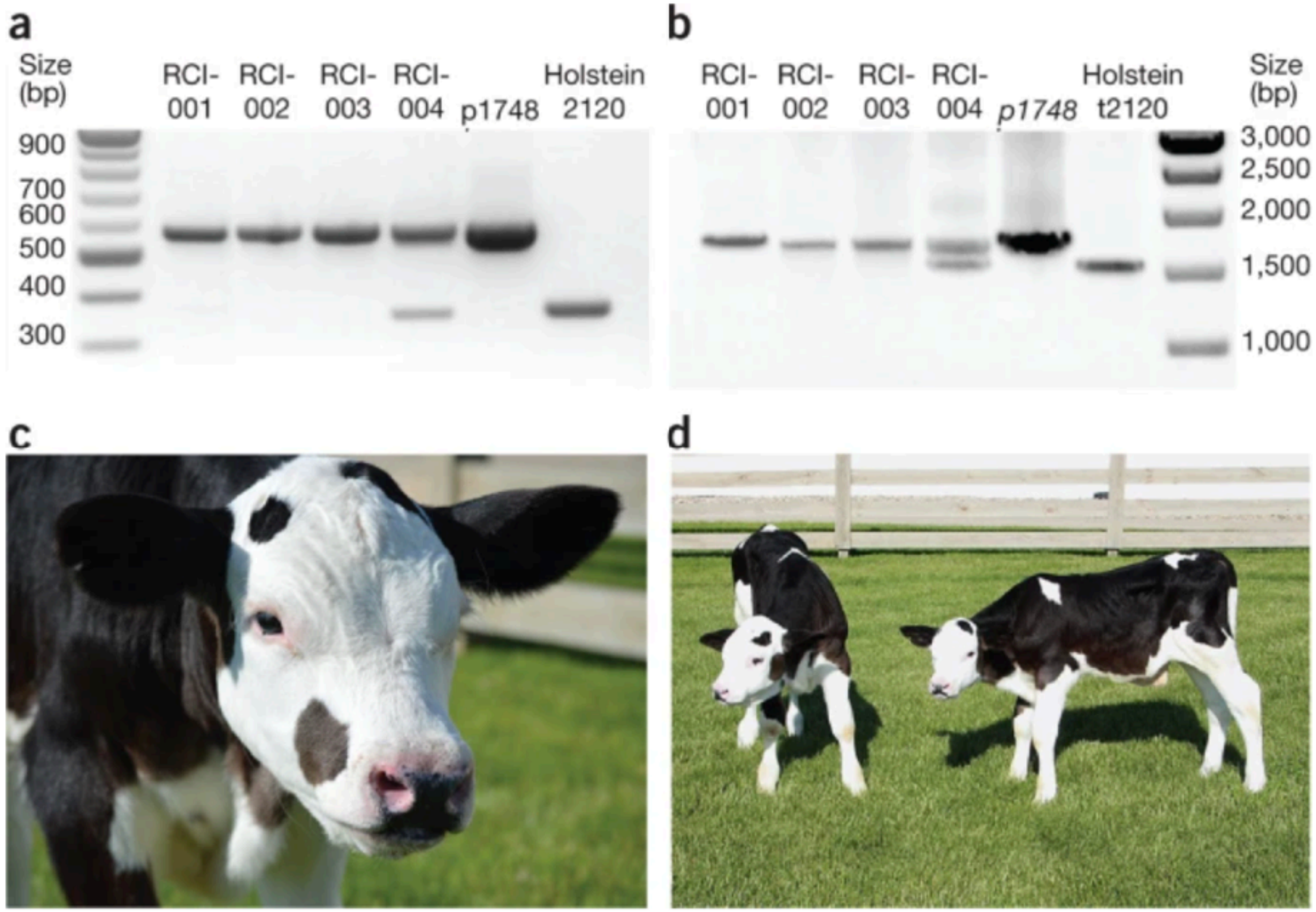




Medugorac I, Seichter D, Graf A, Russ I, Blum H, et al. Bovine Polledness – An Autosomal Dominant Trait with Allelic Heterogeneity. PLoS ONE (2012) 7(6):e39477.

Hornless dairy cattle from genome-edited cell lines

- Polled Holstein dairy cattle are not attractive for farmers due to lower milk production (a likely result of *POLLED* introgression from non-diary animals)
- The *POLLED* locus has a low frequency in US Holstein populations and over 20 years of classic breeding would be needed to replace 50% of animals
- Genome-editing of fibroblasts for the *POLLED* 202 bp duplication, somatic cell nuclear transfer (cloning), and full-term pregnancies produced hornless animals
- Genome-editing and cloning to introduce causal, beneficial alleles into any cattle breed

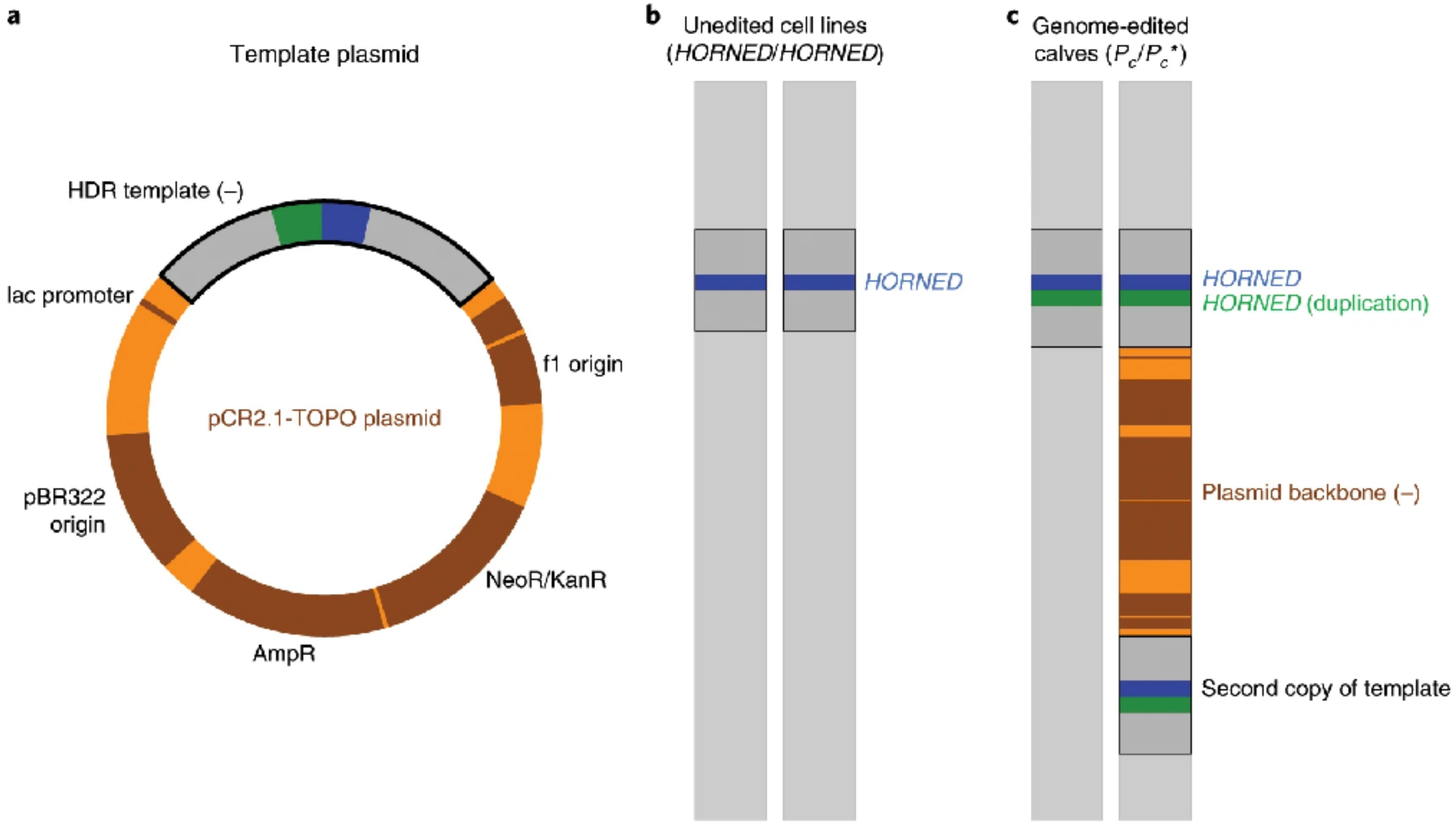


Buri and Spotigy

Carlson, D., Lancto, C., Zang, B. *et al.* Production of hornless dairy cattle from genome-edited cell lines. *Nat Biotechnol* **34**, 479–481 (2016).

Plasmid integration mistakenly introduced into the germline of genome-edited hornless cattle

- Recombinetics researchers reported no unexpected genome alterations as a result of the targeted genome-editing procedure and concluded “our animals are free of off-target events”
- Re-analysis of publicly available genomes of Buri and Spotigy by the US FDA revealed in both animals the full-length plasmid backbone pCR2.1-TOPO
- pCR2.1-TOPO plasmid contains neomycin/kanamycin and ampicillin resistance genes
- Genome-edited animals are a risk for horizontal gene transfer and spread of antibiotic resistance genes



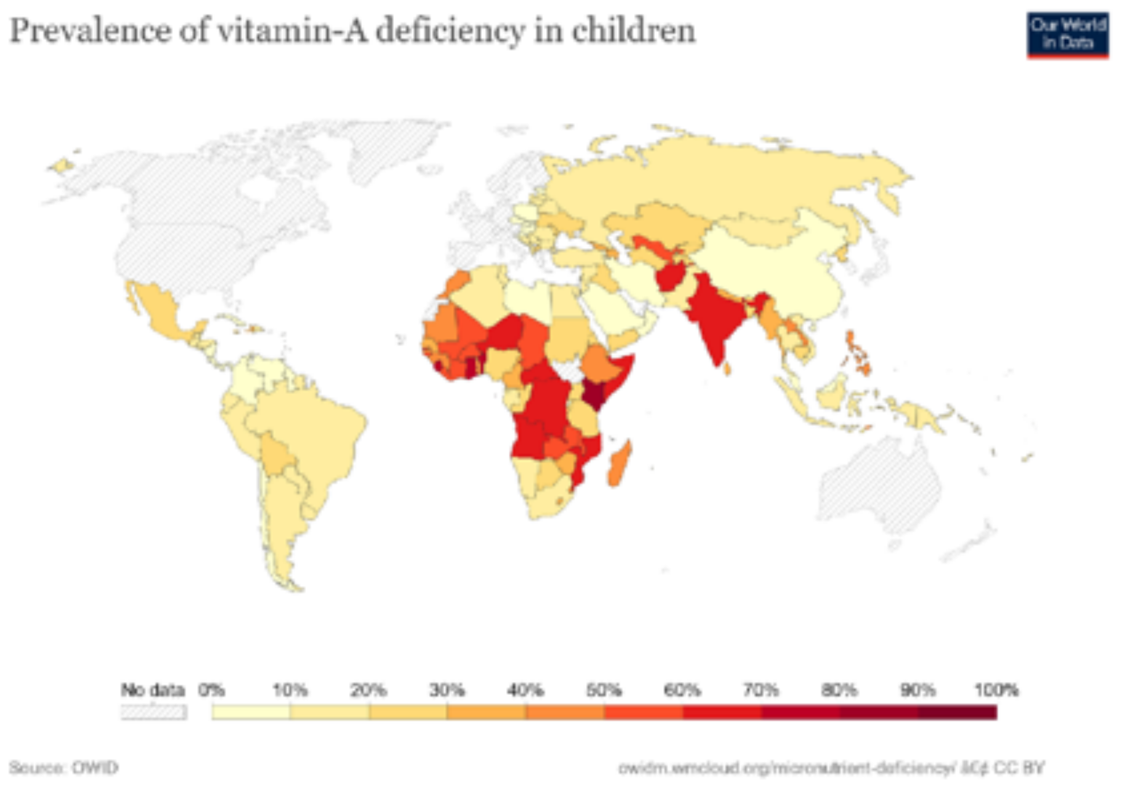
Study led by the Office of New Animal Drug Evaluation, US Food and Drug Administration, Center for Veterinary Medicine, Rockville, MD, USA

Norris, A.L., Lee, S.S., Greenlees, K.J. *et al.* Template plasmid integration in germline genome-edited cattle. *Nat Biotechnol* **38**, 163–164 (2020).

Case study and discussion

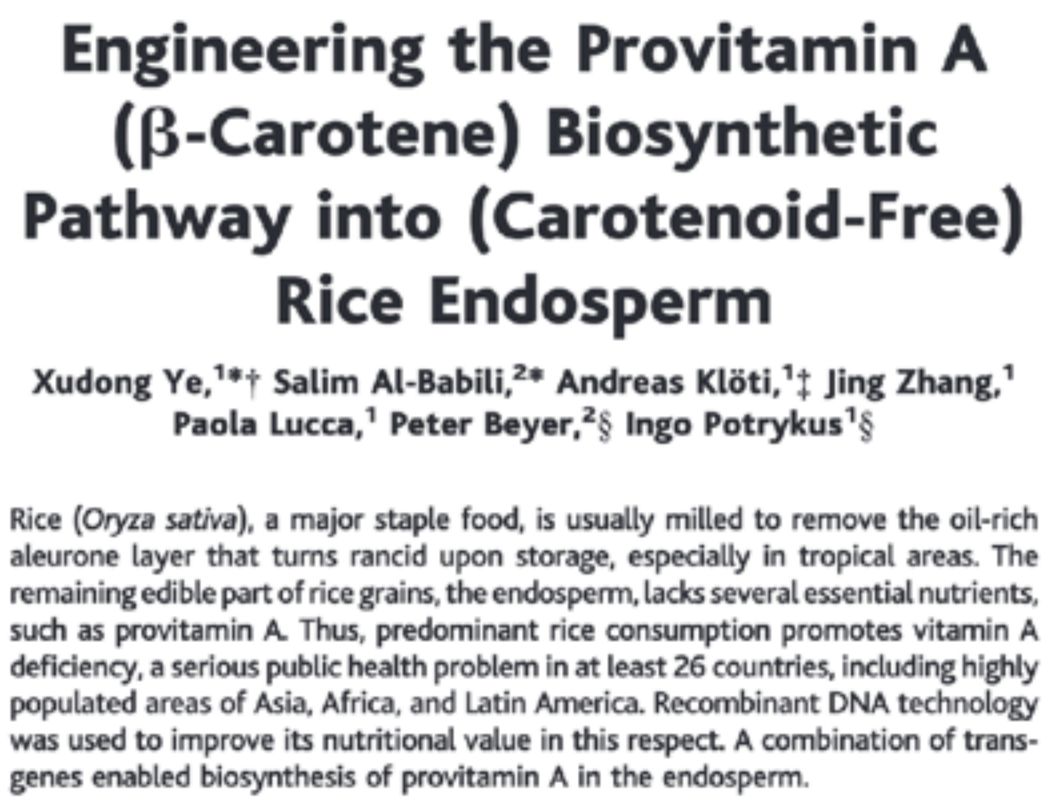
- Vitamin A deficiency impairs vision and can lead to blindness
- Vitamin A deficiency is most common in African and Southeast Asian countries
- The golden rice is a genetically-engineered variety of rice to biosynthesize beta-carotene, the precursor of Vitamin A, which our body can convert into Vitamin A
- Two beta-carotene biosynthesis genes (psy, plant origin; ctrl, bacterial origin) were introduced with plasmids into the Asian-cultivated rice species Oryza sativa
- **Discuss in teams environmental concerns and sustainability concerns linked with the introduction of the Golden rice variety into areas with Vitamin A deficiency**

Prevalence of vitamin-A deficiency in children



Source: OWID

owidm.wmcloud.org/micronutrient-deficiency/ â€¢ CC BY



Engineering the Provitamin A (β-Carotene) Biosynthetic Pathway into (Carotenoid-Free) Rice Endosperm

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Rice (*Oryza sativa*), a major staple food, is usually milled to remove the oil-rich aleurone layer that turns rancid upon storage, especially in tropical areas. The remaining edible part of rice grains, the endosperm, lacks several essential nutrients, such as provitamin A. Thus, predominant rice consumption promotes vitamin A deficiency, a serious public health problem in at least 26 countries, including highly populated areas of Asia, Africa, and Latin America. Recombinant DNA technology was used to improve its nutritional value in this respect. A combination of transgenes enabled biosynthesis of provitamin A in the endosperm.