Health and Welfare Traits

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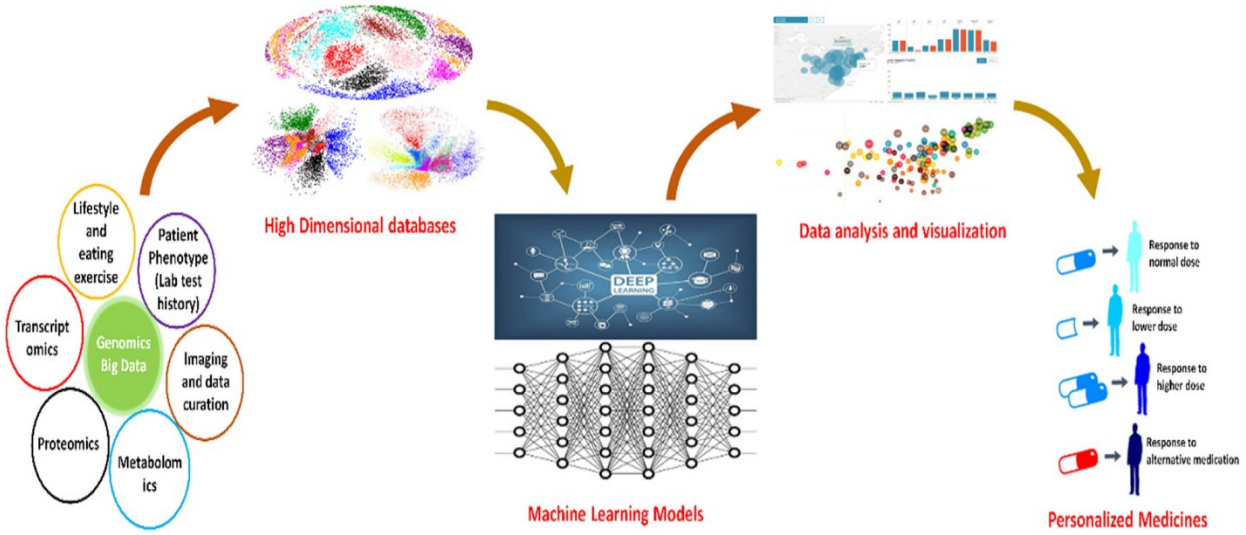
A strong vision for future approaches to health & welfare

Svante Pääbo
Nobel Prize Laureate in
Physiology & Medicine 2022

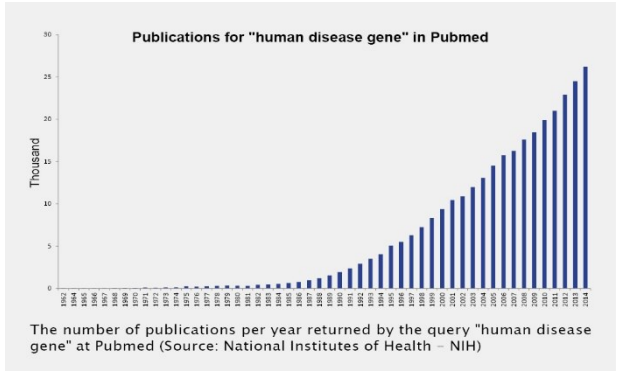
- Sequenced the Neanderthal genome in 2010
- Predicted early on that sequencing of genomes of ancient species will contribute to a revolution in human & veterinary medicine → “Precision medicine will be routine”

Break-throughs in human health genomics

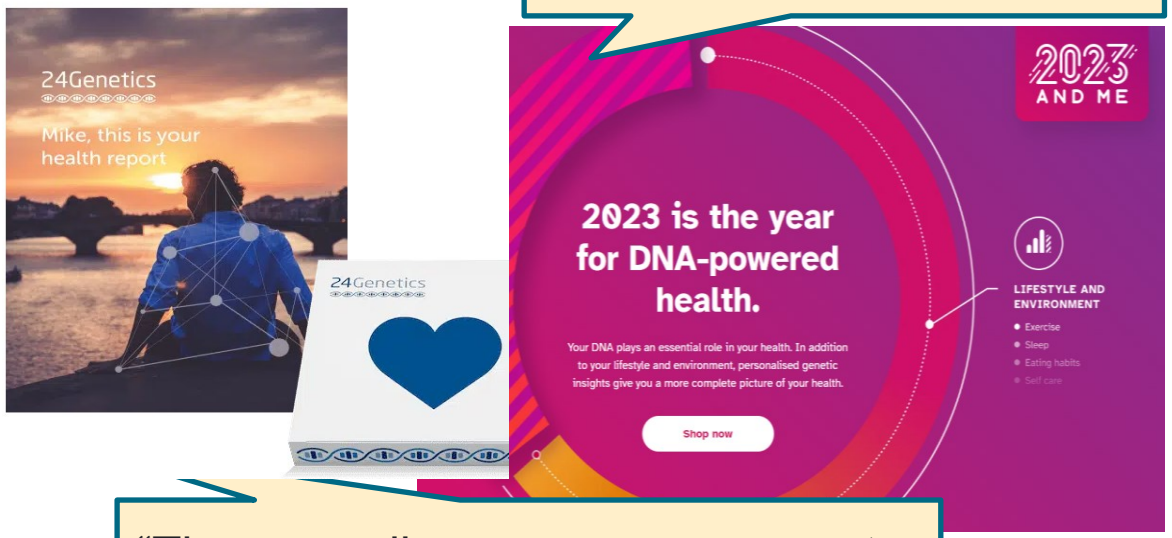
- Over 2000 disease genes discovered to date
- Genomic testing is increasingly used to diagnose, monitor, treat, predict & prevent disease
- Huge advances in 'big data' analytics



Hassan et al., Int. J. Mol. Sci. **2022**, *23*(9)



"A single DNA test has been developed that can screen a patient's genome for **over 50** genetic neurological and neuromuscular diseases." (Garvan Institute for medical research, March 2022)



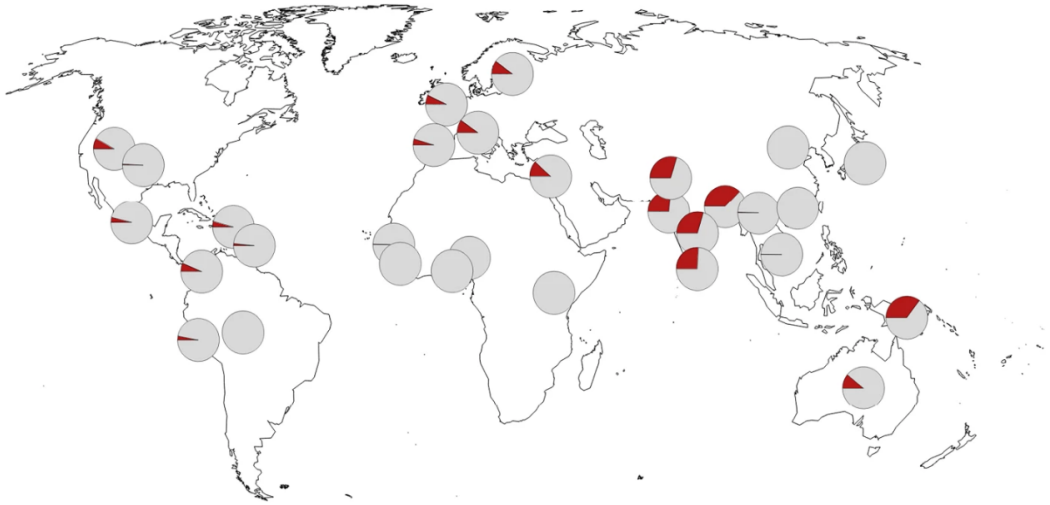
"There are disease we can prevent, & the DNA Health Test can help us identify them" (24 Genetics)

Reality check

Nobel price lecture, Uppsala, Sweden, December 2022

Fig. 3: Geographical distribution of the Neanderthal core haplotype that confers risk for severe COVID-19.

From: The major genetic risk factor for severe COVID-19 is inherited from Neanderthals



Pie charts show the minor allele frequency at rs35044562. Frequency data were obtained from the 1000 Genomes Project[22]. Map source data were obtained from OpenStreetMap[23].

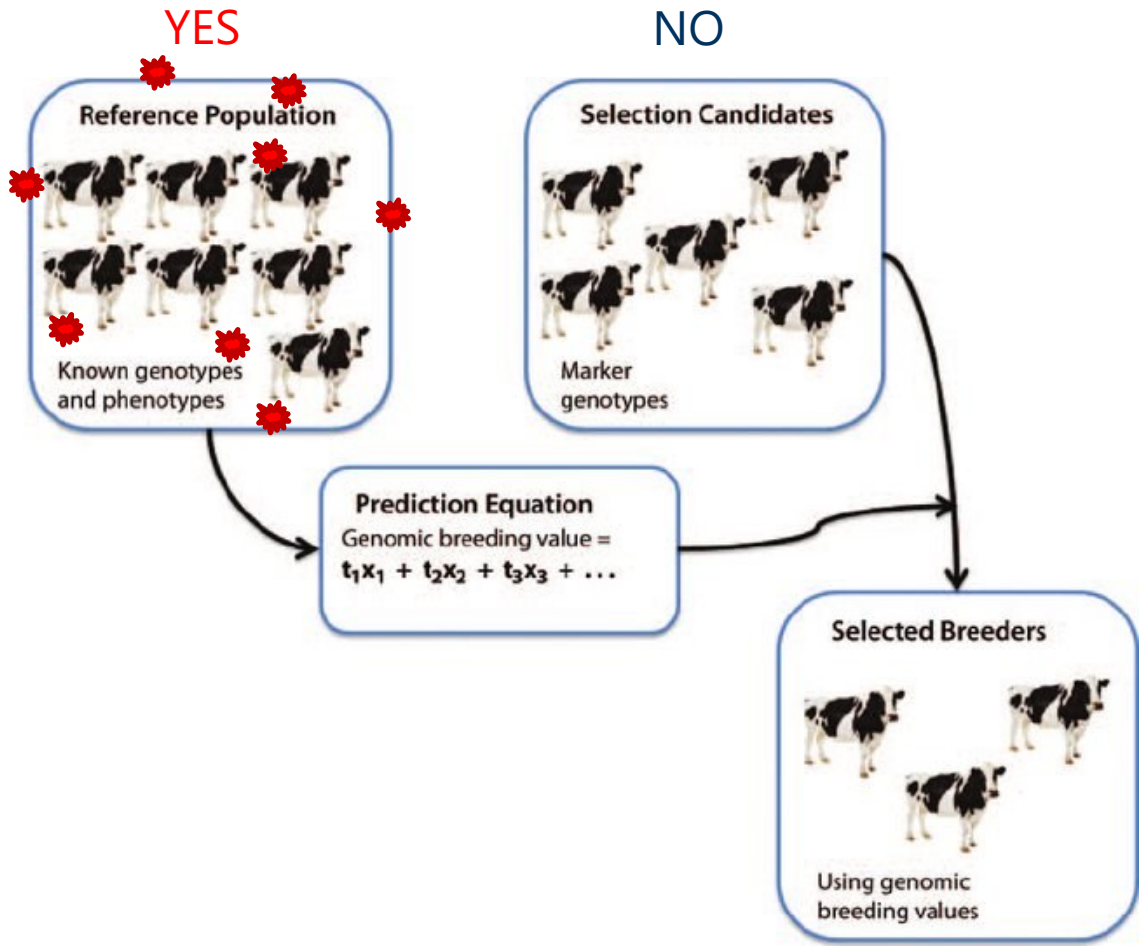
Zeberg & Pääbo, Nature 587, 2020

- Clearly strong scientific advances in health genomics
- But also increased recognition regarding the complexity of the immune system and the challenges for precision medicine

Animal health & welfare genomics

Genomic selection:

Required exposure to pathogens & other stressors:



- Huge expectations for genetic disease control through genomic selection
- But limited genomic selection for health, resilience and welfare traits in practice

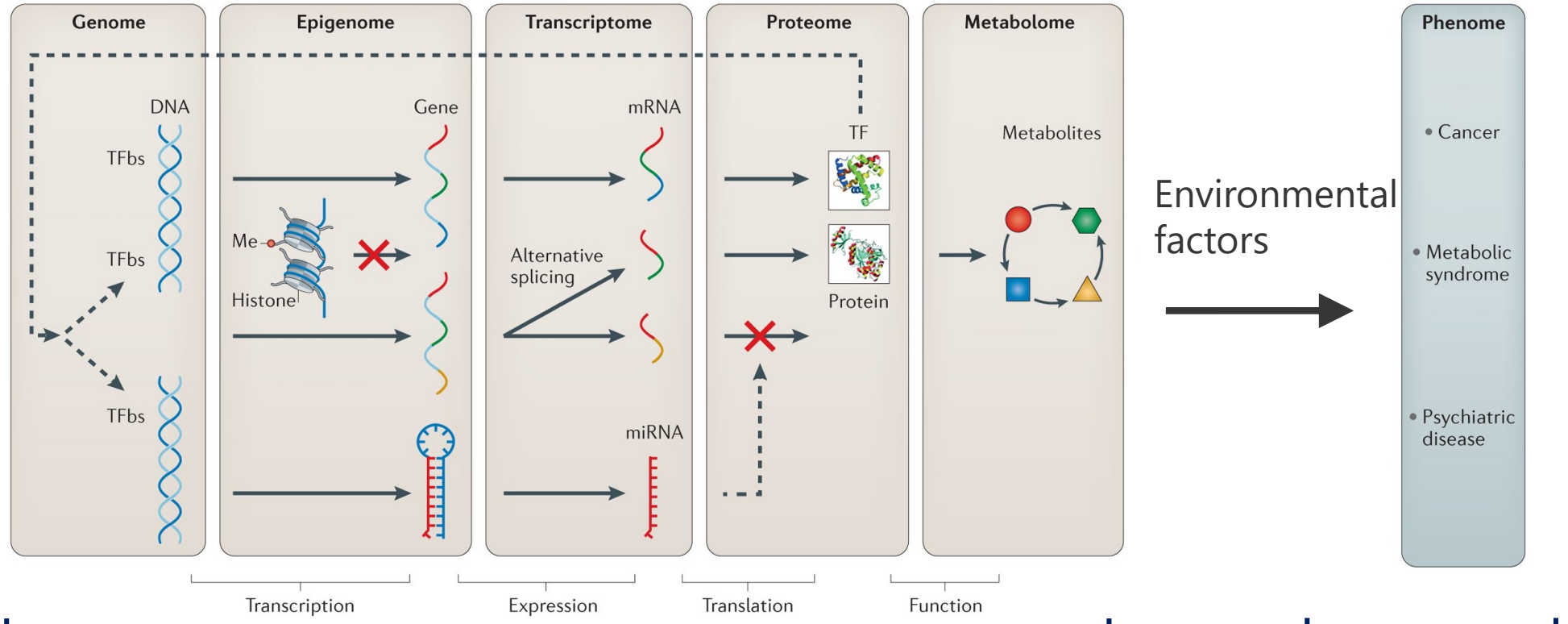
Addressed within the H2020 Smarter project

Smarter
SMAll RuminanTs breeding for Efficiency and Resilience

Key obstacles in health & welfare genomics

- Sparse, highly heterogenous data for rare diseases
- Difficulties in identifying causal variants underpinning associations identified in GWAS
  - and the cell type / physiological function they regulate
- Most common diseases are complex traits
  - Poor prediction accuracies for polygenic risk scores
  - GxG and GxE lead to reduced prediction accuracies
  - Very limited understanding of the functional mechanisms
- Infection and behavioural processes are highly dynamic, stochastic, and affected by interactions between individuals

The route from genotype to phenotype has many steps



New statistical & computational methods for integrating multi-omic data needed

Figure from Ritchie et al., Nature Reviews Genetics **16**(2015)

Health & welfare traits depend strongly on social interactions between individuals

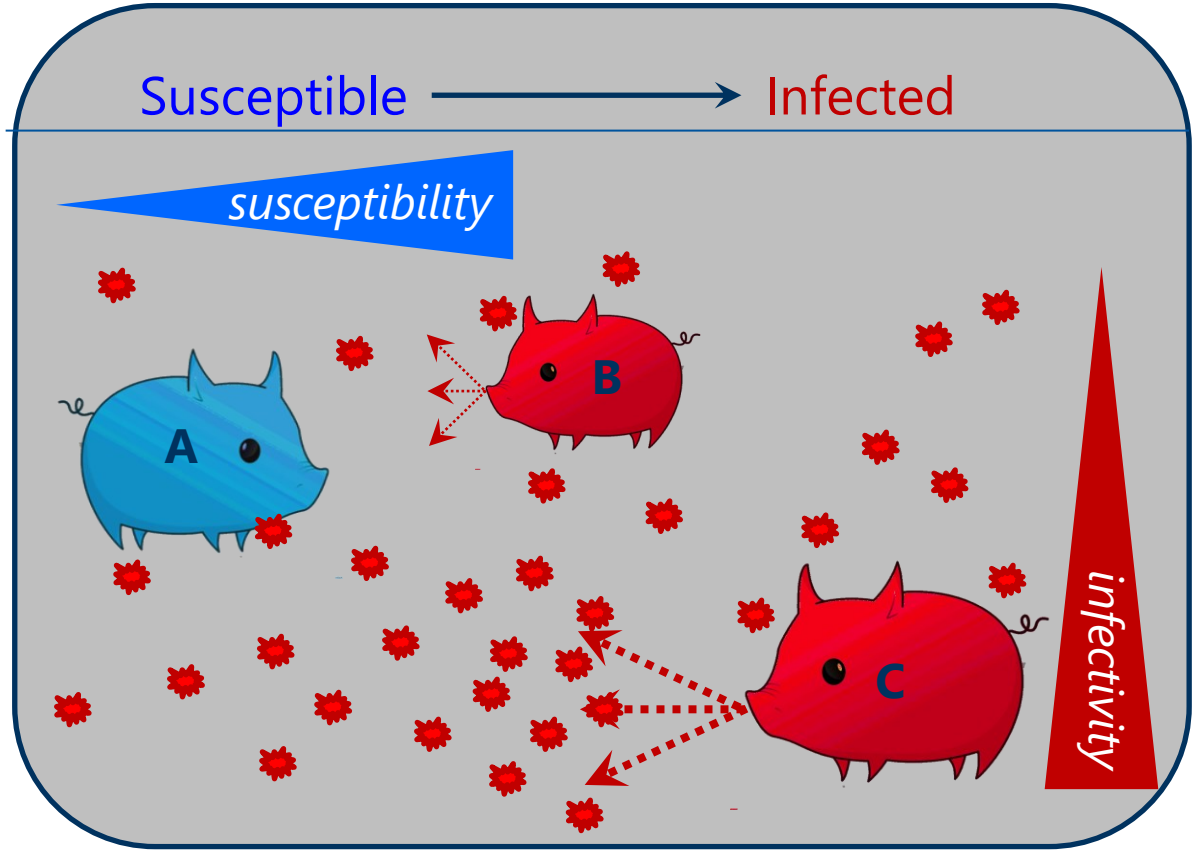


Figure adapted from Doeschl-Wilson et al., Animal 15 (2021)

Genetic effects underlying **disease transmission** poorly understood

It takes Two to Tango

Figure: Courtesy of Dr. Simon Turner, SRUC

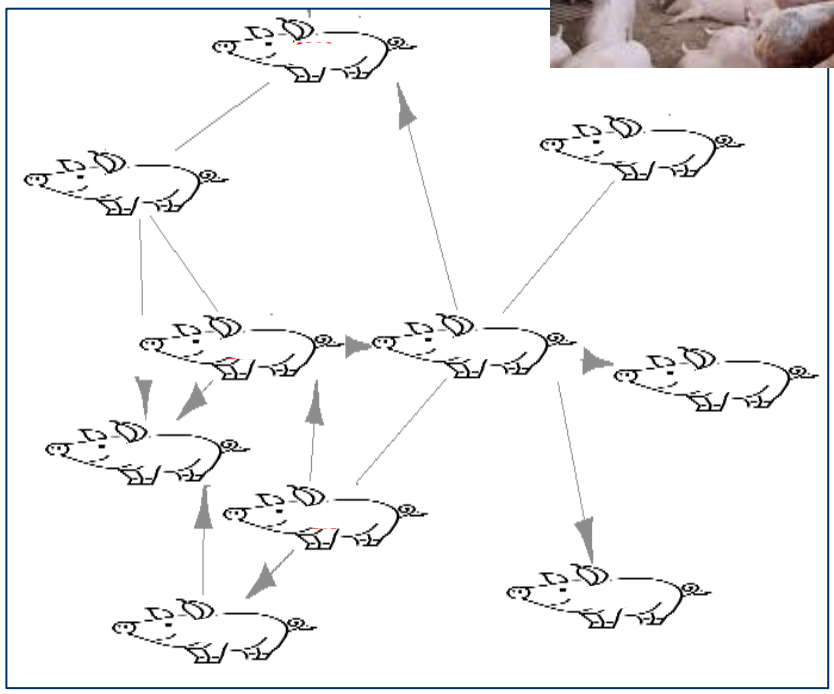


Figure from Agha et al., Genes 2022

Statistical models must account for social (genetic) interactions if the aim is to improve health & welfare at the population level

Speakers of this session

1. **Juan Steibel** (Iowa State University)

Genetics of swine behavior for increased animal welfare and productivity

2. **Everest Castaneda** (Baylor University)

Network Enhanced Similarity Search Increases the Predictive Power of a Highly Heterogenous Network

3. **Gosia Trynka** (Wellcome Sanger, UK)

Moving from GWAS variants to function in immune diseases

4. **Cassie Spracklen** (University of Massachusetts Amherst)

In and Out of Context: Deciphering the Genetic and Genomic Architecture of Type 2 Diabetes