DNA-Profile, DNA-Biobanken und Epigenetik

PSK 1895, am Schlagbaum, 25.3.2018

Prof. em. Jörg T. Epplen, amedes genetics

DNA-Profile, DNA-Biobanken und Epigenetik

- DNA-Profile
- DNA-Biobanken
- Epigenetik
- Schlussfolgerungen

Werkzeuge und Methoden

Begriffe

Allel: Variante eines genetischen Markers

DNA-Profil: genetischer Fingerabdruck

genet. Marker: eindeutig identifizierbarer DNA-Abschnitt, Ort im Genom bekannt

Heterozygotie: Mischerbigkeit

Mikrosatellit $\longrightarrow$ $\longrightarrow$

genetische Marker: Mikrosatelliten

...cttgtatatatatatatatatatatatatatatatatatatagtttt...
...cttgtatatatatatatatatatatatatatatatatatatagtttt...
...cttgtatatatatatatatatatatatatatatatatatatagtttt...
...cttgtatatatatatatatatatatatatatatatatatatagtttt...
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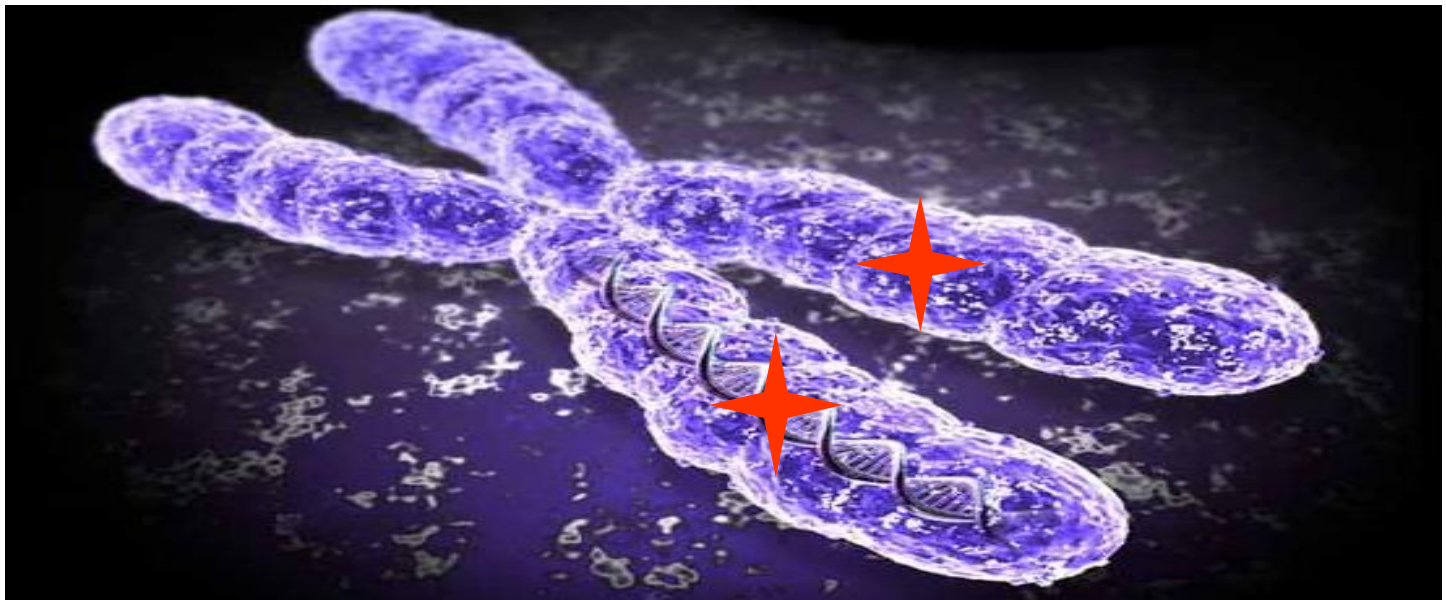
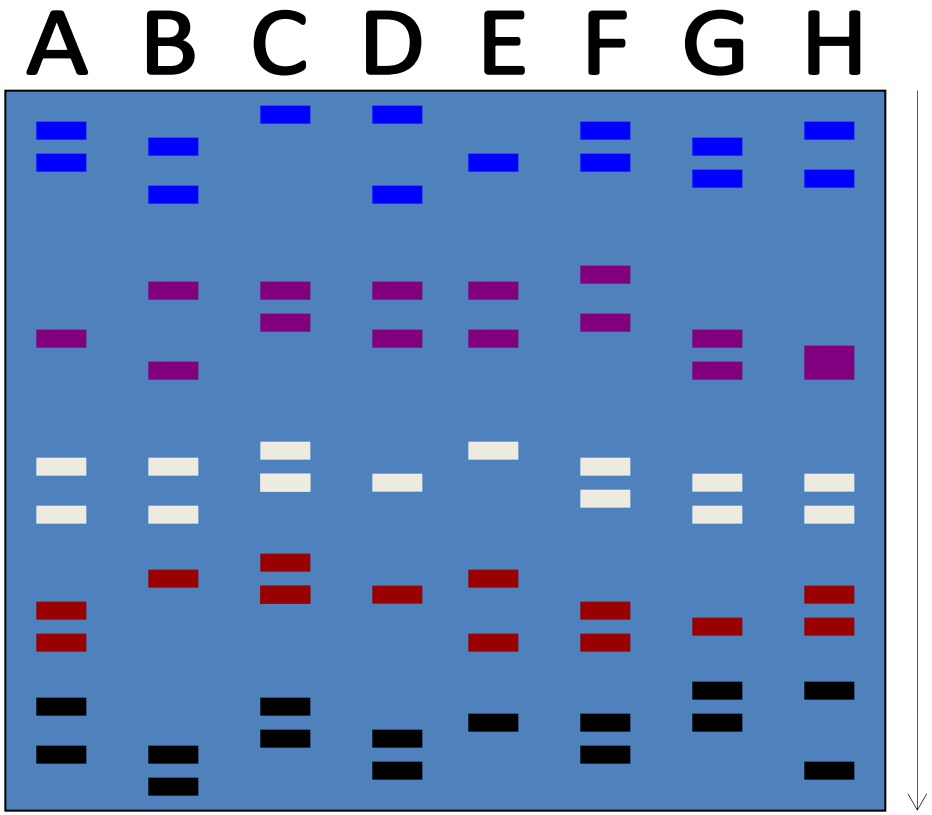
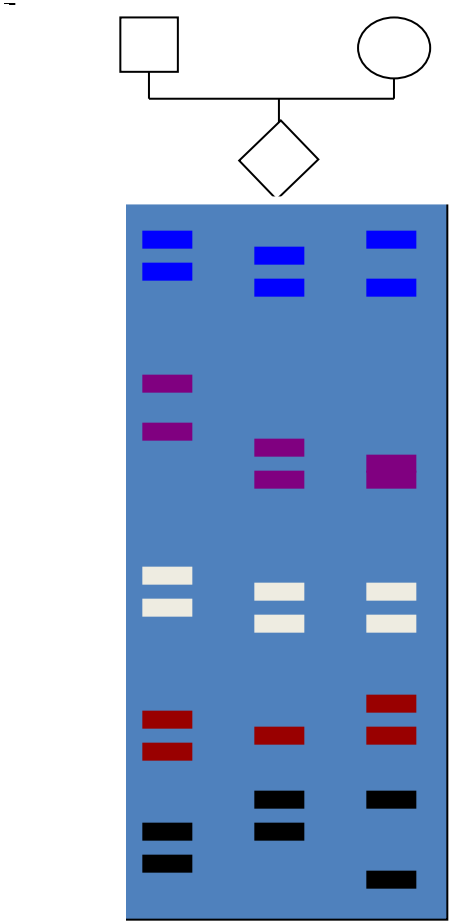


DNA-Profile



mehrere vielgestaltige (polymorphe) Markersysteme gleichzeitig dargestellt; viele Menschen unterscheidbar

DNA-Profile



Mikrosatelliten:
polymorphe
Marker-Allele

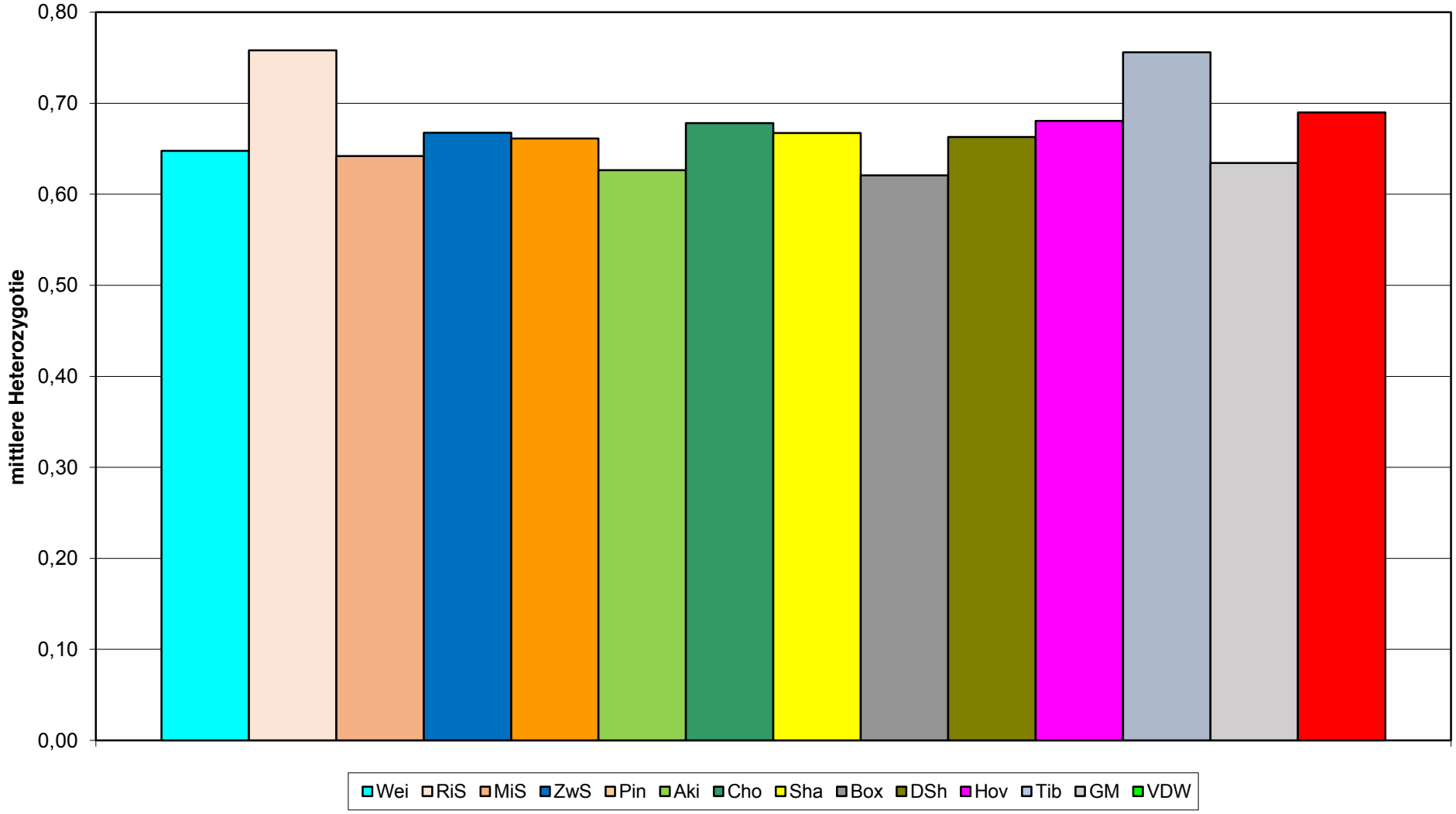
Abstammung

? Mutter ausgeschlossen ?

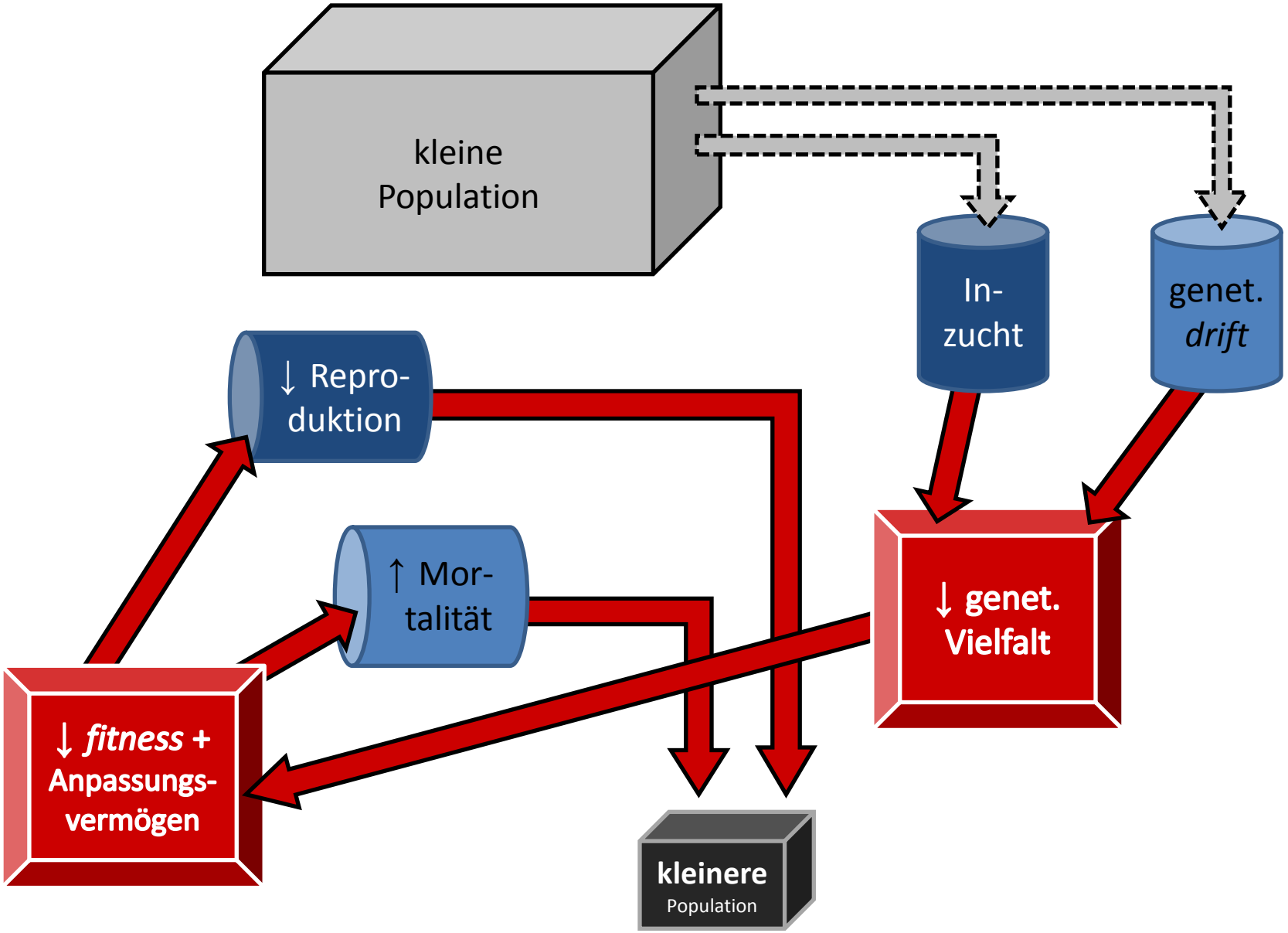
	PEZ02		Zfxy		PEZ17		FH2017		FH2309		PEZ05		FH2001		FH2328		FH2004		FH2361		PEZ21		FH2054		FH3377		FH2107		FH2088		VWFX		FH2010		PEZ16		FH3313	
Großmutter	122	126	158		204	212	262	266	399		101	105,5	124	128	173	188	240		339	351	95		147	163,5	192		363	367	119		155,5		236		290,5	302,5	373	
Großvater	122		158	162,5	204		262		347	399	101		128	132	173	188	232	236	351		87		163,5		186	192	363	367	119	123	155,5	161,5	236		279	302,5	376	400
Hündin	122		158		204	212	262	266	347	399	101		128		173	188	232	240	351		87	95	147	163,5	192		363	367	119		155,5		236		290,5	302,5	373	376
Hündin	122		158		204	212	262	266	347	399	101		128		173	188	232	240	351		87	95	147	163,5	192		363	367	119		155,5		236		290,5	302,5	373	376
Rüde 1	126		158	162,5	204	212	262		387	399	101	109,5	128		173	188	236		343	347	87		147	163,5	235		363	367	119	126	155,5		236		302,5		373	376
Welpe 1	122	126	158	162,5	204	212	262	266	347	399	101	109,5	128		188		236		343	347	87	95	147		192	235	363		119	126	155,5		236		290,5	302,5	373	376
Welpe 2	122	126	158	162,5	204	212	262	266	391	399	101		128		173		236	240	347	351	87	95	147	163,5	192	235	363	367	119		155,5		236		302,5		373	376
Hündin	122		158		204	212	262	266	347	399	101		128		173	188	232	240	351		87	95	147	163,5	192		363	367	119		155,5		236		290,5	302,5	373	376
Rüde 2	126	130	158	162,5	200	204	262		347	395	101	109,5	128		173	184,5	236		339	347	87		163,5		192	235	367	370	119	123	155,5		228	236	279	298,5	391	415
Welpe 3	122	126	158		200	212	262	266	395	399	101		128		173	188	232	236	339	351	87	95	147	163,5	192	235	363	370	119	123	155,5		228	236	298,5	302,5	376	395
Hündin	122		158		204	212	262	266	347	399	101		128		173	188	232	240	351		87	95	147	163,5	192		363	367	119		155,5		236		290,5	302,5	373	376
Rüde 3	126		158	162,5	200		262		347	399	101		128	144	173		236	240	343	439	87		147	163,5	186	235	367	385	126		155,5	161,5	236		290,5	302,5	373	395
Welpe 4	122	126	158	162,5	200	204	262		347	399	101		128		173	188	232	240	347	439	87		147	163,5	192	235	363	385	119	126	155,5	161,5	236		290,5	302,5	373	395

	FH2309		PEZ05		FH2001	FH2328		FH2004		FH2361	
Hündin	347	399	101		128	173	188	232	240	351	
Rüde 1	387	399	101	109,5	128	173	188	236		343	347
Welpe 1	347	399	101	109,5	128	188		236		343	347
Welpe 2	391	399	101		128	173		236	240	347	351

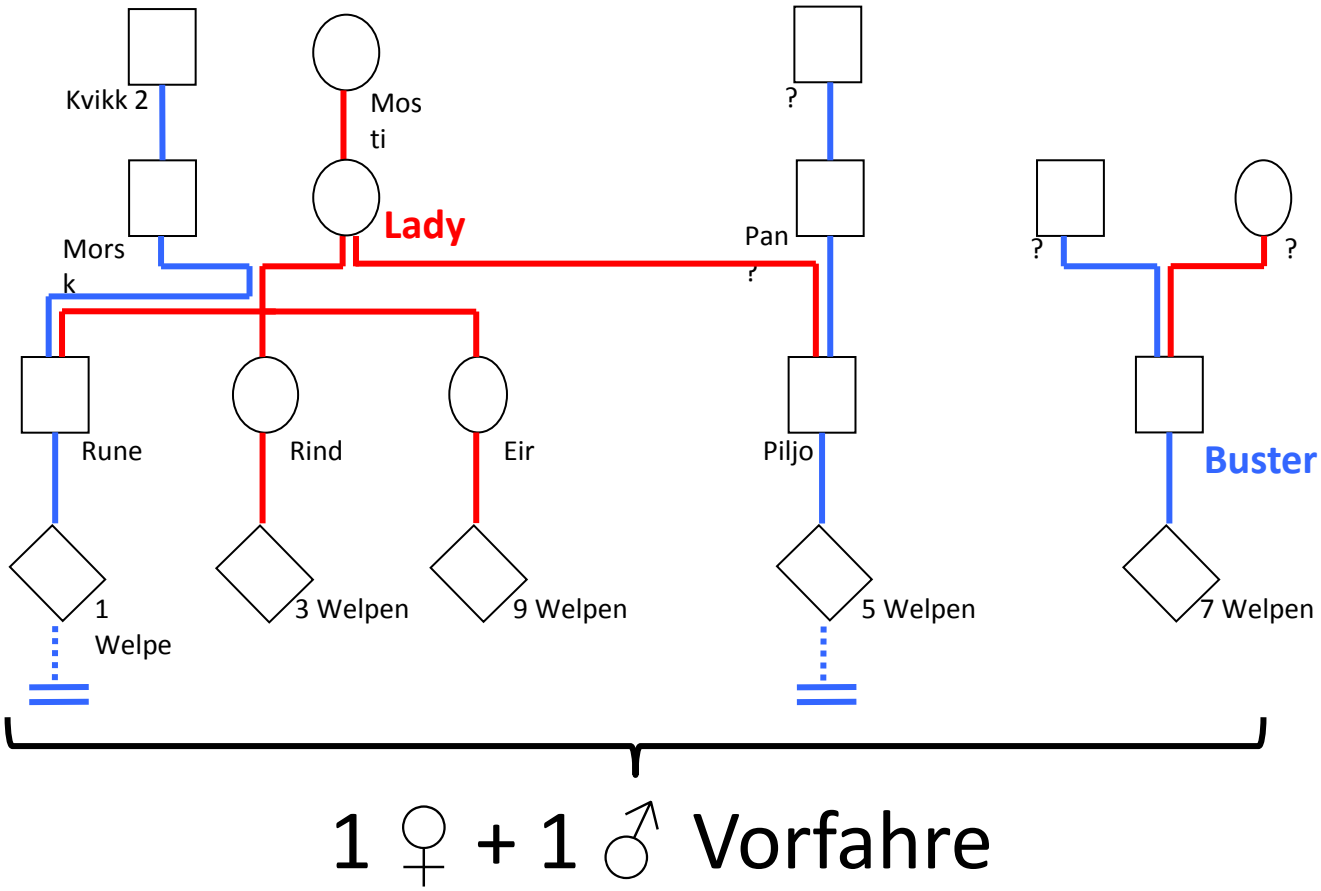
mittlere Heterozygotie in versch. Rassen



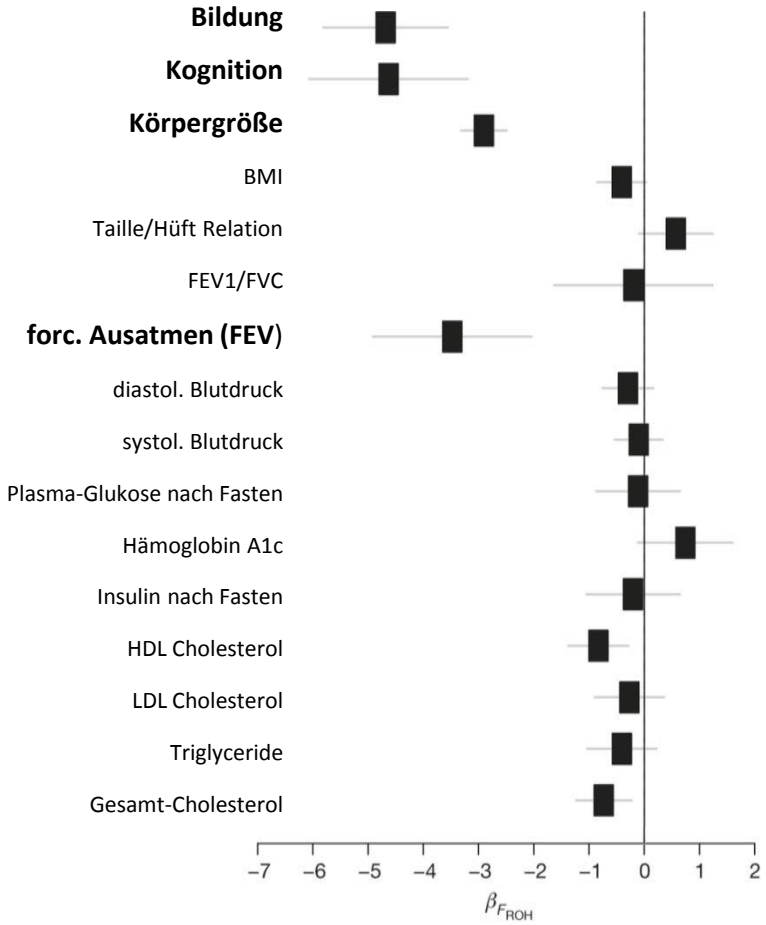
„Strudel“ reduzierter genet. Vielfalt



Lundehund: genetische Flaschenhälse

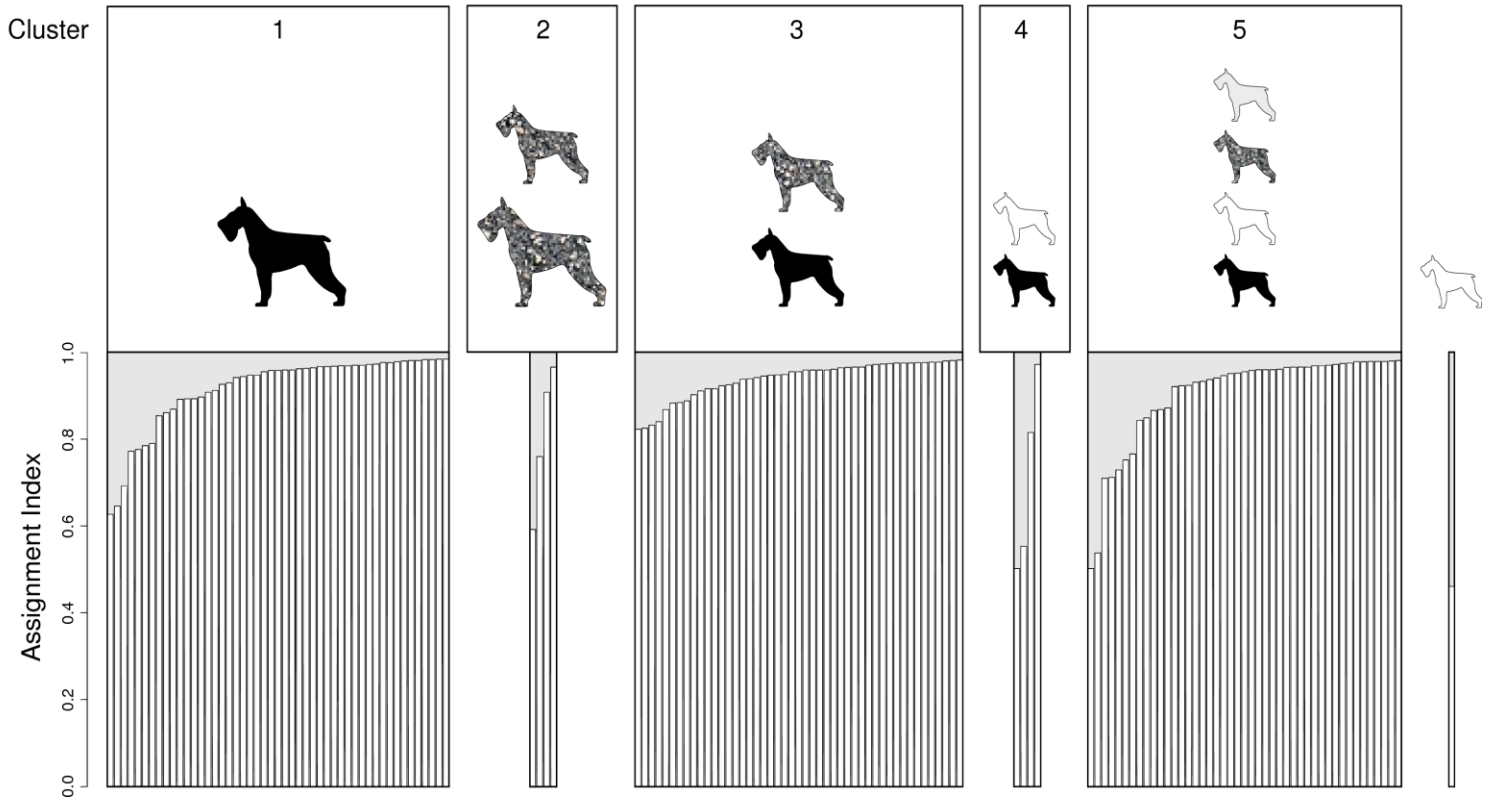


↓ Heterozygotie ist nachteilig



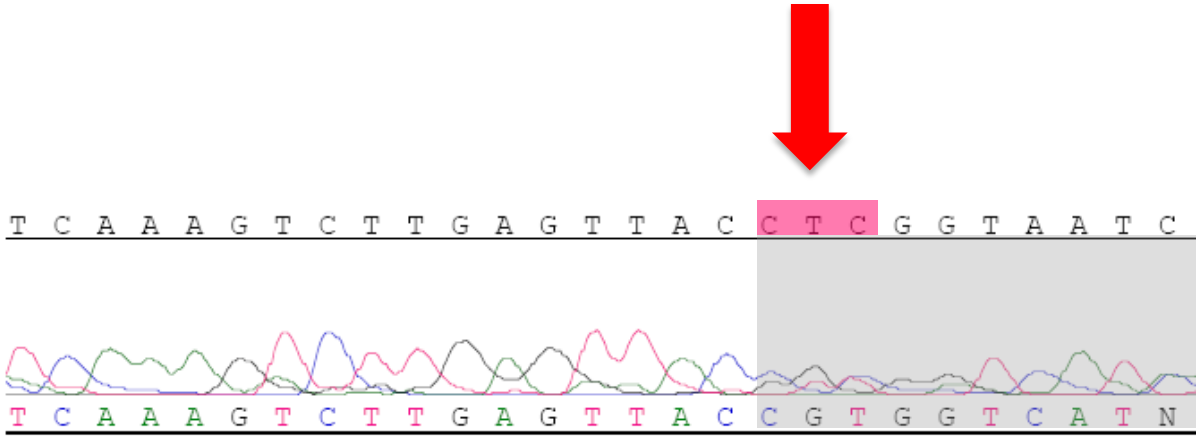
354 224 Menschen untersucht

„Schnauzer-Schläge“ - Verwandschaften

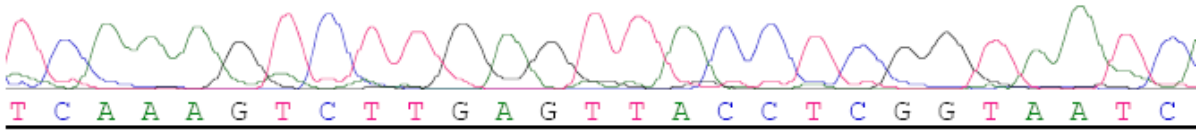


Pointer im Weimaraner-Wurf?

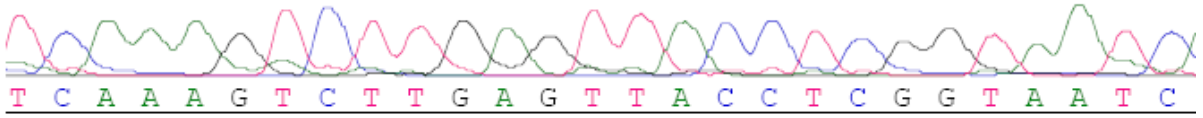
Asta vom Boleko



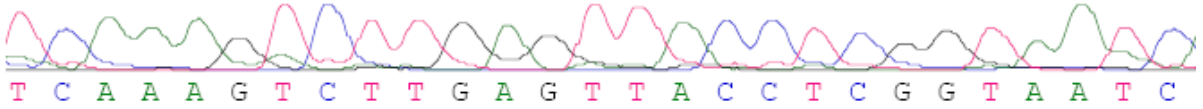
Banjo vom Grauthoff



Jule von der Dianaburg



Aska vom Boleko



KIT Exon 13:

c.1960_1962delCTC p.L654del, heterozygot

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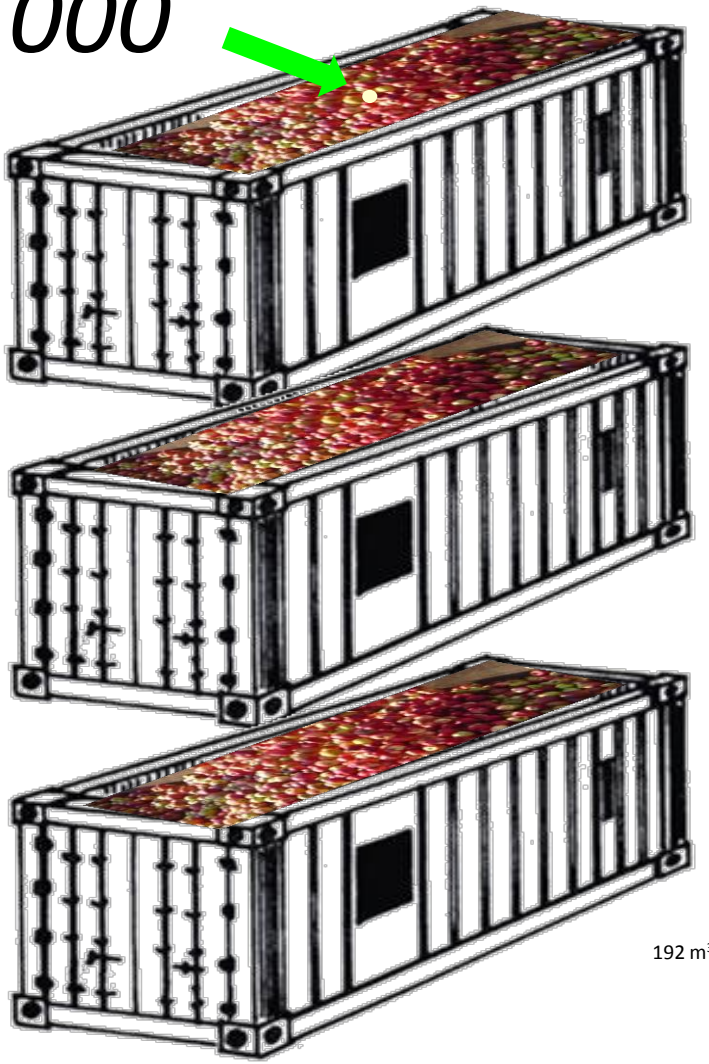
DNA-Biobanken

der einzige wirklich Faulige
unter 372 000



PRA bei Schapendoes + Weimaraner

3/04
genome screen

6/2005
chromosome identified

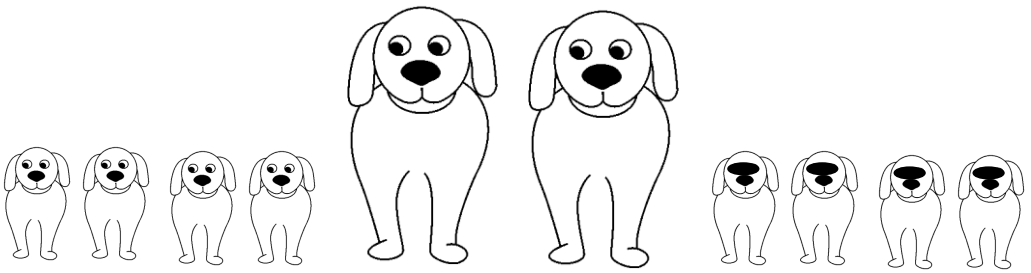
7/05
1. gene
charakterised

8/2006
2. gene

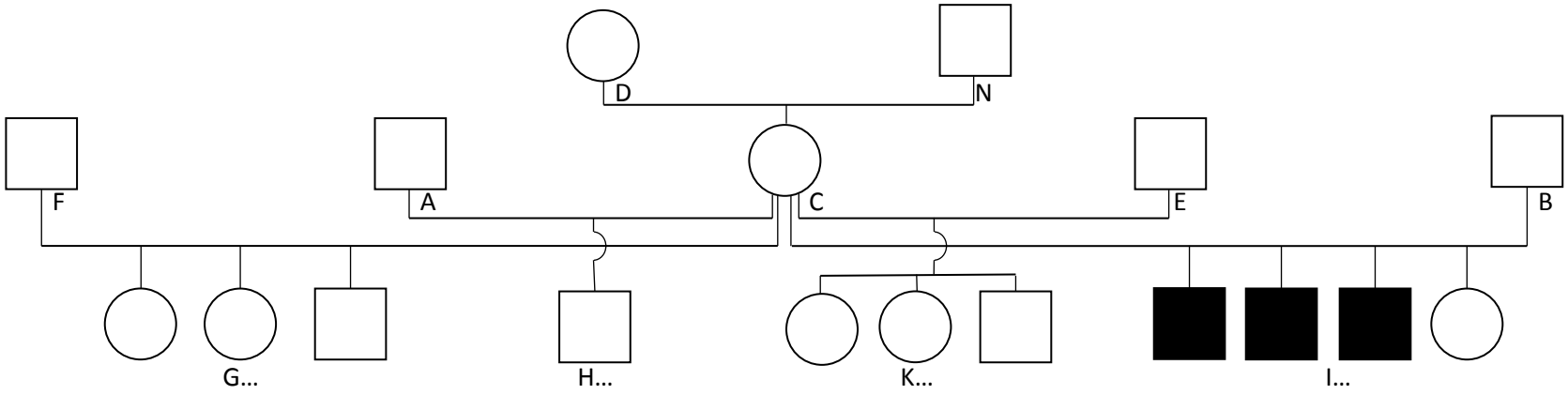
2/08
11. gene

7/15
Exom
sequen-
ziert

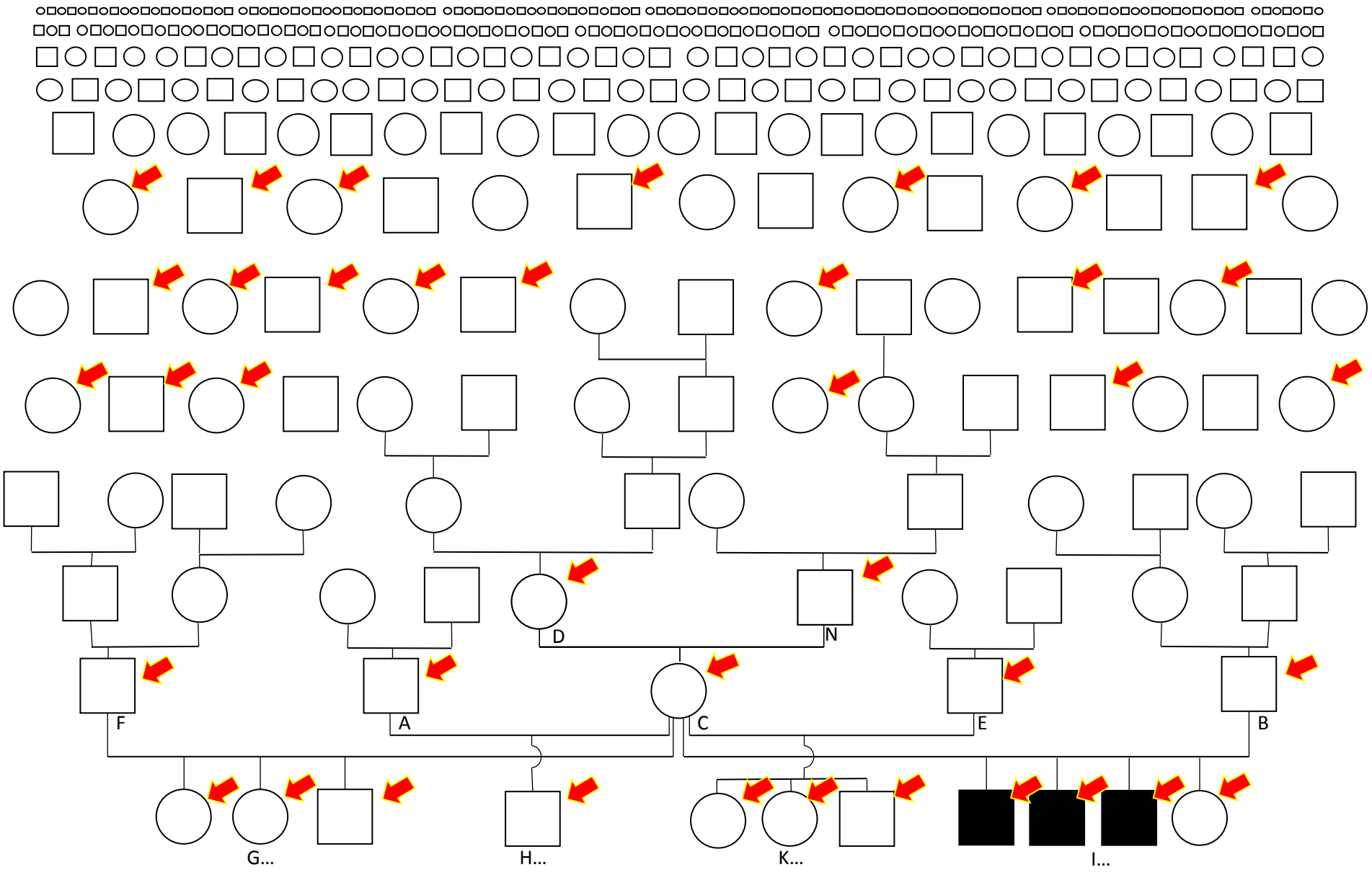
8/15 9/15
1.-15. Gene



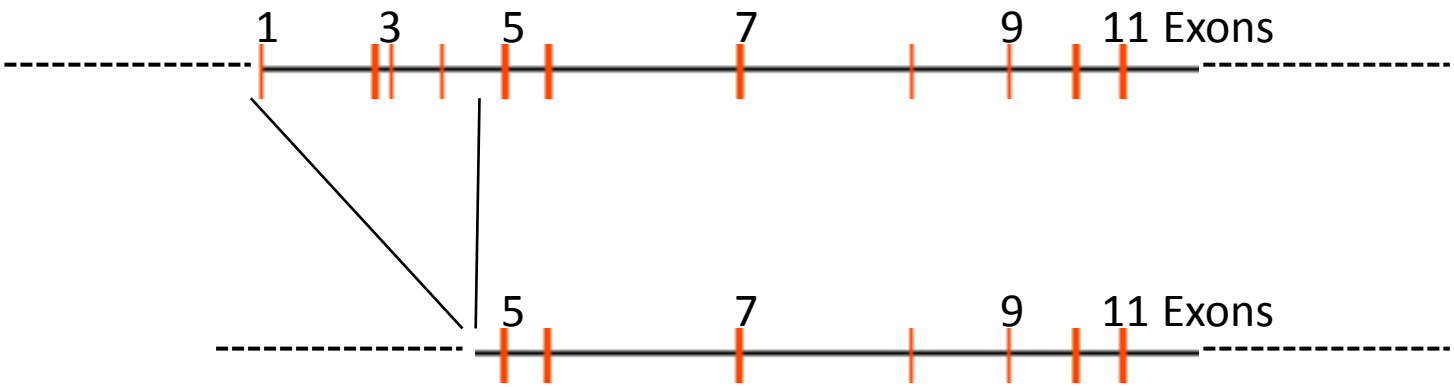
Erbleiden ?



DNA-Biobank



Stückverlust im Gen (Deletion)



→ kein funktionierendes Protein

→ Netzhautdegeneration → Sehstörungen

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PRA in Schapendoes

3/04
Genom-*Screen*

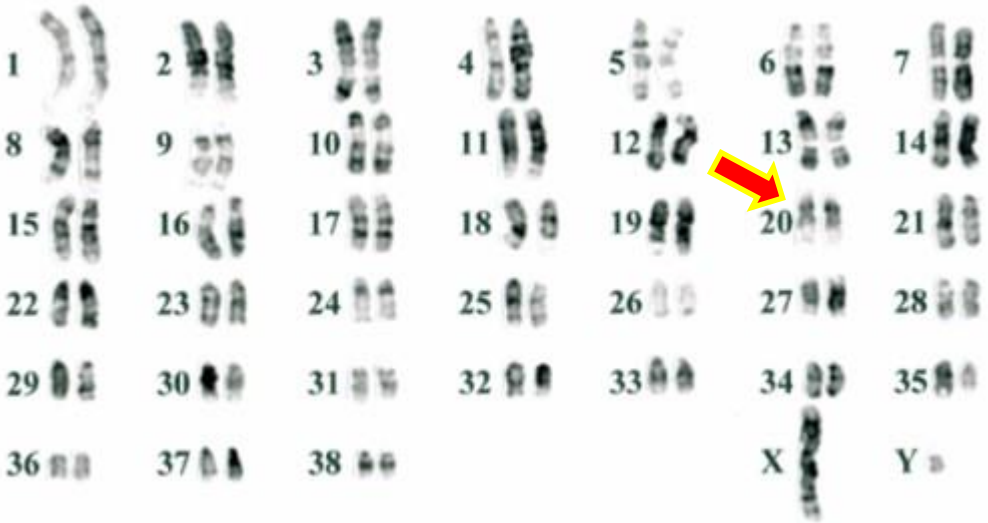
6/2005
Chromosom identifiziert

7/05
1. Gen
charakterisiert

8/2006
2. Gen

2/08
11. Gen

2/15
Konse-
quenzen



Chromosomen des Hundes

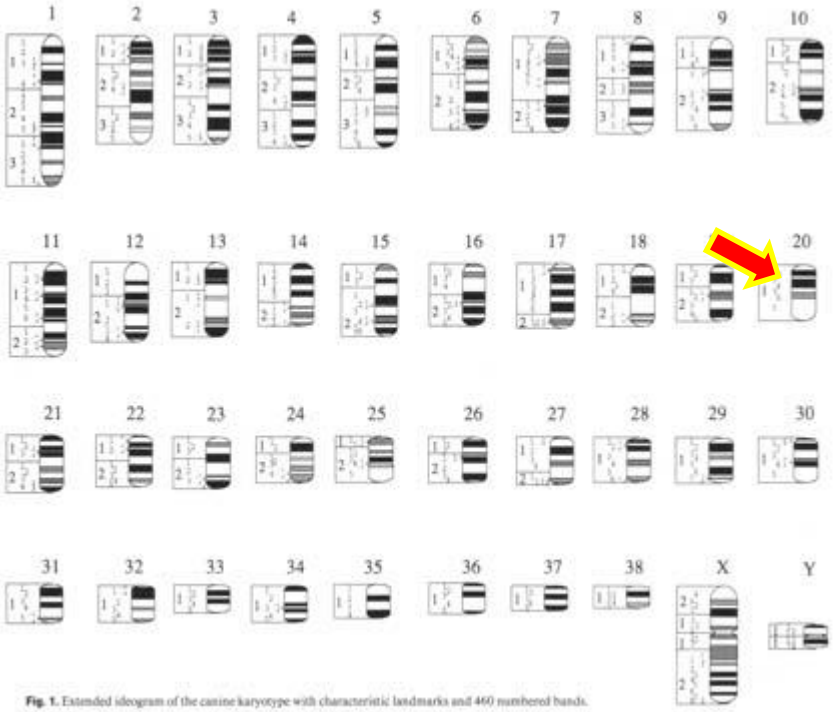
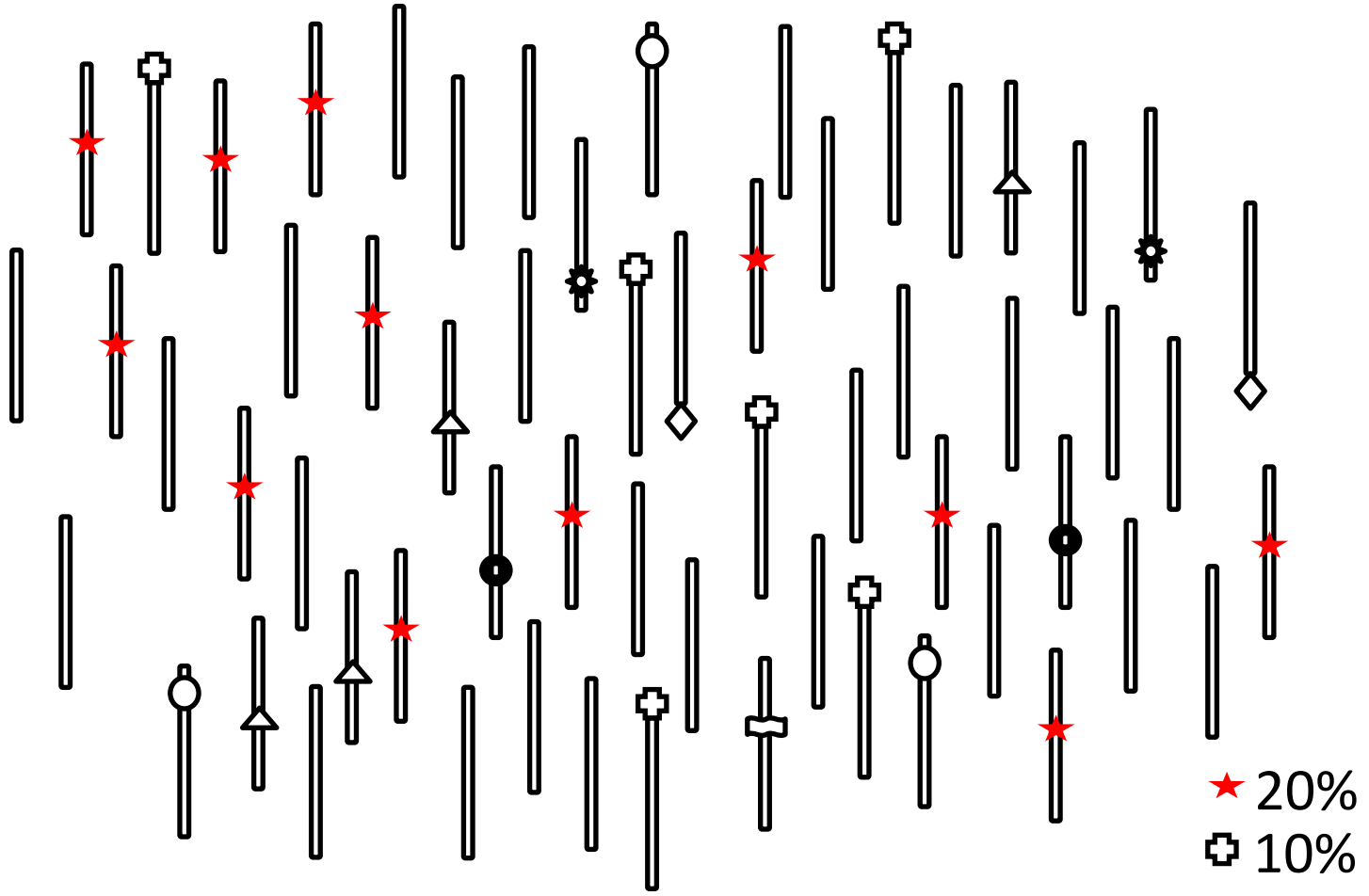
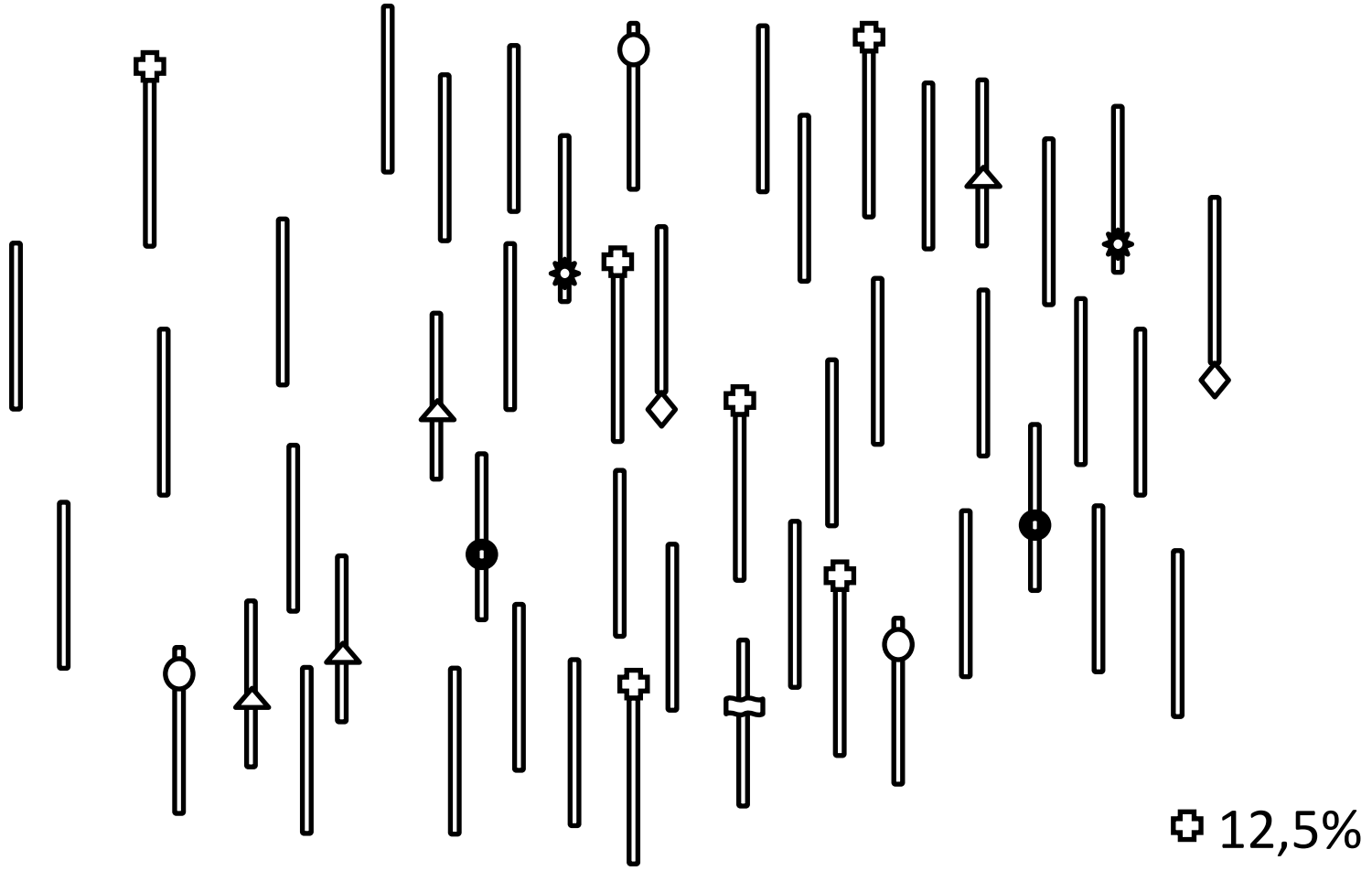


Fig. 1. Extended ideogram of the canine karyotype with characteristic landmarks and 460 numbered bands.

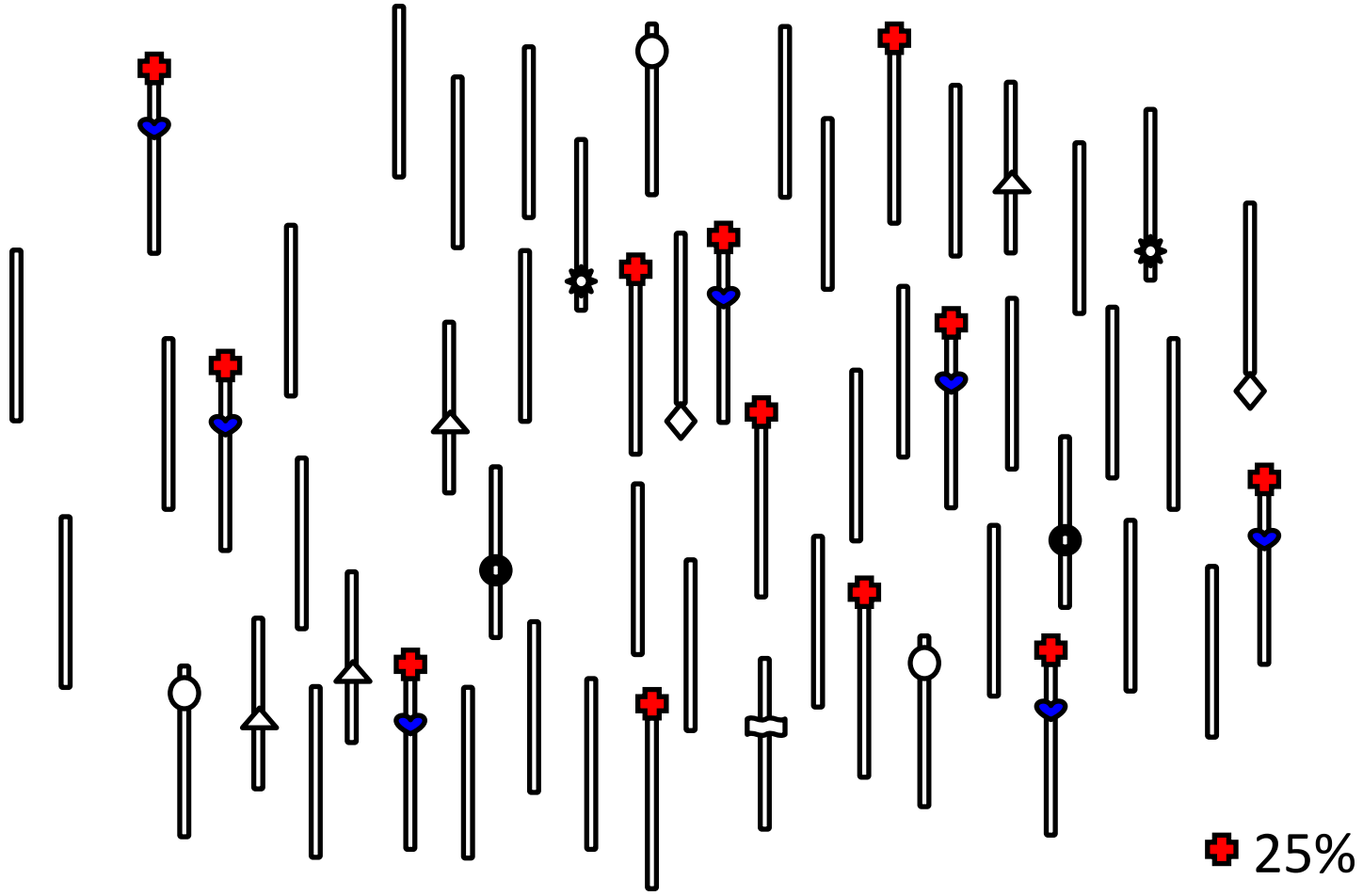
alle Chromosomen 20 vor DNA-Test



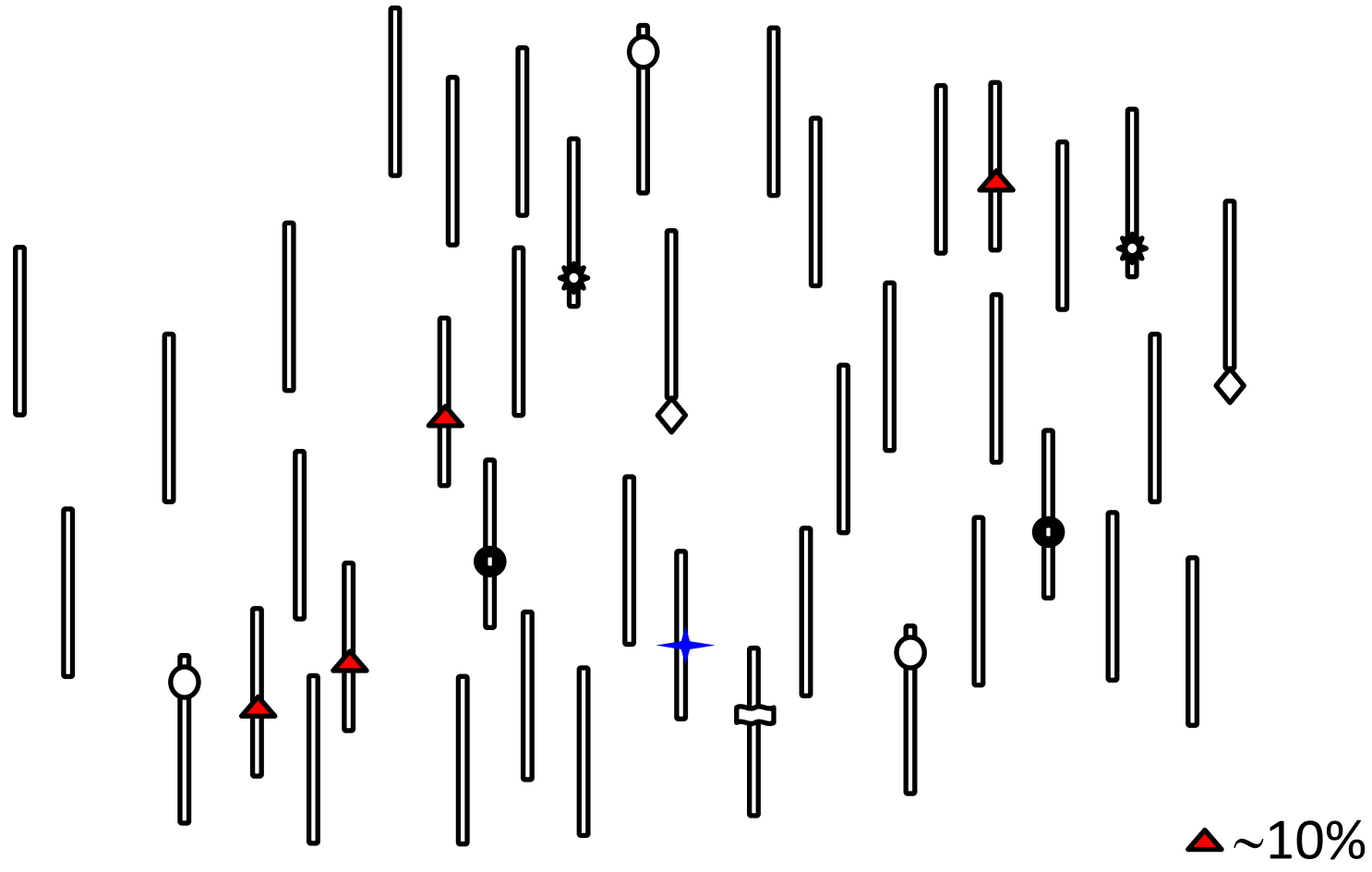
Chromosomen 20 nach selektiver Zucht



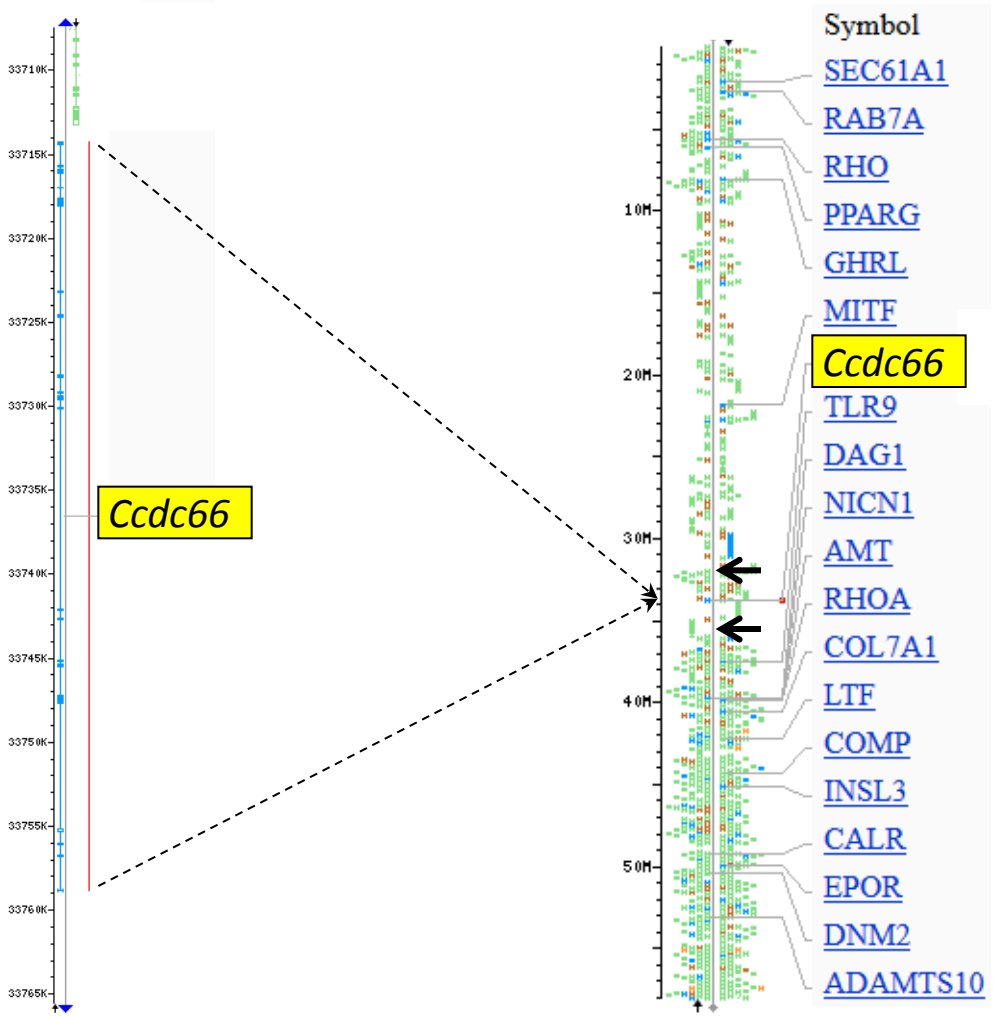
Chromosomen 20 bei Exterieur-geleiteter Zucht



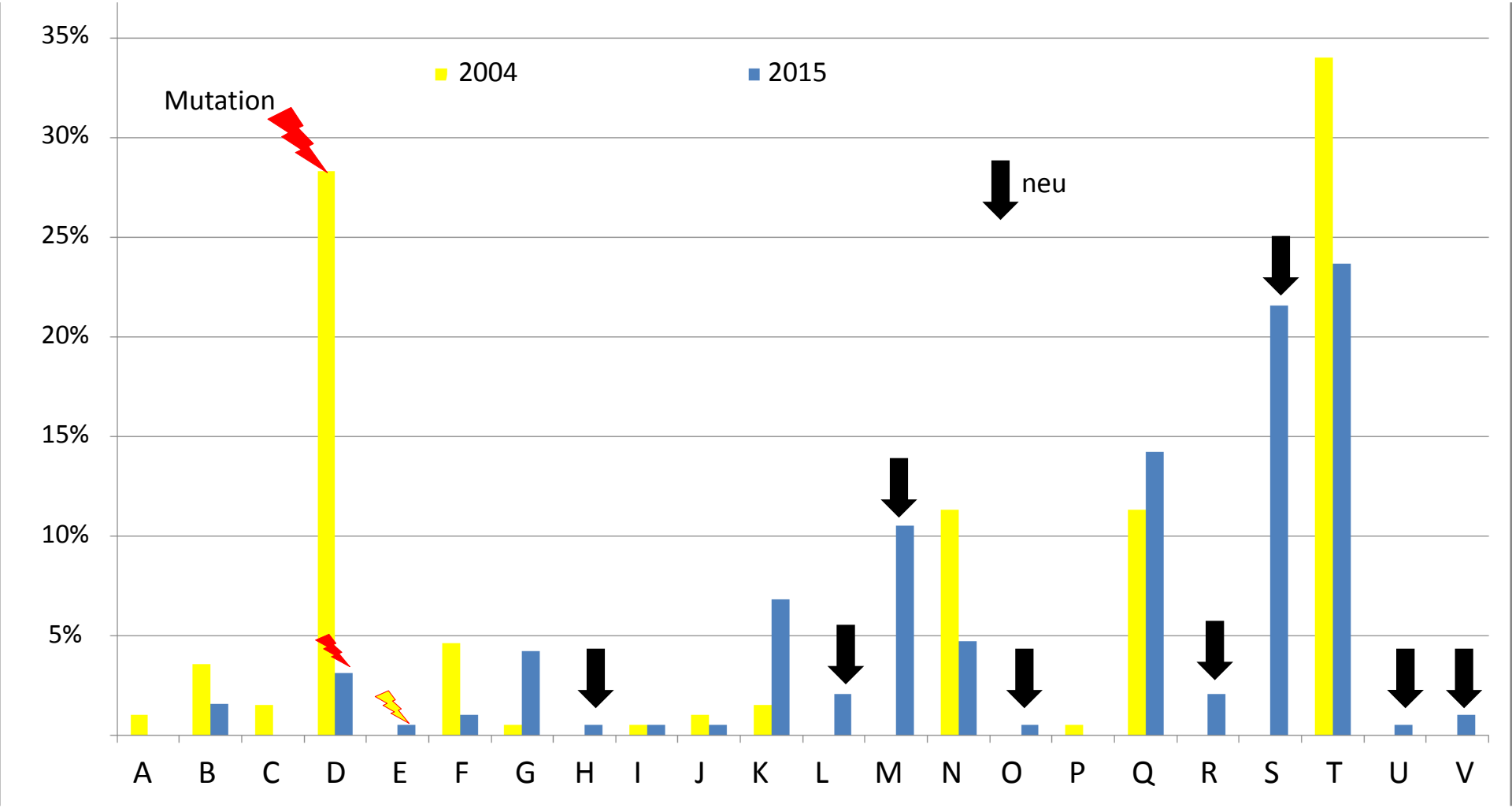
Chromosom 20 ⟶ ↓ variabel



Ccdc66 Gen auf Chromosom 20



variable Marker (be)im *Ccdc66* Gen



→ neue Haplotypen, genetische Variabilität ↑

Folgen konsequenten Ausmerzens: PRA-Mutation Schapendoes

- Mutation-Frequenz ↓
- paradox: genet. Vielfalt ~~↓~~ **sondern** ↑ - warum ?
- andere Zuchtstrategie: alte Linien

  wieder genutzt (Inzucht-Koeffizient 30→20)

→ weise Zucht-Politik

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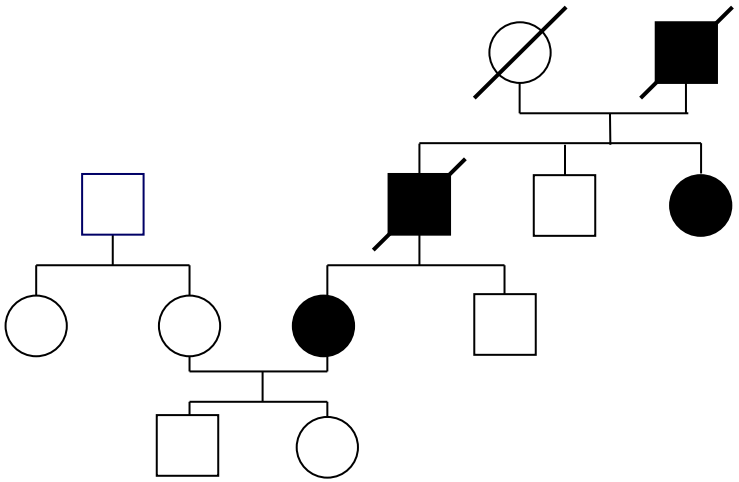
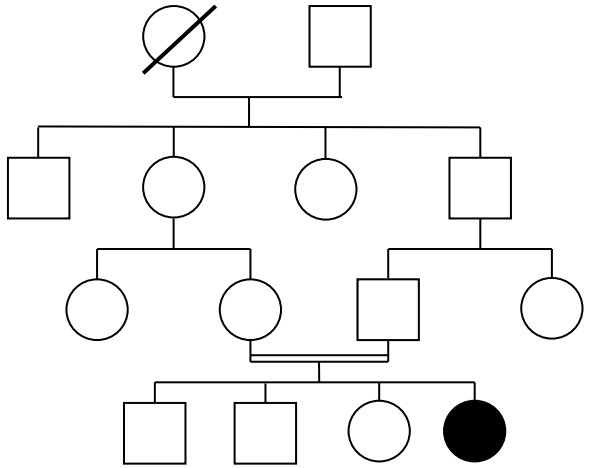
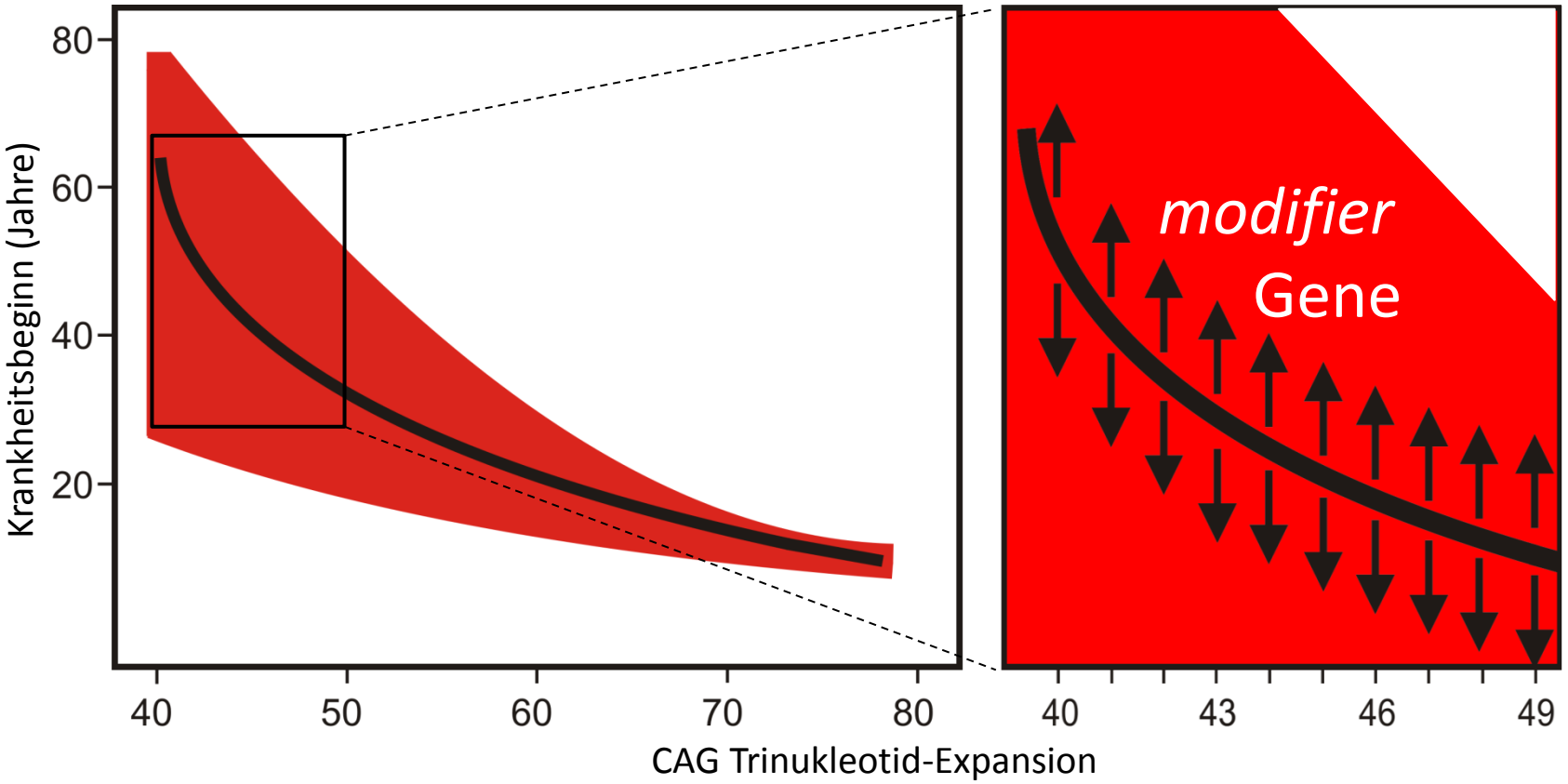
Erbleiden ↔ Epigenetik

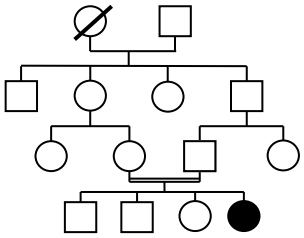




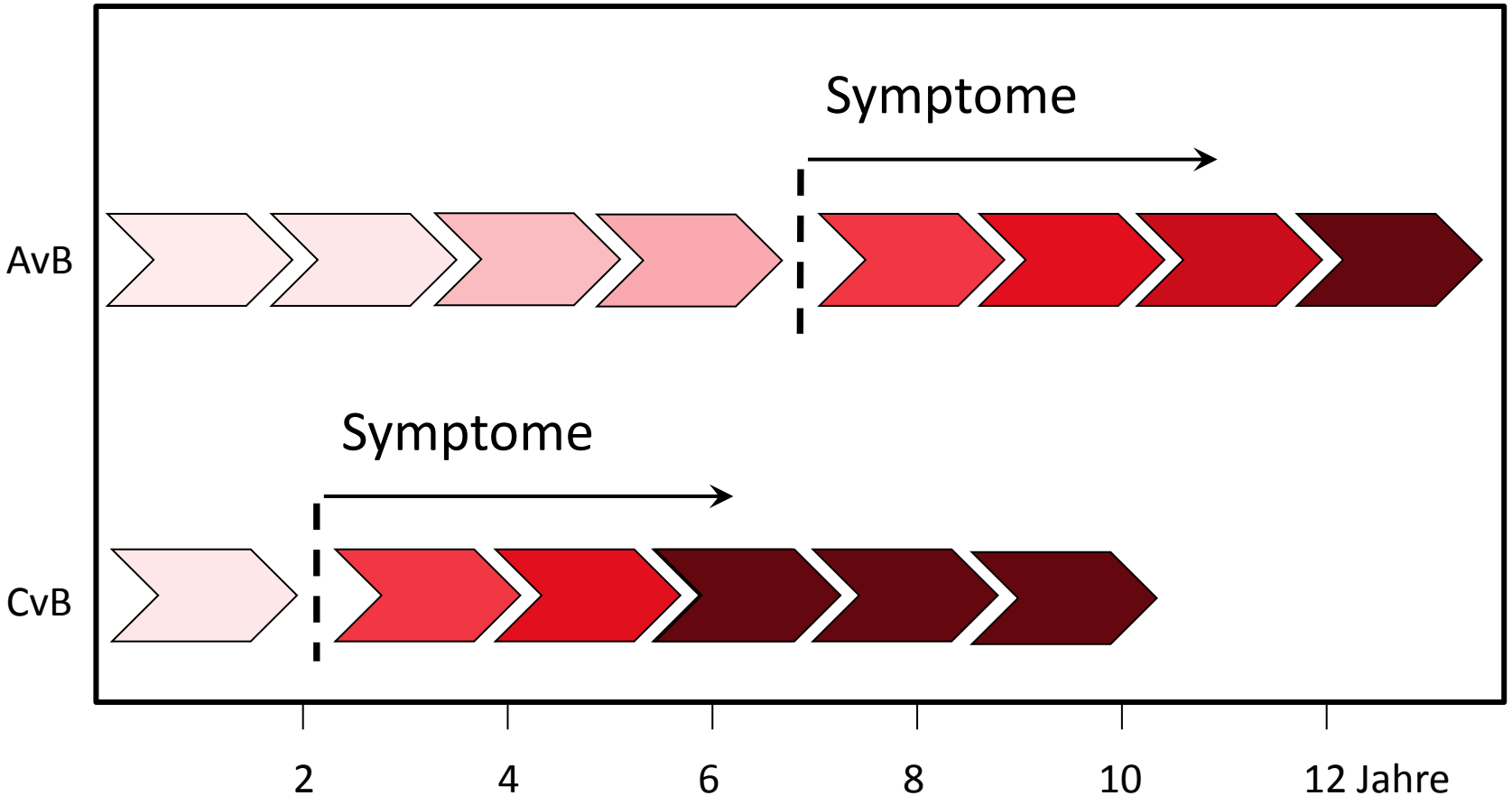
<u>Epistasis</u> (*via modifier* Gene):
Effekt 1 Gens verändert durch 1-x andere Gene

Huntington-Krankheit





(Nacht-)Blindheit



Epigenetik

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Subject: Re: [working-gundog] epigenetics and the origins of pointing

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07/04/2007 7:59 AM

I think we have both argued in the past that the natural point and the trained stand are distinct behaviors. Could the distinction be the result of fundamental differences between brain development processes guided by **epigenetic molecules** working in concert with the genetic foundation and the environment and brain development learning under environmental influence?

Epigenetik: *imprinting* ↔ Prägung

Optimal geprägte Welpen begegnen dem Menschen voller Neugier und Vertrauen.

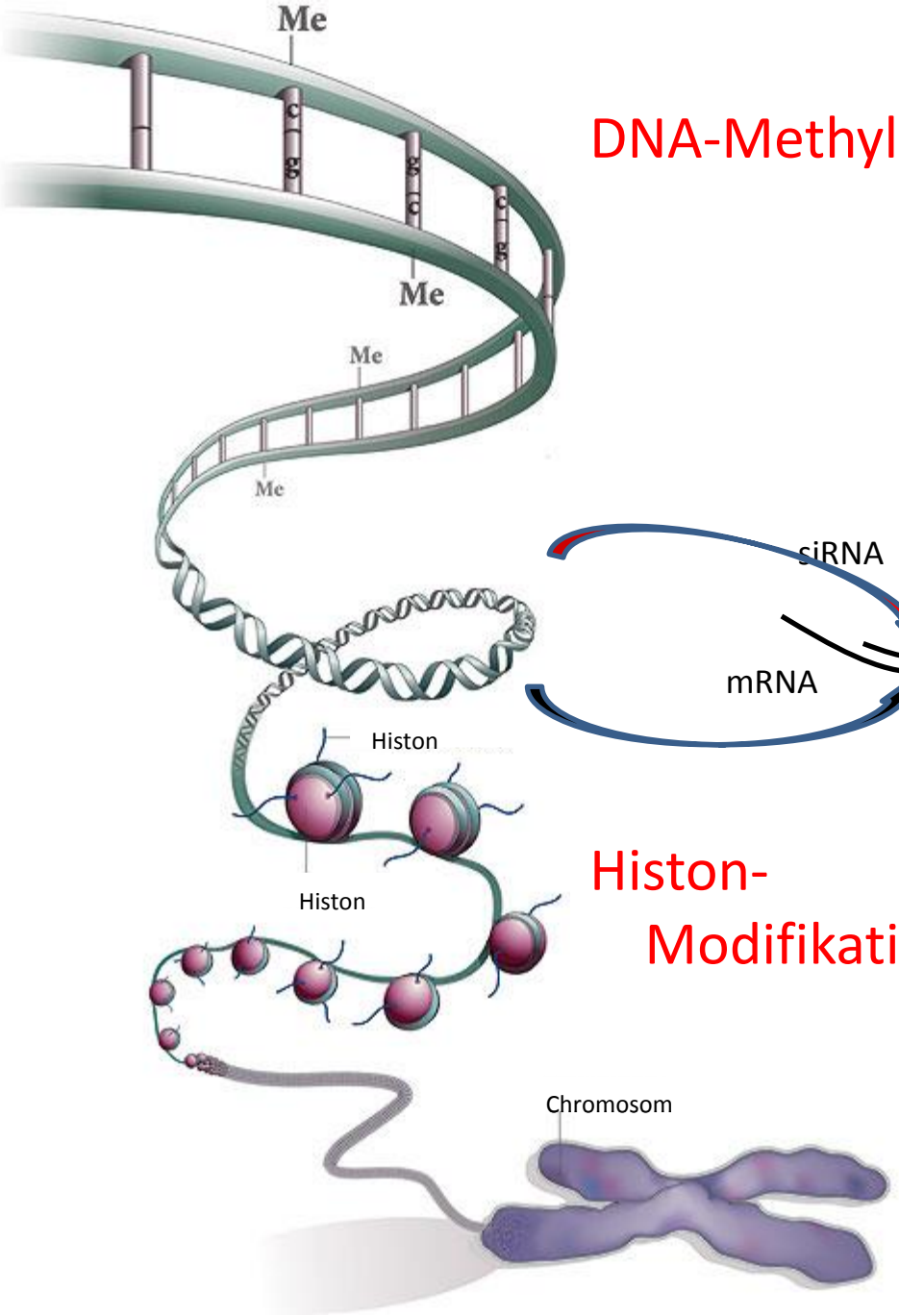
Prägung ist in der Verhaltensbiologie eine irreversible Form des Lernens.

Epigenetik:

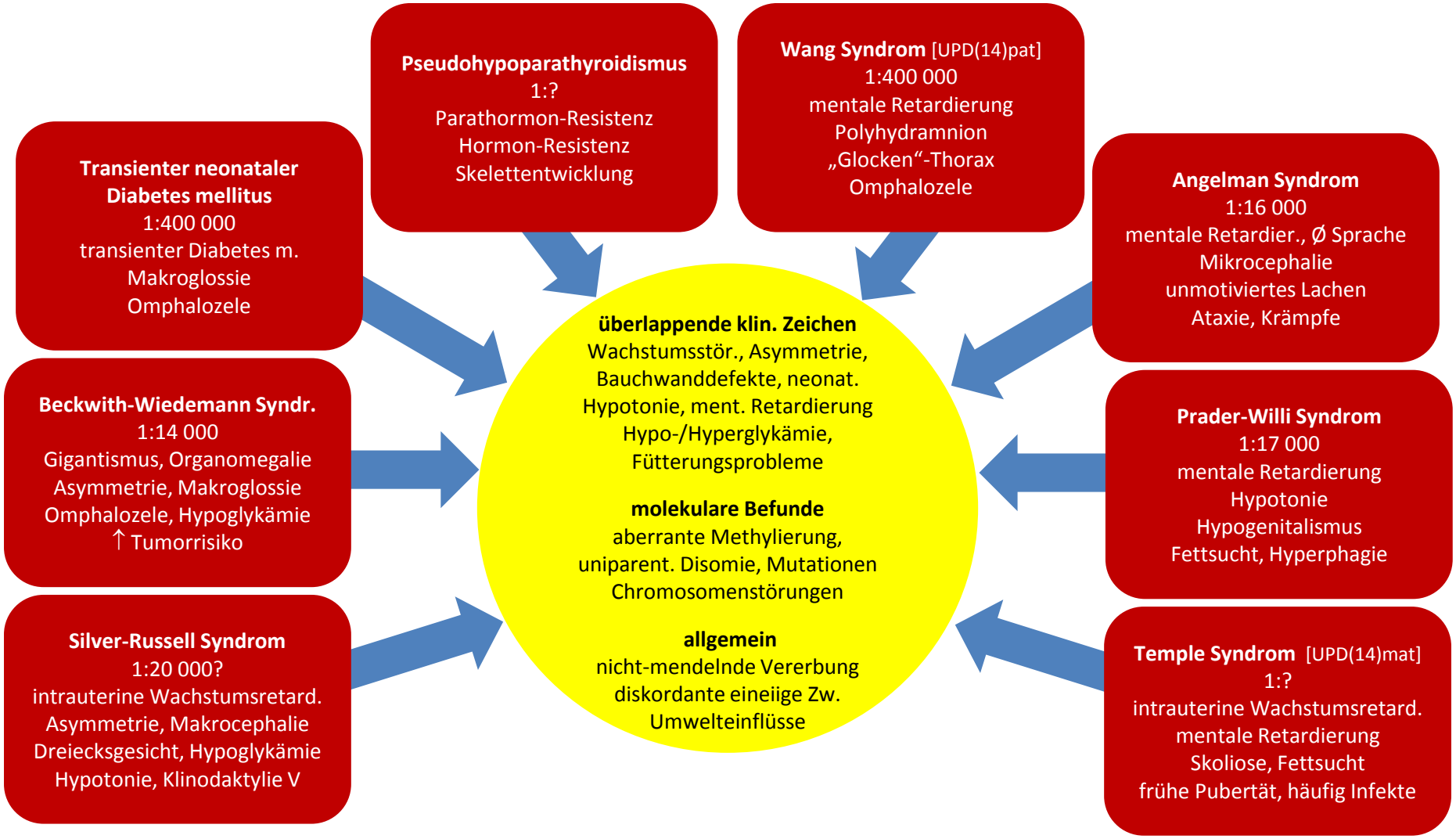
Mechanismen

DNA-Methylierung

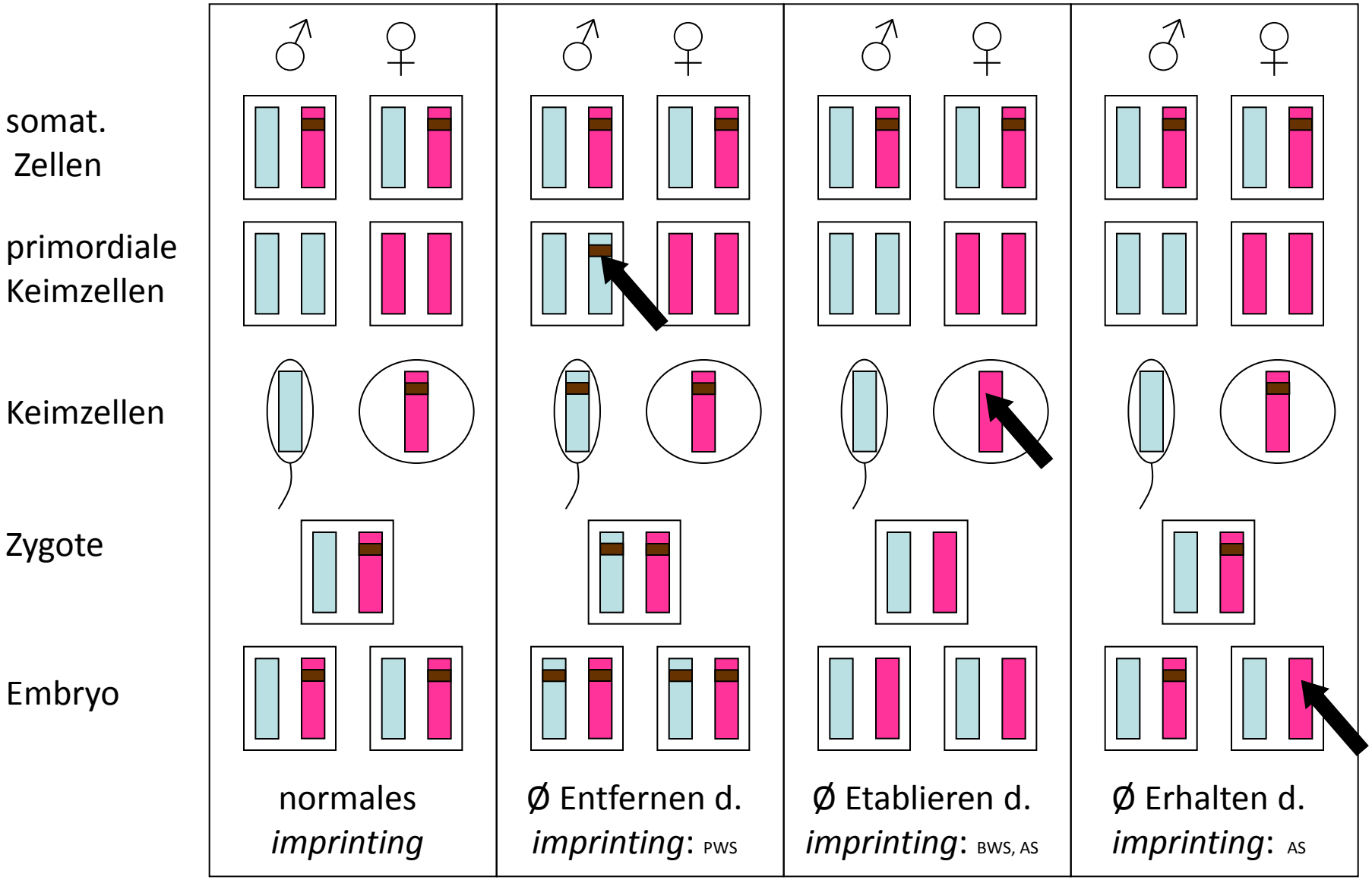
Histon-Modifikation



humane *imprinting* - Erkrankungen

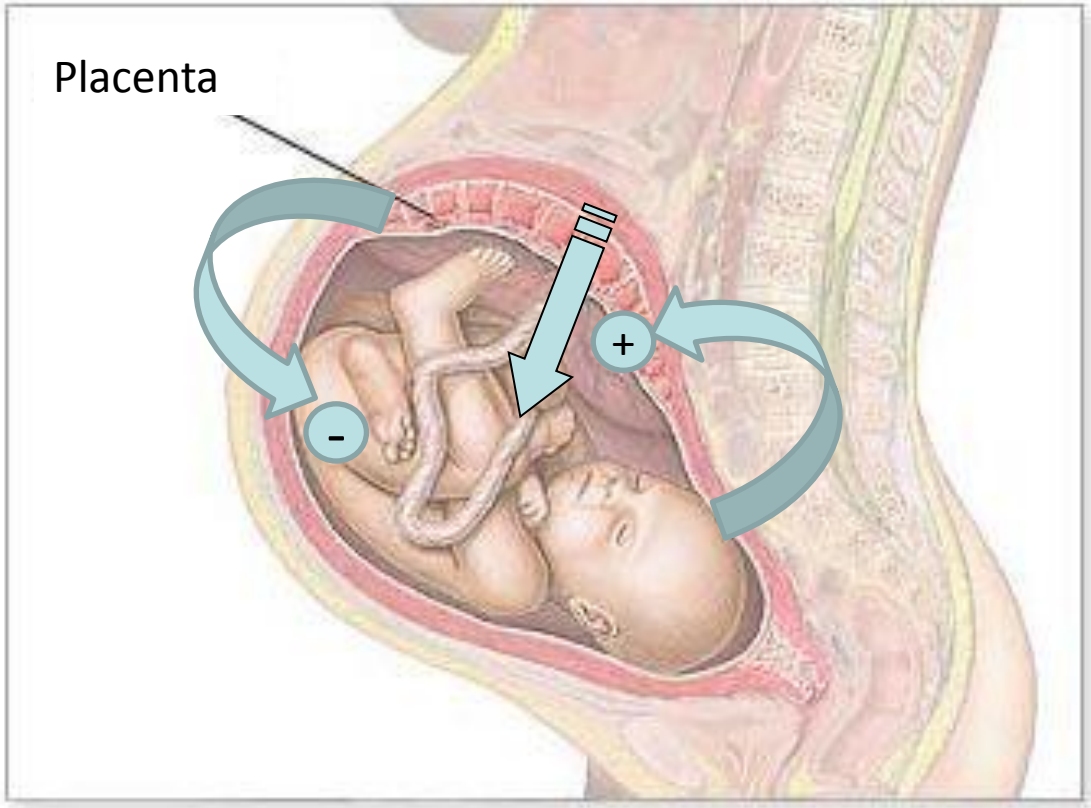


geprägte Gene (*imprinting*)

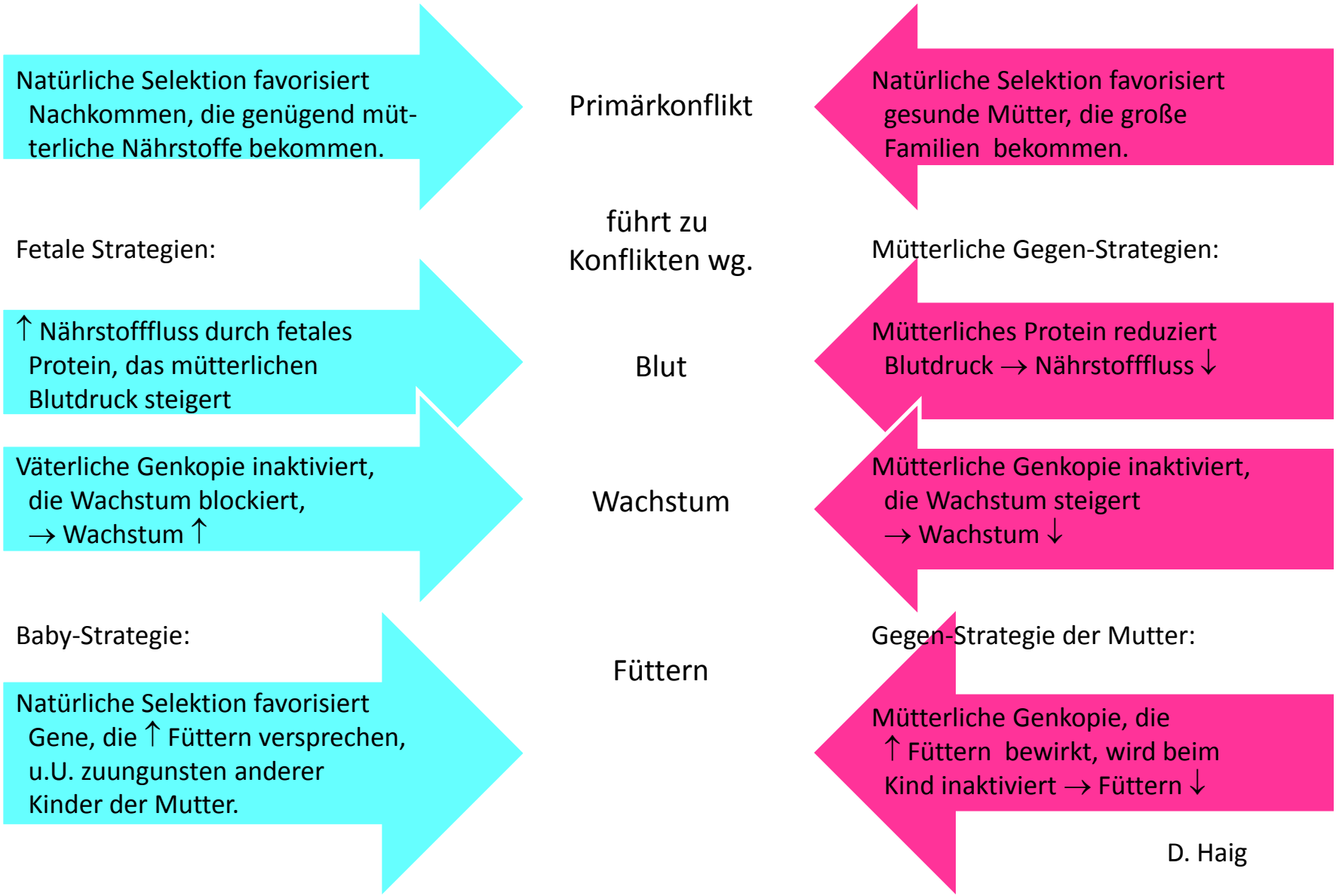


Mutter ↔ Fet (*kinship theory*)

Effekte geprägter Gene auf Resourcen-Bereitstellung



evolutionäre Konflikte: Schwangerschaft



D. Haig

geprägte Gene (*imprinting*)

doi:10.1111/j.1558-5646.2010.01115.x

A MODEL FOR GENOMIC IMPRINTING IN THE SOCIAL BRAIN: ADULTS

Francisco Úbeda[1,2] and Andy Gardner[3]

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[2]*E-mail: fubeda@utk.edu*

[3]*Department of Zoology, University of Oxford, Oxford OX1 3PS, United Kingdom*

Mensch: < 100 geprägte Gene

Sex-Specific Parent-of-Origin Allelic expression in the Mouse Brain

Published as: *Science*. 2010 August 6; 329(5992): 682–685.

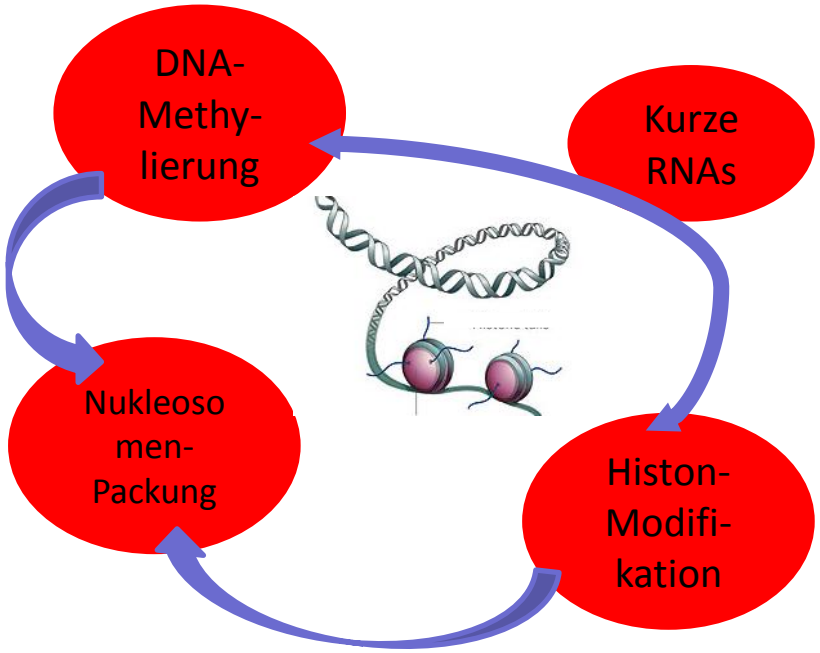
Christopher Gregg[1,2], **Jiangwen Zhang**[3], **James E. Butler**[1,2], **David Haig**[4], and **Catherine Dulac**[1,2,*]

Maus-Gehirn: ~1500

Epigenetik:
geprägte Gene, *Überprogramm* ?

old dogs - new tricks

Schlussfolgerungen
- theoretisch relevant
- “maternaler Großvater-Effekt”
- Forschung !



Schlussfolgerungen

heutige Rassen sind extrem wertvoll

DNA-Tests bedächtig + sparsam einsetzen keine Test-Batterien

genetische Vielfalt bewahren Zuchtpopulation testen

DNA-Biobank einrichten und pflegen Abstammungstest redundant