



IT-Solutions for
Animal Production

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Importance of high quality data base systems in the study of genetic characteristics in horses

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Outline



- ❖ role of genetic defects and characteristics
 - genetic background and examples (cattle, horse)
- ❖ role of data base systems: monitoring and interpretation
- ❖ Warmblood Fragile Foal Syndrome (WFFS) as a famous example
 - disease characteristics
 - statistical analyses: WFFS mutation and equine reproduction data
 - distribution patterns
- ❖ conclusions



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Genetic background

- ❖ replication error during meiosis (parent → offspring)
 - apparent in the next generation
 - consequence could be: neutral, trait, disease or unknown
 - often recessively inherited
- ❖ selection → increase of inbreeding
 - stronger relevance of mutations
- ❖ extensive recording of phenotypes, ancestral and genomic information
 - facilitating the discovery of mutations



Example: Cattle breeding

- ❖ since introduction of genomics
 - discovery of several deleterious genetic defects (BLAD, Brachyspina etc.)
 - as well as: single gene effects without any negative consequences (colour genotypes, polledness, casein etc.)



- genetic characteristics instead of genetic defects



Genetic characteristics in horses

- ❖ routine screening in some horse breeds, e.g.:
 - Arabians (SCID, CA, LFS etc.)
 - Quarter Horses (PSSM, HERDA, HYPP etc.)
- ❖ in the past:
Warmblood breeders not so familiar with molecular genetic testing
- ❖ main point of contact with laboratory work:
 - parentage testing
 - testing for colour genotypes



Role of data base systems

- ❖ how to control, understand and discover genetic characteristics?
 - informative and enough data
 - stored and managed in one central location
- ❖ comprehensive data base system needed for:
 - monitoring and interpretation of genetic characteristics

→ essential for a responsible handling
by the breeding organizations



Warmblood Fragile Foal Syndrome (WFFS)



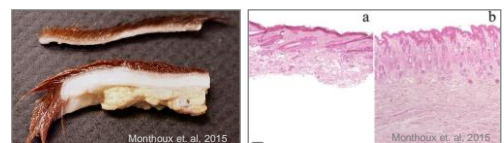
- ❖ hereditary connective tissue disorder in Thoroughbred and Warmblood breeds
- ❖ first described in 2011 (US research group)
 - commercial genetic test since 2013
- ❖ became widely known among breeders in 2018
 - WFFS case in the USA → discussed internationally
- WFFS as an example how to elucidate a genetic characteristic with the help of a comprehensive data base system



WFFS – disease characteristics

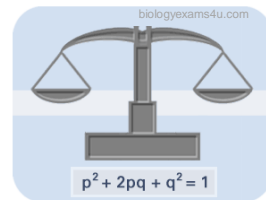


- ❖ point mutation in the PLOD1 gene, recessively inherited
- ❖ consequences of mutation:
 - thin and fragile epidermis – not firmly attached to the subcutaneous tissue
 - even low stress leads to skin rupture
 - hyperextensible joints of the limbs
- ❖ only few affected (homozygous) foals are born → not viable
- what about WFFS related losses?



Hardy-Weinberg equilibrium (HWE)

- ❖ mathematical model from population genetics
 - null hypothesis of relationship between allele and genotype frequencies
- ❖ reported carrier (heterozygotes) frequency of 9.5-15 %
- ❖ mating a carrier sire to the average mare population
 - estimated value of 2.4-3.7 % homozygous offspring (following HWE)



→ 2.4-3.7 % more foal losses (because of WFFS) expected

HWE – Explanation

probabilities of genotypes with random mating (11 % carrier freq.)

sire \ mare pop.	AA (89%)	Aa (11%)
AA (free)	all free (AA)	½ free (AA) ½ carrier (Aa)
Aa (carrier)	½ free (AA) ½ carrier (Aa)	¼ free (AA) ½ carrier (Aa) ¼ affected (aa)

0.25*0.11 = 0.028 ←

expected: 2.8 % homozygous offspring (more foal losses)

Analyses with equine reproduction data



- ❖ covering data from 10 German Horse Breeding Associations
 - N = 426,568 coverings of 10 years (2008-2017)
 - N = 177,582 coverings from stallions with known WFFS status
- ❖ **analyses of variance** with SAS software (v. 9.2, PROC HPMIXED)
 - dependent variable (1/0):
foal was born (1) or foal was not born / died within the first 2 days (0)
 - fixed effects:
WFFS status of the sire, data provider, covering year, age of the mare
 - random effect of the sire himself + random residual

Analysis of variance – Results



- ❖ expectation (following HWE):
 - 2.4-3.7% more foal losses among carriers than free sires
- ❖ results based on all sires with known WFFS status
 - least square means of the foaling rates

dataset restriction	least square means foaling rates		difference free vs. carrier	p-value WFFS status
	carrier	free		
none (a)	0.6393	0.6636	0.0243	0.0304
min. 5 foals per sire (b)	0.6388	0.6638	0.0250	0.0264
min. 5 sire per provider (c)	0.6550	0.6783	0.0233	0.0397
combination of (b) and (c)	0.6552	0.6792	0.0240	0.0347

WFFS – Distribution patterns (I)

- ❖ WFFS known for several breeding populations (cases in USA, SWE, CH, DK, GER)
 - mutation must be rather old
 - first occurrence in a founder who is an ancestor in many populations
 - English Thoroughbred was / is used in many different breeds
- ❖ data analyses: WFFS tested horses (N = 3576) and their ancestry
 - which founder appears in the pedigree of all known carriers?

WFFS – Distribution patterns (II)

- ❖ only horses which appear in every known carrier
 - Dark Ronald xx, born 1905
 - his father Bay Ronald xx, born 1893
 - very influential English Thoroughbred horses
- ❖ skeleton, heart + skin of Dark Ronald xx in a museum in Halle (GER)
 - sample from heart / skin was taken
 - DNA extraction and testing in progress
 - spread of mutation i.a. via Dark Ronald xx and others
- ❖ note: origin of the mutation most likely much older



Conclusions

- ❖ inheritance theory confirmed by foaling rates
 - WFFS as a cause of premature foal losses
- ❖ to avoid affected / stillborn foals and abortion: use the possibilities of modern breeding!
 - WFFS can be controlled by targeted testing and mating
- ❖ one distribution path of the mutation could be found



→ not possible without the power of strong data base systems

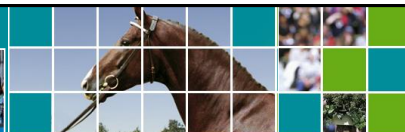


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Thank you !

Take home: frequent mutations → technical advances help elucidating relevant genetic characteristics

→ growing importance of meaningful data collection, responsible data use and strong data base systems



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