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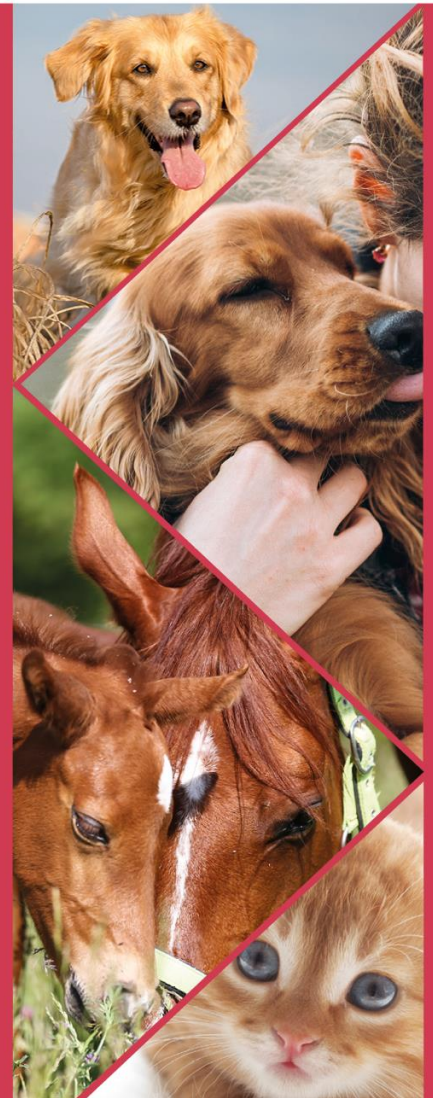
Genetic anomalies in horses

from diagnostics to breeding advice

Leanne van de Goor
VHLGenetics



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- Leanne van de Goor
  - MSc - Animal breeding and genetics, University of Wageningen,
  - PhD - Forensic DNA analysis in animals, University of Utrecht
  - Business Manager VHLGenetics/Combibreed
  - Chair ISAG Equine Genetics and Parentage Testing Standardization Committee
  - No veterinary education/background

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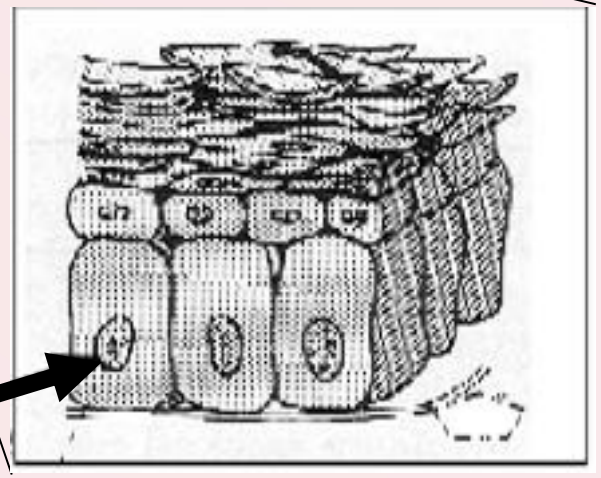
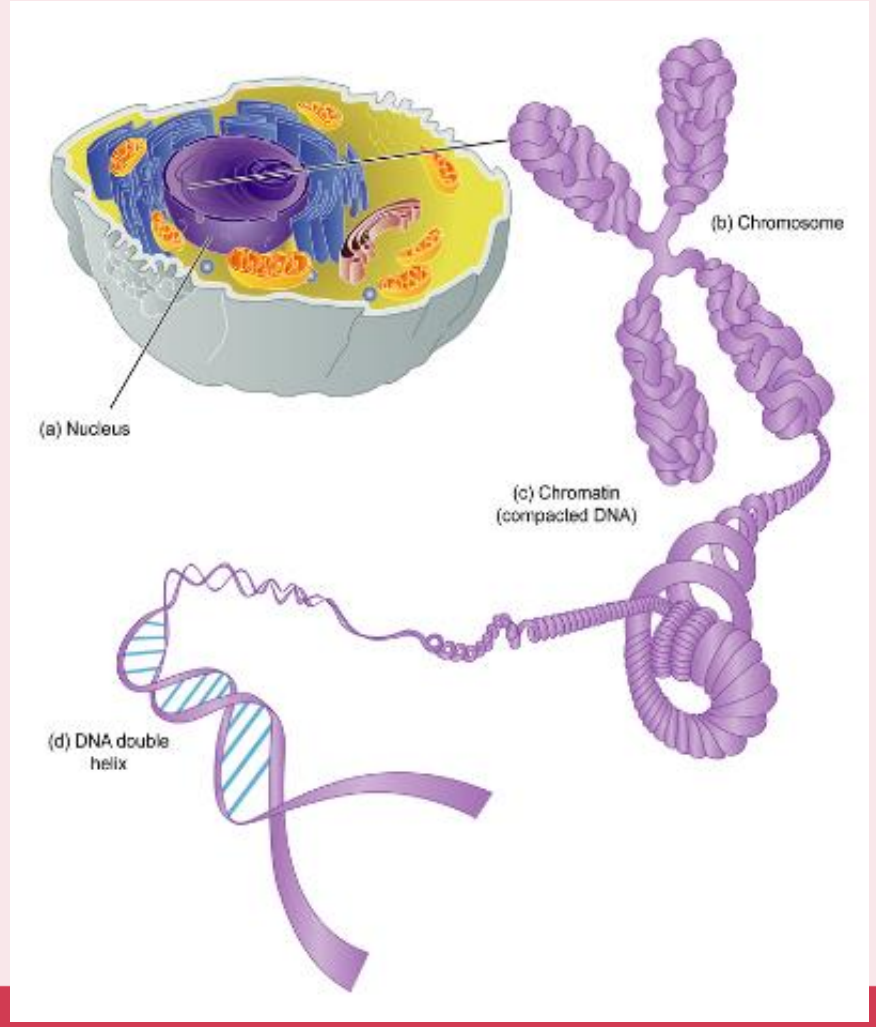
- Genetics and Inheritance
- DNA tests for horses
- Genetics and fertility

Cell to chromosome

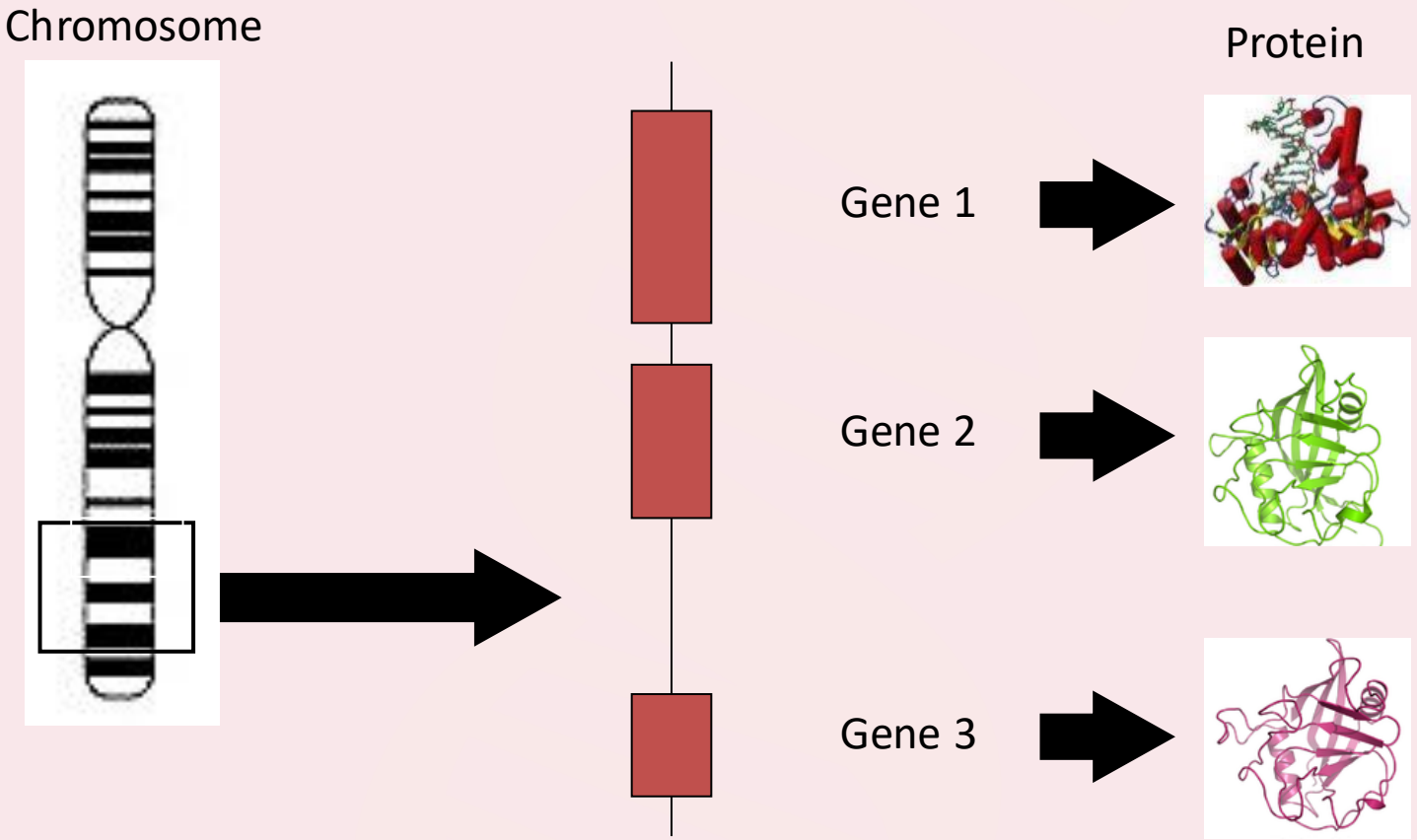
Cell



Nucleus



Chromosome to protein

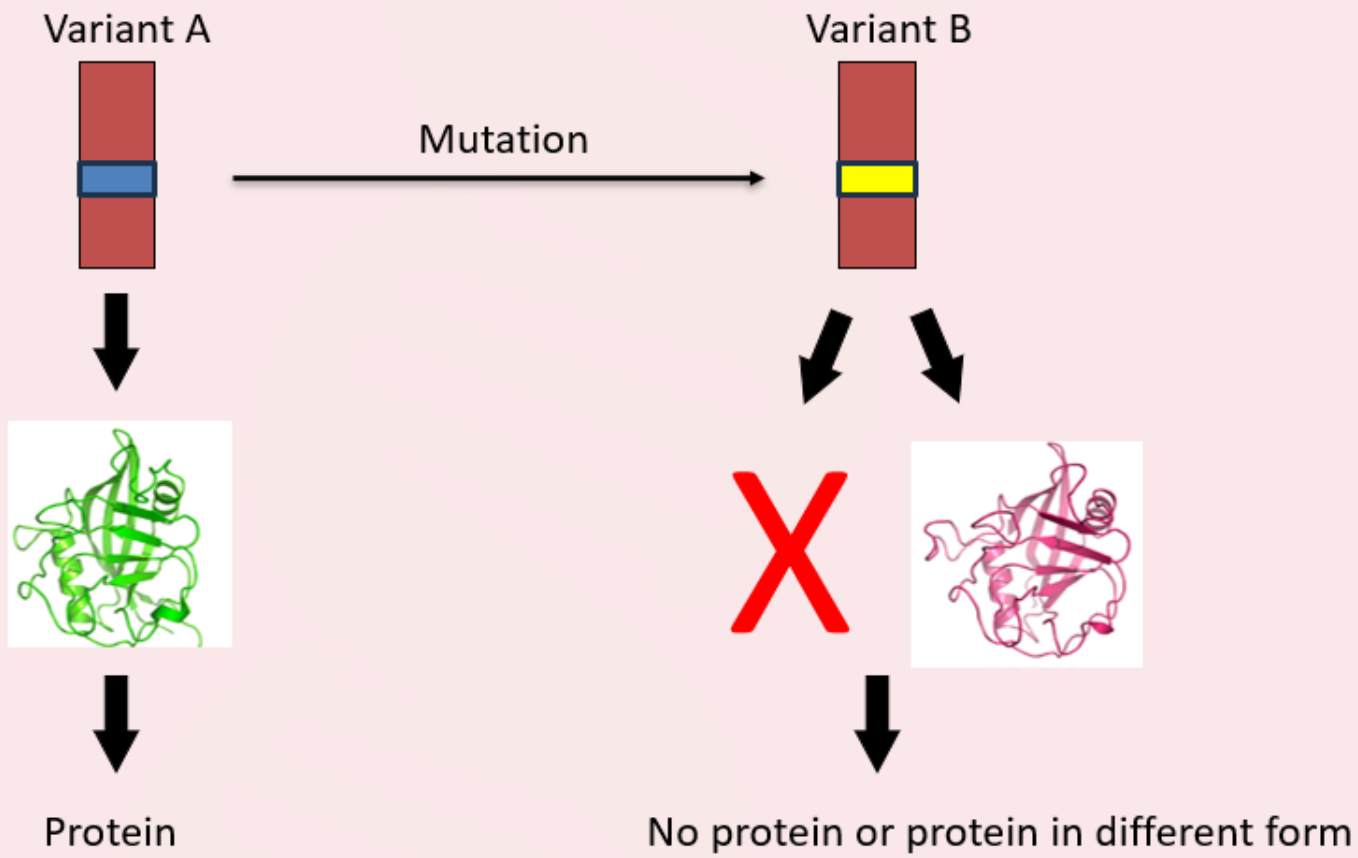


Proteins for example:

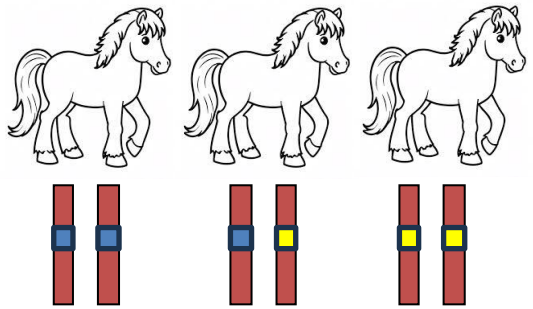
- Hormones
- Enzymes
- Antibodies

Essential for body function

Variation in genes



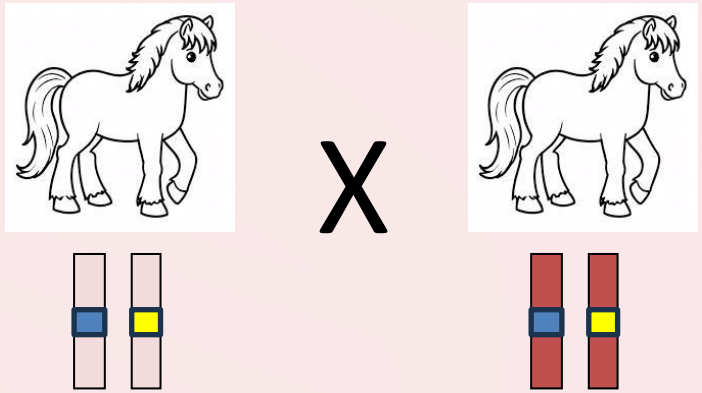
All horses have 2 alleles per gene:
1 from mother
1 from father



DNA Marker: Piece of DNA with variation between individuals
Not all mutations are found in every breed and/or are causal

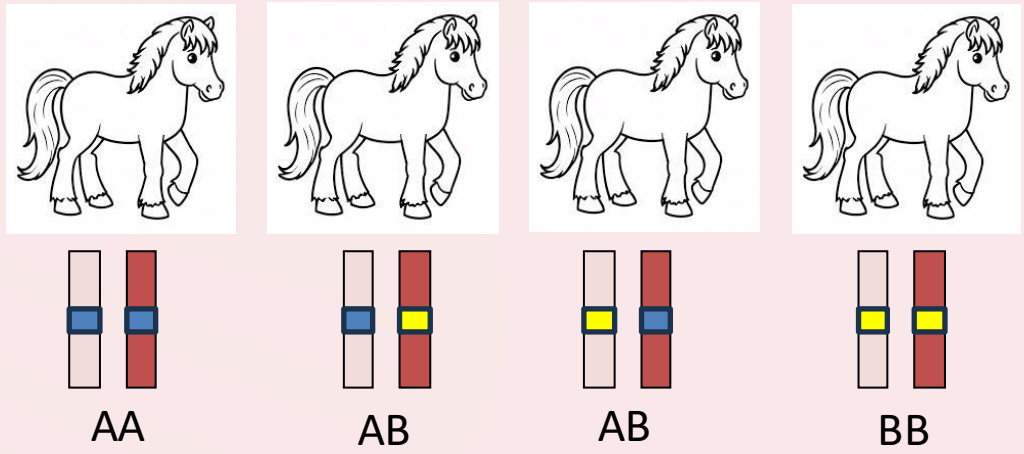
Inheritance of genes

Example mating
carrier (AB) x carrier (AB)



Offspring will inherit the alleles randomly

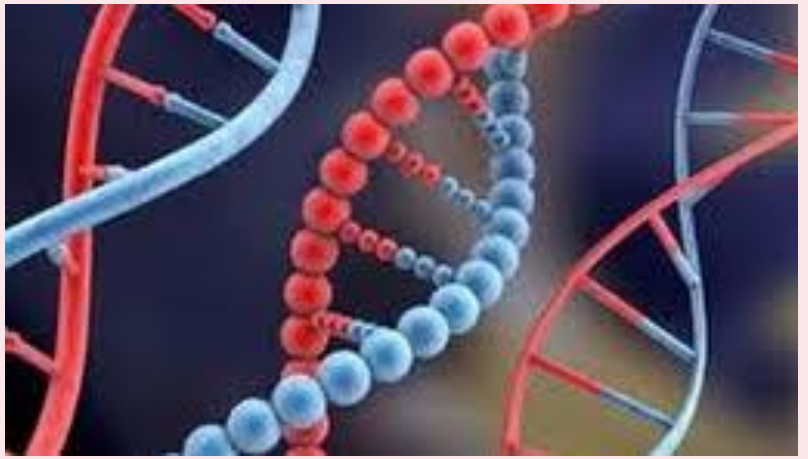
Possible foals



Theoretically:
25% AA (Normal)
50% AB (carrier)
25% BB (affected)

Modes of inheritance

- Monogenic inheritance
  - One gene – direct effect
  - Dominant vs recessive, autosomal vs sex-linked
  - Also incomplete dominant, semi-dominant, co-dominant
  - Relatively easy
- Polygenic inheritance
  - Multiple genes involved, influence each other
  - Complex – risk factor
- Multifactorial inheritance
  - Multiple genes involved, influence each other
  - Also, environmental components involved (e.g. nutrition, exercise)
  - Complex – risk factor



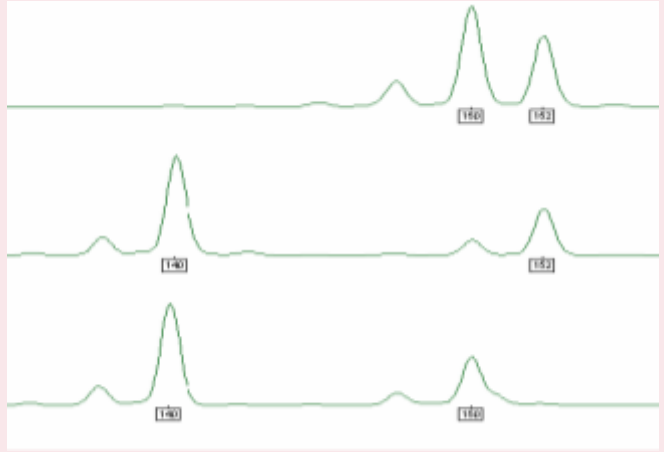
Samples for DNA testing

- Sample collection in horses
  - Hair (± 50 hairs, incl. hairroots)
  - Blood (EDTA, heparin)
  - Reliability results equal

  - ! Karyotyping only sodium heparin blood

Applications DNA-tests horses

- DNA tests can be used for
  - DNA profiles and parentage verification
    - STR vs SNP – profiles are not compatible
    - Samples alleged parents needed
    - Mainly through studbooks
  - Tools for breeding
    - Disorders
    - Traits
    - Genomic Estimated Breeding Value (GEBV)
    - Monitoring
  - Diagnostics (hereditary disorders)
  - Preventative – What can the owner expect
  - Scientific research



Example parentage verification STR

Breed-specific relevance

- Some mutations are ‘breed specific’
  - Not detected in all breeds
    - Scientific research only for breeds in which mutation is detected
  - If mutation appears in ‘new’ breed(s)
    - No scientific research data available
    - Clinical symptoms in ‘new’ breed(s) unkown
    - In case of causative mutation, likely to be causative in other breeds as well

Results DNA tests

- When comparing results of different laboratories
  - Did they test the same disorder or variant of the disorder?
    - Compare gene and mutation
    - Use omia.org when in doubt
      - Online Mendelian Inheritance in Animals
      - Online database of known mutations including scientific publications

Genetic tests relevant for equine vets

- Genetic diseases
  - For diagnosis, for example:
    - Hyperkalemic Periodic Paralysis (HYPP)
    - Polysaccharide Storage Myopathy (PSSM1)
    - Warmblood Fragile Foal Syndrome (WFFS)
    - Hereditary Equine Regional Dermal Asthenia (HERDA)
    - Lavender Foal Syndrome (LFS)
    - Disorders of sexual development (DSD)
    - Repeated Early Embryonic Loss (REEL)
  - For prognosis, for example:
    - Ocular Squamous Cell Carcinoma

Genetic tests relevant for equine vets

- Genetic traits with health concerns
  - Coat colours, for example:
    - Silver Dilution: Multiple Congenital Ocular Anomalies (MCOA)
    - Leopard Complex Spotting (LP): Congenital Stationary Night Blindness (CSNB)
    - Frame Overo: Overo Lethal White Syndrome (OLWS)

Genetics and fertility

- In- or subfertile horses without a medical cause
  - Disorder of Sexual Development (DSD)
  - Repeated Early Embryonic Loss (REEL)

Disorders of Sexual Development (DSD)

- Disorder in which the sex of an animal does not develop correctly
  - Possible at different levels → external genitals, gonads, hormones, chromosomes
  - Some causes are hereditary, some not
  - Possible symptoms:
    - Absent or abnormal oestrus
    - Behaviour not corresponding to sex
    - Body size not corresponding to sex
    - Unusual confirmation or characteristics of the genitals
    - Reduced fertility or infertility

Disorders of Sexual Development (DSD)

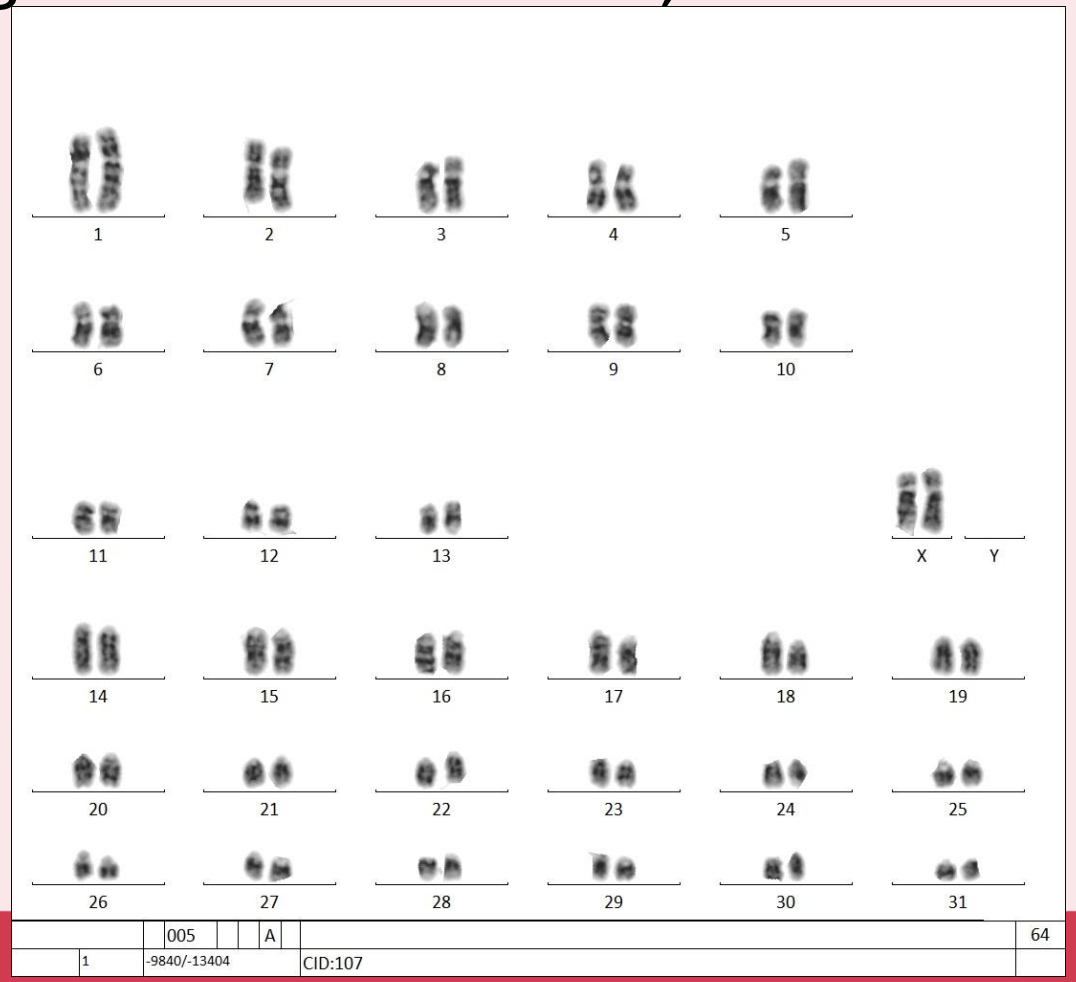
- Genetic cause:
  - Androgen Insensitivity Syndrome (AIS)
    - Mutation in Androgen Receptor gene (AR), X-linked
    - 2 different mutations:
      - Quarter Horse and related breeds
      - Warmblood
    - Hereditary, can be tested with DNA test
    - Impaired function of androgens during embryonic development
    - Development of male characteristics is disrupted
    - Either female-like or male-like genitals, with reduced fertility

Disorders of Sexual Development (DSD)

- Genetic cause:
  - Chromosomal abnormalities
    - Normal 64,XX or 64,XY
      - 31 pair of autosomal chromosomes
      - 2 sex chromosomes
    - Visualisation with karyotyping

Disorders of Sexual Development (DSD)

- Normal karyogram of a mare - 64,XX

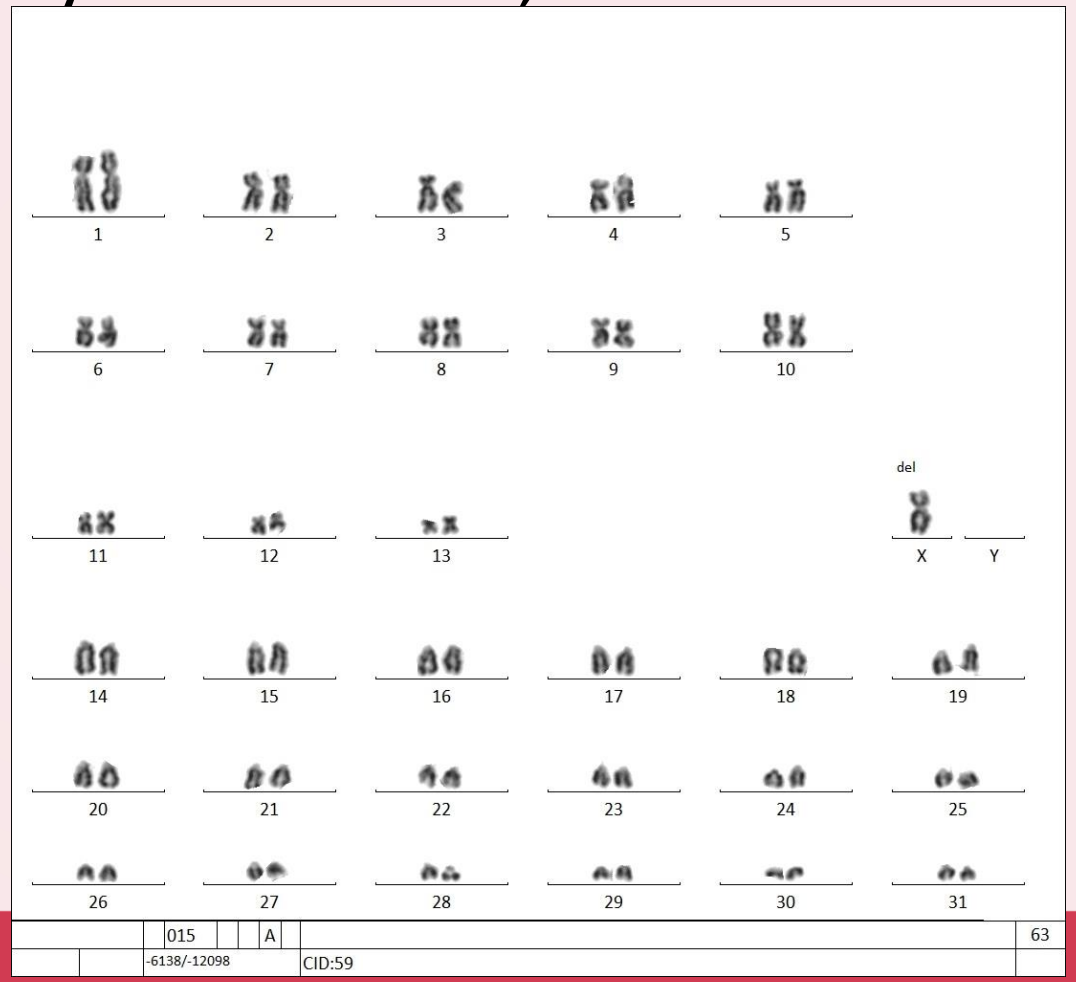


Disorders of Sexual Development (DSD)

- Chromosomal abnormalities
  - Abnormal amount of sex chromosomes, for example:
    - XO – Turner Syndrome
    - XXY – Klinefelter Syndrome
    - Mosaicism – any combination of cells with different sex chromosomes; 64,XX; 64,XY; 63,X; 65,XXY; 66,XXXY etc.
    - YO – not viable, embryonic lethal

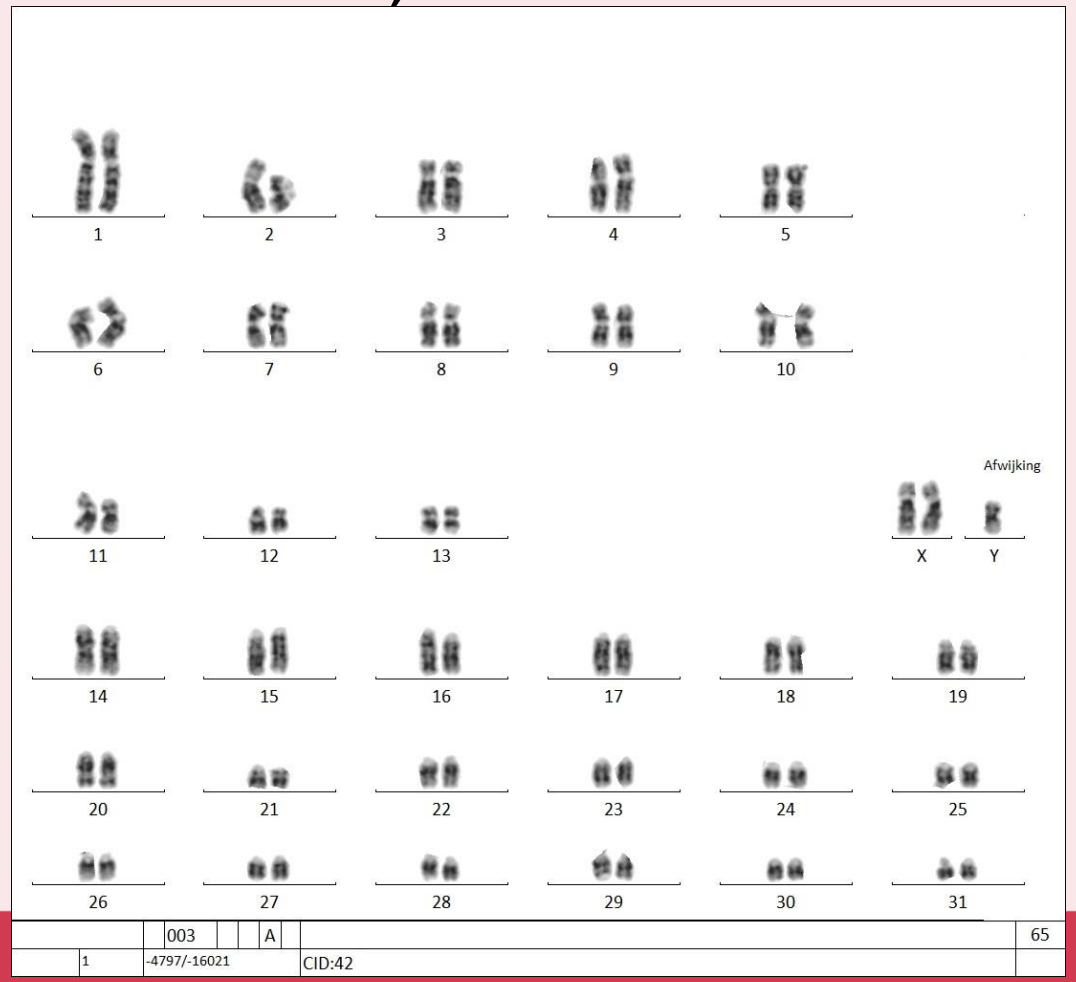
Disorders of Sexual Development (DSD)

- Equine Turner Syndrome - 63,X



Disorders of Sexual Development (DSD)

- Klinefelter Syndrome - 65,XXY



Repeated Early Embryonic Loss (REEL)

- Loss of embryo between fertilization and day 42-65 of gestation
  - Uterine environment
  - Hormonal imbalances
  - Maternal age
  - Embryonic abnormalities
    - Recessive lethal mutations
    - Chromosomal abnormalities
      - Embryo
      - Mare
      - (Stallion)

Repeated Early Embryonic Loss (REEL)

- Chromosomal abnormalities
  - Might cause imbalance in genetic information necessary for embryonal development
    - Depends on exact chromosomal abnormality → is information missing/genes broken?
    - Can be viable or lethal

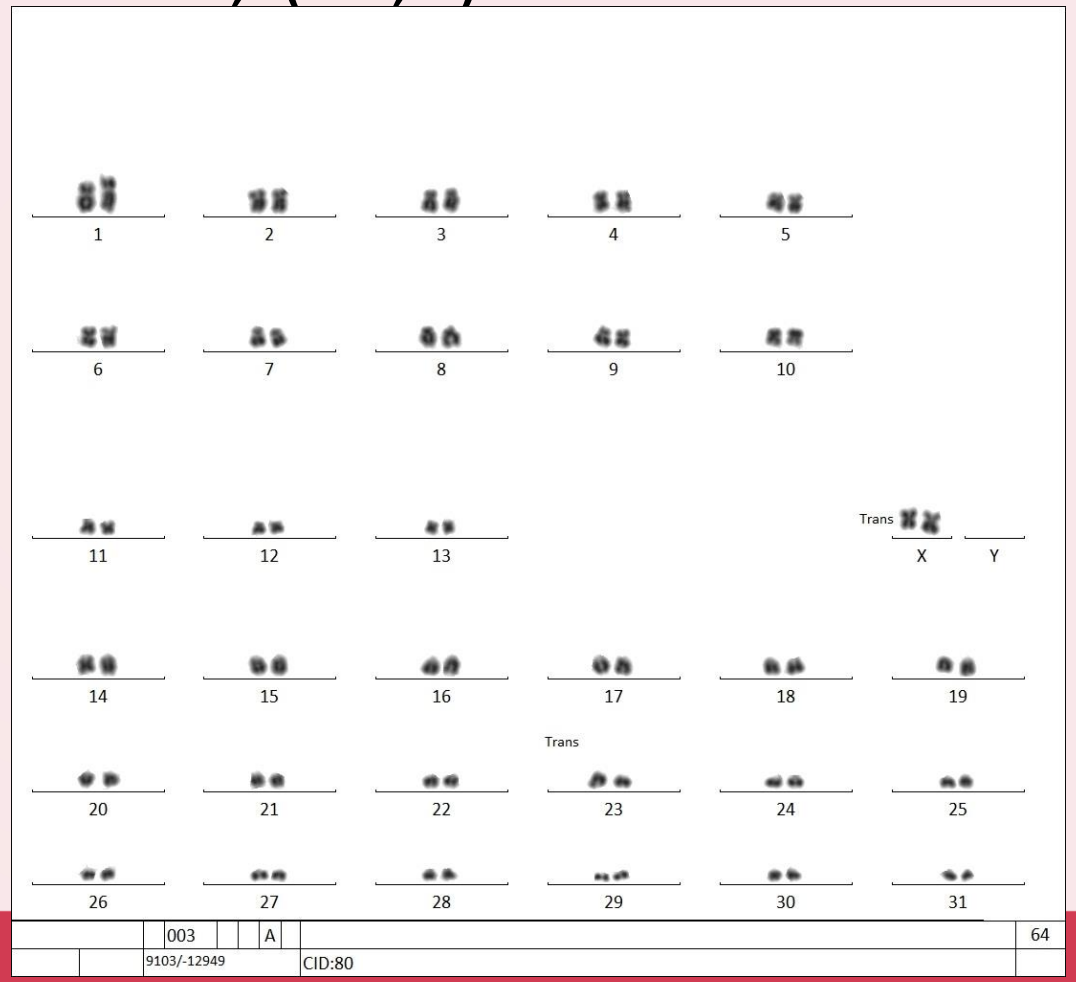
Repeated Early Embryonic Loss (REEL)

- Chromosomal abnormalities
  - Embryo
    - Misarrangement of chromosomes during fertilisation
  - Mare
    - Viable chromosomal abnormality
      - Sex chromosomes → often infertile
      - Autosomal chromosomes → unbalanced gametes → non-viable → REEL

Phenotypically normal mares experiencing REEL may be at risk for carrying a chromosome translocation. Karyotyping can rule out chromosome abnormalities.

Repeated Early Embryonic Loss (REEL)

- Translocation – 64XX,t(23,X)



From karyogram to breeding advice

- Mares with sex chromosome abnormalities are often infertile
  - Cases with viable offspring are described in literature, but unlikely
- Translocations in the mare are a cause of REEL
  - Some causal translocations described in literature
  - Impossible to describe al possible translocations in literature
  - Some translocations might be possible to give viable offspring, but less likely
  - Known to cause reduced litter size in e.g. pigs

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