Analysis of genetic diseases in rabbits and chinchillas

ISAGREED

Modul no. 4: Precision Livestock Farming

prof. Ing. Tomáš Urban, PhD.

Mendel University in Brno

Faculty of Agriscience

Erasmus+ project 2021-1-SK01-KA220-HED-000032068

ISAGREED

Co-funded by the European Union

Genetics diseases

- Genetic disease occurs when a mutation affects the function of genes and thus the physical or functional deviations from the normal state with a negative effect on vitality.
- There are many types, including single-gene, multifactorial and chromosomal disorders.

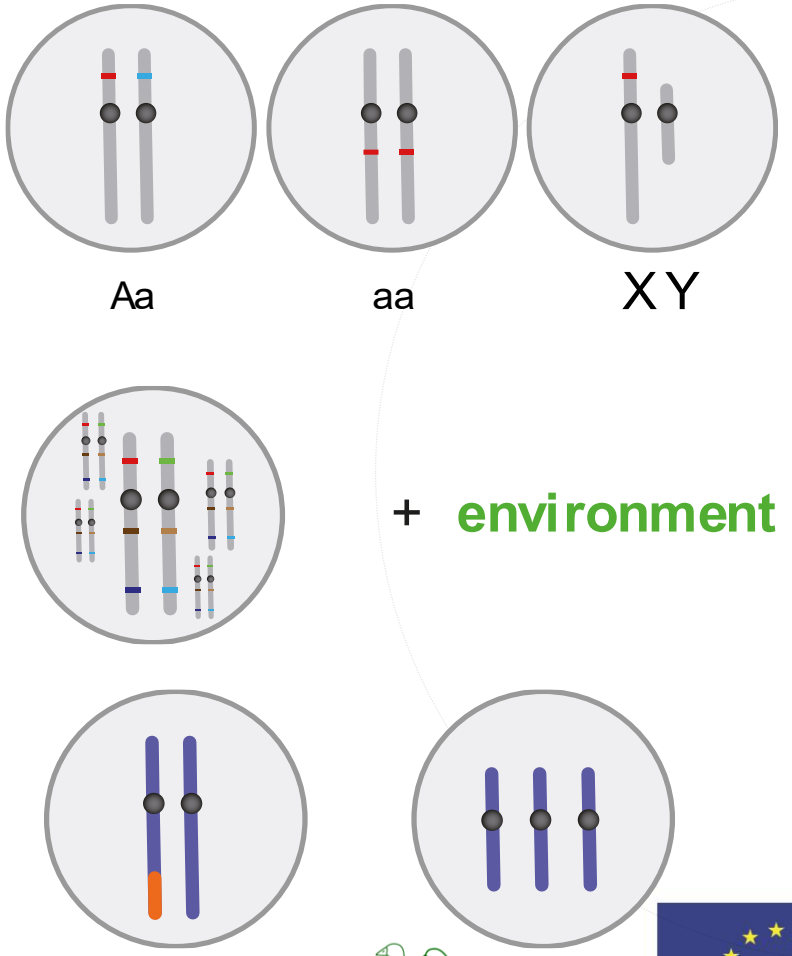
Erasmus+ project 2021-1-SK01-KA220-HED-000032068

ISAGREED
Co-funded by the European Union

Causes responsible for genetic diseases

Genetic disease arises as a result of a mutation and its transmission (~ inheritance) to offspring.

1. **Monogenic diseases** -> mutations in one gene (on one or both chromosomes) - e.g. cystic fibrosis, sickle cell anaemia (mainly metabolic disorders)
2. **Multifactorial inherited diseases** -> combination of variability of many genes and environment (quantitative, complex diseases) - heart disease, diabetes, most cancers, hip dysplasia in dogs
3. **Chromosomal diseases** -> increase or decrease in the number and functions of genes by changing the number of chromosomes, or structural changes in chromosomes



ISAGREED

Erasmus+ project 2021-1-SK01-KA220-HED-000032068

ISAGREED
Co-funded by the European Union

The Genetic Structure of Domestic Rabbits

- The domestic rabbit (*Oryctolagus cuniculus*) is one of the most recently domesticated species (most likely within the last 1,500 years) and is characterized by an exceptionally high phenotypic diversity with more than 200 breeds recognized worldwide
- Breeds vary extensively in weight, body conformation, fur type, coat color, and ear length, and this visible morphological variation dramatically exceeds the phenotypic diversity of their wild counterparts

doi: 10.1093/molbev/msr003

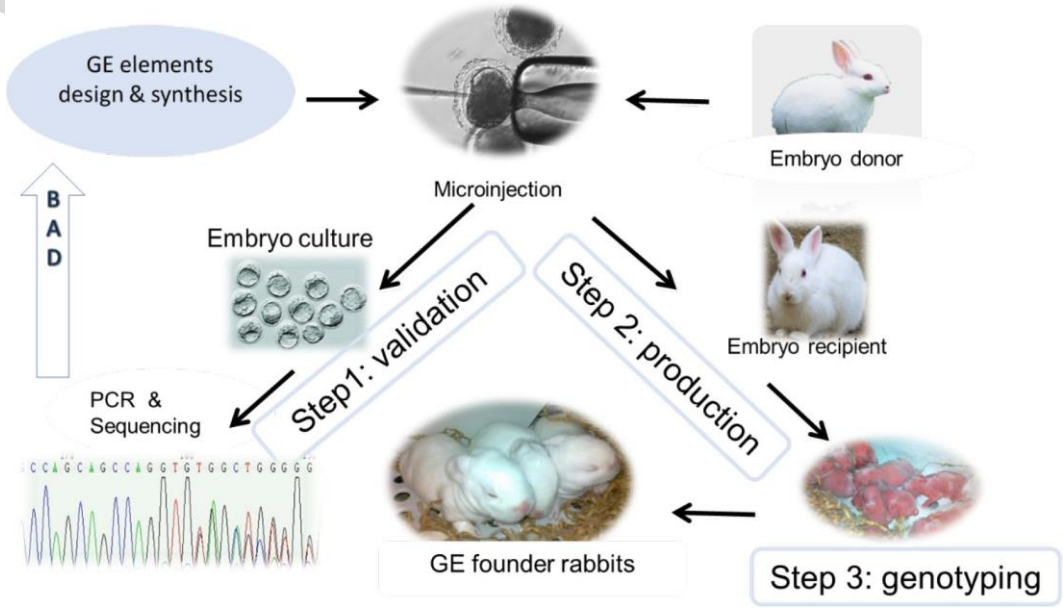
Erasmus+ project 2021-1-SK01-KA220-HED-000032068

Co-funded by the European Union

Rabbit as a model organism for study of human disease

- Normal rabbits serve as models to study human diseases as hyperlipidemia and related diseases, cancer and diabetes mellitus, tuberculosis, papillomavirus infection, atherosclerosis, obesity and type II diabetes, prion diseases, lung and airway morphometry…
- Rabbit is used as bioreactors to produce pharmaceutical proteins - recombinant human C1 inhibitor in milk
- Transgenic/gene edited rabbits are widely used as model organisms for biomedical research (Cystic Fibrosis, susceptible to HIV-1 infection, Human Papillomavirus pathogenesis, Cardiovascular Diseases, Ocular Diseases, Muscular Dystrophy)
- More than fifty gene knockout or knock-in rabbit models have been reported in the past decade
- a new role for rabbits to serve as special tools, especially as models to image organs and tissues *in situ* and *in vivo*

GE rabbit production



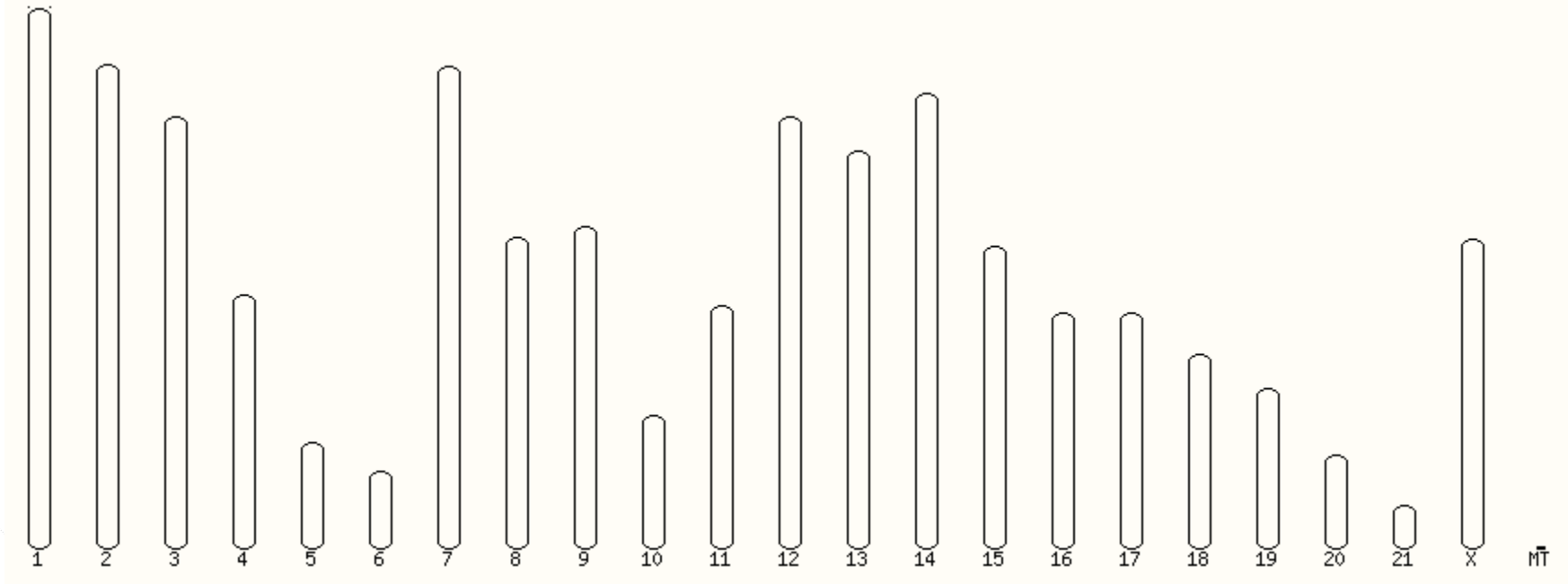
doi.org/10.3389

Erasmus+ project 2021-1-SK01-KA220-HED-000032068

ISAGREED
Co-funded by the European Union

Rabbit genome

- The rabbit genome, RABBIT (OryCun2.0) is 2.7 Gbp in size and contains 20612 protein-coding genes (Ensembl release 54)
- First sequenced in 2009



http://www.ensembl.org/Oryctolagus_cuniculus/Info/Index

Erasmus+ project 2021-1-SK01-KA220-HED-000032068

Co-funded by the European Union

Database of mendelian traits - OMIA

- https://www.omia.org

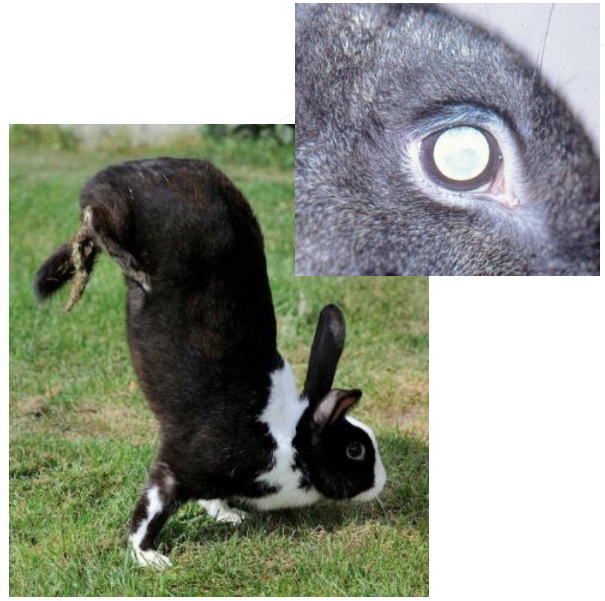
Summary

	dog	taurine cattle	cat	pig	sheep	horse	chicken	rabbit	goat	Other	TOTAL
TOTAL TRAITS/DISORDERS	888	642	415	367	310	268	251	125	116	1128	4611
Mendelian trait/disorder	407	300	138	136	122	62	137	75	25	363	1833
Mendelian trait/disorder; likely causal variant(s) known	345	207	106	66	58	49	58	16	17	204	1144
Likely causal variants	508	271	178	72	90	106	72	20	30	172	1538
Potential models for human traits	570	330	270	207	133	151	87	74	54	633	2556

Co-funded by the European Union

Autosomal recessive disease

- **Oculocutaneous albinism type I** (OCA1), TYR-related
  - Gene ***TYR*** (tyrosinase), 1th chr.
  - 1118C>A substitution giving rise to a missense mutation (Thr>Lys) at codon 373
- **Abnormal gait, retinal dysplasia, cataracts** - disrupts saltatorial locomotion
  - Gene ***RORB*** (RAR-related orphan receptor B), 1th chr.
  - s^{am} allele - g.61103503G>A (in the 5' donor site of intron 9)
- **Adrenal hyperplasia** - Due to the hypersecretion of adrenalin causes death right after parturition
  - Gene ***CYP11A1*** (cytochrome P450, family 11, subfamily A, polypeptide 1),
  - *ah* allele - a large deletion mutation
- **Long hair** - hair growth regulation
  - Gene - ***FGF5*** (fibroblast growth factor 5), 15th chr.
  - Missense mutation, c.571T>C, p.(L191S)



doi: 10.1371/journal.pgen.1009429.g003

doi: 10.1186/s12864-023-09405-2

Erasmus+ project 2021-1-SK01-KA220-HED-000032068

Co-funded by the European Union

Autosomal incomplete dominant

- **Dwarfism**
  - Gene ***HMGA2*** (high mobility group AT-hook 2), 4th chr.,
  - *dw* allele - deletion, a ~12.1 kb deletion overlapping the promoter region and first three exons of the HMGA2 gene leading to inactivation of this gene

doi: 10.1534/genetics.116.196667

Erasmus+ project 2021-1-SK01-KA220-HED-000032068

ISAGREED
Co-funded by the European Union

Chinchilla (*Chinchilla lanigera*)

- Chinchillas are rodents belonging to the Chinchillidae family and are related to guinea pigs and degus.
- There are two species of chinchilla, the short-tailed chinchilla, *Chinchilla chinchilla*, and the long-tailed chinchilla, *Chinchilla lanigera*
- **Chinchilla genome – 2n = 64; first sequenced in 2012**
- Long-tailed chinchilla (ChiLan1.0) with a total sequence length of 2.39 Gbp
- Contains 17809 protein-coding genes

http://www.ensembl.org/Chinchilla_lanigera/Info/Index

Erasmus+ project 2021-1-SK01-KA220-HED-000032068

ISAGREED
Co-funded by the European Union

Fur-chewing

- Many chinchillas kept in captivity develop **fur-chewing**. This behavior does not only affect fur price, but most importantly it can be the result of an animal welfare problém - negative physiological and productive consequences
- Estimated heritability $h^2 = 0.16$
- The selection and management practices used in fur-farming should be improved in order to decrease the incidence of this behavior.

ISAGREED

Erasmus+ project 2021-1-SK01-KA220-HED-000032068

Co-funded by the European Union

Urolithiasis

- Formation of calculi ('stones') in the urinary tract, or the condition associated with the presence of such calculi.
- There is no direct evidence for this disorder being inherited in this species. It has been included because the same disorder is definitely inherited in other species, and there is no reason to believe that the same situation does not apply in chinchillas

Erasmus+ project 2021-1-SK01-KA220-HED-000032068

ISAGREED
Co-funded by the European Union

Skin disease

- *Fur slip:* Fur slip often occurs when the chinchilla is handled roughly or is extremely stressed. The lost fur will grow back, but it may take some time.
- *Fur ring:* Fur rings commonly occur in male chinchillas. A ring of fur can become wrapped around the penis inside the prepuce. This must be removed before it constricts the blood flow to the end of penis. Males, especially those in breeding colonies or housed with other chinchillas, should be checked regularly.
- *Ringworm:* The ringworm organism *Trichophyton mentagrophytes* can cause alopecia in chinchillas. The commonly affected areas include the top of the nose and the pinnae. Often, antifungal powder can be added to the sand bath to treat this condition.

Erasmus+ project 2021-1-SK01-KA220-HED-000032068

Co-funded by the European Union

Infertility

- Poor reproduction may be due to any of several possible causes: malnutrition, abnormal sperm, hormonal imbalance, infectious disease, lack of experience, and lethal genes from inappropriate crosses.
  - For instance, mating between or among chinchillas with matched genes for white and velvet coat color should be avoided.
  - Infectious and dietary factors as well as poor conditioning may also cause infertility in both male and female chinchillas.

Erasmus+ project 2021-1-SK01-KA220-HED-000032068

ISAGREED
Co-funded by the European Union

ISAGREED

Partners:

Mendel University in Brno

Siedlce University of Natural Sciences and Humanities

Czech University of Life Sciences Prague

Thank you for your attention!

This presentation has been supported by the Erasmus+ KA2 Cooperation Partnerships grant no. ***2021-1-SK01-KA220-HED-000032068 "Innovation of the structure and content of study programs in the field of animal genetic and food resources management with the use of digitalisation - Inovácia obsahu a štruktúry študijných programov v oblasti manažmentu živočíšnych genetických a potravinových zdrojov s využitím digitalizácie"****. The European Commission support for the production of this presentation does not constitute an endorsement of the contents which reflects the views only of the authors, and the Commission cannot be held responsible for any use which may be made of the information contained therein.*

Tomáš Urban

urban@mendelu.cz

ISAGREED

Co-funded by the European Union