
# GENETICS VME205

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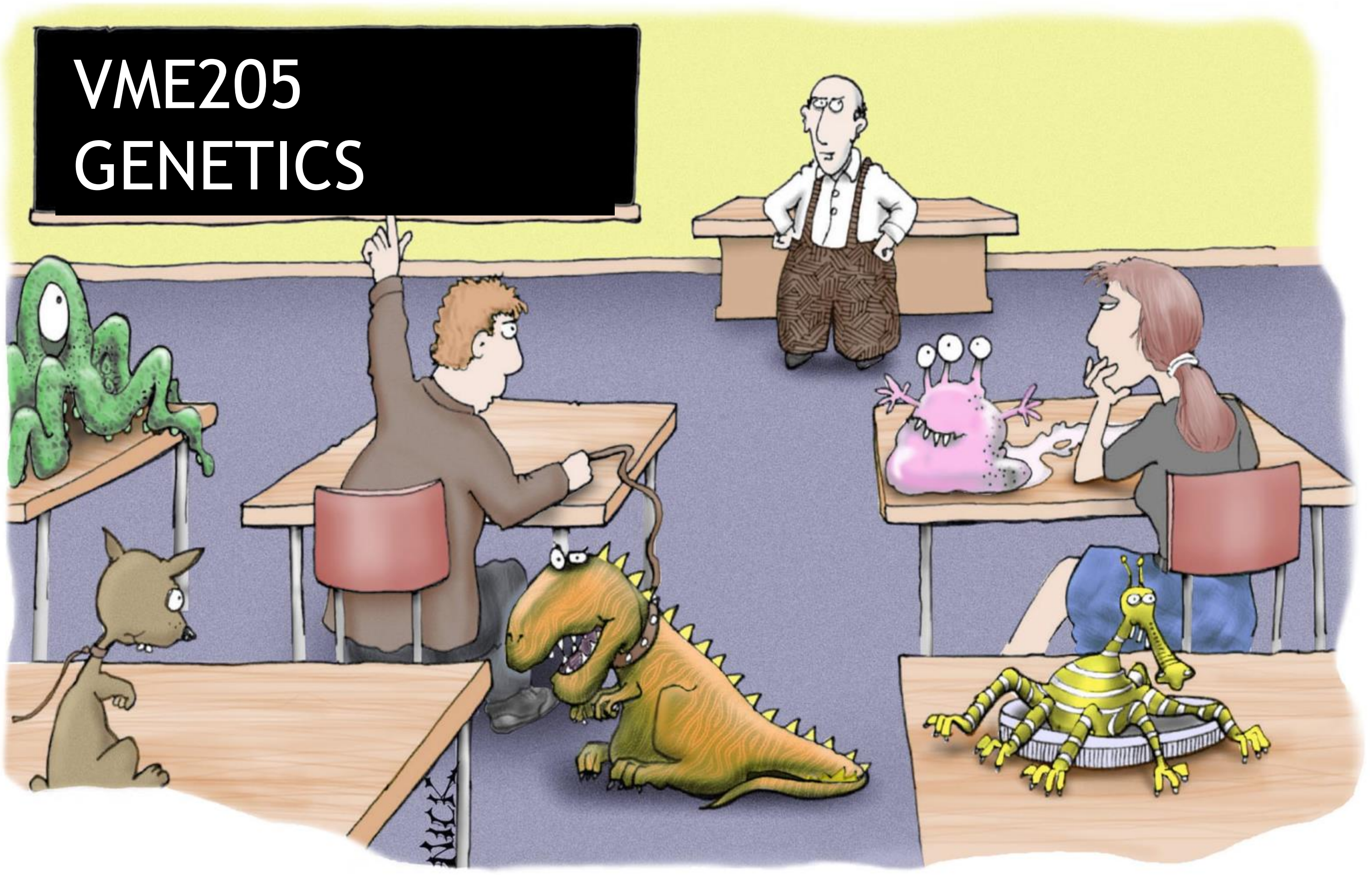
Ankara University Faculty of Veterinary Medicine Department of Genetics

| **Main goals of this lecture:** | |
|---|---|
| | **to learn**<br>**-genetic mechanisms affecting the phenotypic and genotypic characteristics**<br>**-organizing DNA into the chromosomes**<br>**-structure and function of the genomes and genes,**<br>**-mutations types,**<br>**-inherited disorders in animals.** |

**Evaluation**;
40 %  mid term exam
60% final exam
written essay answers, short text answers and multiple choice questions

Homework??.

# VME205 GENETICS

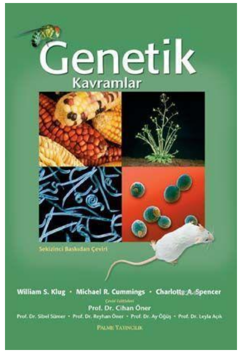


*"Okay—is there anybody ELSE whose homework ate their dog?"*

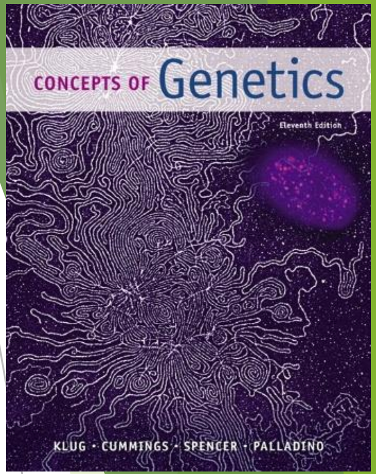
## Lecture content

| Week | Subject |
|---|---|
| 1 | Introduction; History; Definitions, The Place and Importance of Genetics in Veterinary Medicine, Variations; Genotype and Phenotype |
| 2 | The Genetic Make-up of a Cell; Definition of Organism; |
| 3 | Cell divisions; Mitosis and meiosis, Crossing Over; |
| 4 | Mendelian Genetics; Mendel’s Laws |
| 5 | Non-Mendelian inheritance; Interaction of Genes; Interaction of Alleles; Pleiotropy, Penetrance, Expressivity; Interaction of Non-Allele Genes; Epistasis; |
| 6 | Structure of DNA and RNA; Structure of Genes and Genomes; Chemical Composition of DNA and RNA |

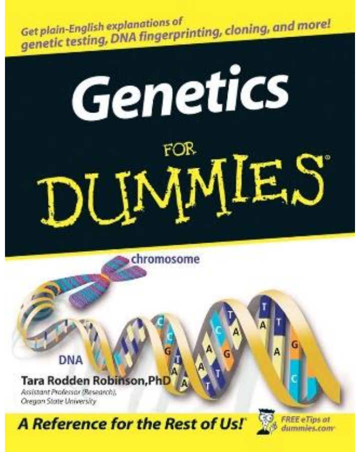
| Week | Subject |
| --- | --- |
| 7 | Structural Features and Organisation Chromosomes; Inheritance of Gender; Gender Defects, Inheritance of Characters Related with Gender; |
| 8 | DNA Replication in Prokaryotes and Eukaryotes |
| 9 | Transcription, gene expression |
| 10 | Translation and Protein synthesis |
| 11 | Mutations; Causes of Mutation; Chromosomal Aberrations; Numerical and Structural Chromosome Aberrations, Point Mutations (Base Mutations) |
| 12 | Multiple Alleles; Polymorphism |
| 13 | Inherited disorders in Livestock; Identification and elimination of Detrimental Genes, Pedigree Analyses |
| 14 | Role and Importance of Biotechnology in Veterinary Medicine; Analysis of DNA Sequence; Polymerase Chain Reaction; Analytical Approaches to Solve Genetical Problems |




Klug, W. S., & Cummings, M. R. *Concepts of genetics* Pearson Education, Inc.

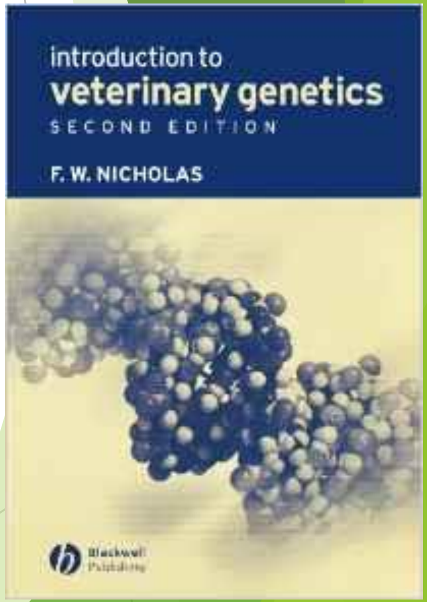



Genetik Kavramlar, (Türkçe Çeviri) Öner C., Palme Yayınevi




Robinson, T. R. *Genetics for dummies*. John Wiley & Sons.

Nicholas, F.W. *Introduction to Veterinary Genetics*. Oxford University Press Inc




You are wellcome to our library, whenever you want


To the laboratories...


**Research Projects Completed by Undergrads.**

-**TUBİTAK →** The Scientific and Technological Research Council of Turkey
2209-Undergraduate Research Projects Funding Program

-**BAP →** Ankara University Scientific Research Projects Coordination Unit

**TUBİTAK -2209 –**
**Title: İdentification of the *BoLA-DRB3 gene Polymorphism in ANATOLIAN BLACK CATTLE by PCR-RFLP***
**Researcher:** Mustafa Yenal AKKURT
**Supervisor:** Prof. Dr. Okan ERTUĞRUL

**BAP**
*Title: DNA sequencing of the Melanocortin1 Receptor Gene in KANGAL Dog Breed.*
**Supervisor :** Prof. Dr. Okan ERTUĞRUL
**Researcher :** Ahmet YURTSEVEN

# We will begin this course with a quick question:
# What is Genetics?

- This question will take us fourteen lectures to answer…
- the answer is hidden in the milestones of genetics…

# History of Genetics

**People have known about inheritance for a long time…**


**Offsprings resemble their parent**

**Person can be identified as a member of a particular family through particular traits.**

**Selective breeding for desired characters**

# Ancient theories

**several incorrect ideas generated and overcome…**

- ✓ "preformation" tiny, fully-formed human in each sperm (or egg)

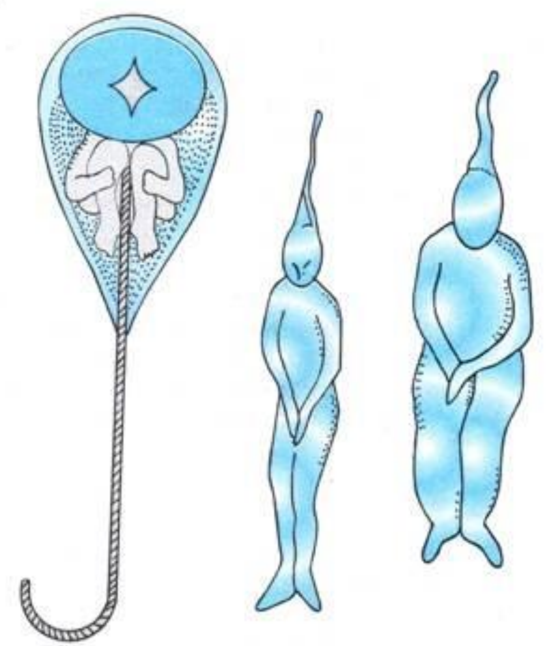
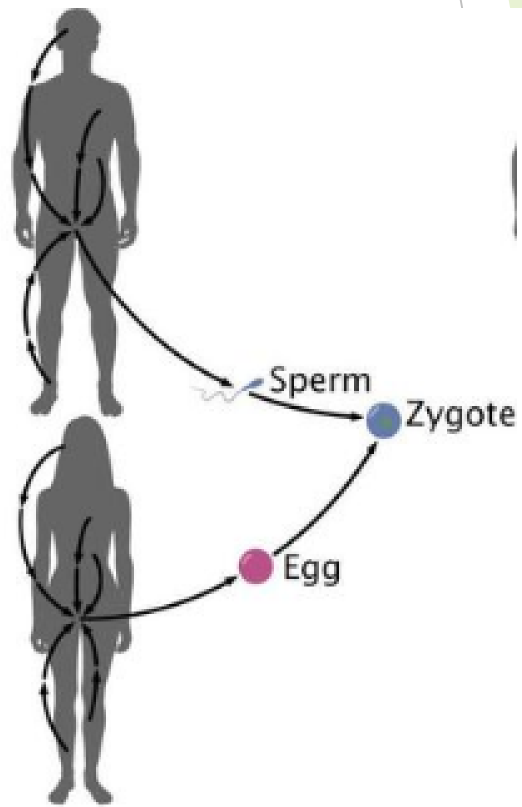


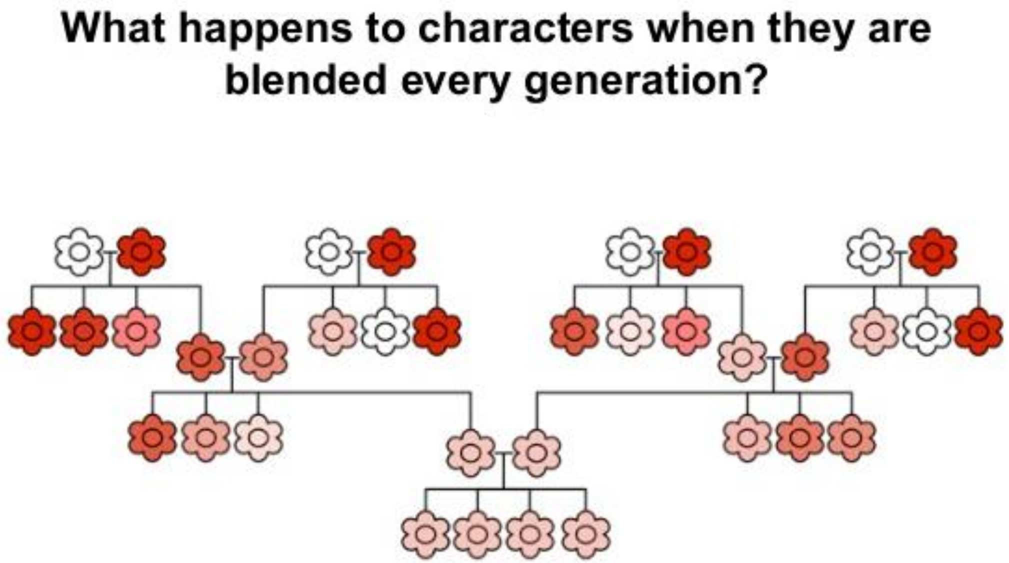
Fig. 5.2. 'Homunculus' "little man in a sperm cell"
(From journal des Scavans, Feb. 7, 1695).

# Ancient theories

- ✓ ancient Greek idea: male plants a “seed” in the female “garden”.
- ✓ Aeschylus: the male as the parent and the female as a nurse for “the young life sown within her”
- ✓ Hippocrates: “seeds” were produced by various body parts and transmitted to offspring at the time of conception



- ✓ **Blending theory:** The mixture of sperm and egg resulted in progeny that were a “blend” of two parent’s characteristics.

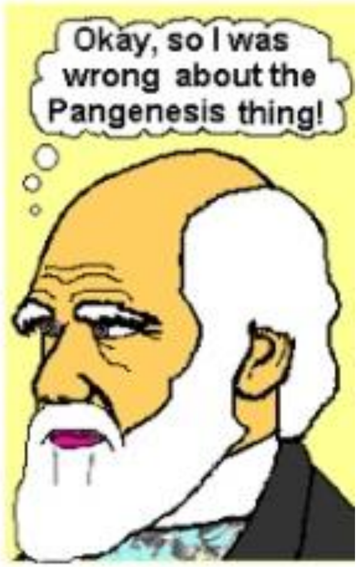



## **Pangenesis theory:** every part of the body contribute to egg or sperm.

Darwin's hypothesis of Pangenesis

"Gemmules" travel from every part of the body to the reproductive system to pass the traits to future generation.

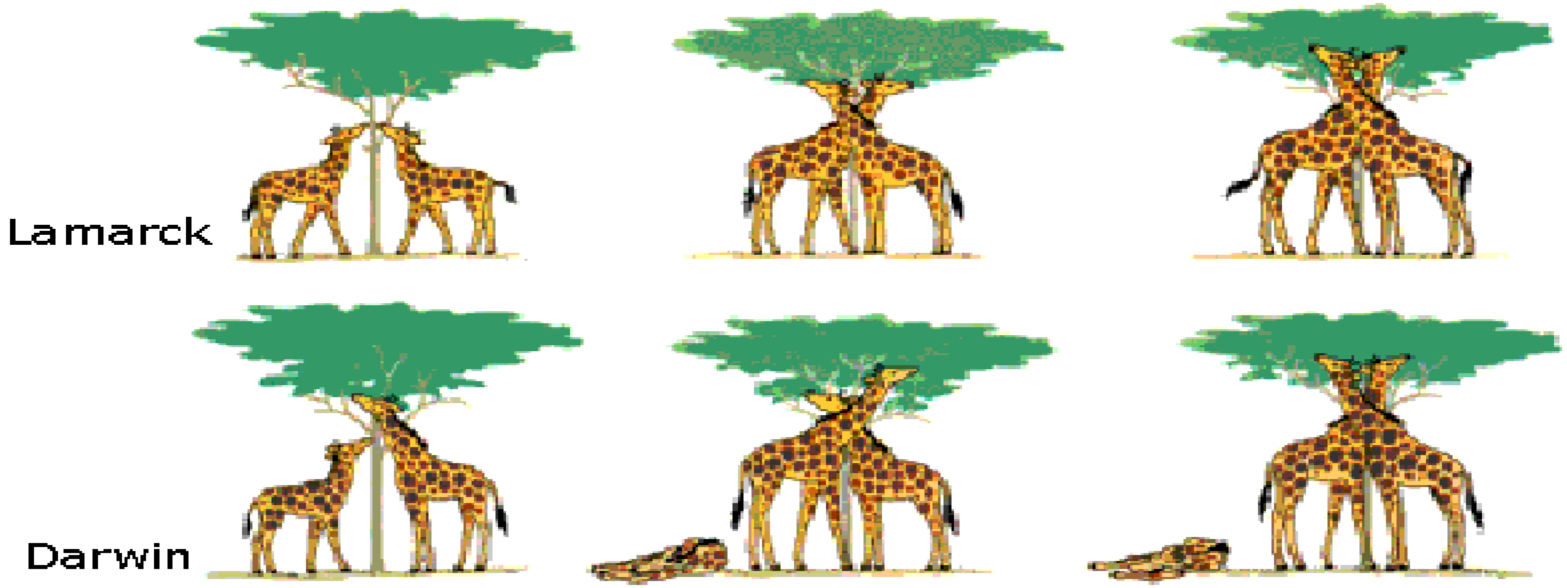
Hypothesis **NOT** supported by scientific evidence.




O'Connor, C. & Miko, I. (2008) Developing the chromosome theory. Nature Education 1(1):44

# Acquired characters inheritance =Lamarckism (Jean Baptiste Lamarck)

Individuals inherit traits are strengthened by their parents




Homework: can this theory accept as true in nowadays? or Is it still wrong?

# Comparing Lamarck's and Darwin's Theories

Question: Why is it that giraffes have long necks?

Lamarck's answer:

→ giraffes stretched their necks in order to reach the leaves in trees to eat (law of use and disuse)

→ the stretched neck acquired throughout a parent's life was passed on to its offspring (inheritance of acquired characteristics)

Darwin's answer:

→ in the beginning, there were giraffes with short necks and giraffes with long necks

→ the long-necked giraffes could reach the food easier while short-necked giraffes could not. The short-necked giraffes died off due to starvation

→ the long-necked giraffes produced more giraffes with long necks, and eventually all giraffes has long necks

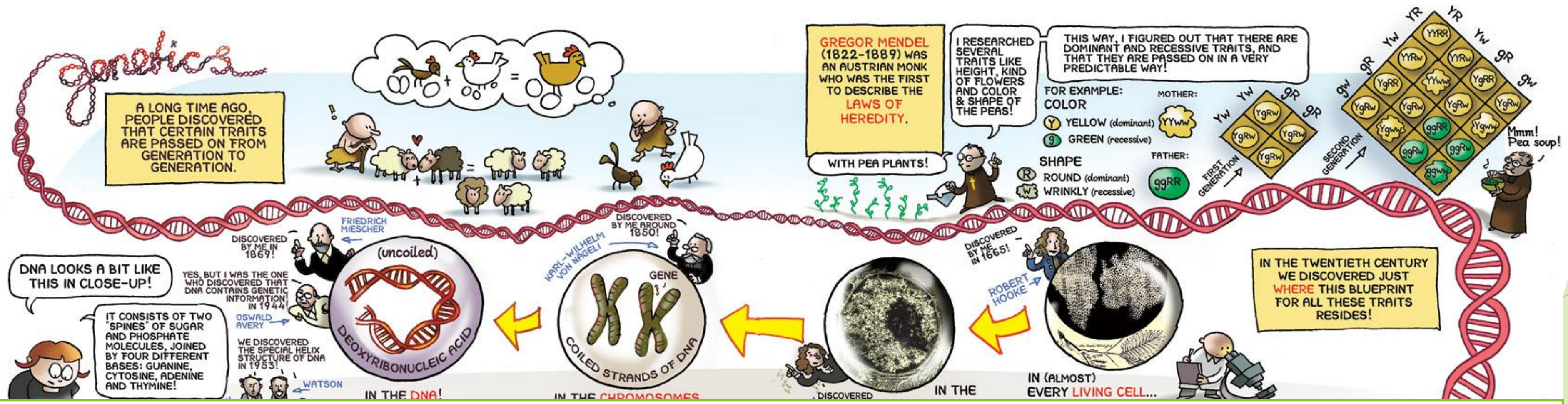
# 1800's milestones

- **Three major events** in the mid-1800's led directly to the development of modern genetics.

1859: Charles Darwin publishes *The Origin of Species*, which describes the theory of evolution by natural selection.

1866: Gregor Mendel publishes Experiments in Plant Hybridization, which lays out the basic theory of genetics. It is ignored until 1900.

1871: Friedrich Miescher isolates "nucleic acid" from pus cells.



# 20th Century's milestones

- 1900: Mendel's work rediscovered by three scientists working independently in different countries.
- Robert Correns, Germany
- Hugo de Vries, Holland
- Erich von Tschermak, Austria

(a) Gregor Mendel

(b) Carl Correns

(c) Hugo de Vries

(d) Eric von Tschermak

Mendel published in 1866, was not appreciated in his lifetime.

- 1902: Archibald Garrod discovers that alkaptonuria, a human disease, has a genetic basis.
- 1904: Gregory Bateson discovers linkage between genes. **Also coins the word "genetics".**
- 1910: Thomas Hunt Morgan proves that genes are located on the chromosomes (using Drosophila).

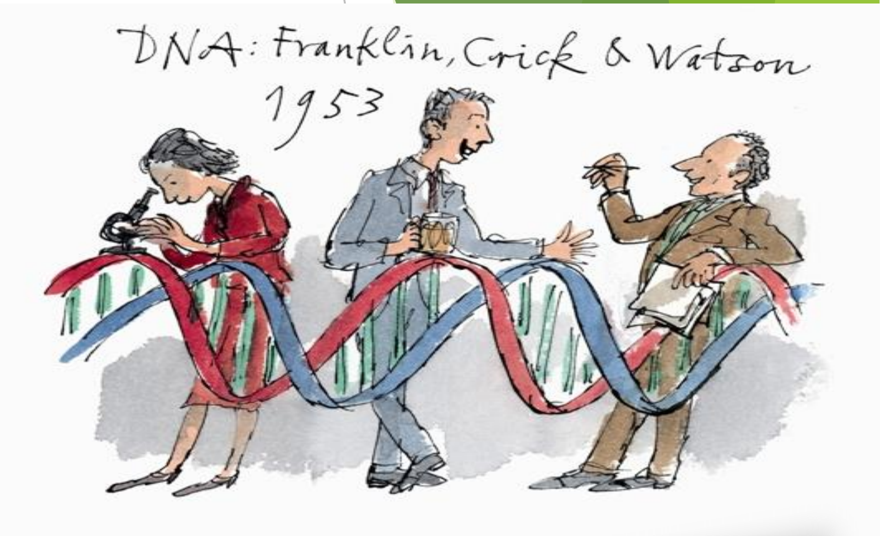
- 1926: Hermann J. Muller shows that X-rays induce mutations.
- 1944: Oswald Avery, Colin MacLeod and Maclyn McCarty show that DNA can transform bacteria, demonstrating that DNA is the hereditary material. In an era when it had been widely believed that it was proteins that served the function of carrying genetic information

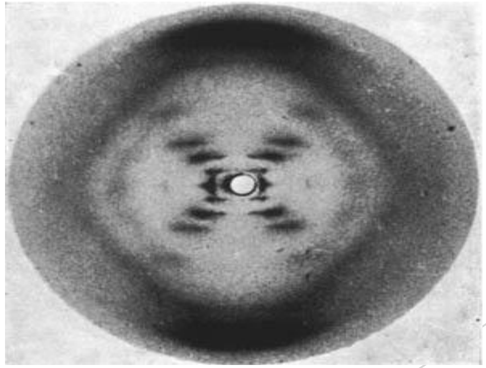
# James Watson and Francis Crick

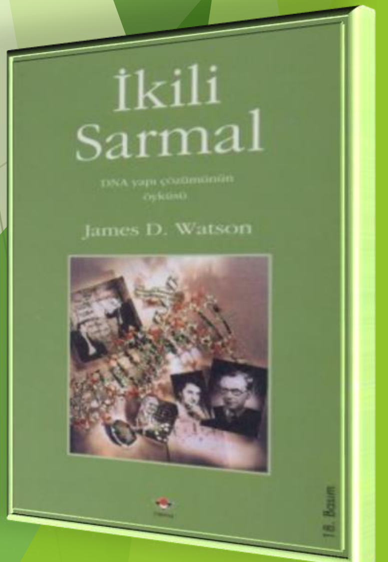
1953: James Watson and Francis Crick determine the structure of the DNA molecule.

Courtesy of Cold Spring Harbor Laboratory Archives and Svenskt Press Photo, Stockholm, Sweden.
Noncommercial, educational use only.

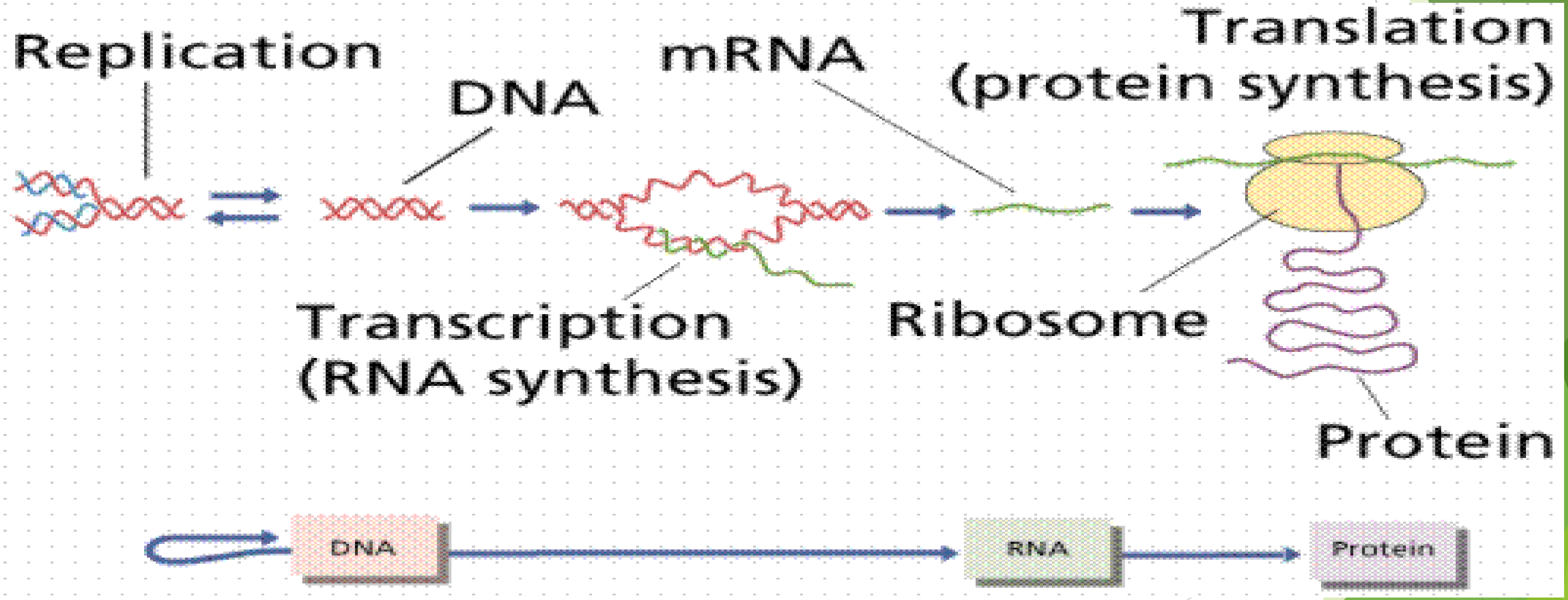
- Used Franklin’s x-ray models
- Determined the structure to be a double helix
- Lead to understanding of mutation and relationship between DNA and proteins at a  molecular level
- 1959 – “Central Dogma”
    - DNA→RNA→protein





# Central Dogma of Biology

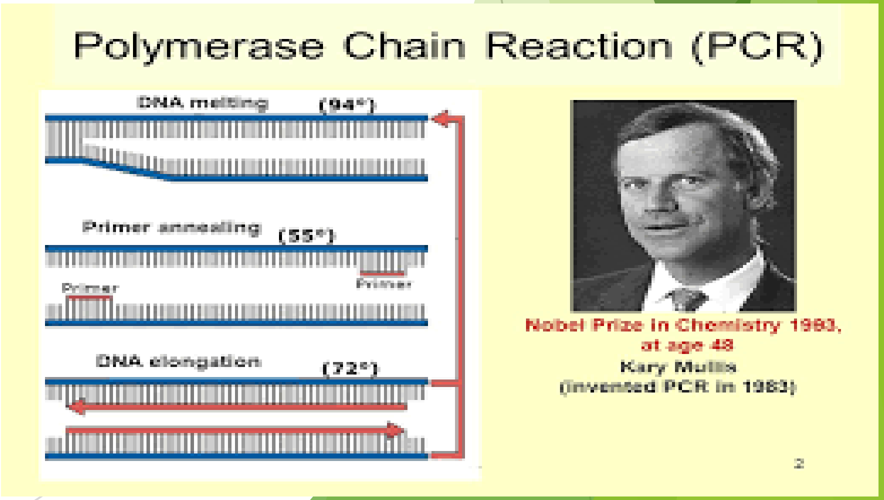


- 1966: Marshall Nirenberg solves the genetic code, showing that 3 DNA bases code for one amino acid.

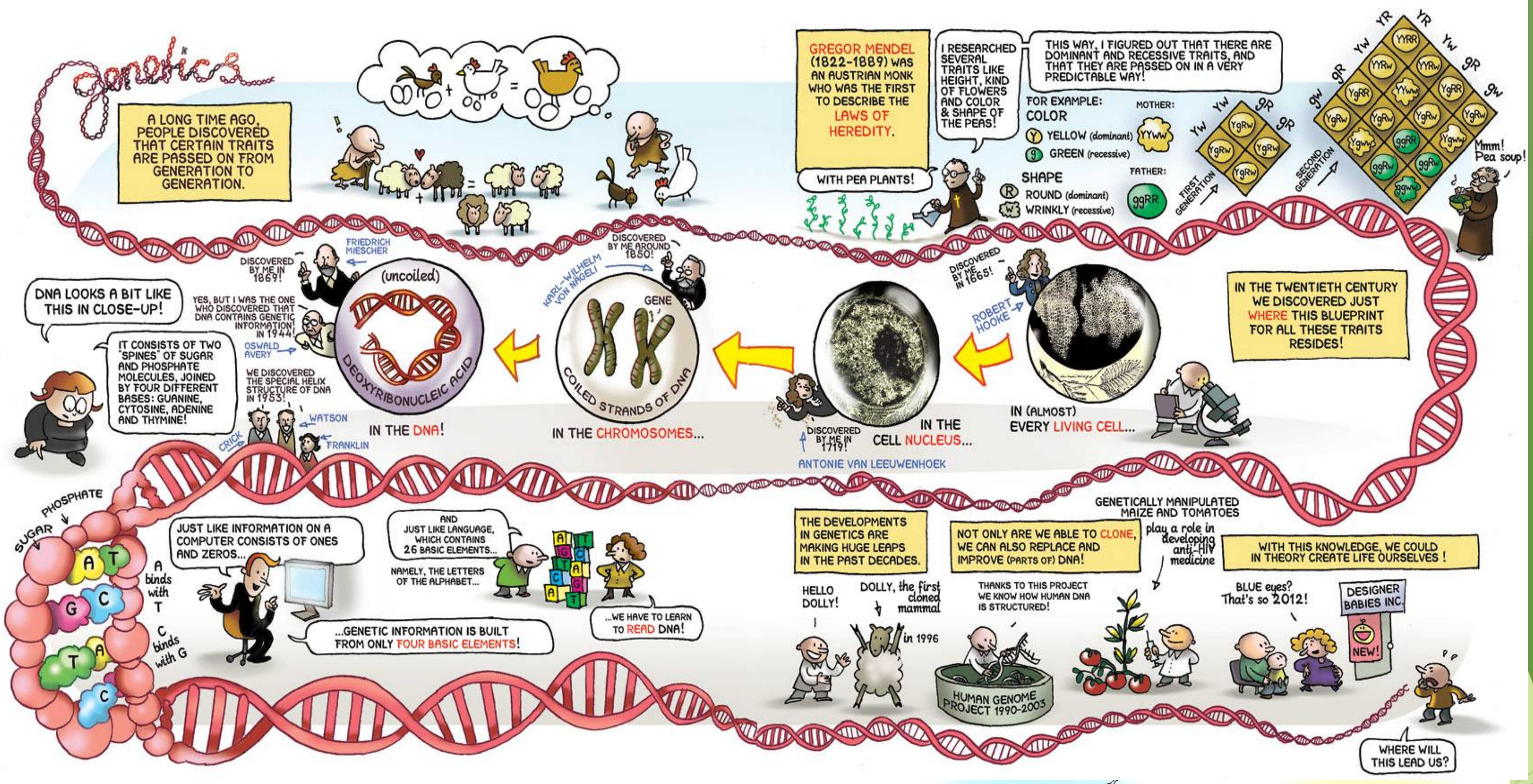
Seond letter

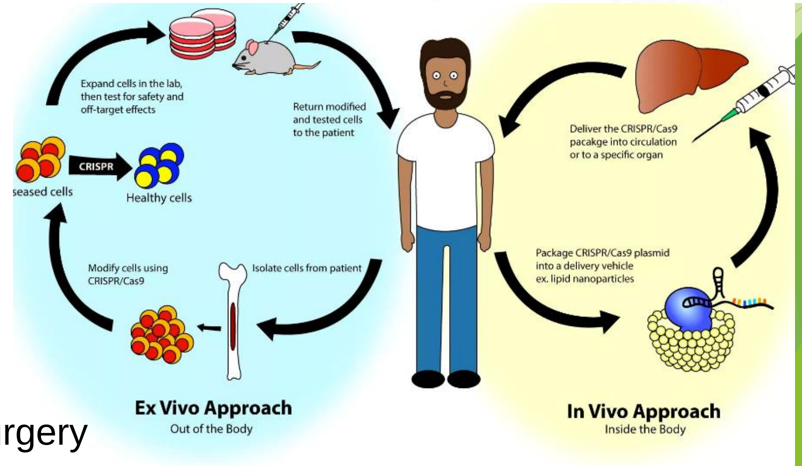
| First letter | U | C | A | G | Third letter |
|---|---|---|---|---|---|
| U | UUU, UUC: Phe; UUA, UUG: Leu | UCU, UCC, UCA, UCG: Ser | UAU, UAC: Tyr; UAA: Stop; UAG: Stop | UGU, UGC: Cys; UGA: Stop; UGG: Trp | U C A G |
| C | CUU, CUC, CUA, CUG: Leu | CCU, CCC, CCA, CCG: Pro | CAU, CAC: His; CAA, CAG: Gin | CGU, CGC, CGA, CGG: Arg | U C A G |
| A | AUU, AUC, AUA: Ile; AUG: Met | ACU, ACC, ACA, ACG: Thr | AAU, AAC: Asn; AAA, AAG: Lys | AGU, AGC: Ser; AGA, AGG: Arg | U C A G |
| G | GUU, GUC, GUA, GUG: Val | GCU, GCC, GCA, GCG: Ala | GAU, GAC: Asp; GAA, GAG: Glu | GGU, GGC, GGA, GGG: Gly | U C A G |

- 1983: Kerry Mullis developes the PCR



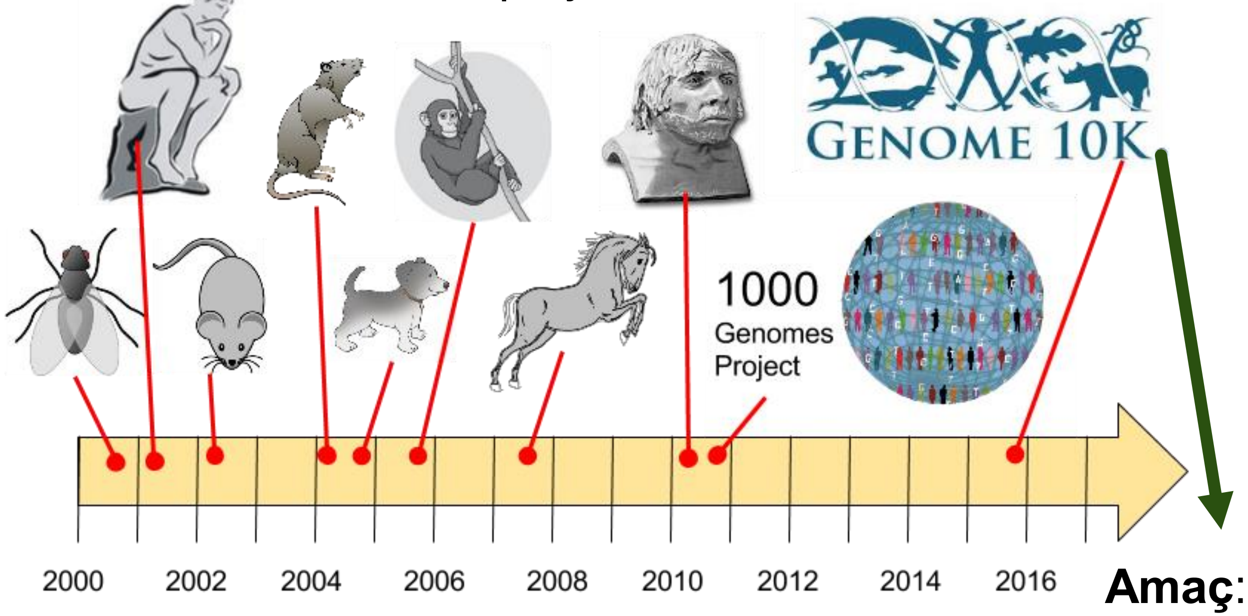
- 2001: Sequence of the entire human genome is announced.

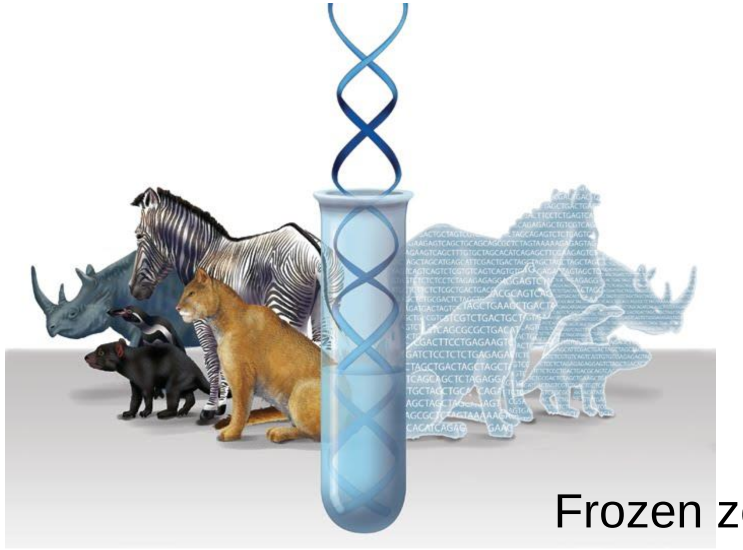




Genetic surgery

Genom projeleri




**Amaç**:
66.000 farklı tür içinden en az 10.000 türün tüm genomunu sekanslamak

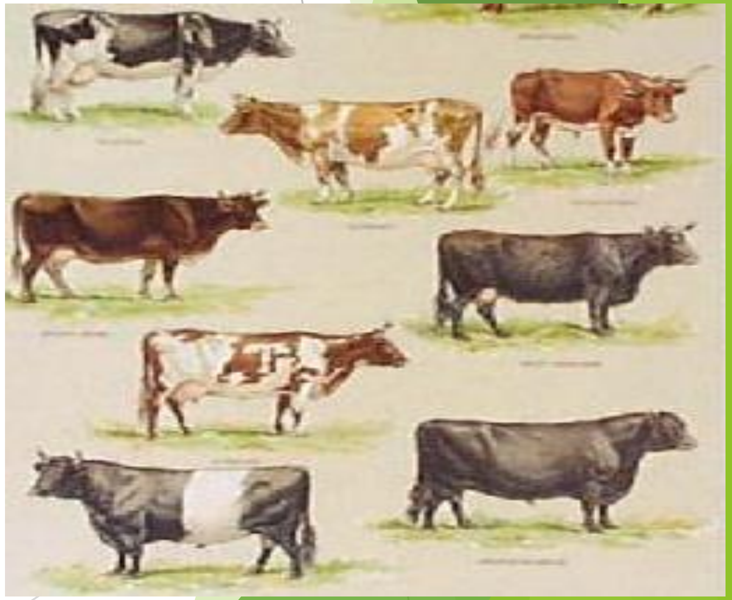


Frozen zoo

# What is Genetics?

# When people began to be interested in genetics?

**Variation and Inheritance**



***Inheritance***: Inheritance is the process by which genetic information is passed on from parent to child. This is why members of the same family tend to have similar characteristics.

*Merinos ram*

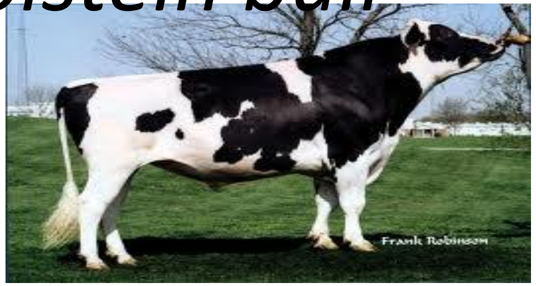
X

*Merinos sheep*

→

*Merinos lamb*

*Holstein bull*




X

*Holstein heifer*

→

*Holstein calf*

- ✓Body shape,
- ✓Tail shape,
- ✓Horn and wool characteristics.....

# What is Inheritance?

- http://learn.genetics.utah.edu/content/basics/inheritance/

**Character/trait:**

"a distinguishing phenotypic characteristic, typically belonging to an individual". In practice this means anything you can record or measure on an individual.

A phenotype is that what you observe or measure on the animal for a certain trait.

It can depend both on the genetic background of the animal (provided it is heritable) and external circumstances such as level of nutrition

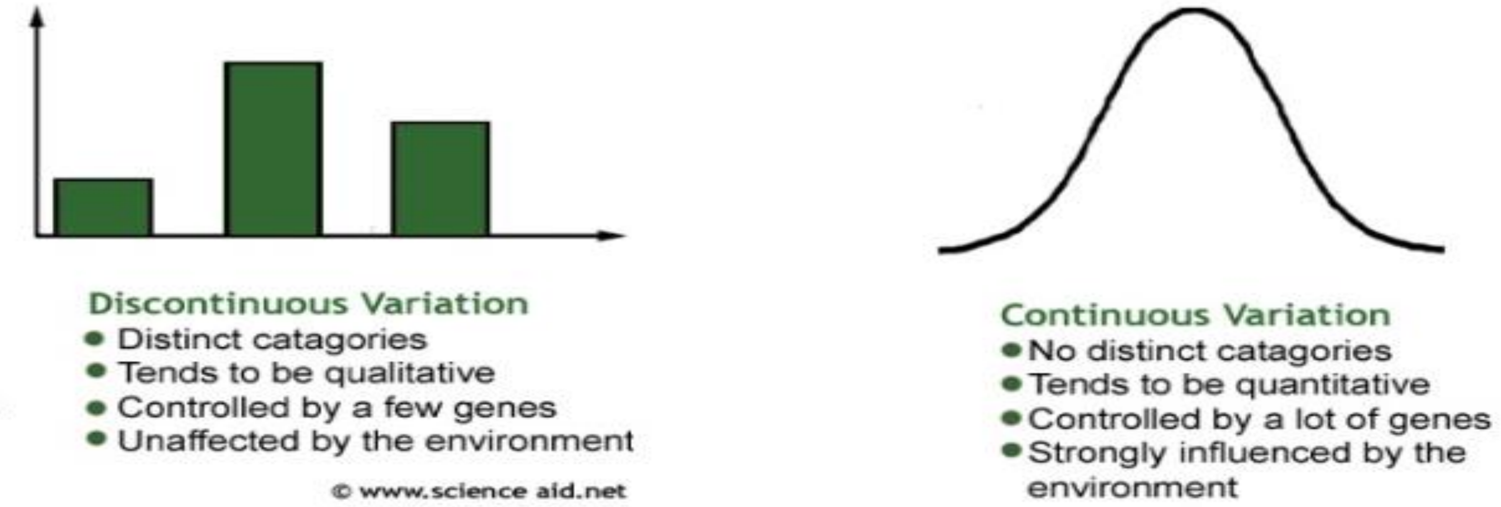
- **qualitative character;** a discrete heritable character that has transmitted well-defined limits and is in a simple alternate manner **:** a typical Mendelian character

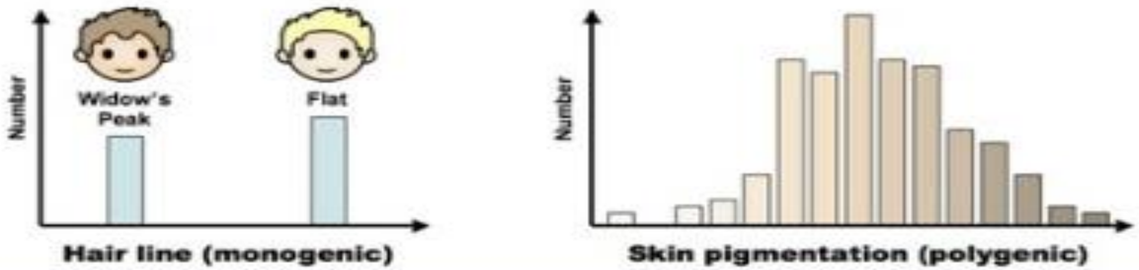
**Discrete or discontinuous traits:** traits occur in distinct Categories:
Trait is there or it is not (examples: albinism, cystic fibrosis, Huntington's disease)
Mendelian inheritance, single genes, dominance, recessiveness

- **quantitative character**; an inherited character that is expressed phenotypically in all degrees of variation between one often indefinite extreme and another **:** a character determined by polygenes.

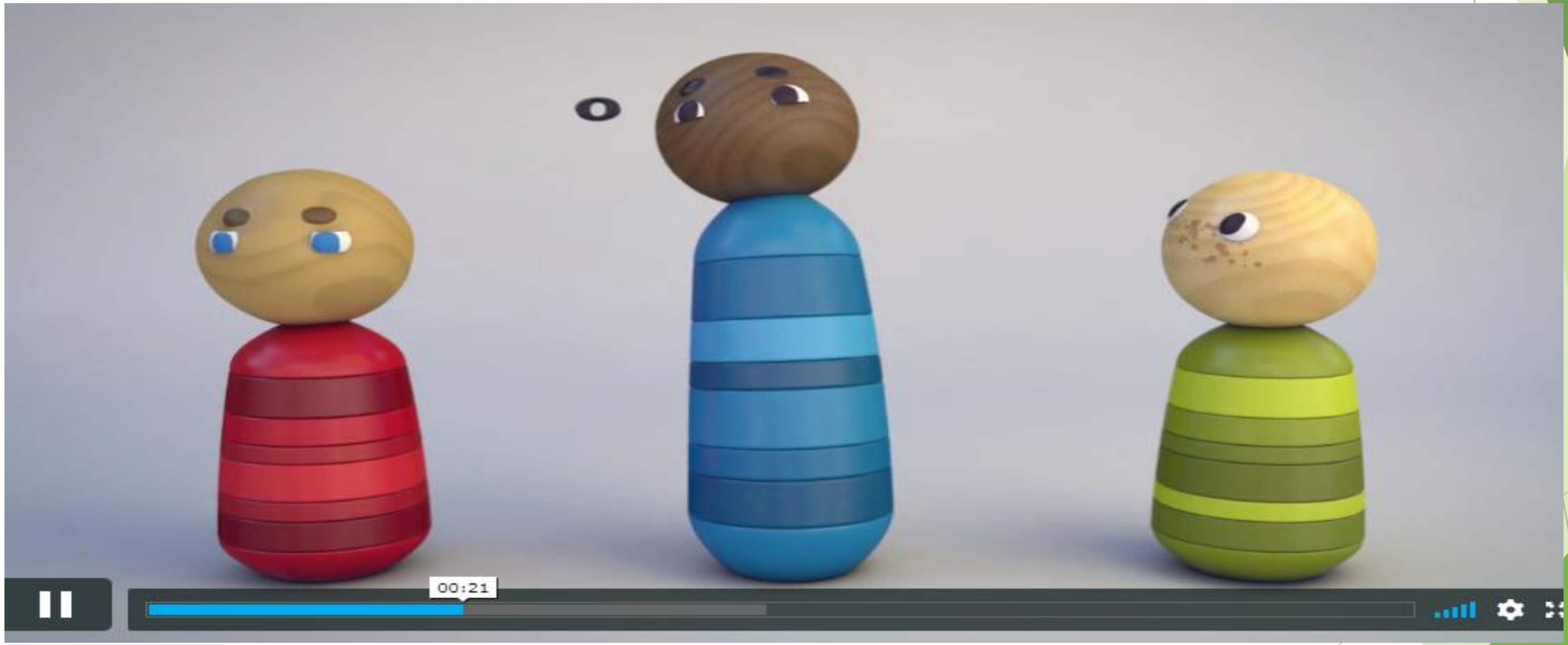
**Continuous traits**: Distribution of phenotypes in the population varies along a continuum. Individuals differ by small degrees.
(examples include height, blood pressure, reaction time, learning ability)
Polygenic quantitative or multifactorial inheritance. Genes act additively.

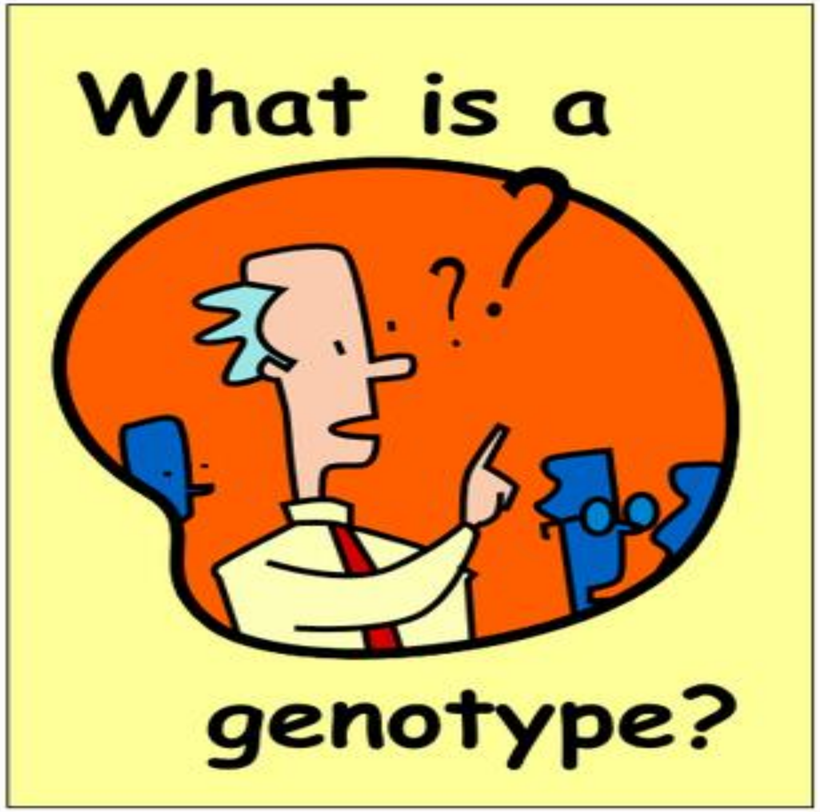
- **Metric: continuous scale**
- **Meristic: discrete scale**
- **Threshold: present or absent**


Discontinuous Variation
Distinct catagories
Tends to be qualitative
Controlled by a few genes
Unaffected by the environment
© www.science aid.net
Continuous Variation
No distinct catagories
Tends to be quantitative
Controlled by a lot of genes
Strongly influenced by the environment

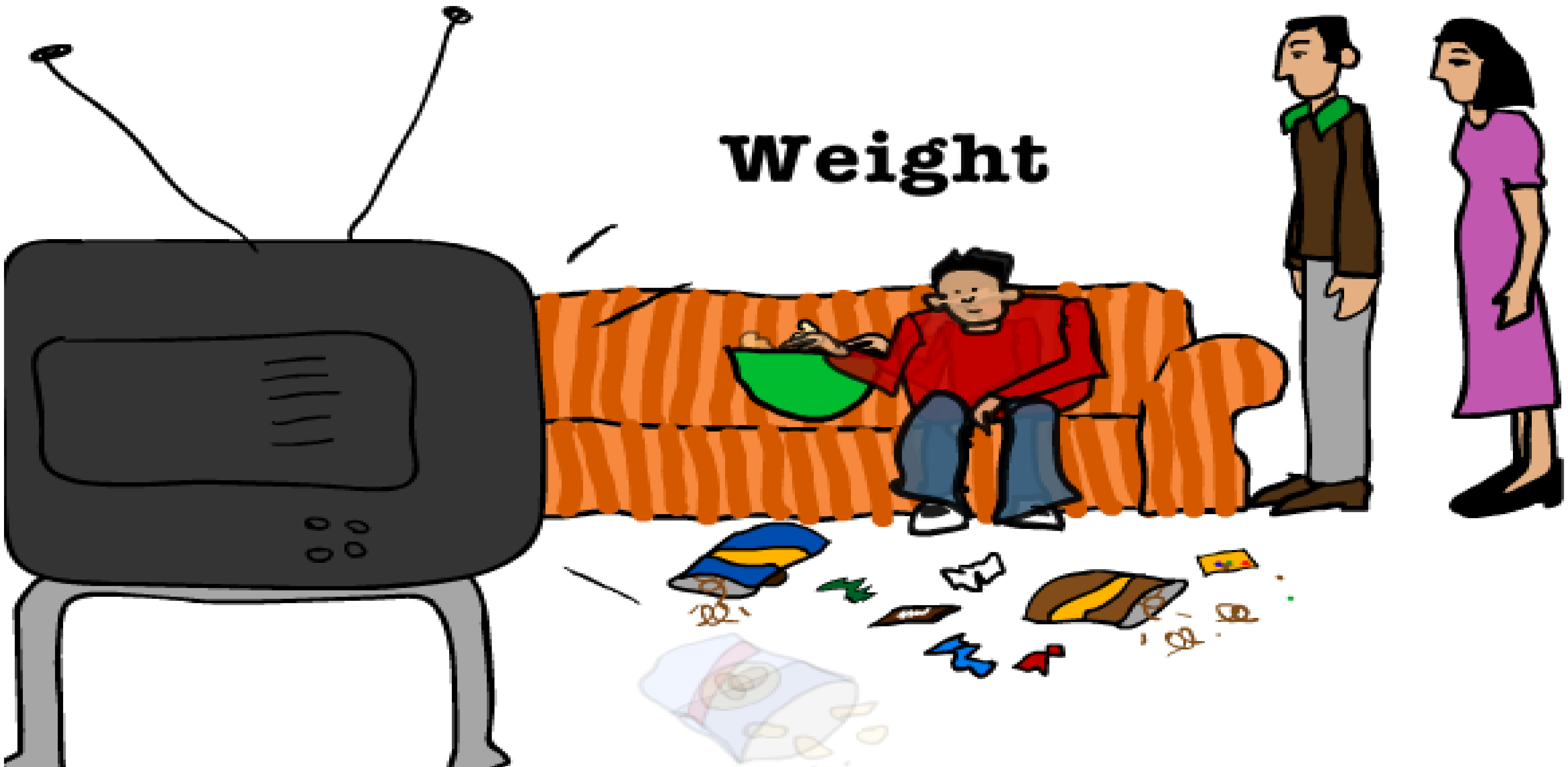

Number
Widow's Peak
Flat
Hair line (monogenic)
Number
Skin pigmentation (polygenic)

http://learn.genetics.utah.edu/content/basics/traits/






# Phenotype??
# Genotype??


Weight

- **Gene** – Genes are segments of <u>DNA</u> located on <u>chromosomes</u> that contain the instructions for protein production.
- Scientists estimate that humans have as many as 25,000 genes. Genes exist in more than one form.
- These alternative forms are called <u>alleles</u> and there are typically two alleles for a given trait. Alleles determine distinct traits that can be passed on from parents to offspring.

Genetics is concerned with genetic development of organisms:

- How to transfer characters to next generations?
- What are the differences and similarities between the characters?
- What are the molecular reasons for the differences and similarities?
- Which mechanisms affect the inheritance?


**Genetic variation is a term used to describe the variation in the DNA sequence in each of our genomes. Genetic variation is what makes us all unique, whether in terms of hair colour, skin colour or even the shape of our faces.**

**Genetic variation is a result of subtle differences in our DNA.**

**Single nucleotide polymorphisms (SNPs, pronounced 'snips') are the most common type of genetic variation amongst people.**

provided by Hoard's Dairyman

provided by Dr Alberto Zorloni

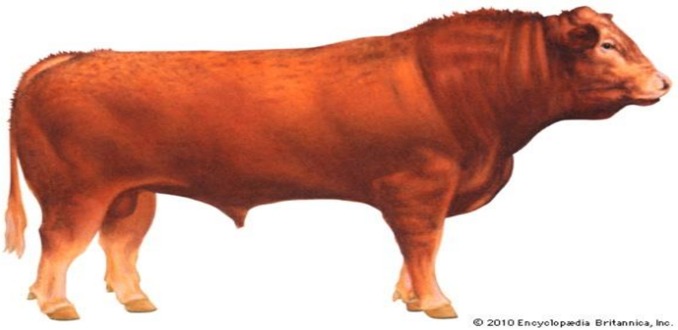
provided by Prof. Dr. M. Ihsan SOYSAL and Research Asst. Emel ÖZKAN

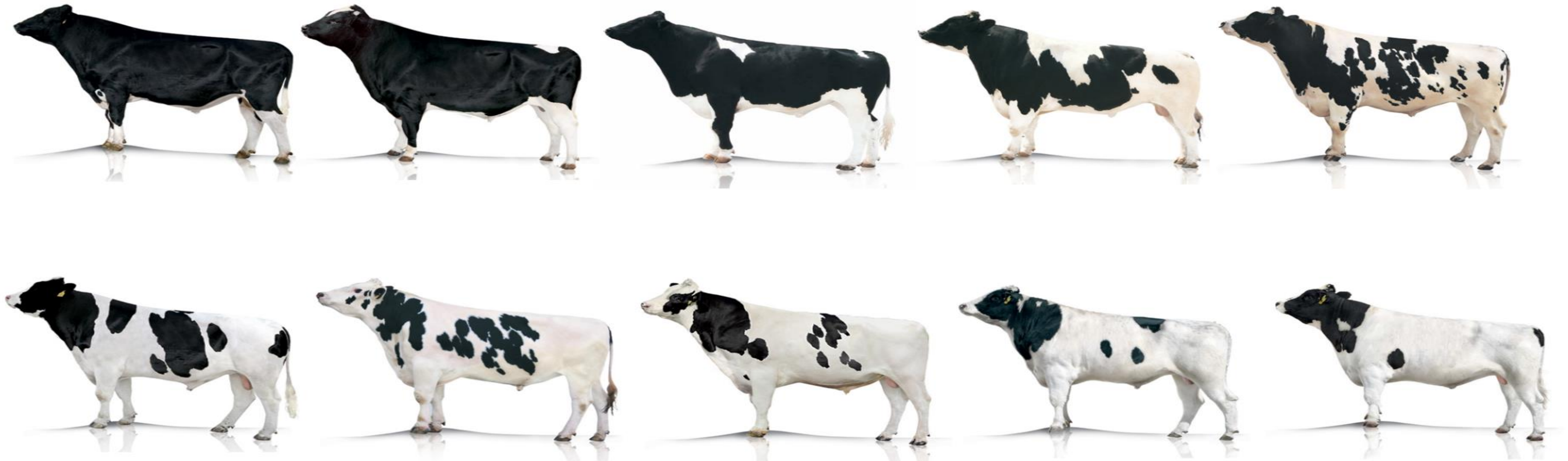
provided by Dr. Zafer Ulutas

provided by Prof. Dr. M. Ihsan SOYSAL and Research Asst. Emel ÖZKAN

provided by Dr G

Provided by Pierre Bonard





# Canis lupus familiaris melanocortin 1 receptor (MC1R), mRNA

NCBI Reference Sequence: NM_001014282.2

GenBank    Graphics

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>NM_001014282.2 Canis lupus familiaris melanocortin 1 receptor (MC1R), mRNA
ATGTCTGGGCAGGGCCCCCAGAGAAGGCTGCTGGGCTCTCTCAATGGCACCTCCCCAGCCACCCCTCACT
TCGAGCTGGCTGCCAACCAGACCGGGCCCCGGTGCCTGGAGGTGTCCATTCCCGACGGGCTGTTCCTCAG
CCTGGGGCTGGTGAGCGTTGTGGAAAATGTGCTGGTGGTGGCCGCCATTGCCAAGAACCGCAACCTGCAC
TCGCCCATGTATTACTTCATCGGTTGCCTGGCTGTGTCCGACCTGCTGGTGAGCGTGAGCAATGTGCTGG
AGACGGCCGTCATGCTGCTGGTGGCGGCAGGCGCCTTGGCTGCTCAGGCTGCTGTGGTGCAGCAGCTGGA
CGACATCATTGACGTGCTCATCTGTGGTTCCATGGTATCCAGCCTCTGCTTCCTGGGCGCCATTGCCGTG
GACCGCTACCTCTCCATCTTCTACGCGCTGCGATACCACAGCATCGTCACACTCCCGCGGGCGTGGCGGG
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CTTGCCCGCGCCTGCCAGCACGCCCGAGGTATTGCCCGGCTCCATAAGAGGCAGCACTTCATCCCCCAGG
GCTTTGGCCTCAAGGGCGCTGCCACACTCACTATCCTGCTGGGCATTTTCTTTCTCTGCTGGGGCCCCTT
CTTCTTGCACCTCTCACTCGTGGTCCTCTGCCCTCAACACCCCATCTGTGGCTGCGTCTTTCAGAACTTC
AACCTCTTCCTCACCCTCATCATCTGCAACTCCATCATTGACCCCTTCATCTACGCCTTCCGCAGCCAGG
AGCTCCGAAAGACTCTCCAAGAGGTAGTGCTATGTTCCTGGTGA
```

# https://www.ncbi.nlm.nih.gov/pubmed/

tps://www.ncbi.nlm.nih.gov/nuccore/NM_001014282.2

NCBI Resources How To bengikul My NCBI Sign Out

Nucleotide Nucleotide Search
Advanced Help

GenBank Send to:

## Canis lupus familiaris melanocortin 1 receptor (MC1R), mRNA

NCBI Reference Sequence: NM_001014282.2
FASTA Graphics

Go to:

```
LOCUS       NM_001014282             954 bp    mRNA    linear   MAM 07-SEP-2017
DEFINITION  Canis lupus familiaris melanocortin 1 receptor (MC1R), mRNA.
ACCESSION   NM_001014282 XM_546772
VERSION     NM_001014282.2
KEYWORDS    RefSeq.
SOURCE      Canis lupus familiaris (dog)
  ORGANISM  Canis lupus familiaris
            Eukaryota; Metazoa; Chordata; Craniata; Vertebrata; Euteleostomi;
            Mammalia; Eutheria; Laurasiatheria; Carnivora; Caniformia; Canidae;
            Canis.
REFERENCE   1  (bases 1 to 954)
  AUTHORS   Ciampolini R, Cecchi F, Spaterna A, Bramante A, Bardet SM and
            Oulmouden A.
  TITLE     Characterization of different 5'-untranslated exons of the ASIP
            gene in black-and-tan Doberman Pinscher and brindle Boxer dogs
  JOURNAL   Anim. Genet. 44 (1), 114-117 (2013)
   PUBMED   22524303
  REMARK    GeneRIF: The results of this study suggest that differential
            expression of ASIP determine pigment-type switching in a MC1R and K
            allele-dependent manner in dogs.
REFERENCE   2  (bases 1 to 954)
  AUTHORS   Wang GD, Cheng LG, Fan RX, Irwin DM, Tang SS, Peng JG and Zhang YP.
  TITLE     Signature of balancing selection at the MC1R gene in Kunming dog
            populations
  JOURNAL   PLoS ONE 8 (2), E55469 (2013)
   PUBMED   23424634
  REMARK    GeneRIF: high heterozygosity and allelic differences at the MC1R
            locus may explain both the mixed color coat, of yellow and black,
            and the difference in coat colors in both Kunming dog populations
```


Change region shown

Customize view

Analyze this sequence
- Run BLAST
- Pick Primers
- Highlight Sequence Features
- Find in this Sequence
- Show in Genome Data Viewer

omia.angis.org.au/home/

THE UNIVERSITY OF SYDNEY

# OMIA - ONLINE MENDELIAN INHERITANCE IN ANIMALS



## WELCOME TO OMIA

Online Mendelian Inheritance in Animals (**OMIA**) is a catalogue/compendium of inherited disorders, other (single-locus) traits, and genes in 239 animal species (other than human and mouse and rats, which have their own resources) authored by Professor Frank Nicholas of the University of Sydney, Australia, with help from many people over the years. OMIA information is stored in a database that contains textual information and references, as well as links to relevant PubMed and Gene records at the NCBI, and to OMIM and Ensembl.

OMIA is manually curated by a team of specialists. If you see an error or wish to submit an entry, please contact us.

To join the OMIA Support Group, register at OMIA Support Group.

From 1st September 2011, the OMIA ID is binomial, with the format OMIA xxxxxx-yyyy.., where xxxxxx is the 6-digit number for a trait/disorder, and yyyy.. is the NCBI species taxonomy id (usually four digits, but sometimes longer).

### Summary

| | dog | cattle | cat | pig | sheep | horse | chicken | rabbit | goat | Japanese quail | golden hamster | Other | TOTAL |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Total traits/disorders | 707 | 517 | 339 | 248 | 243 | 230 | 219 | 91 | 82 | 46 | 41 | 600 | 3363 |
| Mendelian trait/disorder | 303 | 241 | 95 | 67 | 102 | 55 | 129 | 55 | 16 | 34 | 29 | 211 | 1337 |
| Mendelian trait/disorder; key mutation known | 231 | 142 | 62 | 27 | 49 | 41 | 44 | 11 | 10 | 10 | 4 | 102 | 733 |
| Potential models for human disease | 411 | 201 | 206 | 104 | 105 | 128 | 47 | 47 | 36 | 15 | 16 | 318 | 1634 |

## RECENT NEWS

*MENDEL DAY: 8th March 2017:*
Professor Eva Matalova and her colleagues in the Mendelianum in Brno have arranged a wonderful program for Mendel Day 2017, including a guided walking Mendel tour of Brno; an exhibition; a concert of violin music of Leos Janacek, who, as a former organ scholar in Mendel's monastery, arranged the music and played the organ at Mendel's requiem mass; and (on 9th March) a trip to Vienna for a tour of sites associated with Mendel's student days. For details see the Mendelianum website.

http://omia.angis.org.au/home/

# OMIA 000187-9615 : Chondrodysplasia in *Canis lupus familiaris*

See the equivalent entry at NCBI

**In other species:** domestic pig , cattle , domestic cat

**Possible human homologue (MIM number):** 225500

**Mendelian trait/disorder:** yes

**Mode of inheritance:** Autosomal

**Considered a defect:** no

**Key mutation known:** yes

**Year key mutation first reported:** 2009

**Cross-species summary:** Abnormal growth of cartilage, leading to disproportionate dwarfism.

**FGF4**

**Mapping:** In a mammoth GWAS on 95 chondrodysplastic dogs from 8 breeds and 702 non-chondrodysplastic dogs from 64 breeds, each genotyped with the Affymetrix version 2.0 SNP chip (yielding 41,635 informative SNPs for analysis), Parker et al. (2009) highlighted a 431kb region on chromosome CFA18.

By conducting a proof-of-principal across-breed GWAS on 18 affected (from 6 breeds, and including 3 crossbred dogs) and 27 control dogs from 11 breeds (and including 4 crossbred dogs), each genotyped with the Affymetrix Version 2 Custom Canine SNP (comprising 49,663 SNPs), Bannasch et al. (2010) highlighted the same region on chromosome CFA18 that had been shown by Parker et al. (2009) to harbour the causal FGF4 retrogene.

**Molecular basis:** Sequencing within the candidate region (see Mapping section) by Parker et al. (2009) revealed the causal mutation to be a 5kb insertion containing a FGF4 retrogene, i.e. a processed pseudogene of FGF4: "Neither the introns nor the upstream promoter sequences of the gene were present in the insert, however all exons were present, with no alterations in the coding sequence, as well as the 3' UTR and poly-A tail characteristic of retrotransposition of processed mRNA". Furthermore, "The retrogene is inserted in the middle of a LINE with both LINEs and SINEs upstream". The authors suggested "that atypical expression of the [retrogen] FGF4 transcript in the chondrocytes may be causing inappropriate activation of one or more of the fibroblast growth factor receptors such as FGFR3", mutations in which account for the majority of dwarfism cases in humans. The insertion containing the FGF4 retrogene starts at 23,431,136 on CFA18, which is 25Mb away from the complete FGF4 gene, which is located at 48413479-48415205. Because the retrogene is not included in NCBI's Gene database, the table below lists the normal FGF4 gene.

**Clinical features:** Even though chondrodysplasia is normally regarded as a defect, this canine mutation is not classified as a defect because, as noted by Parker et al. (2009), it is a "a short-legged phenotype that defines at least 19 dog breeds including dachshund, corgi, and basset hound".

**Associated gene:**

# FGF4 based variation (case for Chondrodysplasia )

**Generally,** Chondrodysplasia is a defect in, however it is a breed characteristics for several breeds.

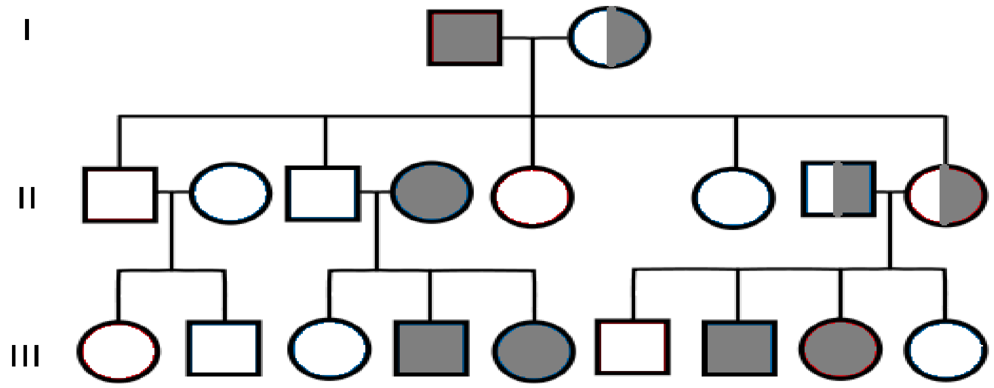
corgi

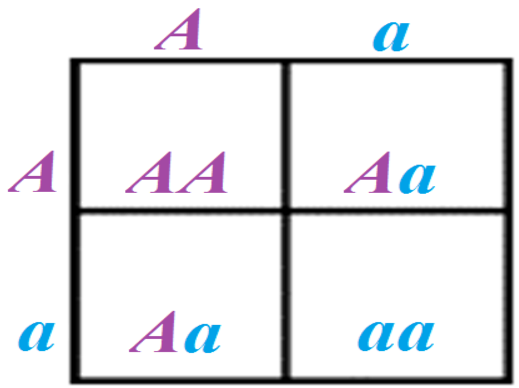
Basset hound

dachshund

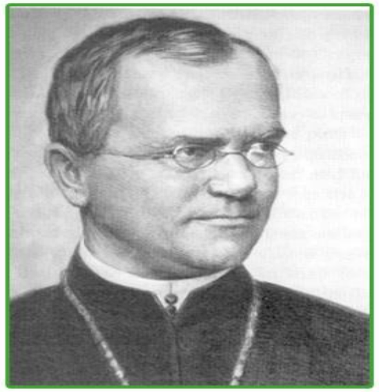
# genetics subfields

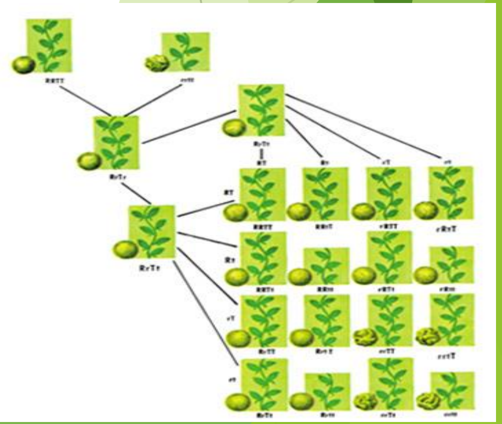
## Classical Genetics

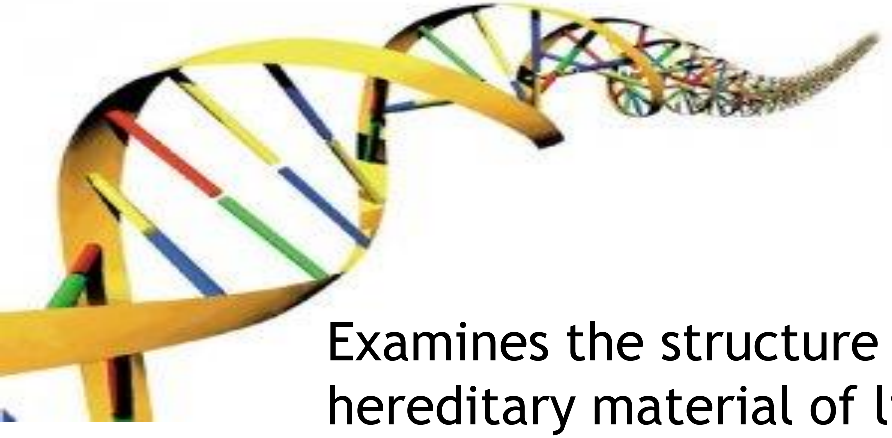


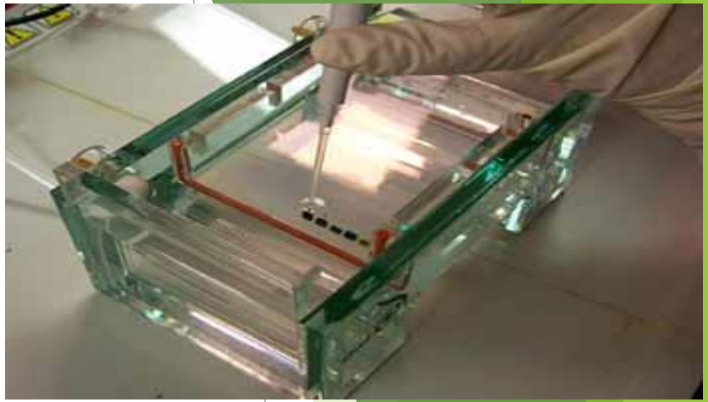

It is the branch of genetics based on visible results of reproductive acts.
It is the oldest discipline in the field of genetics, going back to the experiments on Mendelian inheritance by Gregor Mendel.



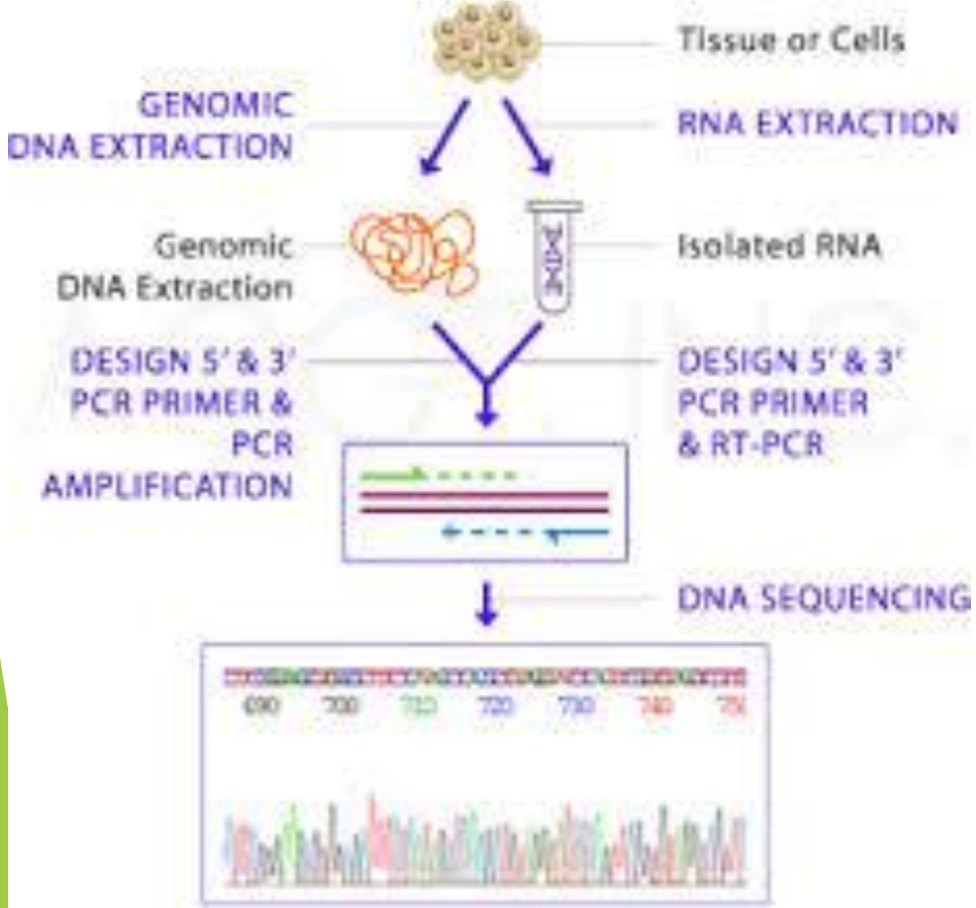


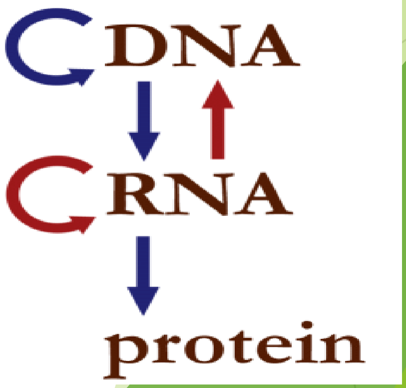


# Molecular Genetics

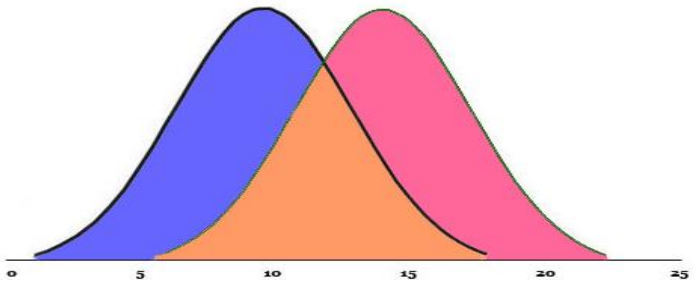


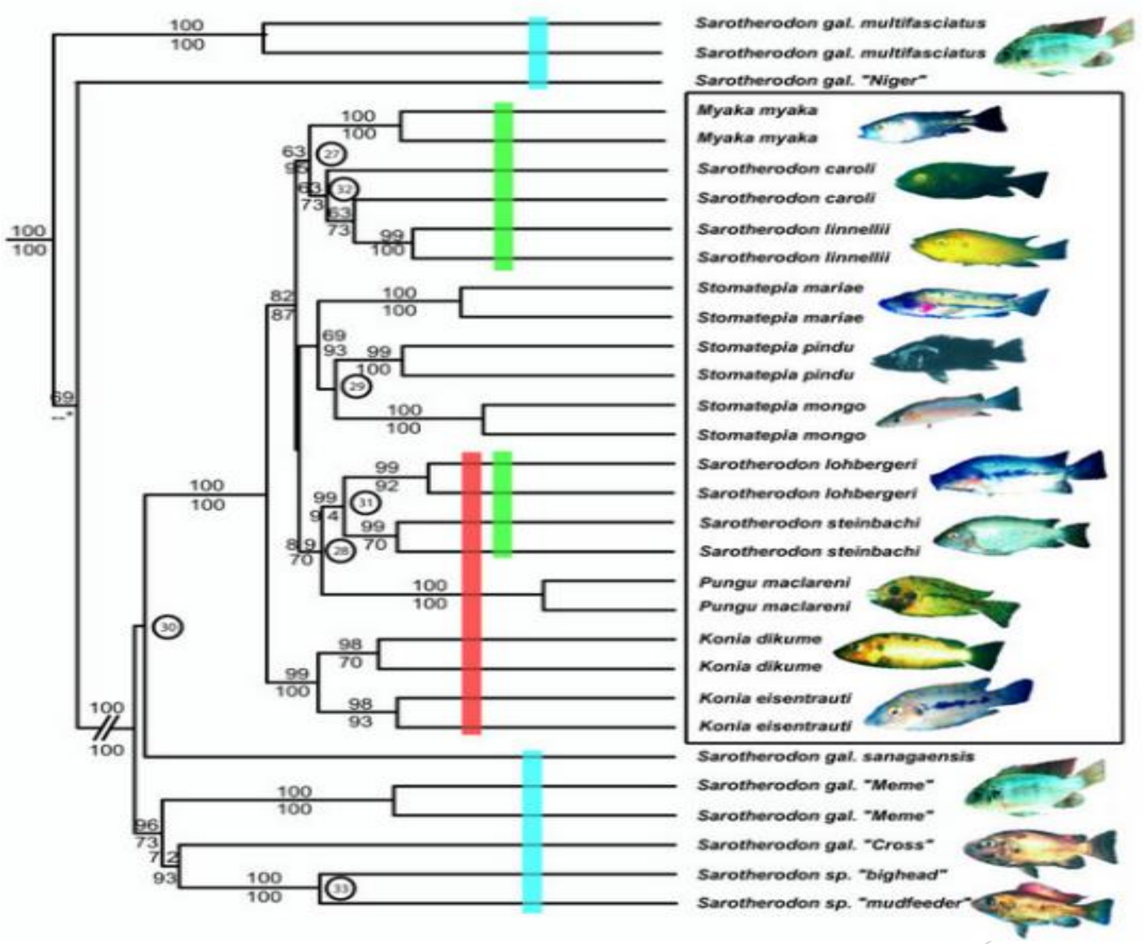
Examines the structure and functions of genes that are hereditary material of living things at the molecular level.

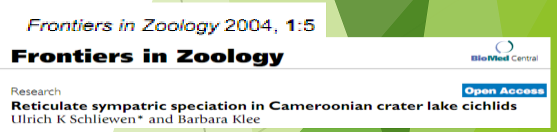


# Population, Quantitative and Ecological Genetics





*Frontiers in Zoology* 2004, **1**:5

**Frontiers in Zoology**

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**Reticulate sympatric speciation in Cameroonian crater lake cichlids**

Ulrich K Schliewen* and Barbara Klee

# GENETICS IN ANIMAL BREEDING

- Genetic researches, made significant contributions to many areas in animal husbandry.
- Genetic studies related to animal research is conducted in many fields such as biotechnology and drug development.
- Some milestones :

✓ DNA structure

✓ Restriction enzymes

✓ rDNA

✓ The birth of Dolly

✓ PCR

✓ Genome sequence


# The use of molecular genetic in veterinary medicine

- The identification of the genes associated with hereditary diseases
- screening of hereditary diseases in populations
- treatment with gene transfer
- diagnosis of disease agents
- measurement of treatment effectiveness

- forensic cases

- to clarify the evolutionary history of domestic species
- establishing the protection programs for animal species and breeds under risk of extinction.

- to produce bioreactive organism
- embryo cloning
- gender control of embryo
- genomic selection
- .............