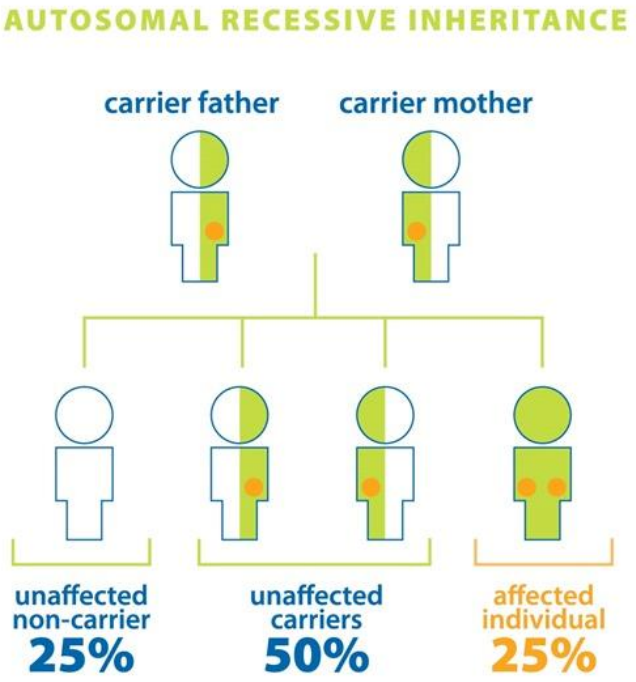
Inherited Diseases in Animals

Assoc. Prof. Dr.Bengi ÇINAR KUL

- Inherited disorders are passed to the offspring from a parent.
- A genetic disease may or may not be a heritable as some genetic disorders are passed down from the parent's genes, but others are almost always caused by new mutations.
- They are caused by inborn abnormalities in genes or chromosomes, which are affect one animal in every several thousands or millions (depends on the species, breed, phenotype etc.)
- Most of them occur rarely and are of minor concern, but some increase in their frequency to the point that they become a significant economic concern and need to be selected against.

- The genetic diseases occur in all breeds of animals however some defects are strongly associated with certain breeds (such as ‘BLAD’ in Holstein)
- The most common <u>inheritance pattern of genetic diseases is autosomal recessive inheritance</u>.

The defective offspring receives the recessive genes from both parents.



- Currently DNA tests are available for several genetic diseases like equine SCID, canine Factor IX, bovine Citrullinemia, which can be diagnosed at very young age of animal and screened for potential sires with undesirable alleles.
- it is necessary to know

- genetic cause/type of mutation,
- clinical symptoms and
- frequency of occurrence in population,

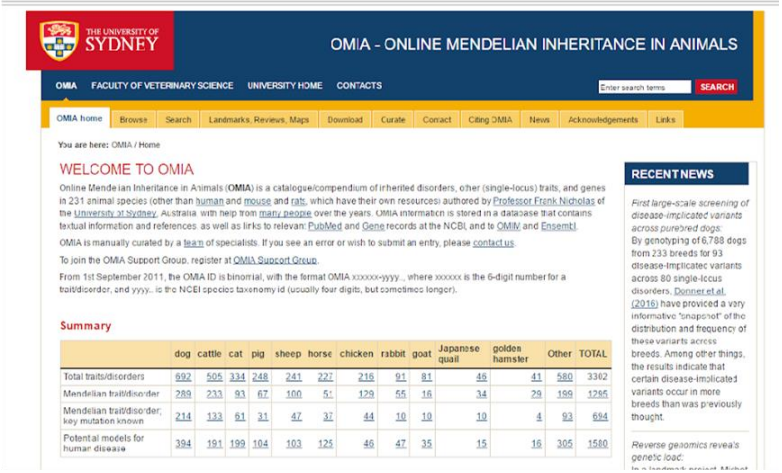
to find out possible strategies to eliminate the genetic disease and avoid economic losses.

- There are several free online resources (databases)

Online Mendelian Inheritance in Animals (OMIA)

The Online Mendelian Inheritance in Animals (OMIA) database is hosted by the National Institutes of Health and it includes several species.

Go to link and examine



Canine Inherited Disorders Database (CIDD)

The goal of the Canine Inherited Disorders Database (CIDD) is *"… to reduce the incidence of inherited disorders in dogs by providing information to owners and breeders, and to facilitate the best management possible of these conditions by providing current information to veterinarians."*

Some genetic diseases in cow

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Table-1

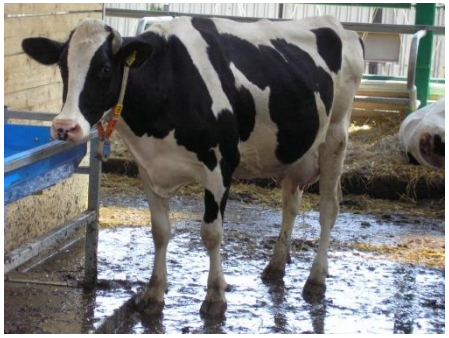
Sr. No.	Specific Tissue	Dairy Cattle	Beef Cattle
1	Skeletal	a. Chondrodysplacia b. Complex Vertebral Malformation c. Osteogenesis Imperfecta d. Osteopetrosis e. Syndactylism	a. Osteopetrosis b. Arachnomelia c. Arthrogryposis Multiplex d. Congenital Contractural Arachnodactyly f. Syndactylism
2	Central Nervous System	a. Weaver Syndrome b. Spinal Dysmielination c. Spinal Muscular Atrophy	a. Ideopathic Epilepsy b. Neuronal Ceroid Lipofuscinosis c. Hydrocephalus d. Spastic Paresis
3	Blood	a. BLAD b. Hereditary Zinc Deficiency c. Citrullinemia	Nil
4	Skin	a. Epitheliogenesis Imperfecta b. X-Linked Anhydrotic Ectodermal Dysplacia	a. Hypotrichosis
5	Muscle Function Disorder	Nil	a. Congenital Pseudomyotonia b. Crooked Tail Syndrome
6.	Opthalmic	a. Anapthlmos and Micropthalmos b. Congenital Cataract c. Optic Nerve Colobomas	d. Anapthlmos and Micropthalmos e. Congenital Cataract f. Optic Nerve Colobomas

Bovine Leukocyte Adhesion Deficiency (BLAD):

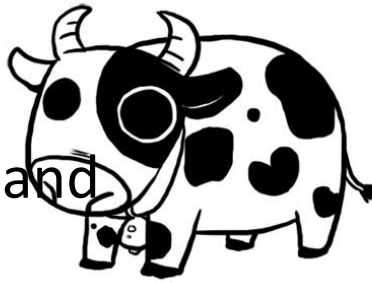
Bovine leukocyte adhesion deficiency (BLAD) disease is immunological disorder. It is an autosomal recessive congenital disease reported in Holstein cattle.

due to a single base substitution of adenine with guanine at nucleotide 383 in the CD18 gene (ITGB2), which subsequently leads to replacement of aspartic acid with glycine at position 128 in the corresponding protein (D128G)

What kind of mutation???



BLAD



- Clinically such individuals are more prone to recurrent and prolonged mucosal and epithelial infections.
- Widespread ulcerative and necrotising stomatitis,
- periodontitis,
- loss of teeth and alveolar periostitis are frequent lesions in the oral cavity.
- Extensive dermatophytosis may occur.
- Multifocal chronic ulcerative and necrotizing enteritis also observed, rhinitis and suppurative bronchopneumonia are frequent additional necropsy findings.
- High mortality

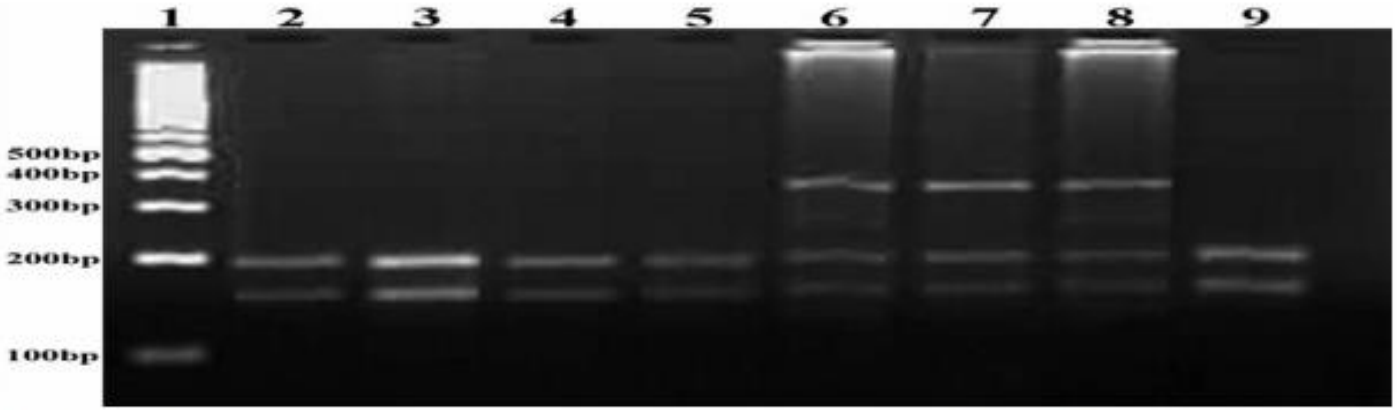
BLAD

- Diagnosis:

Normally 8000/ 1mm^3 leukocytes,

Affected more than 100.000/1mm^3

- PCR (polymerase chain reaction)+ RFLP



Şekil 1. BLAD geninin TaqI enzim kesim ürünlerinin agaroz jeldeki fotoğrafı. Hat 1: 100 bp'lik DNA belirteci, Hat 2-5 ve 9: 152 ve 191 bp'lik homozigot normal hayvanlara ait bantlar, Hat 6-8: 152, 191 ve 343 bp'lik BLAD alleli taşıyan heterozigot hayvanlara ait bantlar

Kafkas Univ Vet Fak Derg
16 (2): 519-521, 2010

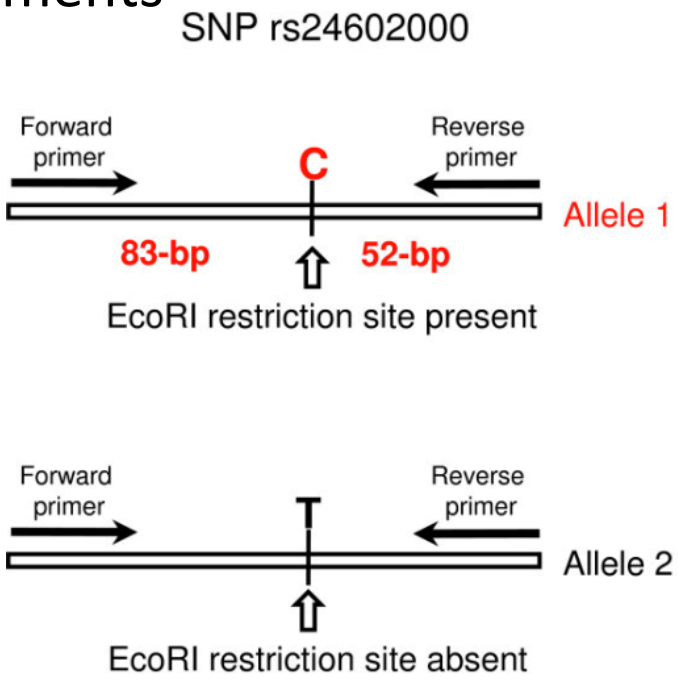
SHORT COMMUNICATION

Detection of Bovine Leukocyte Adhesion Deficiency (BLAD) Allele in Holstein Cows Reared in Kayseri Vicinity

Bilal AKYÜZ * Okan ERTUĞRUL ** Özgecan KORKMAZ AĞAOĞLU **

PCR-RFLP

The first step in a PCR-RFLP analysis is amplification of a fragment containing the variation. This is followed by treatment of the amplified fragment with an appropriate restriction enzyme. Since the presence or absence of the restriction enzyme recognition site results in the formation of restriction fragments of different sizes, allele identification can be done by electrophoretic resolvement of the fragments



Citrullinemia:

- Bovine citrullinemia is a unusual Holstein and Holstein-Friesian-specific metabolic genetic disorder of cattle worldwide
- Similar to leukocyte adhesion deficiency and uridine monophosphate synthase deficiency, this inherited disease is autosomal recessive and breed specific.
- The inherited disorder results in a deficiency in argininosuccinate synthetase, leading to enzymatic disruption of the urea cycle. The mutation involves a single-base substitution (C-T) in exon 5 of argininosuccinate synthetase (ASS), which converts the CGA codon that codes for arginine-86 to TGA, a translational termination codon.
- This results in a shortened peptide product (85 amino acids instead of 412) depressed the functional activity.
- Clinically, citrullinemia causes ammonemia (increased circulatory ammonia) and related neurological signs. Affected calves present with ataxia, aimless wandering, blindness, head pressing, convulsions and death.

Some genetic diseases in horse

- SCID → Severe combined immunodeficiency
- LFS → Lavender Foal syndrome
- PSSM-1 → Polysaccharide storage myopathy tip I
- GBED → Glycogen Branching Enzyme Deficiency

SCID,
Severe Combined Immunodeficiency

- is a fatal disease of Arabian and part-Arabian foals.
- It is caused by a genetic defect transmitted as an autosomal recessive trait. 5bp deletion in DNA-protein kinase catalytic subunit
- Similar to the "bubble boy" condition in humans, an affected foal is born with no immune system, and thus generally dies of an opportunistic infection.
- Affected foals that attain colostral antibody transfer are clinically normal until the colostral antibodies decrease.
- No functional B and T lymphocytes are produced which leads to a complete lack of antibody production and defective cell-mediated immunity.

SCID

- Diagnose:
- Affected foals are lymphopenic (less than 1,000 lymphocytes per mm3), develop infections and die by 4.5 months of age
- PCR

Ankara Üniv Vet Fak Derg, **61**, 59-63, 2014

Investigation of severe combined immunodeficiency (SCID) disease of Arabian horses raised at the state stud farms in Turkey

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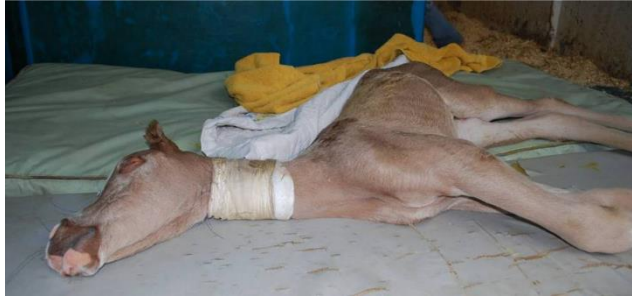
[1] Ankara University, Faculty of Veterinary Medicine, Department of Genetics, Ankara; [2]Mehmet Akif Ersoy University, Faculty of Veterinary Medicine, Department of Animal Science, Burdur; [3] General Directory of Agricultural Farms (TIGEM), Karacabey Agricultural Farm, Bursa, Turkey.



LFS,
Lavender Foal Syndrome

- Also called Coat Color Dilution Lethal (CCDL).
- The condition gets it name because most affected foals are born with a coat color dilution that lightens the tips of the coat hairs, or even the entire hair shaft.
- Foals with LFS are unable to stand at birth, often have seizures, and are usually euthanized within a few days of birth.

LFS

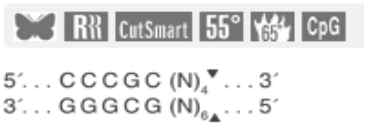
- autosomal recessive trait
- Deletion in Miyozin VA,frameshift mutation
- PCR-RFLP

PCR+RFLP

PCR product 769bp

Enzyme	Affected *MYO5A*	Normal *MYO5A*	Carrier
FauI	**287bp and 482bp**	**287bp, 96bp and 396bp**	**287bp, 96bp, 396bp and 482bp**

FauI



TATTTTAGTCACCATTTCCTATGAACCTTTCAAAAGAGCTAAAATGCTCCTGTTTCT**CAG**
GGCCTTTGAGAACTTTGTATTTGTAGCAGGAATTCAGAAAGACACAAATATGAGAGCATT
CATTTCTGGCCTTTGTTTGAATTTCTTGACTTTAATCAAGTCAGAAGTTACACAGACACT
AAAGAGCACCCACTTTTCCTGCCCTTGCAAGTGAGCACGAAGCCTTGCACCCACCAGGCA
GGGACTCTAGGGTCATCTCCGTTTCCTACCTGTGTGGCTTCTCCACAG**GCTCCTGGAATC**
CCAGCTCCAGTCGCAGAAGAGGAGCCATGAGAATGAGGCTGAAG↓CCCTCCGCGGGGAGAT
CCAGAGCCTGAAGGAGGAGAACAACCGGCAGCAGCAGCTGCTGGCCCAGAACCTGCAGCT
GCCCCCAGAGGCCCGCATCG↓AGGCCAGCCTGCAGCATGAGATCACCCGGCTGACCAACGA
AAACTTGGTAAGAGGAGGTGCCTGGGCCCACACACTCAGCCAGAAGCGCCTGGCCCTGCA
GGACGGTCCTAGTTTCTTTCTTTTTAAAGATTTTATTTTTTTTTCCTTTTTCTCCCCAAA
GCCCCCCGGTACATAGAGTTGTATATTCTTCATTGTGGGTCCTTCTAGTTGTGGCATGTG
GGACGCTGCCTCAGCGTGGTTTGATGAGCAGTGCCATGTCCGCGCCCACGATACGAACCA
ATGAAACACTGGGCTGCCTGCAGCCGAGGGCGCGAACTTATCCACTCGGCCACGGGGCCA
GCCCCAGTCCTAGTTTCTTTTTGATT**AAACCCATCTTTCATGGCTG**GAAAACTCACTGCT

The first step in a PCR-RFLP analysis is amplification of a fragment containing the variation. This is followed by treatment of the amplified fragment with an appropriate restriction enzyme. Since the presence or absence of the restriction enzyme recognition site results in the formation of restriction fragments of different sizes, allele identification can be done by electrophoretic resolvement of the fragments

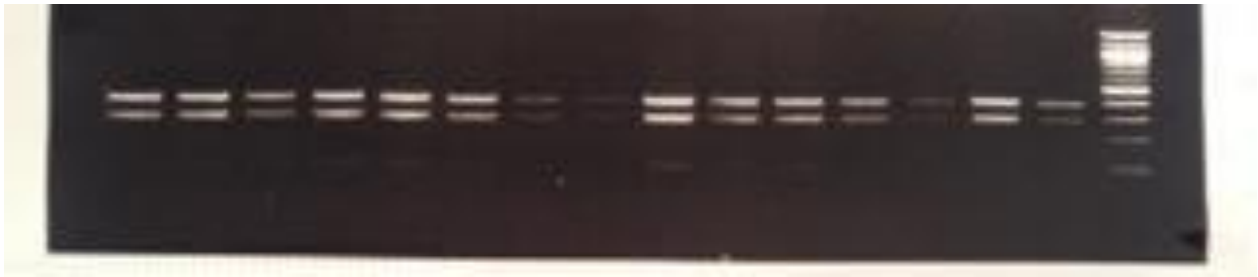
Enzim	Hasta *MYO5A*	Normal *MYO5A*	Taşıyıcı
FauI (Smu)	287bç ve 482bç	287bç, 96bç ve 396bç	287bç, 96bç, 396bç ve 482bç

CAG
GGCCTTTGAGAACTTTGTATTTGTAGCAGGAATTCAGAAAGACACAAATATGAGAGCATT
CATTTCTGGCCTTTGTTTGAATTTCTTGACTTTAATCAAGTCAGAAGTTACACAGACACT
AAAGAGCACCCACTTTTCCTGCCCTTGCAAGTGAGCACGAAGCCTTGCACCCACCAGGCA
GGGACTCTAGGGTCATCTCCGTTTCCTACCTGTGTGGCTTCTCCACAG**GCTCCTGGAATC**
CCAGCTCCAGTCGCAGAAGAGGAGCCATGAGAATGAGGCTGAAG

CCCTCCGCGGGGAGAT
CCAGAGCCTGAAGGAGGAGAACAACCGGCAGCAGCAGCTGCTGGCCCAGAACCTGCAGCT
GCCCCCAGAGGCCCGCATCG

AGGCCAGCCTGCAGCATGAGATCACCCGGCTGACCAACGA
AAACTTGGTAAGAGGAGGTGCCTGGGCCCACACACTCAGCCAGAAGCGCCTGGCCCTGCA
GGACGGTCCTAGTTTCTTTCTTTTTAAAGATTTTATTTTTTTTTCCTTTTTCTCCCCAAA
GCCCCCCGGTACATAGAGTTGTATATTCTTCATTGTGGGTCCTTCTAGTTGTGGCATGTG
GGACGCTGCCTCAGCGTGGTTTGATGAGCAGTGCCATGTCCGCGCCCACGATACGAACCA
ATGAAACACTGGGCTGCCTGCAGCCGAGGGCGCGAACTTATCCACTCGGCCACGGGGCCA
GCCCCAGTCCTAGTTTCTTTTTGATT**AAACCCATCTTTCATGGCTG**

Normal *MYO5A*
287bç, 96bç ve 396bç



Şekilde görülen bütün örnekler normal, hasta birey yok.

Some genetic diseases of the dog

Basset

-Daschund

- **Chondrodysplasia** Gene: Fibroblast growth factor 4 (FGF4) 5kb insertion
- **Von Willebrand disease I** Gene:VWF, exon 43 (c.7437G > A)
- **Progressive retinal atrophy** Gene: CNGB1, exon 26 (c.2387delA;2389_2390insAGCTAC)
- **Cystinuria** Gene: SLC3A1
- **Haemophilia A ve B** Gene: PNPLA1

- **Degenerative Myelopathy (DM)**
- **Primary Lens Luxation (PLL)**
- **Fanconi Syndrome (Fanconi)** for Basenjis
- **Neonatal Encephalopathy with Seizures (NEwS)** Standard Poodles
- **Neuronal Ceroid Lipofuscinosis (NCL)** American Bulldogs, & Tibetan Terriers

- Development of DNA based tests for all the genetic diseases will aid to identify the affected animals very early in life, so as to prevent further propagation of undesirable alleles in future generations.
- Cytogenetic and molecular genetic testing of every elite male and female carriers is necessary to prevent dissemination of undesirable, recessive lethal alleles of various genetic diseases.