# Inherited skin diseases in dogs and their genetics.

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## Abstract

**Canine genodermatoses encompass a wide range of illnesses with various manifestations. Modern genetic technology, such as whole genome sequencing, has considerably aided in the discovery of novel genes and the establishing of genetic diagnoses in such diverse illnesses. A precise genetic diagnosis of a heritable skin disorder is required for proper owner counselling on the disease's progression, prognosis, and breeding consequences. To design specific, targeted, or personalised therapy approaches, it is necessary to first understand the underlying pathophysiology. This review seeks to provide a detailed overview of canine genodermatoses and their genetic aetiologies that have been identified thus far. It is critical to raise awareness of genodermatoses in dogs, and this study may assist physicians in applying contemporary genetics in daily clinical practise to obtain exact diagnosis in suspected genodermatoses.**

**Keywords**: Genodermatoses, FOXI3 mutation, KRT10 variations, Syndromic disorders.

## Introduction

Humans have 6000–8000 uncommon diseases, the majority of which are inherited as monogenic characteristics. More than 5600 monogenic disorders have been linked to specific genetic variations. Despite the fact that each of these diseases is rare, it is estimated that up to 10% of the human population in the United States is affected by at least one of them. In humans, there are around 500 heritable skin illnesses (genodermatoses) [1]. Despite this, additional patients with unidentified genodermatoses continue to be discovered. An outstanding study on human genodermatoses provides compelling evidence for the expanding importance of genetic studies in clinical practise.

There are substantially fewer heritable skin diseases in dogs with recognised molecular aetiologies. We accumulated 19 canine genodermatoses five years ago [2]. This number is constantly increasing because to collaborations between private physicians, veterinary dermatology specialists, and veterinary dermatopathologists, as well as breakthroughs in genetics and sequencing technologies. We will summarise data on 36 canine genodermatoses and the genes that cause them in this review.

Many genodermatoses are similar in dogs and humans, which is not surprising. Their comparative research in related species could be classified as a One Health strategy, with benefits to both human and veterinary care. While the majority of newly found canine genodermatoses have a well-characterized human comparable condition, there are a few exceptions where the causal gene was discovered in dogs first. This means that more genes involved in the formation and maintenance of healthy skin are likely to be uncovered in the future [3].

The focus of this review is on skin illnesses that have a monogenetic inheritance or have well-defined main genetic risk factors. Except in cases when a specific coat colour is clearly connected with a skin illness, we did not include normal hair morphological features or normal coat colour variance. There were also a few syndromic disorders with significant cutaneous involvement [4]. The review will not cover multifactorial disorders like atopic dermatitis, which are likely influenced by (many) modest genetic risk factors. We present a list of all known canine genodermatoses as well as the genetic variations that cause them. The use of genetic analysis as a complementary method to clinical and histological exams, as well as its prospective impact on precision medicine, will be briefly discussed in the review.

### *Canine genodermatoses with known genetic aetiology*

There were a total of 36 genes linked to heritable skin diseases discovered. to be fa There were a total of 36 genes linked to heritable skin diseases discovered. We classified these genes by phenotype/disease to make it easier for physicians to use. We divided the diseases into three groups: ichthyoses and other keratinization disorders, epidermolyses and blistering disorders, and all other genodermatoses. Our affiliations aren't mutually exclusive. The epidermolytic hyperkeratosis produced by KRT10 variations, for example, is classified as ichthyoses and epidermolyses.

The great majority of canine genodermatoses are caused by harmful alleles that have emerged as a result of spontaneous mutation events in recent decades. This explains why most genodermatoses are limited to a single dog breed or a group of closely related breeds with recent genetic exchange. The ancient FOXI3 mutation, which causes ectodermal dysplasia

in some hairless dog breeds, and the various MLPH alleles, which cause coat colour dilution in many dog breeds and mixed breed dogs, are notable outliers.

### *Mixed breed dogs vs purebred*

The demographic structure of mixed breed dogs is similar to that of most human communities. As a result, monogenic heritable disorders in mixed breed dogs are uncommon in general. Dominant diseases, on the other hand, are equally likely to infect mixed-breed and purebred dogs.

Purebred dogs are bred in small, self-contained groups. This necessitates some inbreeding and encourages the expression of recessive alleles. As a result, recessive disorders are more common in purebred dogs than in mixed breed dogs. This is similar to the scenario that exists in some isolated human populations where consanguineous marriages are widespread [5]. The problem is aggravated in purebred dogs by the overuse of elite breeding animals. Every dog has a tiny number of detrimental recessive alleles. As long as the effective population size is large enough and the breeding dogs are used equally, the population will have a significant number of harmful alleles with low individual frequencies. Due to inbreeding, the likelihood that any of these detrimental alleles may come together in a homozygous condition in an offspring is not zero, but it is still low. The overuse of a small number of breeding animals may quickly lead to a situation in which certain of the detrimental genes reach extremely high frequency. Monogenic recessive disorders in purebred dogs may thus quickly progress from rare to widespread diseases if adequate breeding strategies are not implemented.

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