



# Orange's DNA results



# The road to less wild

Simply put, our cats are still wild little beasts. The history of cat domestication is vastly different from the domestication of other companion or agricultural animals. Whereas dogs went through thousands of years of selective breeding for behavioral and physical traits, cats have largely remained similar to their wild ancestors. This is why our home-based felines still have excellent hunting skills, feeding and grooming habits and the ability to pounce into action at any given moment.

So, how exactly did cats become part of human life? The pathway to domestication began as human agriculture flourished. The rodent population drastically increased with food storage. Cats played their welcomed role as nature's exterminator. Since cats chose to live with us, a systematic breeding program was never imposed on them for traits responsible for cohabitation. Our cats are unique and in some sense, the only animals known to have domesticated themselves to live with us. Due to this relatively short breeding process, the vast majority of modern cats are not the result of intentional breeding, nor have ancestors of a defined breed.

Unlike other dog or human ancestry tests, we cannot make the assumption that your cat was descended from a mixture of pedigree lines since pedigree cats are so new. However, using a large panel of purebred and pedigree cats that we have sequenced, we can try to find parts of your cat's genome that are similar to a known cat breed.

93% of all cats in the world are random-bred moggies. This is all we knew about them until now! With genetic data, we can learn more about what makes each mixed-breed polycat unique! As we gather more purebred data and trait information, we will be able to start narrowing down the parts of the genome that are responsible for certain traits and thus will continue to explore what makes YOUR polycat unique!

# **Breed Analysis**

#### Breed groups

We used high coverage whole genome sequencing pedigree cat data to generate what we call a genetic proximity map. This map visualises the underlying genomic differences between known cat breeds. For instance, breeds that are close to each other on the map share a high degree of genetic similarity. In many instances, such breeds are known to have a shared origin. The observed genetic similarity between breeds results in the formation of 4 foundational breed groups - Eastern, Western, Persian and **Exotic**. The genetic proximity map allows you to see how the breeds closest to your cat relate to other known breeds and breed groups.

## Chromosome map

Cats have 18 autosomal and 1 sex chromosome pairs. Our genetic analysis looks for regions on your cat's autosomal chromosomes that are most similar to different breed groups and individual cat breeds. We quantified these results, indicating what percentage of your cat's DNA is most similar to each respective breed or breed group. Keep in mind that genomic regions showing similarity to a particular breed do not necessarily indicate pedigree ancestry.

# Breed Analysis

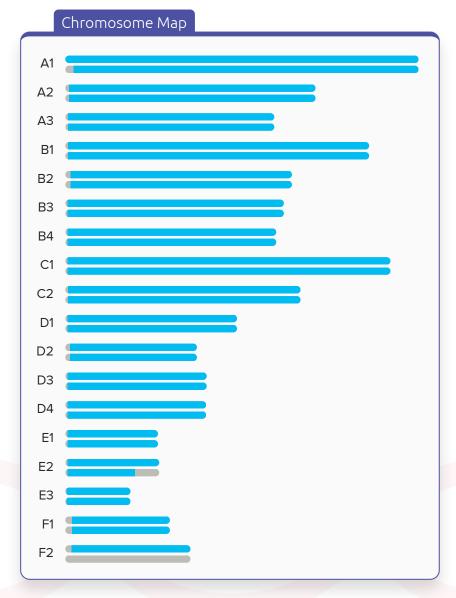


The **Chromosome Map** shows your cat's chromosome pairs with regions of genomic similarity to different breed groups shown in different colors. Mouse over a specific breed on the left and you will see which chromosomal regions in your cat are the closest match to this breed. Click on each breed in the Breed Groups to read more about each breed!

You can use the slider below to modify results to reflect different degrees of statistical confidence.



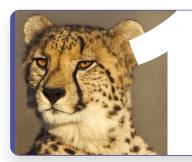
Western	93.92%
Maine Coon	93.05%
Ragdoll	0.88%
Polycat	6.08%



# Wildcat Index - What is it?

All cats around the world share the same common ancestor from about 10.8 million years ago. The progressive evolution of the common ancestor eventually led to the development of 37 modern cat species. However, as the evolution progressed bringing cats from the jungles into our homes, some domestic kittens inherited more or less DNA from particular wild relatives. Tiny differences and minimal amounts, yet this gives us a chance to better understand our cat, and all cats, with the help of genetics.

We compared your cat's DNA to the DNA of four wildcats and we ranked the results based on genomic similarity. For the majority of domestic cats, these results will look very similar as they broadly reflect the evolutionary history of domestic cats. These results should NOT be interpreted as evidence that your cat is part wildcat.



The cheetah is the world's fastest land animal, reaching speeds of over 110 km/hr (70 mph) in 3 seconds. With its unique anatomy, characterized by long legs, flexible spine and slender body frame, the cheetah is very different from other cats and is the only member of its genus – Acinonyx. Today, cheetahs are found in only 9% of their historic habitat and are considered functionally extinct, with 7,100 adults in the wild. They are classified as vulnerable on the IUCN Red List, considered a protected species in Namibia and endangered under the Endangered Species Act in the United States.



The cougar, also known as panther, puma and mountain lion, is found across the Americas. Cougars used to be abundant in the United States, often considered a nuisance as they prey on livestock. However, since the beginning of the 20th century, the cougar population has drastically decreased in the United States as they are hunted for their fur and partially due to them being killed to protect livestock. Eastern cougars, originally found in the Northeastern United States, are considered to be extinct. The Florida panther, a sub-species of cougars, is among the world's most endangered mammals.



Leopards are considered a young species, having originated around 500,000 years ago. Typically, leopards are light colored, with dark rosette shaped spots. Leopards are comfortable in trees and often stalk and hunt their prey by pouncing from trees. They are great swimmers and occasionally hunt fish and crabs while in the water. Leopards inhabit sub-Saharan Africa, northeast Africa, Central Asia, India and China. However, outside of Africa, most leopard populations are considered endangered. In addition, human expansion has resulted in a loss of 66% of leopards' habitat in Africa itself.



Tigers are the largest known cat species, with males from the largest subspecies, the Amur tiger, weighing up to 660 pounds (300 kg) and measuring 10 feet (3 meters). The smallest sub-species, the Sumatran tiger, can still reach an impressive 310 pounds (140 kg) and 8 feet (2.4 meters). The black stripe patter is unique to each tiger and can serve as an identification tag. Tigers are considered critically endangered although numbers are starting to stabilize in slowly increase in India, Nepal, Bhutan, Russia and China. It is estimated that there are around 3,900 tigers living in the wild today.

#### Kitty Genetics 101: Critical Reading

Genotype is the portion of your cat's genome that encodes the physical expression (phenotype) of a particular trait, such as eye color, coat color, or disease predisposition. Genes comprise the genotype. Every gene in your kitty's genome is present in two copies - one inherited from each parent. These two copies can be the same or different. If they are different, we say that the cat has two different alleles (gene variants) and is, therefore, heterozygous for this gene. On the contrary, if the two copies of the gene are the same, the cat is homozygous for the gene of interest.

When it comes to the phenotype, alleles can have different contributions. If the two gene alleles are the same, then they will both contribute to the phenotype equally. If the two alleles are different however, which allele will contribute to the phenotype depends on their relationship. Some alleles are dominant, meaning that they have the ability to "hide" other alleles and thus be the sole contributor to the phenotype. In contrast, the allele that is "hidden" in a heterozygous state is known as a recessive allele. A recessive allele can only contribute to the phenotype when your cat is homozygous for that allele, i.e., there is no dominant allele to hijack the phenotype expression.

#### How Does It All Relate To Disease?

Genetic disorders are conditions that are present at birth or develop later in life and are caused by one or more genetic mutations. We tested your cat for genetic health markers associated with genetic disorders. Genetic health markers are mutated gene alleles associated with an increased likelihood of developing a particular genetic disorder. With the exception of hypertrophic cardiomyopathy (HCM), which has more complex genetics, the conditions included in this report have either a dominant or a recessive pattern of inheritance. This means that for diseases with a dominant inheritance pattern, having just one mutated gene allele will result in the cat developing the disease. Conversely, for diseases with a recessive inheritance pattern, the cat will only develop the disease if it has 2 mutated alleles. Having just one mutated recessive allele makes the cat a disease carrier, meaning that it will not develop the disease, but it can pass down the mutation to its kittens.

In this part of the report, you will see your kitty's results for 38 genetic markers associated with 16 diseases. 'Clear' status indicates that your cat tested negative for a particular genetic marker. 'Carrier' status means your cat has one copy of a recessive genetic marker and should only be a concern if you plan to breed your cat. 'At risk' and 'At high risk' status means that your cat has tested positive for a dominant allelic mutation or has two copies of a recessive allelic mutation. If you see one of these two result designations, contact your veterinarian.

Please note, Basepaws results should not replace the evaluation and the clinical diagnosis made by a veterinarian. We also want to point out that a 'Clear' result does not mean your cat is guaranteed to not develop the disease. It simply means your cat is negative for the mutation we tested. There may be environmental factors and other not yet known genetic mutations contributing to developing the disease.

In this section, you will find a brief description for each of the genetic diseases you currently have results for. Each of these disease is represented by at least one known health marker. In addition to your cat's results, we have also included details on the genes and genetic mutations included in our test.

Clear – The cat is negative for the disease-associated marker we tested

Carrier – The cat has one copy of an autosomal recessive disease-associated marker

At Risk – The cat has one copy of a marker associated with hypertrophic cardiomyopathy

At High Risk – This designation can mean one of three things:

The cat has 1 or 2 copies of a marker associated with an autosomal dominant disease

The cat has 2 copies of a marker associated with hypertrophic cardiomyopathy

The cat has 2 copies of an autosomal recessive disease-associated marker

IMPORTANT: Not all health reports might be available initially, and more markers and results can be added over the coming weeks and even months! Stay close to your results and check often to see any new health markers and diseases added.

#### Polycystic kidney disease

Polycystic kidney disease (PKD) is the most common genetic disease in cats. PKD is characterized by the formation of small fluid-filled cysts in the kidneys that lead to kidney failure.

Gene	Mutation	Status	
PKD1	C>A	Negative	Clear

## Cardiomyopathy, hypertrophic

Hypertrophic cardiomyopathy (HCM) is the most common feline heart disease characterized by tachycardia.

Gene	Mutation	Status	
MYBPC3	G>A *Frequent in Rag Doll	Negative	Clear
MYBPC3	C>G *Frequent in Maine Coon	Negative	Clear

# Retinal degeneration II

Progressive retinal atrophy (PRA) is a disease marked by the deterioration of retinal caused by the progressive death of retinal cells.

Gene Mutation Status

CEP290 A>C Negative Clear

## Mucopolysaccharidosis I

Mucopolysaccharidoses are a group of metabolic disorders characterized by a deficiency in the production or functioning in lysosomal enzymes required for digestion of glycosaminoglycans (GAGs).

Gene Mutation Status

IDUA GTC>del Negative Clear

\*Type I

# Mucopolysaccharidosis VI

Mucopolysaccharidoses are a group of metabolic disorders characterized by a deficiency in the production or functioning in lysosomal enzymes required for digestion of glycosaminoglycans (GAGs).

Gene Mutation Status

ARSB A>G Negative Clear

\*Type VI

# Mucopolysaccharidosis VII

Mucopolysaccharidoses are a group of metabolic disorders characterized by a deficiency in the production or functioning in lysosomal enzymes required for digestion of glycosaminoglycans (GAGs).

Gene	Mutation	Status	
GUSB	G>A *Type VII	Negative	Clear
GUSB	T>G *Type VII	Negative	Clear
GUSB	C>T *Type VII	Negative	Clear

## Gangliosidosis, GM1

Gangliosidosis is a group of lipid storage disorders characterized by the accumulation of lipids – gangliosides in neurons. GM1 gangliosidosis (type 1) is caused by a deficiency of an enzyme called beta-galactosidase.

Gene	Mutation	Status	
GLB1	C>G	Negative	Clear
	*GM1		

### Gangliosidosis, GM2, GM2A deficiency

Gangliosidosis is a group of lipid storage disorders characterized by the accumulation of lipids – gangliosides in neurons. GM2AB gangliosidosis (type AB) is associated with a deficiency in beta hexosaminidase A.

Gene	Mutation	Status	
GM2A	GACC>del	Negative	Clear
	*GM2. GM2A deficiency		

# Gangliosidosis, GM2, type II (Sandhoff or variant 0)

Gangliosidosis is a group of lipid storage disorders characterized by the accumulation of lipids – gangliosides in neurons. GM2AB gangliosidosis (type AB) is associated with a deficiency in beta hexosaminidases A and B.

Gene	Mutation	Status	
HEXB	T>del *GM2 Type II	Negative	Clear
HEXB	TACTGGATATTGTGACTATGAATAC>inv *GM2 Type II	Negative	Clear
HEXB	C>T *GM2 Type II	Negative	Clear

## Cystinuria, type B

Cystinuria is an inherited metabolic disease, relatively common in dogs and rare in cats, associated with high cysteine levels in urine.

Gene	Mutation	Status	
SLC7A9	C>T *Type B	Negative	Clear
SLC7A9	G>A *Type B	Negative	Clear

# Cystinuria, type I - A

Cystinuria is an inherited metabolic disease, relatively common in dogs and rare in cats, associated with high cysteine levels in urine.

Gene	Mutation	Status	
SLC3A1	C>T	Negative	Clear
	*Type I-A		

# Porphyria, acute intermittent

Porphyria is a group of diseases associated with the accumulation of porphyrins. The buildup of porphyrins in the acute diseases primarily affect the nervous system.

Gene	Mutation	Status	
HMBS	ACAG>del *Acute intermittent	Negative	Clear
HMBS	T>ins *Acute intermittent	Negative	Clear
HMBS	G>A *Acute intermittent	Negative	Clear
HMBS	C>T *Acute intermittent	Negative	Clear
HMBS	G>A *Acute intermittent	Negative	Clear
HMBS	GAG>del *Acute intermittent	Negative	Clear

# Porphyria, congenital erythropoietic

Porphyria is a group of diseases associated with the accumulation of porphyrins. The buildup of porphyrins in the acute diseases primarily affect the nervous system.

Gene	Mutation	Status	
UROS	G>A *Congenital erythropoietic	Negative	Clear
UROS	C>T *Congenital erythropoietic	Negative	Clear

# Autoimmune lymphoproliferative syndrome

Mutation

Autoimmune Lymphoproliferative Syndrome (ALPS) is a lethal disease distinguished by massive enlargement of lymphatic nodes and spleen caused by the accumulation of lymphocytes.

Gene	Mutation	Status	
FASLG	A>ins	Negative	Clear

## Factor XII deficiency

Factor XII deficiency, or Hageman deficiency, is a blood clotting disorder characterized by deficiency in the coagulation factor XII.

Gene	Mucacion	Status	
F12	C>del	Negative	Clear
F12	G>C	Negative	Clear

# Hypothyroidism

Feline Conginetal Hypothyroidism with Goiter is a rare autosomal recessive disease that affects the thyroid levels in the blood.

Gene Mutation Status

TPO C>T Negative Clear

#### Mannosidosis, alpha

Alpha mannosidosis is a lysosomal storage disorder characterized by the deficiency of the alpha-D-mannosidase enzyme. A defective alpha-mannosidase causes progressive accumulation of mannose-rich oligosaccharides in all tissues, which subsequently disrupts the cellular functions and causes apoptosis.

Gene Mutation Status

MAN2B1 CTGG>del Negative Clear

# Myotonia

Myotonia Congenita (MC) is a hereditary neuromuscular disorder characterized by persistent contraction (or delayed relaxation of muscles), particularly during the muscle movement.

Gene Mutation Status

CLCN1 G>T Negative Clear

# Niemann-Pick disease, type C1

Niemann-Pick disease is a group of hereditary lysosomal storage diseases. Feline Niemann-Pick disease C coincides with the human type C of this disorder, and it is classified in two subtypes: C1 and C2.

Gene Mutation Status

NPC1 T>G Negative Clear

# Primary hyperoxaluria type II (Oxalosis II)

Hyperoxaluria is a congenital, potentially lethal condition characterized by disrupted metabolism of oxalates and their excessive urinary excretion.

Gene Mutation Status

GRHPR G>A Negative Clear

## Pyruvate kinase deficiency of erythrocyte

Pyruvate kinase deficiency is an inherited metabolic disorder characterized by disrupted survival of erythrocytes (red blood cells).

Gene Mutation Status

PKLR G>A Negative Clear

# Vitamin D-deficiency rickets, type I

Rickets or osteomalacia is a disease associated with the softening of bones and increased rate of bone deformities and fractures.

Gene Mutation Status

CYP27B1 C>del Negative Clear