Thermo Fisher SCIENTIFIC

Scientist spotlight

Understanding the feline genome with advanced microarray technology

Meet the scientist advancing the field of feline genetics

The field of feline genetics has helped cultivate our understanding of cat breeds. Insights include pinpointing diverse genetic traits such as coat variation, tracing the origin and evolution of domestication, and uncovering disease mechanisms. Dr. Leslie Lyons, one of the world's leading feline geneticists and Gilbreath-McLorn Endowed Professor of Comparative Medicine at the University of Missouri College of Veterinary Medicine, has been at the helm of this discipline for more than three decades. Her research has resulted in breakthrough discoveries that have laid the groundwork for improving feline and human health, such as uncovering the first-ever domestication of cats in the Fertile Crescent [1].

Today, her laboratory at the University of Missouri aims to bring precision and genomic medicine to companion animals. Her research focuses on the genetic aspects that influence feline inherited diseases, phenotypic and morphological traits, and population dynamics. Applications of her research include translational medicine, genetic testing, and forensics [2]. Advanced analytical technologies and refined sequencing techniques have been instrumental in furthering the broader goal of Dr. Lyons' research, which is to use cats as a biomedical model to study diseases that impact both cats and humans, such as polycystic kidney disease, blindness, and dwarfism [3].

To achieve this goal, Dr. Lyons has been building a toolkit of genotyping technologies and genomic resources, including domestic cat microsatellite markers, short tandem repeats (STRs), and single-nucleotide polymorphisms (SNPs), as well as a domestic cat DNA array [4]. Her focus on creating robust technologies that support advanced feline genomics and complex disease studies has made way for innovation, including the development of a higher density feline microarray with Thermo Fisher Scientific.

Developing a high-density feline microarray

Dr. Lyons' research has been instrumental in developing SNP genotyping technologies for cats. The first cat microarray, a 63,000 SNP array, used over 2,000 feline samples and represented 41 cat breeds, one random-bred population, and four wild felid species [5]. While lower density, this array has helped researchers find

Dr. Leslie Lyons, Gilbreath-McLorn Endowed Professor of Comparative Medicine, University of Missouri

mutations in fancy cat breeds, such as Bengal and Savannah cats. However, the majority of cats in the world are mixed-breed and randomly bred [6]. There was a need for a higher density array to prove significant associations and answer health questions about random-bred cats. Dr. Lyons and Thermo Fisher collaborated to make this powerful microarray technology with higher resolution, throughput, and increased sample size a reality.

Working with bioinformatics specialists at Thermo Fisher, Dr. Lyons and her colleague, Dr. Reuben Buckley, a postdoctoral fellow at the University of Missouri, designed a customized, high-throughput 630,000 SNP microarray that offers 10 times the density of the currently available cat SNP array. It was critically important that the array could be used to help researchers answer health questions, such as comparing single-gene disorders and conducting association studies of complex diseases in random-bred cats, so the design needed to have good spacing, high density, and the most polymorphic markers that the team could get on the chip.

This array used the full cat genome sequence that was available because of the 99 Lives Cat Genome Sequencing Initiative, a community-based research project that aims to sequence the genome of 99 or more cats to improve coverage of the cat genome, improve future assemblies of the cat genome, and identify genetic

variation and mutations present in diseases [7]. The data collected via this project include DNA from healthy cat breeds and populations around the world, plus wild felids, such as lions, tigers, and cheetahs. Because of the data from the 99 Lives project, Dr. Lyons and the team at Thermo Fisher could prioritize specific genomic regions and select the right type of markers for this array.

In addition to the higher density, the team worked to optimize marker distance across the array, which helps to decrease poor genotyping or errors. The excellent genome sequence enabled the bioinformatics team to space these markers out properly. This high-density, multipurpose array holds immense potential for future users—from large, direct-to-consumer corporations to smaller academic labs who are interested in using innovative technology to further genetic studies and generate more accurate data.

The cat-human genome comparison

Scientists' understanding of genetic information has transformed our modern world. For example, the study, diagnosis, and treatment diseases; improvement of crop growth and building of the food supply; and DNA-based forensic analysis are all application areas where innovation is led by cutting-edge genomic technologies. Microarray solutions have helped researchers build a trove of genomic data on humans, primates, rodents, and companion animals, such as dogs and horses. Over the years, there has been an increased interest in feline genetic research, and a variety of genomics resources and tools have been developed to further the field.

Understanding genetic aspects of domestic cats and wild felids can play a vital role in veterinary care, but it can also help to improve human health and further disease research, as the feline genome and human genome are structurally similar [8]. According to Dr. Lyons, studying the genetic causes and treatments of diseases in cats could one day be useful for treating humans with the same diseases [9]. For example, the currently available treatment for cats with polycystic kidney disease can have negative side effects, such as liver failure. Dr.Lyons, along with other academic researchers, used feline genetic insights to develop an alternative, diet-based treatment [10]. If successful in cats, this research could help inform alternative treatment plans for humans.

There are other disorders, such as dwarfism, where feline DNA has helped point disease researchers toward a better understanding of the disorder in humans. Dwarfism in humans is often caused by a very specific genetic mutation, but Dr. Lyons was able to find that a completely different gene was affected in cats with the same disorder. This understanding has the potential to be applied to undiagnosed human cases of dwarfism. Other disorders, like retinal degeneration, can also be studied by learning more about feline and human DNA, how the genes work, where mutations happen, and even which medications might be most effective. A high-density array is critical for this type of advanced research.

Choosing the Axiom microarray portfolio to genotype companion animals

Thermo Fisher has been a trusted provider of innovative microarray technologies for decades. From predesigned and validated content to custom solutions, many scientists choose Applied Biosystems™ Axiom™ microarrays to accelerate their unique research needs. These advanced microarrays often offer greater resolution and rapid, reliable results, allowing researchers to verify pedigrees and the genetic health of companion animals, such as dogs, cats, and horses, or even genotype entire animal populations.

Axiom microarrays are a powerful solution for a wide range of applications including studying marker–trait association, evaluating elite lines, and identifying reference populations consisting of multiple genetic lines, as well as research applications for genome-wide analysis and selective sweep analysis studies. Predesigned arrays from Thermo Fisher are available as low-, medium-, and high-density arrays, so scientists or breeders can choose the best array based on their research needs. For some, a custom marker panel or multiple-species array may be needed to target important parentage and traits, as well as markers associated with defects in the breeds and varieties of interest. By collaborating with Thermo Fisher, customers can design fully or semi-customized arrays containing 300 to 2.6 million markers without any restrictions on the number of markers per species.

Technologies within the Axiom microarray portfolio help breeders, veterinarians, and researchers target the most informative parentage, trait, and genetic markers for their breeds and varieties, making way for novel research. Thermo Fisher is committed to working with scientists around the world, like Dr. Lyons and others at the forefront of discovery in their fields, to offer scalable and affordable genotyping solutions for a variety of applications.

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