FEATURE

Let's talk about innovation

How can veterinary medicine leverage recent advances in genomics?

By David Haworth and Aaron Massecar

Highlights:

- Falling costs and advancing technology mean genetic research holds big possibilities for veterinary medicine, including improved patient care and revenue.
- New genomic testing makes it possible to figure out what conditions pets might be genetically susceptible to so veterinary teams can take preventive steps.
- Genomic testing—which many pet owners are already using—could lead to more individualized treatment, making the technology a potentially powerful tool for veterinary teams.

Every week, new publications appear demonstrating the power of genetic analysis to help us understand and treat disease in our patients. Developments that started in 2002 when the human genome was first sequenced are maturing and finally becoming applicable to veterinary medicine thanks to the plummeting cost of genetic sequencing and the entry into our market of readily available DNA tests.

While basing diagnoses on genetics certainly isn't new in our profession, these new research and product developments open even more possibilities for improved care and revenue.

Two kinds of genetic problems

Problems in the genome happen two ways: Either the patient was born with it, or the genome changed during the patient's lifetime. Both play a role in disease.

Mutations happen all the time. Every time a cell divides and the billions of base pairs that make up the genome replicate themselves, mistakes happen. Those mistakes are the basis of evolution (probably a good thing) and genetically related disease (not such a good thing).

One of the reasons genomic sequencing failed to live up to the hype of radical medical advancement had to do with the complexity of identifying specific genetic diseases. We thought there would be a few common themes that would become apparent as we started to explore the genetic landscape. Alas, biology turned out to be more complicated than that, and the mountains we thought we would find and conquer turned out to be an incredibly varied and nuanced landscape of hills and valleys.

But with time and adequate resources, even nuanced landscapes can be mapped. Plus, we can often leverage research on human diseases like diabetes and cancer for the species our profession is focused on. Outcomes that cost billions to find in humans can be confirmed or denied in dogs, cats and horses for a few million. And that price is coming down dramatically thanks to reductions in the costs of genome sequencing and computing power.

It is rare that a single mutation causes disease. If it does, that patient usually does not make it out of the womb alive. More commonly, there is a series of genetic "switches" that need to all be flipped in the right combination to cause disease. This is where "germ line" mutations—those we inherited from our parents—interact with "somatic" mutations: those that happened spontaneously during cell division. If you are born with a bunch of the genetic switches already flipped in the way they need to be in order to cause a certain disease, it doesn't take many mutations in other genes in that pathway to cause the disease to manifest. This is the nature of breeds predisposed to certain conditions. Of course, overwhelming assaults on the genome—high exposure to mutagens like radiation or cigarette smoke—can also cause all the switches to flip during a single lifetime.

Prognostics and diagnostics

But here is another place where genomic diagnostics come in. They can tell us which switches are flipped and which ones are normal. When genetic testing of healthy dogs was introduced in 2007 (two short years after the first canine genome, a Boxer named Tasha, was sequenced), it was really a fancy breed test: interesting at cocktail

parties but of limited medical use. Current tests look for hundreds or thousands of known heritable traits and diseases.

Having one gene flipped one way or the other doesn't necessarily mean disease is inevitable, but smart owners and vets should use this information to predict and watch for specific diseases, and not just in breeding decisions. Some even go so far as distinguishing this field as separate from diagnostics because of the predictive nature of the work, calling it "prognostics." If I know the dog in front of me has an increased risk of, say, hemangiosarcoma, why wouldn't I suggest that we proactively ultrasound the spleen and liver twice a year? Good medicine and certainly good revenue.

Couple prognostics, focusing on the state of an animal's germ line mutations, with diagnostics that look at somatic mutations inside a specific disease state like cancer, and we begin to get a complete picture of which genetic switches are flipped the wrong way. And knowing which mutations are driving the disease also gives us insight into which specific molecular pathways are impacted and therefore which molecules can be inhibited or supplemented to help treat the disease.

In this way, prognostics can become part of a larger set of tools veterinary professionals can use to narrow in on a particular disease and treatment plan. There are challenges, however, with being able to implement prognostics in the average practice. For example, unless the DNA test was recently performed, it becomes difficult for a veterinarian to dig into the patient record for the genetic information that would be required to supplement the diagnosis. Additionally, it's far too easy for records to be lost when owners change clinics, and the valuable information contained within these reports might not be available when the time comes. Last, there are challenges associated with the production of viable information because not every genetic testing company is providing the highest level of quality control measures.

These challenges, though, are neither trivial nor insurmountable, and the information generated by these test results and their applicability in solving complex medical conundrums will necessarily drive the market toward solutions for each of these obstacles.

Individualized medicine

In veterinary medicine, we have always practiced "individualized" medicine—tailoring diagnostics and therapeutics to the individual patient in front of us. With new, powerful tools becoming available, we can further refine that tailoring process to a finer and finer resolution. You don't need a deep understanding of genomics any more than you need a deep understanding of biochemistry to interpret small-animal biochemistry panels.

Are there limitations and drawbacks to these tests? Absolutely. There is a ton we don't understand, and the path from genetic mutation to disease state involves RNA, proteins and other compensatory and accelerating mechanisms. Biology is complicated. But we are making huge strides in the areas of molecular medicine, and to ignore those or wait for them to become perfect is probably denying a whole lot of our patients the care they deserve.

Because of this potential, we are advocating for more veterinary professionals to look into and explore the use of genomic testing in their clinics. It's very likely clients are already using it, so why not engage those progressive-minded owners and bring the tests into the cycle of care?

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