The Resistome: What is it, and why should I care?

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Did you know that you currently have dozens – maybe even hundreds – of antimicrobial resistance genes in, on and around your body? While this sounds alarming, it is probably normal. In fact, scientists have identified antimicrobial resistance genes in places as remote as the Antarctic permafrost, and even in the frozen stomach contents of "Ötzi" the Iceman (who certainly didn't benefit from modern antibiotics)! We term this universal collection of antimicrobial resistance genes the "resistome". It is just like the "microbiome" (aka the collection of microbes in our world) -- but for antimicrobial resistance.

To understand research that uses the resistome, I first need to give a short primer – so bear with me! Antimicrobial resistance is generally thought of as the ability of microbes to resist the effects of antibiotic drugs. In the past, researchers have studied antibiotic resistance by growing (or "culturing") a pathogen in a Petri dish, and then bathing the pathogens in an antibiotic drug. If the pathogens are able to grow in the antibiotic, they are termed "resistant". This approach yields useful information, especially if a doctor or veterinarian is trying to treat a patient that has an illness caused by a specific pathogen. However, our bodies, homes and environments contain thousands of different microbes – the pathogen making us sick is just one of these thousands. Therefore, when we limit our investigation to a single pathogen, we are missing thousands of bacteria that may also be carrying resistance DNA.

Today, we can overcome this limitation by harvesting all of the microbial DNA in a sample and "reading" it using a next-generation sequencing machine. Just like you can have your own human DNA sequenced, we can also sequence the DNA of all of the microbes that inhabit your body, home, pets or farm. Once we sequence this DNA, we can then look at it closely to identify all of the resistance genes that are present – this is the "resistome" of the sample. Of course, it takes supercomputers and bioinformatics to accomplish this task, but many scientists are now performing these types of analyses on a fairly routine basis.

The big question is: who cares? What does all of this DNA and the resistome mean for animal production? Or even human health? Well, this is early days for resistome research, and therefore those questions are still being answered (and probably will be for the foreseeable future). However, in our own research, we have found some emerging trends that I believe have some important implications for the work that you do on your farm, as well as policy development, and public, human and animal health. In this MSHMP report, I will detail two of these five trends, and stay tuned for the next three!

1. ***The resistome is everywhere, and it usually contains many dozens (and sometimes hundreds and thousands) of unique resistance genes***. As I mentioned earlier, resistance genes have been identified in numerous and diverse "pristine" environments, such as caves that have been untouched by humans for thousands of years, or the feces of remote, indigenous human populations where antibiotics have not been used; resistance DNA is found commonly in the meconium of newborn infants and animals. Given all of this evidence, there is now a strong consensus that the DNA that codes for antibiotic resistance is a "natural phenomenon", and that this "natural" resistome can be very diverse. So why does this matter? Well, it makes it tricky to define a baseline, and therefore tricky to identify specific management practices that might be causing the resistome to become "worse". Every veterinarian knows: if you can't define normal, it's hard to define abnormal.

2. ***The resistome that we detect in a sample is determined largely by the microbiome in that same sample***. This might seem intuitive, but it has important implications for resistance research and control. Because what this means is that *anything* that we do to change the microbiome will most likely have a big impact on the resistome as well. And many things can change the microbiome, including changing our diet, moving to a new home (or farm), undergoing stress, getting sick, and becoming pregnant. Therefore, if any of these changes are occurring in our herd, we should expect to see changes in the resistome profiles of our animals. And as producers and veterinarians, I'm sure you realize that most of your livestock are undergoing at least one (if not multiple) of these "life events" nearly every day. So if we want to understand specifically how *antibiotic use* impacts resistance in our herd, we need to take into account all of these *other* things that might be occurring in our livestock at the time of antibiotic administration. By the same token, we need to realize that experimental conditions (for instance, putting animals in small groups in a research facility) may induce microbiome (and thus resistome) shifts that are completely different than those we would see in commercial production. Certainly such experimental studies are a rational and solid starting point, and I don't want to discredit their utility; however, in order to develop meaningful and concrete policies and guidelines, I believe we need well-controlled, large-scale studies in livestock animals being raised under true commercial conditions. Without such studies, it is impossible to generate practical, evidence-based guidelines regarding antibiotic use and resistance. And in the absence of evidence, it is all too easy for people to react out of fear, which can result in irrational and/or ineffective policy. This point is especially significant as scrutiny over preventive antibiotic uses grows.

Check back next week for points 3, 4 and 5! And in the meantime, the following links contain research summaries from studies that have utilized a resistome approach in commercial livestock populations:
https://meg.colostate.edu/wp-content/uploads/2016/08/MEG_Take-Home_Summary_-_eLife_04MAR2016.pdf
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