

## **Genome Sequence Analysis in Veterinary and Human Medicine**

The science of genome sequencing and analysis has undergone radical changes in the past several years. Projects that 10 years ago cost hundreds of thousands of dollars and took several months to complete can literally be done for hundreds of dollars and take a total of three weeks from start to finish. There are many possible applications of “High-Throughput Sequencing” (HTS) in infectious disease studies, including generation and analysis of region-specific vaccines, strain typing of pathogens, and studies of normal flora in health and disease. Many applications also exist for use of these tools for study of other aspects of animal health and well being. The following discussions show how these tools are being used in the Biomedical Sciences department of our College of Veterinary Medicine, most often through interactions with the O.S.U. Center for Genome Research and Biocomputing (CGRB).

### **Genome sequencing of chlamydial pathogens**

A graduate student in Dr. Dan Rockey’s laboratory, Tim Putman delivered a well-received talk to the members of the Chlamydia Basic Research Society meeting in San Antonio in March. Tim is a third year graduate student in the OSU Molecular and Cellular Biology Program. He investigates novel technologies for doing very rapid and inexpensive genome sequencing in different Chlamydia species. His talk addressed the use of clinical swab material to generate complete genome sequences in the absence of culture, and the subsequent analysis of the collected genomes. While this talk directly addressed the human pathogen Chlamydia trachomatis, the technology is being applied to chlamydia pathogens of sheep, and could be used for many different pathogens of significance in human and veterinary medicine. A manuscript describing this work should be submitted soon. Previous work by this group involved the examination of recombination within chlamydiae, using genome sequencing of parental and recombinant strains as a tool of discovery. Genome sequence analysis by Dr. Brendan Jeffrey, previously in the Rockey Lab, led to significant understanding of this process, and his work was published in the journals Infection and Immunity and BMC Microbiology. More work in this area will also be published in the near future.

### **Studies of novel viral infections of mammals and fish species**

The laboratory of Dr. Ling Jin has used genome sequence analysis to examine new viral pathogens in animals and fish, including a coronavirus of alpacas, a herpesvirus of rabbits, and a novel viral pathogen of goldfish. Each of these viruses was isolated from diseased animals and represents an emerging infection in that species. This group used the HTS technology to complete the genome sequence of an alpaca coronavirus, which was first identified by Dr. Chris Cebra of the Clinical Sciences Department. These investigators also isolated and characterized Leporid Herpes Virus-4, an important and unique herpesvirus that is highly lethal in production rabbits. An additional herpesvirus sequence was also completed by the Jin laboratory- a strain of human herpesvirus that causes human ocular infections with high frequency of recurrent infections.

Dr. Jin and her doctoral student, Dr. Aimee Reed, DVM, also used genome sequencing to examine an interesting and unique viral pathogen identified in goldfish from a Willamette Valley ornamental pond. A novel viral pathogen was identified from these goldfish, from tissue exhibiting an unusual neurofibroma (NF) tumor of the skin. This virus was isolated in koi fin (KF-1) cells infected with tumor tissue extracts. Dr. Reed is working to assemble this genome following generation of data at the CGRB. Dr. Reed has also been involved in assembling a herpesvirus sequence from cows, Bovine Herpesvirus 2 associated with a bovine skin condition.

### **Microbiome analyses in the mammalian intestine**

A new faculty member in Biomedical Sciences, Dr. Natalia Shulzhenko studies interactions between the intestinal immune and metabolic functions and the commensal microorganisms (microbiota), using mouse models of human disease. This is a rapidly progressing area of understanding in the health of virtually all animal species. Because there are so many different microbes in the mammalian intestinal tract, and because so many of these

cannot be cultured in the laboratory, contemporary genomic technologies are essential components of these analyses. The Shulzhenko laboratory makes use of genomic techniques to simultaneously analyze global gene expression by the host and the composition of microbiota. Most of these technologies center on sequence analysis of the conserved 16S rRNA gene to identify the microbial taxa and a metagenomics “shotgun” approach to uncover the functional capacity of microbiota. They hope to reconstruct the networks of interaction between the host and the microbes in order to understand which commensals drive which immune and metabolic functions in the gut.

### **Determining the mechanisms of pathogenesis in different *Mycobacterium* spp.**

*M. avium* complex is an opportunistic intracellular pathogen that can infect a variety of hosts and is commonly found in the environment. There are several established clinical isolates of *M. avium* that have differing phenotypes both in vitro and in vivo. Brendan Jeffrey and others in the laboratory of Dr. Luiz Bermudez lab have used the HTS technologies in the CGRB to sequence the genomes of several clinical isolates of *M. avium*, with a goal of identifying genomic regions within these strains that are associated with unique aspects of pathogenesis. Along with the genome sequencing, they will examine the transcriptional profiles of *M. avium* strains, to determine what genes are specifically upregulated in different growth conditions. Taken together, these approaches will help the researchers determine regions of the genome that are important in the mycobacterial disease process.

### **Pathogens in an important laboratory animal species: the zebrafish**

Zebrafish are a well-established vertebrate model for development, toxicology, cancer, and several infectious diseases. The most prevalent pathogen diagnosed in laboratory zebrafish is the microsporidian parasite, *Pseudoloma neurophilia*. The laboratory of Dr. Mike Kent is working to use the zebrafish/*P. neurophilia* model to study both vertical (i.e. direct parent to offspring) and horizontal (i.e. fish-to-fish) transmission of the pathogen. This group is working to complete the genome sequence of *P. neurophilia*, which will enable them to investigate the genetic basis of virulence in their transmission studies. These investigators are working with scientists at the University of Ottawa, and expect the genome sequence to be completely assembled in the next few months. These individuals are conducting state of the art research addressing significant infectious disease problems in veterinary and human medicine. Each research plan uses an integrative approach that involves connecting clinical aspects of the disease with the genomic sequences of the pathogen responsible for the problem. There are also researchers in the Clinical Sciences department using similar approaches for other problems in veterinary medicine. Individuals in the college will continue to use contemporary technologies to investigate these and many other conditions, with a goal of helping treat diseases of animals both in the present and the future.