Tuesday Sepember 4th – Langeve / Cartier
Zebrafish / Lab Animal Health
Moderator – Michael Kent (Oregon State University)

9:30 AM	Zebrafish / Lab Animal	Kent - Overview of Diseases of Zebrafish in Research Facilities
9:45 AM		Farmer - Challenges and Opportunities for Management of Disease Control and Biosecurity in Biomedical Zebrafish Facilities
10:00 AM		Sanders - Overview of Impacts of Common Zebrafish Pathogens
10:15 AM		Murray - Reversibility of Proliferative Thyroid Lesions Induced by Iodine Deficiency in a Laboratory Zebrafish Colony

Overview of Diseases of Zebrafish in Research Facilities

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The use of zebrafish *Danio rerio* as an in vivo model in biomedical research has expanded at an incredible rate over the last few decades. Originally it was mostly used as model in developmental genetics, but now is widely used in a variety of research areas that utilize adult zebrafish as research endpoints. Concurrently, the importance of acute diseases that cause high mortality, as well as those that are chronic or subclinical have become more important. The Zebrafish International Resource Center has been providing a diagnostic service to the research community since 1999, in which histopathology is our primary diagnostic tool. We have evaluated over 17,000 fish from laboratories around the world, and the following summarizes the patterns of infections and diseases that we have seen. *Pseudoloma neurophilia* is the most common pathogen, infecting the central nervous system in about 50% of the facilities, with about 10% prevalence in number of fish examined. Other common diseases and pathogens are as follows: Mycobacteriosis, caused by *M. chelonae*, *M. marinum* or *M. haemophilum*, *Pseudocapiillaria tomentosa*, *Myxidium streisingeri* and transmissible intestinal neoplasms associated with a *Mycoplasma* sp. *Edwardsiella ictaluri* is uncommon, but has caused severe disease. Other very common neoplasms are seminomas and ultimobranchial tumors. Common water quality related diseases include gas supersaturation and idiopathic gill diseases.

Conference Session Designation: (Zebra Fish or Lab Animal Medicine)
Presentation Format: (Oral)

Challenges and Opportunities for Management of Disease Control and Biosecurity in Biomedical Zebrafish Facilities

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The presence of zebrafish (*Danio rerio*) as an animal model for human diseases has grown tremendously in recent years, and they now are the second most commonly used research species in Great Britain (Home Office annual statistics for 2015). A literature review suggests that more than 5 million zebrafish are used yearly in research performed at more than 3,250 institutions in over 100 countries. Zebrafish are a popular model for a variety of reasons, including that they are genetically similar to humans, are more easily and economically housed and maintained than many other animals, and are robust breeders. Efficient genetic manipulation of zebrafish is possible using several approaches. In addition, zebrafish are a valuable model for pharmacology and toxicology studies as a given test substance may be added to their tank water, reducing a need for more invasive animal manipulations like injection or gavage. However, the rapid expansion of this animal model has led to challenges in facility disease control and biosecurity. When zebrafish were first used in biomedical research, there were no commercial vendors providing pathogen defined zebrafish. While there are now vendors who provide specific pathogen-free zebrafish and health testing of zebrafish on a fee for service basis, some institutions still do not routinely test their colonies or share this information when sharing fish. Because many facilities now operate as centralized resources, it has become critical that zebrafish facility personnel and scientists understand which diseases must be carefully excluded to reduce negative research results in particular studies. This talk will focus on the diseases that are most important to exclude from research colonies, the advantages and disadvantages of available testing methods for performing health surveillance, and characteristics of a robust biosecurity program. The use of these approaches is crucial to ensure the quality of research produced using this animal model and to reduce variation between research done at different institutions and laboratories.

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Overview of Impacts of Common Zebrafish Pathogens

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Zebrafish used in laboratory research can harbor pathogens such as mycobacteria, microsporidia and helminths. Some of these infections can be clinical and lead to significant mortalities. However, subclinical infections can impact experimental endpoints, resulting in non- protocol induced variation. As the use of zebrafish has rapidly expanded to include a wide range of studies involving immune function, microbiome composition, and behavior, it is important to understand how subclinical infections by these pathogens can impact experimental results. The results of several experiments will be presented demonstrating the impacts of the most common pathogens, Pseudoloma neurophilia, Mycobacterium chelonae, and Pseudocapillaria tomentosa, on several experimental endpoints including fecundity, immune function, microbiome, and behavior.

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Reversibility of Proliferative Thyroid Lesions Induced by Iodine Deficiency in a Laboratory Zebrafish Colony

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Zebrafish (*Danio rerio*) in a large laboratory facility experienced a widespread occurrence of red nodular lesions that were located predominantly in the ventral mandibular region. This facility housed approximately 37,000 fish distributed among 2040 tanks, of which, 220 tanks (~10%) were overtly affected. Among affected tanks, approximately 25% of the fish had externally visible masses. The masses were observed in wild-type, mutant, and transgenic lines, without apparent predilection for sex, researcher, or room location, and lesion occurrence was not associated with increased morbidity or mortality. Initially, twelve fish with visible masses were submitted to the Zebrafish International Resource Center (ZIRC, University of Oregon, Eugene, OR) diagnostic service for histopathologic processing and evaluation. Following humane sacrifice, fish were preserved as whole body specimens in Dietrich's fixative, processed routinely for paraffin embedding, sectioned in the parasagittal plane, and stained with H&E. All twelve fish were determined consequently to have proliferative thyroid lesions, in pharyngeal and/or ectopic locations, which were diagnosed as follicular cell hyperplasia, adenoma, or carcinoma in accordance with published morphologic criteria. Although salt had been used previously to maintain low levels of salinity within the containment systems, the thyroid lesions regressed dramatically throughout affected populations following transition to a brand of salt that contained a higher iodine content. Within five months the thyroid masses were no longer grossly visible, and eleven months after the salt change, there was no macroscopic or microscopic evidence of thyroid proliferative disease based on repeated diagnostic sampling. These findings suggest that at least in zebrafish, both hyperplastic and neoplastic thyroid proliferation may be hormone dependent, and such dependency may persist even following full lesion development. In addition, these results underscore the adaptive ability of zebrafish to absorb iodine from water and food, which has implications for the current campaign to standardize diets and include minimum environmental parameter recommendations in zebrafish publications.

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