

Department of Molecular and Cellular Biology DISTINGUISHED SPEAKER SEMINAR SERIES

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“Microbial regulation of host nutrient metabolism in the zebrafish intestine”

**Wednesday, February 15, 2012
at 12:30 p.m. in ANNU 156**

The intestinal microbiota has been identified as an important environmental factor that enhances the ability of the host to harvest dietary nutrients and promotes fat storage in adipose tissues. I will present recent work from my lab utilizing the zebrafish model system to understand the molecular and ecological mechanisms underlying these host-microbe relationships.

The ability of the microbiota to promote fat storage is caused in part by the microbial suppression of intestinal epithelial expression of a circulating inhibitor of lipoprotein lipase called angiopoietin-like 4 (Angptl4/Fiaf). To define the *cis*-regulatory mechanisms underlying intestine-specific and microbial control of *angptl4* transcription, we utilized the zebrafish system in which host regulatory DNA can be rapidly analyzed in a live, transparent, and gnotobiotic vertebrate. Using structure-function and comparative evolutionary approaches, we define a minimal set of regulatory sequences at the zebrafish *angptl4* locus that mediate intestinal expression. The microbiota suppressed the transcriptional activity of a distinct intestine-specific regulatory sequence similar to the endogenous *angptl4* gene. These results suggest that the microbiota regulates host intestinal Angptl4 protein expression and peripheral fat storage by suppressing the activity of an intestine-specific transcriptional enhancer.

Although the gut microbiota is known to impact host nutrition and energy balance, its role in dietary fat absorption in the intestine is unclear. We used *in vivo* imaging of fluorescent fatty acid (FA) analogs delivered into gnotobiotic zebrafish to reveal that the microbiota stimulates FA uptake and lipid droplet (LD) formation in the intestinal epithelium. Comparison of animals that were starved or fed a sterile diet revealed that the microbiota promotes epithelial LD number, but not size, in a diet-dependent manner. The presence of food results in enrichment of Firmicutes bacteria in the microbiota of the zebrafish intestine, but not in the surrounding water. Monoassociation studies reveal that LD number is increased by diet-enriched Firmicutes and LD size is increased by other bacterial types. Our results establish that members of the gut microbiota regulate intestinal FA absorption via distinct mechanisms, and that diet can influence FA absorption indirectly by modifying microbiota membership.

Faculty Co-Hosts: Dr. Emma Allen-Vercoe & Dr. Terry Van Raay

Coffee, Tea & Timbits

EVERYONE IS WELCOME TO ATTEND!

“A great opportunity to hear leading researchers in the scientific community discuss their work”