2016 Webb-Waring Biomedical Research Awards
Investigator Research Profile

Timothy J. Stasevich, Ph.D.

Colorado State University

Dr. Stasevich is currently an assistant professor in the department of biochemistry and molecular biology at Colorado State University in Fort Collins. He was recently a visiting fellow in Single-Molecule Imaging at the Howard Hughes Medical Institute, Janelia Research Campus (Ashburn, VA). He completed postdoctoral training at Osaka University (Suita-shi, Japan) and the National Cancer Institute (Bethesda, MD) and earned his Ph.D. and M.S. degrees in physics at the University of Maryland, College Park.

Select Honors

Dr. Stasevich has been the recipient of a Japan Society for the Promotion of Science Foreign Postdoctoral Research Fellowship.

Medical Focus

Although cancer pathogenesis has been intensely studied for many decades now, its origin remains shrouded in mystery. While genetic mutations are clearly central to cancer development, less well-known, but of increasing interest, are the variety of epigenetic factors implicated in cancers that can also result in gene misregulation. By definition, epigenetic modifications are heritable changes in patterns of gene expression and function that create a new phenotype without changing the genome sequence. These factors include chemical modifications to proteins and DNA that are not encoded in the genome, but nevertheless are heritable and confer aberrant properties to cancer-causing genes. Among the chemical modifications that are implicated in cancers, modifications to histones—the proteins that package our genome within the cell nucleus—are arguably the most diverse and numerous. Histones are heavily modified at evolutionarily conserved residues, and these modifications are thought to act in specific combinations to help switch genes on or off. In normal cells, this added layer of control makes gene expression go smoothly, but in cancerous cells the layer itself goes awry. Modifications are misappropriated, so oncogenes are switched on, while tumor suppressors are switched off. The chemical rather than genetic nature of these modifications makes them incredibly difficult to visualize and interrogate in vivo (for example, they cannot be directly tagged with fluorescent proteins). It therefore remains unclear if these marks exert a causal influence on cancer pathogenesis, or instead are just symptoms of the disease.

Research Proposal

The goal of Dr. Stasevich's proposed research is to better understand how epigenetics contribute to cancer development. In particular, he will examine how epigenetic modifications to histones influence MYC-driven cancers. MYC is a proto-oncogene that is overexpressed in the majority of tumors, leading to approximately 100,000 deaths each year. Precisely how this occurs remains a complete mystery. To confront this outstanding issue, Dr. Stasevich's lab is developing a highly innovative suite of technologies, including advanced single molecule microscopy, novel antibody-based probes and photoactivatable dyes that will allow him to image and quantify epigenetic histone modification dynamics in living cells with record- breaking resolution. With this technology, his team is uniquely positioned to directly visualize and interrogate the causality of histone modifications in cancer gene expression networks for the first time. The results of this work hold great biomedical promise because—unlike genetic mutations—histone modifications are reversible, making them incredibly attractive therapeutic targets. With this one-of-a-kind technology, Dr. Stasevich's team will be able to visualize the epigenome in action, to test how it interacts with specific oncogenes, and more directly investigate whether or not these interactions

causally influence malignant cell transformation and tumorigenesis. The results of this research will shed new light on the cancer epigenome with the long-term goal of discovering novel strategies to prevent and reverse cancer pathogenesis.