

Six new faculty

CSHL continues its historic commitment to attracting and promoting world-class research faculty. According to Director of Research David L. Spector, who heads the institution's recruitment efforts, "in the last year, we have strategically invested in research faculty who are at the forefront of cancer therapeutics, genetics and genomics of human disease, computational biology and bioinformatics. We look forward to the significant impact that we know these exceptional scientists will have in shaping the future of biomedical research."

David Tuveson, M.D., Ph.D.

Professor
Deputy Director, CSHL Cancer Center

Dr. Tuveson obtained a bachelor's degree in chemistry at MIT, followed by M.D. and Ph.D. degrees at Johns Hopkins. After a faculty position at the University of Pennsylvania, he moved to the University of Cambridge to develop preclinical and clinical therapeutic strategies. CSHL recruited Dr. Tuveson to direct the Cancer Therapeutics Initiative (CTI) and serve as Director of Research for the Lustgarten Foundation. He continues to practice medical oncology with an adjunct appointment at Memorial Sloan-Kettering Cancer Center.

The Tuveson laboratory investigates fundamental aspects of cancer biology and applies this knowledge to the development of new diagnostic and therapeutic strategies. Dr. Tuveson focuses on pancreatic ductal adenocarcinoma (PDAC), the most lethal common cancer with a 5-year survival rate of only 6%. His lab developed the first mouse models of PDAC, which have been instrumental in the discovery of biomarkers of early disease; identified pathways and druggable targets involved in the initiation, progression and metastasis of PDAC; and developed new therapeutic strategies. Following his observation that PDAC tumors contain a deficient and compressed vasculature, which limits drug delivery and therefore efficacy, Dr. Tuveson

has uncovered several methods to correct or target these vascular deficits and promote drug response. This has led to the initiation of several clinical trials. At CSHL, he continues the search for new vulnerabilities in PDAC neoplastic cells and the tumor surroundings, called the micro-environment. His team will evaluate candidate drug targets in an advanced testing facility being developed as part of the CTI.

Jesse Gillis, Ph.D.

Assistant Professor

The Gillis laboratory is working to understand how genes interact, relating to gene function and the effect on disease. Using computational biology and data derived from gene association studies, he interprets the functions of genes in the context of the networks they form. Historically, attempts to understand gene function through networks make use of a principle known as "guilt by association" (GBA). This concept implies that genes with related functions tend to share properties (e.g., physical interactions). GBA has become a favored way to grapple with the complex genetic interdependencies in the face of floods of genomics and proteomics data. Dr. Gillis is making fundamental improvements to GBA, applying it to neuropsychiatric gene network data to understand disease.

Molly C. Hammell, Ph.D.

Assistant Professor

The Hammell laboratory is interested in understanding — on a system-wide basis — how multiple types of regulatory factors in cells interact within and among gene networks. Dr. Hammell uses computational algorithms to integrate multiple



Christopher R. Vakoc

types of profiling data gathered from genomes and "transcriptomes" — readouts of all genes active in a given cell at a particular moment in time — to develop models of regulatory circuits in human disease. Her team is creating new tools for the statistical analysis of high-throughput data, novel algorithms for modeling the flow of signals through genetic pathways, and testing these models using the tools of molecular genetics. The goal is to understand how human diseases like cancer take advantage of the cell's innate adaptability by rewiring its regulatory networks.



Ivan Iossifov, Ph.D.

Assistant Professor

The Iossifov laboratory studies the genetics of common diseases in humans using two main tools: next-generation sequencing and molecular network models, which represent functional relationships among specific locations along the genome, called genetic loci. The laboratory applies advanced machine learning and statistical modeling techniques to analyze massive amounts of biomedical data. Used in combination, these tools enable Dr. Iossifov and colleagues to conduct the large-scale studies necessary for furthering our understanding of complex diseases such as autism, bipolar disorder and cancer.



Molly C. Hammell

Gholson J. Lyon, M.D., Ph.D.

Assistant Professor

The Lyon laboratory focuses on analyzing human genetic variation and its role in severe neuropsychiatric disorders by studying large groups of related individuals living in the same geographic location. Dr. Lyon's lab is utilizing sequencing of whole

genomes and of the exome — the small portion of the genome that encodes proteins — to find mutations that distinguish disease syndromes in populations from Utah and elsewhere. He is interested in the discovery of families with rare diseases and/or increased prevalence for syndromes such as Tourette syndrome, ADHD, obsessive compulsive disorder, mental retardation, autism and schizophrenia.

Christopher R. Vakoc, M.D., Ph.D.

Assistant Professor

The Vakoc laboratory investigates how molecules that regulate chromatin are integrated within the cancer-promoting signaling pathways that drive cancer cell growth. Chromatin is the combined package of DNA and proteins around which it is coiled within the nucleus of cells. The lab's focus is on acute myeloid and lymphoid leukemias, and is expanding its research on epithelial tumors. Dr. Vakoc employs genetically engineered mouse models of cancer that recapitulate the main features of human disease, particularly with respect to therapeutic response. Through a genetic screen, the laboratory recently identified a protein called Brd4 as a critical vulnerability in acute myeloid leukemia — a protein the cancer depends upon for its survival. Brd4 helps control the pattern of which genes are switched on and how they work. Dr. Vakoc's work coincided with the independent development of small-molecule drug inhibitors of Brd4 and related proteins. Using these agents, he has pharmacologically validated Brd4-inhibition as a therapeutic strategy in preclinical animal models of leukemia and his findings are being tested in clinical trials.



Jesse Gillis