

King Hung

Category: Cell & Molecular Biology

 $\textbf{Essay title:} \ Oncogenes \ out \ of \ context-cancer \ genes \ break \ free \ from \ the \ regulatory \ constraints \ of \ chromosomes$

Biography

King L. Hung received an undergraduate degree from the University of Washington and a PhD from Stanford University. He started his postdoctoral fellowship at Scripps Research Institute in September 2024. His research focuses on the basic principles of how cells dynamically regulate genomic and signaling processes in cancer and tissue homeostasis.

Abstract

Genes that promote cell growth are often amplified in cancer via increased DNA copy numbers outside chromosomes, driving tumor formation. How this extrachromosomal DNA is regulated and inherited by dividing cancer cells was poorly understood. We used fluorescence imaging, genomics and computational modeling to study the DNA sequences, physical interactions, and activities of extrachromosomal DNA in cancer cells. We found that these extrachromosomal DNA molecules dynamically rearrange in sequence, physically activate one another in space and are inherited together by dividing cancer cells. These properties defy the normal constraints of chromosomes and allow cancer cells to become hyperactive. Studying the dynamic DNA of cancer will ultimately help us understand how cancer cells grow and evolve, and design better treatments to target them.



Liam Lachs

Category: Ecology & Environment

Essay title: Balancing between evolutionary rescue and extinction – the adaptive potential of reef-building corals in a warming world

Biography

Liam Lachs received an undergraduate degree from the University of Galway, a master's from Vrije Universiteit Brussel, and a PhD from Newcastle University. Since helping to conceptualize the CORALADAPT project, Liam is now a postdoctoral research fellow in the Marine Spatial Ecology Lab at the University of Queensland. His research focuses on how coral reef management can leverage spatial variations in heat wave exposure and the adaptive potential of corals to support reefs in a warming world.

Abstract

Marine heatwaves are causing unprecedented declines across the world's coral reefs. Losses owing to mass coral bleaching and mortality events have been particularly severe for fast-growing yet heat-sensitive corals such as many Acropora species. It remains uncertain whether such corals may undergo evolutionary rescue or are facing an extinction vortex. I addressed this knowledge gap using a combination of field and lab experiments, historic environmental and ecological data, and evolutionary metapopulation modelling of corymbose Acropora corals in Palau. Together, this work uncovers new insights into the adaptive capacity of corals, suggesting that reefs may already be adjusting to ocean warming. Both rapid emissions reductions and strategic reef management will be essential to maintain conditions in which evolution can help corals persist in our warming world.



Nitzan Tal

Category: Genomics, Proteomics & Systems Biology

Essay title: Nucleotides on the frontline – nucleotide-centric defense systems reveal a core principle in bacterial antiviral immunity

Biography

Nitzan Tal received an undergraduate degree from the Hebrew University of Jerusalem and a PhD from Weizmann Institute of Science. She is currently a postdoctoral fellow at the European Molecular Biology Laboratory (EMBL Heidelberg), where she explores how bacteria respond to threats in their environment.

Abstract

Genes that promote cell growth are often amplified in cancer via increased DNA copy numbers outside chromosomes, driving tumor formation. How this extrachromosomal DNA is regulated and inherited by dividing cancer cells was poorly understood. We used fluorescence imaging, genomics and computational modeling to study the DNA sequences, physical interactions, and activities of extrachromosomal DNA in cancer cells. We found that these extrachromosomal DNA molecules dynamically rearrange in sequence, physically activate one another in space and are inherited together by dividing cancer cells. These properties defy the normal constraints of chromosomes and allow cancer cells to become hyperactive. Studying the dynamic DNA of cancer will ultimately help us understand how cancer cells grow and evolve, and design better treatments to target them.



Uche Medoh

Category: Molecular Medicine

 $\textbf{Essay title:} \ \text{The missing piece-solving the 50-year puzzle of BMP synthesis in} \\$

neurodegeneration

Biography

Uche Medoh received an undergraduate degree from Yale University and conducted his PhD and postdoctoral research at Stanford University. He started his laboratory at the Arc Institute in 2024, where his research focuses on discovering and characterizing protein-metabolite interactions that can be leveraged to modulate aging and agerelated diseases.

Abstract

Neurodegenerative diseases often result from lysosomal dysfunction, where cells fail to properly degrade lipids. The lysosomal lipid bis(monoacylglycero)phosphate (BMP) promotes this breakdown and prevents toxic lipid accumulation, but how BMP is made has been unknown for over half a century. I identified that CLN5—a gene mutated in Batten disease—encodes the long-sought BMP synthase. Through lipidomic, biochemical, and cellular analyses, I demonstrated that CLN5 catalyzes the condensation of two lysophosphatidylglycerol molecules to generate BMP within lysosomes, revealing an unexpected biosynthetic capacity of lysosomes. Furthermore, I found that CLN5 deficiency causes severe BMP depletion, lipid accumulation, and neuronal dysfunction characteristic of Batten disease. My work opens therapeutic avenues for restoring BMP levels to treat Batten disease and potentially other neurodegenerative disorders linked to lysosomal dysfunction.