Albert Einstein College of Medicine
Bronx, NY
Lucas Sjulson, Mats Nilsson
$1,000,000

Fluorescence microscopy is a foundational tool of the biomedical sciences because it can visualize almost any molecule of interest. However, traditional fluorescence microscopy is limited to 6-7 colors, far fewer than many applications require. This limitation is imposed not by optics, but by the unavailability of a large panel of dyes with distinct colors. A team from the Albert Einstein College of Medicine and Stockholm University will develop FRAINBOW (Fluorescence Resonance-Assisted IdentificatioN Based On Wavelength), an innovative technology that can generate up to 128 spectrally unmixable colors. The project aims to visualize large numbers of diverse mRNA molecules in thick, clarified brain tissue sections, with the potential to revolutionize the understanding of the functional roles of distinct cell types. Two FRAINBOW-based methods will be developed: PUFRFISH (Probes Unmixed in First Round Fluorescence In Situ Hybridization), which can image 128 distinct mRNAs, and PUMAFISH (Probe Unmixing Multi-round Analog FISH), a multi-round imaging technique with theoretical full-transcriptome capacity. The team will also develop user-friendly software tools and an open-source microscope upgrade module to ensure these methods are accessible to the entire community. Successful completion of this project has the potential to revolutionize not only multiplexed RNA FISH, but any fluorescence-based application in the biomedical sciences, from flow cytometry to cancer diagnostics.

Oregon State University
Corvallis, OR
Edward Brook Christo Buizert
$1,200,000

folded over one another, leaving a discontinuous historical record that precludes traditional methods of interpretation. This work seeks to answer fundamental questions about past natural climate cycles by developing and applying new methodologies to decipher old ice from the Allan Hills. The new tools would (1) determine the "arrow of time" of individual ice segments; (2) determine the relationship between global Ice Age cycles, Antarctic climate, and changes in incoming solar energy during the early Pleistocene; and, (3) determine if and how changes in greenhouse gases impacted those early Ice Age cycles. Antarctic ice is the only Earth material that can answer these questions, yet the complications of this folded archive make deciphering it a challenging, high-risk endeavor.

Purdue University
West Lafayette, IN
Niranjan Shivaram, Chris H. Greene
$1,200,000

A team of researchers from Purdue University plan to generate high photon rate, ultrabroadband extreme ultraviolet and soft x-

University of California, Los Angeles
Los Angeles, CA
Steven Jacobsen
$1,300,000

A fundamental problem in eukaryotic biology is how transcription factors and other proteins gain access to DNA, given that DNA is wrapped around chromatin proteins within nucleosomes. For example, genome editing approaches rely on CRISPR-Cas nucleases that must gain access to specific DNA target sequences to induce sequence changes. However, CRISPR-mediated genome editing is highly inefficient at DNA sequences that are tightly associated with nucleosomes. This work aims to tackle this problem by developing fusion proteins that can efficiently edit nucleosomal DNA in plants and other organisms. Planned experiments revolve around a key discovery made recently by our laboratory, that fusion of certain protein domains to CRISPR or to zinc finger systems can cause massive accumulation of the fusion proteins at target genomic sites, while sequestering these proteins away from non-target chromatin sites. This discovery will be leveraged to design and test new CRISPR-based editi/e5l.2 (m)-t4 ( )11 (s)-4.-52 (a) (m)-7 t (o)-7.0(a)8 eeygm (y)1.5z.2 2(f)-1 (h)-

qu.74(6)a2 dy9dR

activity will be supported by a vigorous theoretical program at the intersection of condensed matter physics and quantum electrodynamics. If successful, these studies will lead to a paradigm shift in the understanding of emergent matter and open a new field of quantum fluctuations engineering.

University of Washington
Seattle, WA
Devin Schweppe, Brian Beliveau, Keriann Backus
$1,300,000

Multicellular life is defined by trillions of unique cells. Understanding how cells work together and what makes each cell unique is the key to understanding organism function. Using techniques developed to measure nucleic acids (RNA and DNA) in individual cells, recent studies have revealed some of the true scope of cell-to-cell differences that define life. However, proteins, not nucleic acids, are the molecular machines responsible for most cellular functions. A comprehensive understanding of multicellularity requires single-cell quantitative measurements of proteins. State-of-the-art single cell protein detection methods (e.g., mass spectrometry, microscopy, and flow cytometry), are useful for providing single-cell biochemical readouts for modest numbers of cells and specific proteins, but these methods fail to scale. Two key reasons for the failure to scale are the inherent challenges of: (1) performing proteomics on small amounts of material and (2) the inability to amplify proteins. This collaboration