Kentucky Center for Epitranscriptomics Research

A major effort in biology is the understanding a biological system as an entity, a field known as systems biology. Such understanding requires a deep knowledge of all modes of the regulation of gene expression and metabolism. Ribonucleic acid (RNA) is a critical molecule that dictates or influences almost all cellular functions. Messenger RNAs (mRNAs) encode proteins, and non-coding RNAs serve a variety of other discrete functions. The recent exciting discovery that mRNA modifications can regulate protein production gave birth to the emerging field of *epitranscriptomics*, which is in its infancy but is already appreciated to be of great importance. Widespread mRNA modifications would constitute a heretofore undiscovered aspect of regulation that may well play a role in nearly all biological processes. Therefore, epitranscriptomics was named *Nature Methods*' METHOD OF THE YEAR for 2017.

We propose to establish a multidisciplinary, state-wide consortium called the Kentucky Center for Epitranscriptomics Research (KCER), the mission of which is to develop methodologies and approaches to elucidate epitranscriptomes. The focus of KCER will be to (i) develop innovative technologies to identify RNA modifications, (ii) develop large scale bioinformatics tools to discover, identify and quantify RNA modifications, and (iii) apply these technologies and tools to examine mRNA modifications in various biological systems. The nature of these proposed efforts is multidisciplinary and aligns well with the Application side of the *Kentucky Advanced Manufacturing Ecosystem* theme - the outcomes of this consortia will have direct impacts on big data, agriculture, and human health. We have assembled a multidisciplinary team to develop new epitranscriptomic technologies: biologists and biochemists to generate RNA samples; analytical chemists for separation, identification, and localization of RNA modifications; computer scientists and statisticians for big data mining and knowledge discovery; organic chemists and biochemists for synthesizing the modified RNAs *in vitro* for verification; and biologists and biochemists to explore the function of a modification in each specific biological system.

The workforce in KCER will be organized into three cores: Technology, Bioinformatics, and Biology. Although each Core has its own focus, their synergy will contribute to the overall mission, and each Core will closely interact at all project levels. The Technology Core will develop bioanalytical technologies for epitranscriptome mapping and quantification using chemical reagents that can react with particular features in biomolecules to 'fish out' RNA with particular modifications. The Bioinformatics Core will develop bioinformatics tools to discover, identify, and quantify RNA modifications using advanced data mining and machine learning approaches. The Biology Core will study the mechanisms and functions of RNA modifications in biological systems by examining the generation and maintenance of bacterial biofilms and by probing the gene regulation triggered by insect juvenile hormone, both of which have agricultural and human health implications.

Our long term goal is to make KCER a self-sustainable infrastructure for multidisciplinary education and research in the Commonwealth of Kentucky that will eventually be shared nation-wide. We will achieve this goal by developing state-wide expertise in epitranscriptomics, training the next generation of scientists at the interfaces of disciplines, promoting collaborative research, and contributing to Kentucky economic development. These activities will be quantitatively measured and examined annually by our education and outreach program, research productivity, research funding, and state-of-the-art services provided to the community.

KCER will be the first national center performing organized, collaborative epitranscriptomics research and providing state-level services on a large scale. Faculty and students from all Kentucky Universities will be work together to develop state-of-the-art technologies to reveal the secrets of the epitranscriptome. The innovation and discoveries by KCER will aid in understanding the mechanisms of biological processes in research projects of green energy, agriculture, and health science, and nearly all biological systems, thus making major contributions to science. The technologies developed in KCER will also have direct applications in academia and industry. They can be immediately applied to aid understanding of the mechanisms of biological processes in research projects of environmental science, insect control, human health and disease, cancer therapy, etc.

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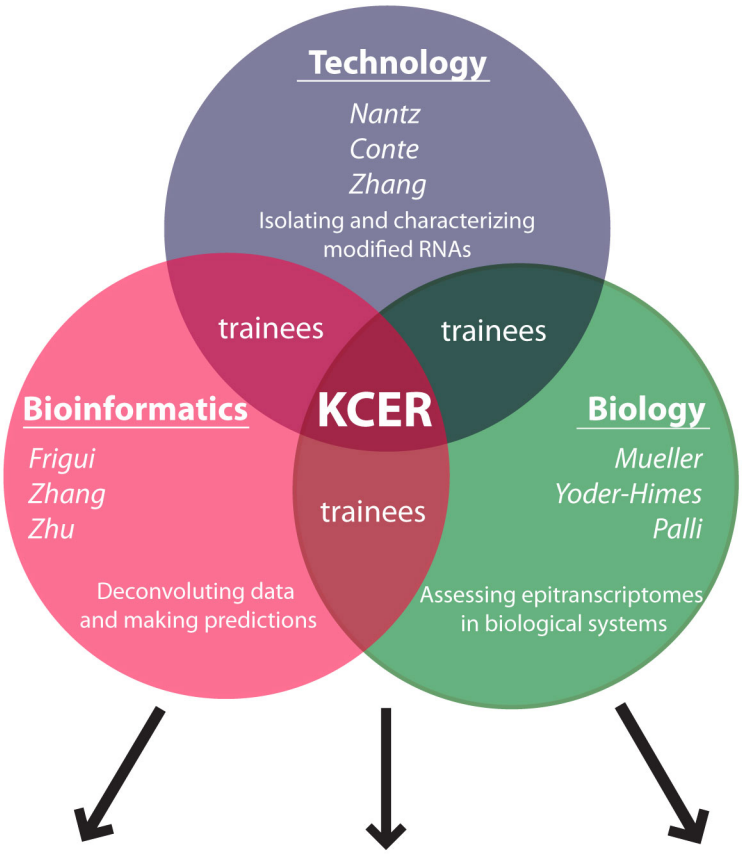
The global epicenter for epitranscriptomics



Kentucky Infrastructure	Collaborative Research	Economic Development
First dedicated national research center for epitranscriptomics	Big data collection and analysis	Contribution to Kentucky agriculture and human health
Training students at a frontier of biology, chemistry, and bioinformatics	Attract talent to Kentucky at all levels	Industrial collaborations
Generating Kentucky-based resources	Expand to include additional Kentucky schools and researchers	Licensing opportunities from resulting patents