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Genomic and physiological impact of transposable elements

Project Number	Contact PI/Project Leader	Awardee Organization
5R35GM122550-03	FESCHOTTE, CEDRIC	CORNELL UNIVERSITY

Description

Abstract Text

PROJECT SUMMARY Transposable elements (TEs) make up more than half of the human genome, and their transposition and rearrangement have been directly implicated in causing more than 100 genetic diseases. Because of these mutagenic properties, TEs are important drivers of genetic variation between and within species. TE activity accounts for most of the DNA that is unique to each mammal species, and is responsible for as much as 30% of structural genomic variation within the human population. However how this enormous source of genetic variation impacts the evolution and physiology of species remains poorly understood. This project is designed to yield transformative insights into the biological significance of TEs in evolution and disease. The central hypothesis tested in this proposal is that prefabricated regulatory and coding activities ancestrally encoded by TEs have been co-opted repeatedly during vertebrate evolution to promote the emergence of new cellular functions. At the regulatory level, we will deploy innovative computational and experimental approaches to test the hypothesis that polymorphic and lineage-specific TEs make a substantial contribution to transcriptomic and cis-regulatory variation within humans and across a diverse set of mammal species, including primates, rodents and **bats**, with an emphasis on the origin and turnover of long noncoding RNA repertoires. Furthermore, we will investigate the role of TEs in the regulatory evolution of a major component of the innate immune system, the interferon response. Experimental manipulations in cell lines, including genome editing and functional assays, will be used to validate the functional significance of TE-derived regulatory sequences. At the protein-coding level, we will combine evolutionary sequence analysis and functional assays to characterize several TE-derived genes co-opted for cellular function in the human genome. Notably we will test the hypothesis that envelope proteins derived from endogenous retroviruses are capable of protecting cells from retroviral infection. We will also investigate several domesticated transposases involved in brain function and development. Together the outcomes of this proposal are anticipated to shift the perception of TEs from inert molecular fossils to active contributors to the evolutionary plasticity of vertebrate genomes. In addition, our studies are bound to reveal crucial new insights into the role of mobile genetic elements in promoting disease states, including cancer, autoimmunity, and neurodevelopmental disorders.

Public Health Relevance Statement

Narrative Transposable element sequences occupy fifty times more space in our genome than those coding for proteins, yet we know surprisingly little about the significance of these elements in health, disease, and evolution. This project combines genomics and functional assays to test the transformative idea that transposable elements have been co-opted to diversify the regulatory and coding repertoires of mammalian genomes, and foster the evolution of physiological and developmental novelties. We seek to harness these new insights in the promotion of human health.

NIH Spending Category

Biotechnology Genetics Human Genome Stem Cell Research

Stem Cell Research - Embryonic - Human

Project Terms

Autoimmunity Biological Biological Assay Brain Cell Line

Cell physiology Cells Chiroptera Code D

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5R35GM122550-03

Contact PI/Project Leader
FESCHOTTE, CEDRIC

Awardee Organization
CORNELL UNIVERSITY

Malignant Neoplasms Mammals Mobile Genetic Elements Molecular
Neurodevelopmental Disorder Outcome Perception Physiological

Read More

Details

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Country
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Department Type
BIOCHEMISTRY
Organization Type
EARTH SCIENCES/RESOURCES

State Code
NY
Congressional District
23

Other Information

FOA
RFA-GM-17-002
Study Section
ZGM1-TRN-5(MR)

Fiscal Year	Award Notice Date
2019	05-August-2019

Administering Institutes or Centers
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

DUNS Number **872612445**
CFDA Code **859**

Project Start Date **08-September-2017**
Project End Date **31-August-2022**
Budget Start Date **01-September-2019**
Budget End Date **31-August-2020**

Project Funding Information for 2019

Total Funding
$507,738
Direct Costs
$323,400
Indirect Costs
$184,338

Year	Funding IC	FY
2019	NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES	$507,738

NIH Categorical Spending

Click here for more information on NIH Categorical Spending

Funding IC	FY Total Cost by IC	NIH Spending Category

Thank you for your feedback!

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- Human;

Sub Projects

No Sub Projects information available for 5R35GM122550-03

Publications

No Publications available for 5R35GM122550-03

Patents

No Patents information available for 5R35GM122550-03

Outcomes

The Project Outcomes shown here are displayed verbatim as submitted by the Principal Investigator (PI) for this award. Any opinions, findings, and conclusions or recommendations expressed are those of the PI and do not necessarily reflect the views of the National Institutes of Health. NIH has not endorsed the content below.

No Outcomes available for 5R35GM122550-03

Clinical Studies

No Clinical Studies information available for 5R35GM122550-03

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Related News Releases

No news release information available for 5R35GM122550-03

History

No Historical information available for 5R35GM122550-03

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