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Characterizing the impact of Yersinia Pestis to the phenotypic evolution of the human immune system

Project Number
1R01GM134376-01

Contact PI/Project Leader
BARREIRO, LUIS BRUNO

Awardee Organization
UNIVERSITY OF CHICAGO

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Description

Abstract Text

Project Summary Pathogens are one of the strongest selective pressures on the human genome. As modern humans migrated out of Africa, they encountered markedly different pathogenic environments, likely resulting in population-specific selection of immune phenotypes. Consistent with this hypothesis, some of the most compelling evidence for local positive selection in the human genome has been detected among genes involved in immunity and host defense. Yet, our understanding of the role that local adaptation plays in shaping phenotypic variation in immune responses across populations is still in its infancy. To better understand the complex relationship between pathogens and host adaptation we propose to study the selective impact on the immune system of one of the most devastating pathogens in history – Yersinia pestis, the agent of the Black Death. Since its emergence in Eurasia 1500 to 6400 years ago Y. pestis has swept Eurasia and North and Central Africa in two major pandemics (Justinian, 541-544; Black Death, starting 1347- 1351) and has subsequently spread nearly worldwide via a third ongoing **pandemic**. Although Y. pestis is proposed to have severely culled the Eurasian population, how groups that differ in their historical exposure to plague respond to the pathogen is not known. Addressing this gap is not only important for understanding the recent evolution of the human immune system, but may also help reveal the molecular basis of ancestry- related differences in susceptibility to infectious diseases, chronic inflammatory disorders, and autoimmune disorders. Using combined expertise in human genomics, immunology, infectious diseases and ancient DNA, we propose: (i) to characterize inter-individual and inter-population variability in immune responses to infection with Y. pestis; (ii) to map expression quantitative trait loci (eQTLs) that are associated with variation in response to infection with Y. pestis; and (iii) to identify genetic loci showing signatures of positive selection by Y. pestis by looking at “real-time” fluctuations in allele frequencies among immune-related genes and immunological QTLs sequenced from skeletal remains of European populations living before, during, and after the Black Death. This work is expected to yield unprecedented insight into the genetic mechanisms associated with increased protection against Y. pestis as well as reveal novel genetic markers involved in the susceptibility to and/or protection against contemporary infectious diseases

Public Health Relevance Statement

Project Narrative Yersinia pestis – the causative agent of Black Death – has been posited to be one of the strongest agents of pathogen-mediated selection in human history. This project uses a unique combination of functional genomics immunology and ancient DNA tools to investigate the genetic basis an evolutionary underpinnings of inter- individual and ancestry-associated differences in immune response to Yersinia pestis infection.

NIH Spending Category

Emerging Infectious Diseases | Genetics | Human Genome | Infectious Diseases | Rare Diseases | Stem Cell Research | Stem Cell Research - Induced Pluripotent Stem Cell | Stem Cell Research - Induced Pluripotent Stem Cell - Human | Vector-Borne Diseases

Project Terms

Address | Africa | African American | American | Autoimmune Diseases | Bacteria | Biological Assay | Bubonic Plague | Cells | Central Africa | Chronic | Collection | Communicable Diseases | Complex | DNA | Data | Disease | Environment | European | Evolution | Exposure to | Gene Expression | Gene Frequency | Genes | Genetic | Genetic Determinism | Genetic Markers | Genetic Transcription | Genetic Variation | Genetic study | Genotype | Growth | Host Defense | Hour | Human | Human Genome | Immune | Immune response | Immune system | Immunity | Immunologics | Immunology | Individual | Infection | Inflammatory | Maps | Measures | Mediating | Modernization | Molecular | Natural Selections | Northern Africa

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Awardee Organization
UNIVERSITY OF CHICAGO

Organization

Name
UNIVERSITY OF CHICAGO

City
CHICAGO

Country
UNITED STATES (US)

Department Type
INTERNAL MEDICINE/MEDICINE

Organization Type
SCHOOLS OF MEDICINE

State Code
IL

Congressional District
01

Other Information

FOA
PA-18-484

Study Section
Genetic Variation and Evolution Study Section[GVE]

Fiscal Year
2019

Award Notice Date
27-August-2019

Administering Institutes or Centers
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES

DUNS Number
005421136

CFDA Code
859

Project Start Date
01-September-2019

Project End Date
31-May-2023

Budget Start Date
01-September-2019

Budget End Date
31-May-2020

Project Funding Information for 2019

Total Funding
$476,663

Direct Costs
$346,999

Indirect Costs
$129,664

Year	Funding IC	FY Total Cost by IC
2019	NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES	$476,663

NIH Categorical Spending

Click here for more information on NIH Categorical Spending

Funding IC	FY Total Cost by IC	NIH Spending Category
NATIONAL INSTITUTE OF GENERAL MEDICAL SCIENCES	$476,663	Emerging Infectious Diseases; Genetics; Human Genome; Infectious Diseases; Rare Diseases; Stem Cell Research; Stem Cell Research - Induced Pluripotent Stem Cell; Stem Cell Research - Induced Pluripotent Stem Cell - Human; Vector-Borne Diseases;

Sub Projects

No Sub Projects information available for 1R01GM134376-01

Publications

No Publications available for 1R01GM134376-01

Patents

No Patents information available for 1R01GM134376-01

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.

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No Clinical Studies information available for 1R01GM134376-01

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Related News Releases

No news release information available for 1R01GM134376-01

History

No Historical information available for 1R01GM134376-01

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