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Researchers apply large-scale sequencing and phylogenomic analysis for in-depth insights into the genomic anatomy of *Escherichia coli* O157:H7 outbreaks

A team of academic and government scientists from the United States published data presenting the genomic blueprints and outbreak dynamics of the human pathogen *Escherichia coli* O157:H7 in previously unprecedented detail. Enterohemorrhagic *E. coli* of the serotype O157:H7 is the major cause of food borne disease, responsible for more than 76,000 cases alone in the US, with a potentially lethal outcome. This included the study of three widely publicized food-associated outbreaks of *E. coli* O157:H7 infections in 2006 that captured the attention of the U.S. Congress as well as the public health, forensic and lay communities, such as the severe 2006 multistate outbreak from ingested spinach that swept through 26 states.

This information allowed the team to develop a high-resolution phylogenomic framework and follow the dynamics of pathogenome evolution at a high level of phylogenetic accuracy and resolution. Published today in the prestigious international journal, Proceedings of the National Academy of Sciences (published online on 11/30/2011), the research using phylogenetic comparison of more than 30 *E. coli* O157:H7 isolates from different outbreak related sources to investigate outbreak-specific genome characteristics of this food borne pathogen.

Funding from the National Institute of Allergy and Infectious Diseases, National Institutes of Health, Department of Health and Human Services, contributed in part to this milestone analysis to help scientists and the medical community better trace and prepare for future outbreaks.

The team included Drs. Mark Eppinger and Jacques Ravel from the Institute for Genome Sciences (IGS) at the University of Maryland School of Medicine. Dr. Eppinger, Research Associate and Dr. Ravel, Associate Director, Genomics at IGS, are experts in microbial genomics and forensics. They sequenced and analyzed several bacterial *E. coli* O157:H7 genomes that allowed detailed insights into the outbreak during the time course of an outbreak. Just as DNA is revolutionizing criminal investigations, it can be used to understand dynamics during an outbreak through the use of evolutionary theory and genomics analysis.

The rapid emergence of *Escherichia coli* O157:H7 from an unknown strain in 1982 to the dominant hemorrhagic *E. coli* serotype in the United States and the cause of widespread outbreaks of human foodborne illness highlights a need to critically evaluate the extent to which genomic plasticity of this important enteric pathogen contributes to its diseases severity. Infected patients present with a range of gastrointestinal morbidities such as severe abdominal cramping and bloody diarrhea. An estimated 15-20% of people infected with *E. coli* O157:H7 present with indications severe enough to require hospitalization. In such cases, symptoms may progress to hemolytic uremic syndrome renal failure (HUS), hemorrhagic colitis (HC) and central nervous system (CNS) failure with potentially lethal outcomes. Yet, little is known about the genomic diversity that exists among extant *E. coli* O157:H7 populations or how various genotypes of this pathogen relate to development and severity of human disease.

The work showed that outbreak-specific clades could be identified by unique mutations they have accumulated in their genomes, even among strains derived from the same outbreak. These genomic architecture signatures will be useful for understanding future disease events involving *E. coli* O157:H7, as this type of DNA fingerprinting can be used to characterize outbreaks derived strains , and ultimately for linking with high accuracy human *E. coli* O157:H7 infection to its source. While the current molecular assays used in public health microbiology laboratories may be adequate for routine surveillance and identification of *E. coli* O157:H7, but they often lack the discriminatory power needed to resolve its genetically homogenous population structure.

Dr. Eppinger, the lead author on the project, said: "The sequencing of additional *E. coli* O157:H7 bacteria was crucial in identifying subtle, yet important sequence and structural differences in this genetically very homogenous lineage to not only discriminate among simultaneously occurring outbreaks caused by different bacterial genotypes but also within outbreaks with a previously unprecedented level of resolution. Our data clearly suggest studying microbial outbreak populations rather than relying on single archetypal reference outbreak strain."

E. coli O157:H7 continues to be a significant public health threat and these data should prove useful for the development of a refined phylogenomic framework for forensic, diagnostic and epidemiological studies in order to better prepare for future outbreaks and better risk assessment in response to novel and emerging *E. coli* O157:H7 resistance and virulence phenotypes and ultimately to prevent or control future infectious disease outbreaks.

Notes to Editors

This research is published on 30 November 2011 in the journal PNAS - Eppinger et al., Genomic anatomy of *Escherichia coli* O157:H7 outbreaks, PNAS (2011, published ahead of print November 30, , doi:10.1073/pnas.1107176108)

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About the Funder

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About IGS

The Institute for Genome Sciences (IGS) at the University of Maryland School of Medicine is an international research center dedicated to advancing the use of genomics to improve biomedicine. Led by Dr. Claire Fraser-Liggett, a preeminent genome scientist and microbiologist, IGS is located on UMB's campus in downtown Baltimore. IGS scientists are pioneers in the expanding fields of genomics, bioinformatics and metagenomics. For more information, see www.igs.umaryland.edu.