Research sheds light on genetic processes underlying meningitis and gastroenteritis

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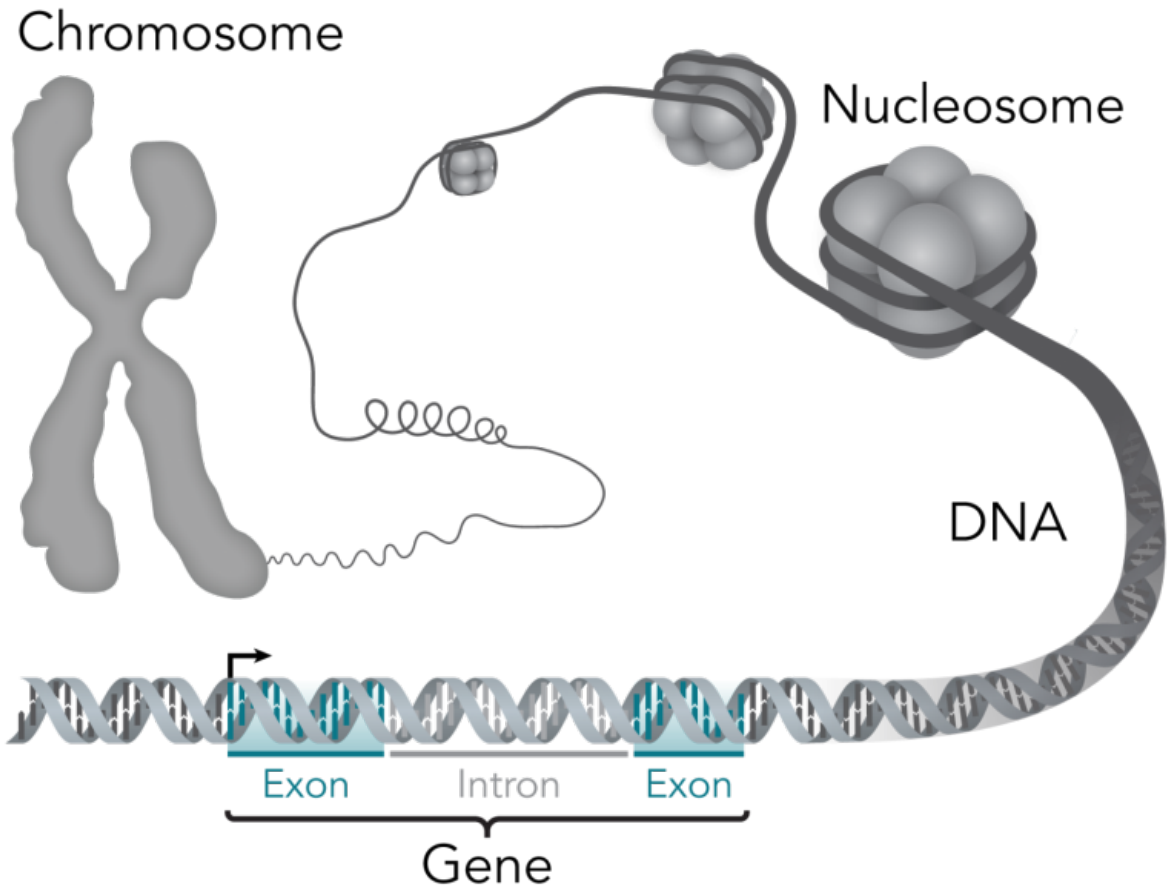

This stylistic diagram shows a gene in relation to the double helix structure of DNA and to a chromosome (right). The chromosome is X-shaped because it is dividing. Introns are regions often found in eukaryote genes that are removed in the splicing process (after the DNA is transcribed into RNA): Only the exons encode the protein. The diagram labels a region of only 55 or so bases as a gene. In reality, most genes are hundreds of times longer. Credit: Thomas

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Innovative computer software developed by University of Leicester scientists is shedding new light on the genetic makeup of deadly pathogens responsible for meningitis and gastroenteritis

The software, called PhasomeIt, rapidly scans through large sets of genomes and identifies their phase variable genes, whilst also comparing all of these genes against one another. This can help in our understanding of the genetic processes underlying a range of deadly diseases.

Researchers from the University of Leicester, led by Dr. Chris Bayliss from the Department of Genetics and Genome Biology, have applied this software to a large number of genome sequences for two families of bacteria – Neisseria meningitidis (a significant cause of meningitis) and Campylobacter jejuni (the most frequent cause of foodborne gastroenteritis). The studies have been published in the journals *PLOS One* and *Microbial Genomics*.

Dr. Bayliss explained: "We and others predict that in-depth analysis of these large sets of genomes will shed light on how these pathogens adapt to life within their human and poultry hosts and how genetic changes may lead to detrimental infections."

Modern DNA sequencing technologies now produce an enormous volume of genomic - the entire genetic content of an organism—information for many different organisms – from humans down to microorganisms.

In many cases there is even too much data to effectively analyse with currently available computer software.

"One mechanism that both of these bacteria use to adapt to environmental and host pressures is the reversible switching ON or OFF of genes that encode molecules responsible for interactions with the host," explains Joe Wanford, a Ph.D. student working on the research in the University of Leicester's Department of Genetics and Genome Biology.

"In many cases this process is advantageous because the ON state gene allows for a tight interaction with host cell surfaces (such as in the throat), whereas the OFF state allows for evasion of host antibodies which may ultimately result in death of the bacteria. Some of these so called phase variable genes can be easily identified because of specific identifying features of their DNA, but until now there was no way to quickly analyse the presence, and distribution of these genes across multiple genomes."

The team's analyses indicated that phase variable genes are largely shared between pathogenic (which cause disease), and commensal (which live in your body, without causing damage) species of bacteria, but that slight differences in either the presence, or expression of these genes may play a role in the transition from asymptomatic colonisation of our bodies, to full-blown disease.

Work is now ongoing in their laboratory to characterise the specific roles of these genes in the disease process.

Dr. Bayliss added: "We believe our new software will be critical in analysing of an ever increasing volume of genome sequences, and will continue to shed key insights into the life cycles of our bacterial symbionts."

More information: Jack Aidley et al. PhasomeIt: an 'omics' approach to cataloguing the potential breadth of phase variation in the genus

Campylobacter, *Microbial Genomics* (2018). DOI: 10.1099/mgen.0.000228

Joseph J. Wanford et al. Phasome analysis of pathogenic and commensal Neisseria species expands the known repertoire of phase variable genes, and highlights common adaptive strategies, *PLOS ONE* (2018). DOI: 10.1371/journal.pone.0196675