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War of the genomes: Diagnosing the genetics of host-pathogen interactions

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Infections and the severity of infections are controlled by a complex interplay of the pathogen's genetics, the host's genetics, and the environment. It is now possible to approach all three parameters using statistical methods which should provide the data to assign individuals to risk groups for infection, and outcome risk groups following infection. Epidemiological studies of environmental factors associated with increased risk of infection or severity of infection have been part of the fabric of medicine for decades.Somewhat more recently familial, case control and population-based human genomic studies have yielded an ever increasing number of susceptibility alleles within the human genome that are predictive of disease and disease outcomes; continuing work in this field will certainly augment our current state of knowledge in this area. Our group is now applying statistical genetic approaches to identify those bacterial genes associated with virulence and pathogenicity. This approach was made possible by the advent of inexpensive routine whole bacterial genome sequencing whichprovided for the comparative analyses of large numbers of independently recovered strains of very many bacterial species.The resultant data from these studies has provided proof of our distributed genome hypothesis and established the bacterial supragenome as a general feature of prokaryotic organisms.These analyses of the composition of the supragenome have, importantly, revealed a very significant "genomic dark matter".This genomic dark matter is composed of very large numbers of unannotated and under- annotated genes and is a feature of all bacteria, including some of the most intensively studied pathogenic species such as *Streptococcus pneumonia* and *Haemophilus influenzae*. We hypothesized that some of these distributed dark matter genes likely played key roles in pathogenesis as our animal model studies demonstrated enormousheterogeneity among the strains of a species with respect to the clinical disease phenotype they induced upon experimental infection.To test this hypothesis we performed a statistical association test for all distributed genesof a species using the gene content data from hundreds ofbacterial strains binned into two phenotype classes: 1) those recovered from sterile sites (i.e. pathogenic); and 2) those recoveredas commensal organisms within the nasopharyngeal mucosa.These analyses have revealed dozens of candidate virulence genes, and our detailed laboratory investigations of the first two of these previously unannotated gene families has provided strong evidence that they are indeed associated with virulence.Thus, we now have a new tool to point the way in the genomic darkness, and ultimately to provide diagnostic and prognostic information about infection risk and disease outcome.The combination of these gene-based bacterial diagnostics with the environmental and host genetic data will provide for a higher degree of personalized medicine than never before achievable.

Biography

Garth D Ehrlich, PhD, is the founder and Executive Director of the Center for Genomic Sciences, and the Center for Advanced Microbial Processing within the Institute for Molecular Medicine and Infectious Disease at the Drexel University College of Medicine (DUCOM).He is also Professor of Microbiology & Immunology, and or Otolaryngology-Head and Neck Surgery at DUCOM.He has received multiple honorary and guest professorships in Asia and Europe. He has over 250 publications including two books on the diagnosis of infectious diseases, and has an H-factor of 54 with citations of his papers exceeding 12,500.

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