Journal of Food Protection, Vol. 67, No. 9, 2004, Pages 2053–2057
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Risk Assessment Prediction from Genome Sequences: Promises and Dreams

TRUDY M. WASSENAAR*

Molecular Microbiology and Genomics Consultants, Tannenstrasse 7, 55576 Zotzenheim, Germany

MS 03-711: Received 25 August 2003/Accepted 12 March 2004

ABSTRACT

The application of bacterial genomics opens new avenues of research on foodborne pathogens. Foodborne pathogens must be able to colonize their hosts and survive transmission from host to host. Different groups of genes are involved in the processes of survival, colonization, and virulence, and such genes are potential targets for risk assessment and intervention strategies. Filtering from genome sequences the genes relevant to these processes is a major challenge, and although many tools are already available for analyses, this type of data mining is just beginning. For the simplest application, gene comparison, it is important to know how gene function, for instance in virulence, is being defined and tested. In other genomic applications, reserachers look for specific properties or characteristics of (virulence) genes to identify novel gene candidates. Each approach has pitfalls, and gene candidates must be tested in the lab to confirm their function. Models for colonization and virulence are available for most although not all pathogens. Models for survival and stress responses are needed to increase the utilization of genomic approaches to risk assessment. Here, I discuss how genome sequences are likely to help in microbial risk assessment of foodborne pathogens and how dreams may become promises.

''Show me your genome and I will tell you who you are.'' With this promise, a vast number of (micro) organisms is being sequenced. The expectations are high. Pathogenic organisms are sequenced with the ultimate prospect of improved treatment and prevention of diseases, and genome sequences of foodborne pathogens could allow researchers to identify new intervention strategies and improve risk assessment. In the first microbial genome report presenting a complete bacterial nucleotide sequence, that of *Haemophilus influenzae,* the authors predicted that ''knowledge of the complete genomes of pathogenic organisms could lead to new vaccines'' *(3).* In a commentary published in 1999, Kuipers *(9)* stated that ''genomics of food microbes, based on rapidly emerging genome sequence information, generates valuable knowledge that can be used for metabolic engineering . . . and development of novel risk assessment procedures will be facilitated.'' The first foodborne pathogen to be sequenced was *Campylobacter jejuni (13).* A year later, the genome sequence of the foodborne pathogen *Escherichia coli* O:157:H7 was compared with that of apathogenic *E. coli* K12 *(14).* The diversity within that species led researchers to the conclusion that ''additional genome sequence data from other *E. coli* strains as well as functional characterization of gene products is necessary before the complex relationship between *E. coli* genotypes and phenotypes can be understood'' *(14).* Thus, instead of one genome sequence per species, multiple genome sequences are now being published for many foodborne pathogens. As of January 2004, at least 13 foodborne pathogen genomes (listed in the Bad Bug Book) had been sequenced, with 24 sequenced strains of these species publicly available and a multitude of these in preparation (see http://www.ncbi.nlm.nih.gov/genomes/static/eub.html for a list of available microbial genomes). With these high expectations and a few words of warning in mind, it is time to evaluate how these genome sequences have been and can be used in pathogenesis research and risk assessment of foodborne pathogens.

THE MAKING OF A FOODBORNE PATHOGEN

In the ideal world of microbial research, all characteristics of microbes would be encoded in their genes. However, not every gene is expressed under every condition, so that microbes can adjust to external conditions by fine-tuning gene regulation. The characteristics that define a foodborne pathogen can be divided into three classes: virulence, colonization, and survival properties (properties conferring tolerance to specific stresses). Virulence properties cause disease and are encoded by virulence-associated genes. Colonization properties are associated with colonization of the human or animal (in the case of a zoonosis) host(s). Stress responses or survival properties are those characteristics that specifically help the organism survive during food processing and storage and in environmental pockets from where they can colonize other animals.

The key features of risk assessment are hazard identification, hazard characterization, exposure assessment, and risk characterization. Microbial genome sequences are of use in the first two steps; either a potential foodborne pathogen could be identified as such by its genome sequence (hazard identification) or a known foodborne pathogen could be identified by those genes relevant to its life style (hazard characterization). Because resources are limited,

* Author for correspondence. Tel: +49 6701 8531; Fax: +49 6701 901803; E-mail: wassenaar_t@yahoo.co.uk.