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How genomics has affected the concept of microbiology

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Genomics influences multiple areas of microbiology, and thus affects key microbiological concepts. Recent reports that describe the large genome and unusual coding capacity of mimivirus, the minimized fungal genomes that contain elements of bacterial metabolism, and the 'signature' eukaryotic proteins in bacteria are introducing grey shades into the black-and-white distinctions between microbial domains. The concept of the 'universal' minimal genome is being challenged, and the ability of minimal genomes to support cellular complexity is under investigation. There have been intriguing insights into microbe–microbe relationships, for example conflict mediation in competing bacteriophages that rapidly evolve survival mechanisms when cooperation is experimentally enforced. Genomics has given birth to metagenomics, but has also stimulated the development of improved cultivation techniques. Lastly, the taxonomic potential of genomics is emerging, as studies of multiple strains allow us to revise and refine the bacterial species concept as well as the idea of a static genome.

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Introduction

Genomics, which explores the biology of organisms through their genetic blueprints, has profoundly affected the discipline of microbiology. It has led us to revise our definitions of microbial entities, reconsider their capabilities and re-evaluate the microbiological toolbox of methods and approaches. In the breadth of its influence on various subdisciplines of microbiology (e.g. metabolism, physiology, ecology, host–pathogen relationships and 'industrial microbiology), and its interaction with other disciplines (e.g. human and veterinary medicine, agriculture, evolutionary biology and structural biology), the impact of genomics on microbiology is arguably unrivaled in this century. In this review, we discuss recent work in genomics that supports, challenges, expands or otherwise affects some key concepts in microbiology.

What is a prokaryotic, eukaryotic or viral microbe?

Recent genomic studies have cast an interesting light on our division of the microbial world into four groups: Bacteria, Archaea, Eukarya and viruses. Some of the ultrastructural and biochemical bulwarks that neatly separated these groups for so many years — for example, the overall level of cellular complexity, cell size, genome size, composition of ribosomes (where present), lipid type and behavioral complexity — began to be chipped away in the pre-genomic era. But genomics has amplified the effect, and has provided a deeper understanding of the rules and exceptions that characterize the four microbial groups.

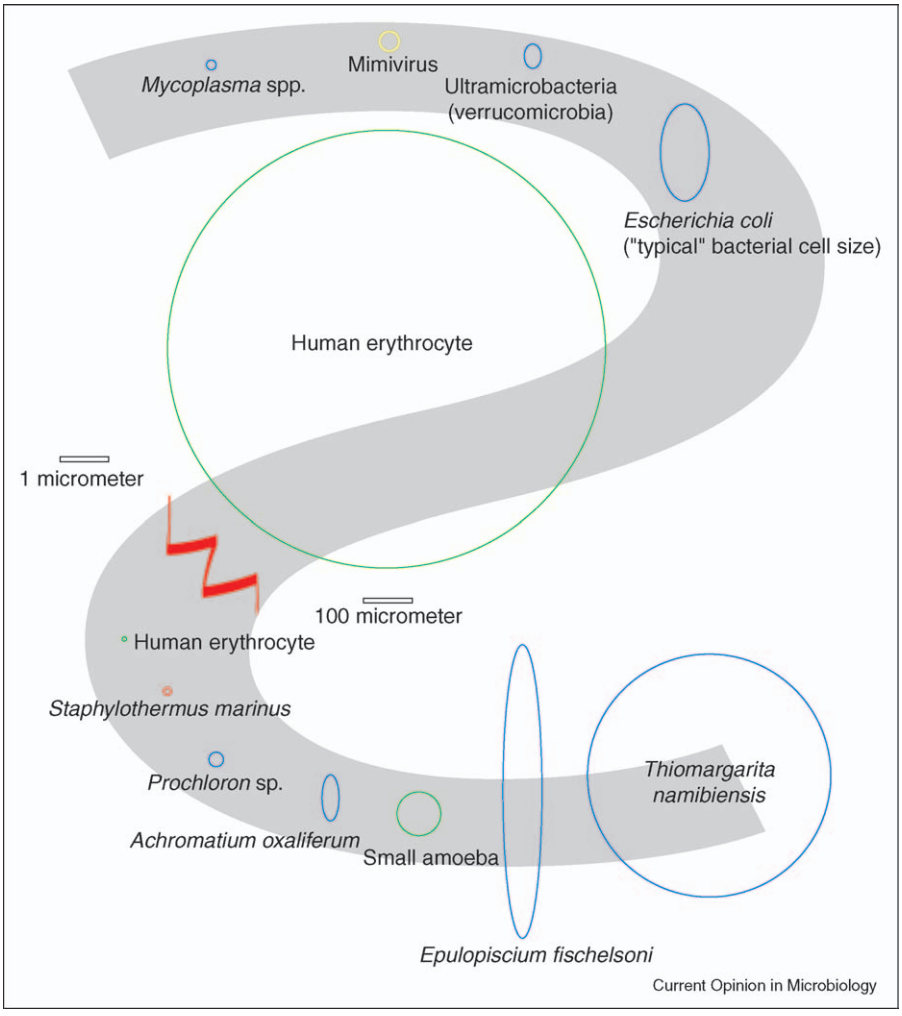
Giant viruses

A good example is provided by recently reported genomic analysis of DNA viruses. Mimivirus is a DNA virus that infects amoebae. It is an extremely large (400 nm) particle that stains Gram-positive and has a genome size of 1.2 Mb [1]. The genome contains genes not previously reported in viruses, encoding proteins involved in translation of proteins and components of metabolic pathways [2••]. Thus in its cell size, genome size and gene content, this mimivirus apes a small bacterium. In a recent review, Desjardins *et al*. [3] argue that the expansion in the viral definition provided by mimivirus is quantitative, but not qualitative, in nature. They attribute the latter trait to the genome of the polydnavirus *Cotesia congregata* bracovirus (CcBv). The mimivirus genome encodes proteins involved in transcription, translation and DNA replication; very few of these are found in the genome of CcBv. In addition, many 'typical' viral genes are absent from the CcBv genome. The fascinating lifecycle of CcBv is tightly associated with two eukaryotic species — parasitic bracovid wasps and their caterpillar prey [4]. Expression of viral genes in the caterpillar obstructs the immune response [5] and helps ensure survival of the parasitic wasp. Genomic analysis of CcBv [6••] revealed oddities such as extremely low coding density, the absence of genes predicted to encode DNA replication proteins, and the high percentage (70%) of genes that appear to contain introns. Collectively, these features resemble a segment of eukaryotic genomic DNA, rather than a viral genome. However, these gene models have not yet been tested *in vitro* (for example, by examination of cDNA sequences), and so their significance cannot be fully evaluated.

Overlapping genome size and content

These shifting boundaries between the microbial domains extend findings that have emerged over the past 15 or so years that similarly complicated our microbial definitions. In the realm of cell size, these findings

Figure 1



Depiction of overlapping cell size in members of the Bacteria (blue), Archaea (red), Eukarya (green) and viruses (yellow). The diagram is divided into two different scales, with the upper portion showing the relative cell sizes of small and 'normal' bacteria, as well as mimivirus, in relation to a human erythrocyte (approximately 9 μm in diameter). The same erythrocyte is used in the magnified lower portion of the diagram, to demonstrate the large cell size present in certain bacteria, culminating in the extremely large cells (average 500 μm diameter) of the giant sulfur bacterium *Thiomargarita namibiensis*.

included the discovery of very large (e.g. *Epulopiscium* [7]) and very small (e.g. ultramicrobacteria [8] and *Nanoarchaeum* [9]) bacterial cells (Figure 1). This has been paralleled by the report of bacterial genome sizes that range from smaller than that of mimivirus to larger than some fungal genomes (Figure 2). In an analysis of the functional content of these larger prokaryotic genomes, Konstantinidis and Tiedje [10] demonstrated an over-representation of some categories of genes, such as regulation of transcription and secondary metabolism. Conversely, other gene categories such as translation and DNA processing contained relatively fewer members in larger genomes. The lack of correlation with non-coding DNA and hypothetical open reading frame content led the authors to conclude that genome expansion favors specific functional classes. Some phylogenetic groups are overrepresented in this analysis, therefore it will be interesting to observe whether or not these trends hold true as a more diverse set of genomes becomes available.

Recent analysis of several fungi has revealed that they have minimized streamlined genomes, some of which appear to have adopted elements of bacterial metabolism. When the genome of the filamentous fungus *Ashbya gossypii* was published in 2004 [11], it was the smallest (9.2 Mb) free-living eukaryotic genome to have been reported. It appeared to be a very compact genome, exhibiting a short distance between genes and only 221 introns. Its high level of homology and synteny with the genome of *Saccharomyces cerevisiae* and the presence of a similar number of proteins suggested that *A. gossypii* represented a minimal genome size for a free-living