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Editorial

MYCOBACTERIUM LEPRAE GENOME SEQUENCE; A LANDMARK ACHIEVEMENT

This edition of *Leprosy Review* is given over to the remarkable achievement, finally realized at the beginning of this year, of the sequencing of the genome of *Mycobacterium leprae.*[1]

M. leprae was one of the first organisms to be associated with a human disease. However, our inability to grow the organism in culture has made it extremely difficult to study in the laboratory. The pioneering work of Charles Shepard in the 1960s,[2,3] in which limited multiplication of *M. leprae* in the footpads of mice was demonstrated, provided new opportunities and eventually paved the way for testing and optimizing new drug regimens. This provided much of the rationale for the introduction of multiple drug treatment. However, we were still unable to address fundamental questions about the organism; why does it grow so slowly? Why has it proved impossible to grow in culture medium? What is its relationship to other pathogenic mycobacteria such as *Mycobacterium tuberculosis*?

The first step on the road to answering these questions was the demonstration that experimental infection of nine-banded armadillos could produce very large numbers of organisms;[4] enough to start looking at the biochemistry and physiology of the organism. Crucially, it was also enough to extract DNA and this marked the starting point of the genome sequencing project.

Now the challenge is to try and understand, as fully as possible, the language of the genes. As you will read in this issue of *Leprosy Review*, we now know that *M. leprae* has been steadily losing genes, and with it the ability to respond to different environments. The reason why it cannot be grown *in vitro* lies in this inability; it has come to rely on its host cell for essential nutrients. Our interpretation of information revealed in the genome sequence is discussed in the papers entitled 'The decaying genome of *Mycobacterium leprae*', 'DNA metabolism in *Mycobacterium leprae*', 'The microbial physiologist's guide to the leprosy genome' and 'Genomic evidence for the retention of the essential mycobacterial cell wall in the otherwise defective *Mycobacterium leprae*'. We can also use the genome sequence to develop new tools, such as rapid methods for detecting drug resistance, as illustrated by Honoré and colleagues ('A method for rapid detection of rifampicin-resistant isolates of *Mycobacterium leprae*'), or methods for differentiating strains of *M. leprae* which could help us to understand more about its transmission ('Repetitive sequences in *Mycobacterium leprae* and their impact on genome plasticity'). We can also now understand the molecular basis of drug resistance and identify potential new targets for drug development ('Genomics and the chemotherapy of leprosy').

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Finally, the papers by Jones *et al.* ('Leproma: a *Mycobacterium leprae* genome browser') and Eiglmeier *et al.* ('The integrated genome map of *Mycobacterium leprae')* explain, in practical terms, how the information can be accessed, and how it has been possible to generate a renewable source of *M. leprae* DNA, which is available to researchers interested in pursuing the molecular biology of *M. leprae*.

This issue marks a historic achievement in the study of leprosy. I am grateful to all of the authors for sharing their ideas and results and hence making it possible. I am particularly grateful to Stewart Cole for his invaluable contribution to the field and for his help in making this special edition of *Leprosy Review* possible.

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