EDITORIAL

Of Microbes and Molecules: Bacterial Virulence

Nowhere are the imperatives of evolution more evident, at least from a human viewpoint, than in the relationships between man and microbes. From minor, everyday, infections to the ravages of tuberculosis (TB) and the Black Death, humans have been constantly prey to the infectious diseases caused by pathogenic microorganisms. The latter half of the 20th century saw spectacular success in the development of antibiotics, and optimistic expectations that many infectious diseases could be consigned to history. Ironically those antibiotics were often the same molecular tools that microbes had developed to use against each other or to colonise their particular niches. The rapid rise in antibiotic resistance reminds us that these bacteria are subtle foes and past masters at adapting to challenge.

In this series of mini-reviews we look at some of the molecular processes through which bacteria interact with their environment, and at the same time highlight the spectacular new opportunities and challenges that come with the genomic revolution. Iain Lamont discusses the remarkable phenomenon of quorum sensing, through which whole bacterial communities regulate or coordinate their behaviour. This behaviour, which depends on secreted chemical signals, can lead to the development of antibiotic resistance or the production of virulence factors. While the secretion and uptake of small molecules is fairly easily understood, the ability to translocate very large biomolecules, and even complexes, through membranes, seems astonishing. Jasna Rakonjac and Marjorie Russel review the complex and varied mechanisms through which this is done – processes that enable pathogenic bacteria to launch their weapons on to unsuspecting host cells. Ries Langley and John Fraser describe those molecular weapons for one particular organism, *Staphylococcus aureus*. This common human pathogen has a remarkable array of toxins. In addition to superantigens, which cause devastating diseases such as toxic shock syndrome, are other protein toxins, only discovered as a result of analysis of the *S. aureus* genome, signalling the existence of virulence mechanisms that are as yet quite unknown. Finally, Shaun Lott discusses *Mycobacterium tuberculosis*, the "captain of all the men of death," as the cause of TB. For a pathogen of global significance it seems appropriate that structural genomics, the subject of this review, should be brought to bear on its unique and poorly understood biology.

Looking to the future, the unknown gene products of the *M. tuberculosis* genome (or for that matter the genome of any pathogen) encapsulate the challenge. Do some of these coordinate the survival of colonies in the lung, as in quorum sensing? Do some represent the machinery of unrecognised secretion systems? Are some of them the weapons through which the human immune response is evaded? One thing is sure. There are exciting opportunities here for the next phase of the battle against infectious disease.

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Cover Illustration –

Mycobacterial molecules. *Cells of the mycobacterium* Tuberculosis bacillus, *the cause of TB, form the background for the cover. This secretive, slow-growing bacterium, known in the past as the white plague, has survived the antibiotic revolution and still today claims more lives every year than any other infectious agent. The protein structures in the central graphics represent two of the first fruits of an international structural genomics initiative aimed at understanding the biology of this organism and characterising potential new drug targets. On the left is an acetyltransferase, implicated in antibiotic resistance. On the right is the catalytic domain of LeuA, an enzyme from the leucine biosynthetic pathway; abrogation of this pathway prevents colonisation of the lung (see Showcase article by Shaun Lott on pages 15-17 of this issue).*

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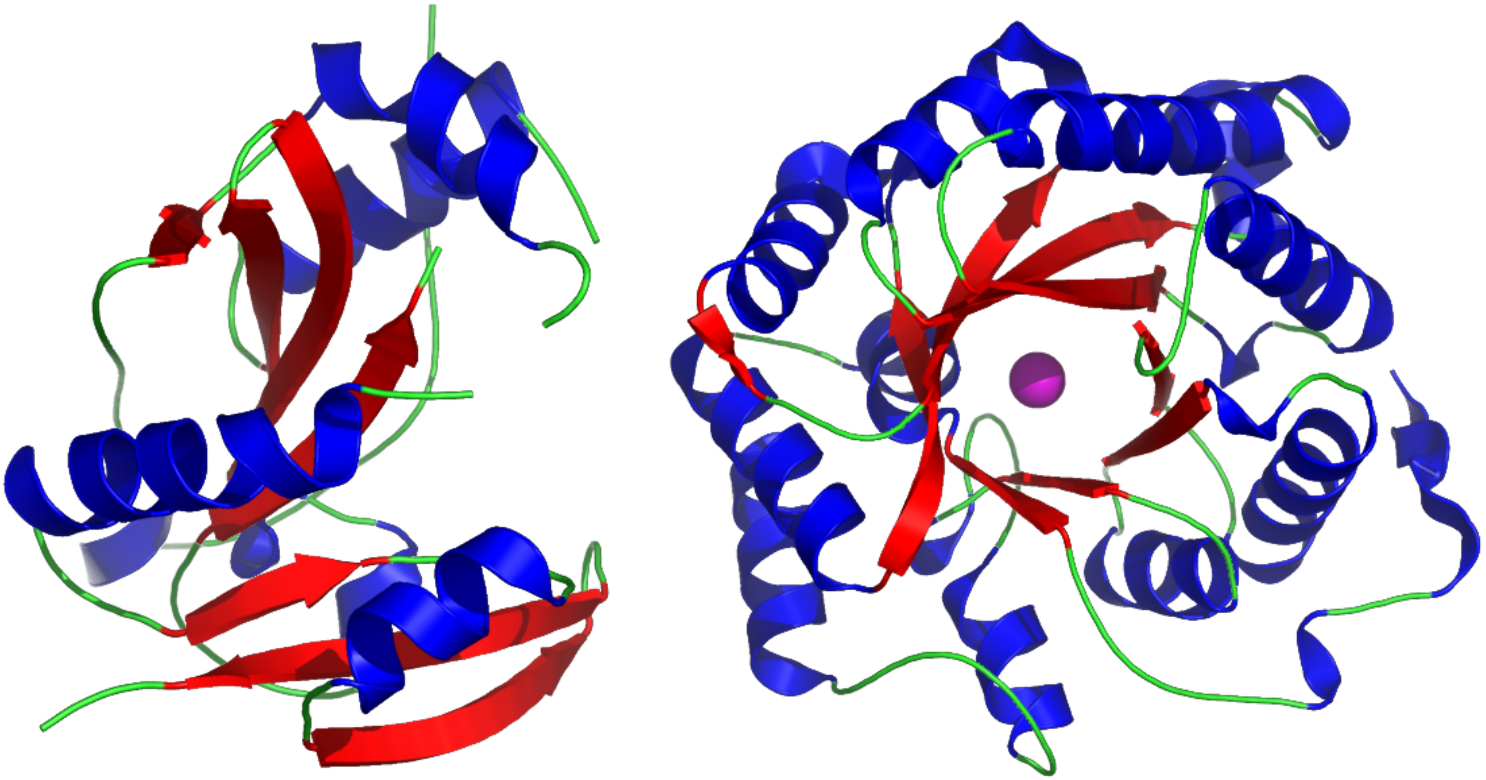
Guest Editor: Ted Baker

Editor's Note: This Showcase on Research emanates from our New Zealand colleagues to mark the participation of NZSBMB in the ComBio2003 meeting in Melbourne this year.

In the Next Issue…

In December, Showcase on Research will be on **Neuroscience –** *Guest Editor: Neil Sims*



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