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CMLS Cellular and Molecular Life Sciences

Introduction

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In this issue of *CMLS*, we present a selection of the best papers presented at the meeting 'Evolution of bacterial virulence and antibiotic resistance' held in Lugano, Switzerland, at the 'Università della Svizzera Italiana', October 15–16, 1998. Although bacterial pathogenesis and antibiotic resistance are, apparently, unrelated, there is a common thread which links them, i.e. their evolution usually responds to a selective pressure. In the former case, it is the immune system of the host, comprising the specific humoral or cellular responses and all the non-specific mechanisms contributing to clearing the bacteria from host tissues or cells. In the case of antibiotic resistance, the selection pressure is obviously represented by the presence of antibacterial drugs not only in the infected and treated body, but also in foodstuffs and the environment. Because they can be essential to bacterial survival, genes that encode pathogenic factors or antibiotic resistance are easily spread among bacteria by genetic transfer mechanisms such as conjugation, transformation, transduction or transposition. Thus, selective pressure coupled with gene transfer leads to the emergence of micro-organisms with increased pathogenicity and/or antibiotic resistance. The aim of the meeting organised in Lugano was to focus on some of the most recent aspects of these issues with contributions from scientists from Switzerland and abroad.

The first review is from Ziebuhr and colleagues. It focuses on the mechanisms of both microevolution, which leads to the emergence in the short term of new pathogenic or resistant variants, and macroevolution which, over long periods of time, leads to the stable fixation in the pathogen genome of sequences encoding improved or new adaptive properties.

Different classes of repetitive DNA sequences are present in bacterial genomes. In his paper, van Belkum analyses their role in microbial pathogenesis and evolution. In addition to providing a modulatory mechanism for the expression of genes, short-sequence repeat (SSR) variability can be used to study the evolution of genetic diversity among bacteria.

According to the report of Boerlin, Shiga-toxin-producing *Escherichia coli* may represent a good example of the evolutionary mechanisms driven by genetic transfers: the DNA sequences encoding the major virulence factors of these micro-organisms are likely the product of horizontal genetic transfers and recombination events involving foreign DNA.

The other papers in this issue deal with the problem of antibiotic resistance, which is of growing concern not only among health workers but also in the general population. Indeed, we are approaching a critical scenario where patients might be infected with multiresistant pathogens unreactive to all current antibiotics on the market, a return to the pre-antibiotic era.

Mazel and Davies focus on the biochemical and genetic aspects of bacterial drug resistance, pointing out the role of gene transfer among distant bacterial populations and emphasising the need for a better understanding of bacterial genetic ecology if we want to control the emergence of antibiotic resistance.

The ecological and global aspect of drug resistance is taken further by Teuber who reviews the role of farm animals and food as reservoirs for resistance genes. The extensive application of antibiotics in agriculture is certainly one of the major factors responsible for the spread of drug resistance among food-borne pathogens.

Methicillin-resistant *Staphylococcus aureus* strains are now of significant importance in many hospital environments: these strains are resistant to all β-lactam antibiotics and, in addition, they often encode many other resistant determinants. The genetic mechanisms leading to methicillin resistance are not yet fully understood, and are addressed by Berger-Bächi in her review.

Multidrug efflux pumps represent a powerful and adaptive bacterial response to the presence of antibiotics in the environment. These systems were probably originally intended as secretion machineries for cellular

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products and as defence mechanisms against harmful substances: they have evolved to develop the capacity for pumping antibiotics out of the bacterial cytoplasm. The contribution of Köhler and colleagues emphasises the role of such systems, which are often characterised by a broad substrate specificity.

Finally, an element of hope is introduced by the paper from Gray and Keck. No new family of antibiotics has been introduced onto the market in the last three decades. However, recent technologies associated with genomic sequencing of pathogens have the potential to identify additional bacterial targets which might lead to the generation of new antibacterial drugs.

The contributions presented in this issue of *CMLS*, as well as many other observations reported during the meeting in Lugano, support the new vision we have been developing during the last years of the bacterial genome as a mosaic genetic structure composed of different DNA sequences originating not only from closely related micro-organisms, but also from distant taxonomic groups. Genes are moving constantly in the global environment and the importance and incidence of particular advantageous encoding sequences may be greatly enhanced by strong selection pressures, contributing to the generation of highly pathogenic and resistant strains. We will have to take these facts into account when deciding on measures intended to control the emergence of such bugs.