Schweizerische Gesellschaft für Mikrobiologie *Berichte der 38. Jahresversammlung*

Société Suisse de Microbiologie *Comptes rendus de la 38e réunion annuelle*

Società Svizzera di Microbiologia *Rendiconti della 38ma sessione annuale*

Swiss Society of Microbiology *Reports of the 38th annual meeting*

Crans, 8–9 June 1979

Honorary Member

Prof. Dr. Ernst Wiesmann, Zürich, has been elected honorary member of the Society in recognition of his contribution to the progress of medical microbiology in Switzerland.

The Society Prize

The Society prize has been allocated to Dr. Riccardo Wittek, Bethesda, USA, in recognition of his contribution to the understanding of the molecular biology of viruses.

Main Lectures

These introduced the main topics of the meeting: Chemotherapy of infectious diseases.

Molecular basis for plasmid epidemiology

by Y.A. Chabbert

Institut Pasteur, 25–28, rue du Dr. Roux, Paris 15e (France)

Evolution in animals and plants takes millions of years. In contrast, we have been able to observe evolutionary changes in pathogenic bacteria which have been submitted to a tremendous selection pressure by antibiotics since 1945. As a result, these bacteria have been able to acquire new genes. Mutation plays a minor role in this evolution. In almost all cases the bacteria acquire extrachromosomal elements which are independent replicons and translocatable fragments of DNA such as transposons which can be inserted either into extrachromosomal elements or even into the chromosome itself.

The infective ability of plasmids is in fact an 'extraordinarily efficient mechanism of accelerated cell evolution' (Reanney). From the medical point of view, it seems to be imperative to try to stop the spread of bacterial resistance to antibiotics by reducing the selective pressure. Any kind of strategy for antibiotic prescription has to be based on the evaluation of the rate of genetic exchange between bacteria or plasmids under normal environmental conditions.

The studies of plasmid epidemiology may solve important problems such as the frequency of genetic transfer in vivo, the phylogenic relationships among plasmids and the role of plasmids in bacterial epidemics and pathogenicity. Bacterial epidemiology makes use of the possibility to differentiate between different taxonomically defined species by using infrequent markers. The epidemiology of plasmids will depend on the relationships between 'molecular species' (a DNA molecule with a high degree of sequence homology) and on the difference in structure between non epidemiologically related plasmids and epidemic plasmids.

The existence of genetic exchanges between replicons might lead us to consider a plasmid as a labile assemblage of small DNA fragments of different origin. Consequently, plasmids from a wild type strain might be completely different from each other.

However the conjugative plasmids from natural isolates of gram-negative rods belong to a limited number of groups with different genetical and physical properties. Plasmids belonging to a particular incompatibility group usually show a high degree of DNA/DNA homology. Conversely little or no homology is detected between plasmids belonging to different incompatibility groups. Heteroduplex analysis of plas-

mids belonging to the same group isolated from strains which are epidemiologically related confirm that they possess large sequences in common. Some groups of plasmids can be considered as 'species'.
It is possible today to classify the main groups which have been identified into several naturally occurring strains belonging to different bacterial genera and isolated in different geographical sites according to their DNA homology. 80% of 150 plasmids from gram-negative rods examined by us belong to the following groups:
1. Groups with large homology with respect to transfer operon and pili formation but subdivided by incompatibility phenomenon. F like plasmids: Inc F, FII, FIII. I like plasmids: IncI1, IncI2.
2. Groups of incomptatible plasmids with poor homology. Complex Inc H: H1, H2, H3. Complex Inc Y: Y1, Y2.
3. Independent groups. - Localisation of R determinants in a few areas (?): Inc M, Inc C. - Several insertions (?): Inc P, Inc N, Inc W. - Others: Inc B.
Assuming that plasmids belonging to a given Inc group are composed of a relatively stable 'core' into which several transposons can be inserted at various preferential sites, one may expect important differences among epidemiologically unrelated plasmids but the maintenance of an identical structure in an epidemic plasmid.

A - Unrelated Inc I1 plasmids

By restriction endonuclease analysis, 5 unrelated plasmids belonging to Inc I1 group share 15 *EcoR1* fragments in common.
The technique described by Southern to detect partial or complete homology between the DNA fragments has been used. In vitro ^{32}P-labelled complementary RNA from pIP111, a 'transfer factor' with no detectable R-determinant, was used as a probe. The autoradiogram shows hybridization with the 15 fragments common to the five plasmids studied (P9, pIP186, pIP112, pIP565 and pIP111).
Electron microscopy of heteroduplex between the transfer factor pIP111 and others shows a unique single stranded DNA insertion loop to be always located at the same distance from a small region with impaired sequence.
A restriction endonuclease map of the inserted regions shows differences between the size and the location of fragments corresponding to the resistance characters. Thus, by means of these analyes it is possible to differentiate between these unrelated plasmids in spite of their large homology.

B - Epidemiologically related plasmids

A plasmid belonging to incompatibility group C coding for gentamicin resistance by an adenylating enzyme and for ampicillin resistance by a peculiar oxacillin hydrolysing β-lactamase, was observed by J. Witchitz at the Claude-Bernard hospital in Paris among 12 different bacterial species, including *Pseudomonas aeruginosa*, between November 1969 and December 1975. DNA/DNA hybridization by A. Roussel showed a high degree of homology between plasmids isolated from these different bacterial species at different period of time.
Analysis after digestion with *EcoR1* and agarose gel electrophoresis showed very few differences among the 10 fragments generated by plasmids isolated in 1969 and 1975. These data indicate a high degree of structural stability among the Inc C plasmids through numerous cycles of replication and transfer in vivo.

In conclusion, when the structure of a plasmid has been almost completely investigated using the sophisticated techniques of molecular biology it is possible to differentiate between epidemiologically related and unrelated plasmids. But simplifications of these techniques are needed which can be easily adopted for real epidemiological surveys.

Antimicrobial chemotherapy - a clinician's viewpoint*

by R. Lüthy

Department of Medicine, Division of Infectious Diseases, University Hospital, CH-8006 Zürich (Switzerland)

Antimicrobial chemotherapy requires a sound knowledge of clinical microbiology, infectious diseases and the pharmacology of antibiotics. Two examples should illustrate the point that usage of antimicrobial agents in Switzerland is far from optimal.
In the first 3 months of 1979, we conducted a quality-of-use study of antibiotic in a surgical clinic in Zürich[10]. A record was kept of every patient treated with an antibiotic, listing the symptoms, the choice of antibiotics, the dosage and duration of therapy, side-effects noted, and the costs of medication, as well as all the available clinical, microbiological and laboratory data. Each treatment course was assessed and divided in to 3 categories according to the criteria of