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Società Svizzera di Microbiologia *Rendiconti della 37e sessione annuale*

Swiss Society of Microbiology *Reports of the 37th annual meeting*

Basel, 16-17 June 1978

The Society Prize

The Society prize has been allocated to Dr Kaspar von Meyenburg, Copenhagen, in recognition of his contribution to the understanding of the molecular biology of cell growth.

Main lectures

These introduced the main topics of the meeting: Transposable genetic elements. The 2 main speakers have not been asked to prepare full manuscripts, since good recent publications on this topic are available.

Transposition and the evolution of antibiotic resistance

by Mark H. Richmond

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It is now a common experience that the introduction of a novel type of antibiotic into clinical use is followed by the emergence of a resistant bacterial population. For example the incidence of penicillinase-producing staphylococci increased rapidly following the introduction of benzyl penicillin into clinical use in 1942[6]. In this case the type of resistance was uniform throughout all the strains involved, and the increase in incidence was due primarily to 2 causes: 1. There was the selective effect of antibiotic use on the numbers of resistant organisms. 2. There was the appearance of penicillinase production in an ever wider range of *Staphylococcus aureus* strains. This was due to the transfer of staphylococcal penicillinase plasmids between staphylococci - probably by transduction.

Another example of the emergence of a resistant population was the appearance and spread of Type 29 *Salmonella typhimurium* which commenced in 1961[1]. In this case the nature of the resistant organisms remained the same in terms of phage typing. The numbers of resistant bacteria certainly increased, but the main characteristic of this outbreak was the increasing complexity of the resistance patterns exhibited by the bacteria as events progressed. In this case the main genetic event involved seems to have been transposition - the acquisition by a plasmid of a succession of resistance transposons - thus giving rise to an ever more complex resistance pattern.

From these 2 sequences of events one can see that the emergence of resistant populations is the result of 3 main types of event. 1. There is the increase in numbers due to the selective effect of antibiotic use. 2. There is the transfer of resistance genes - often carried on bacterial plasmids - from one bacterial strain or species to another. This leads to the appearance of resistance traits in bacteria that have not shown them previously. Finally there is the transfer of resistance genes - organized as a part of a transposon - between bacterial replicons. This process leads to the accumulation of ever more complex constellations of genes on single plasmids and also on bacterial chromosomes - thus broadening the range of resistance characteristics expressed.

Little was said in the lecture about the processes of selection and plasmid transfer. Accounts of these 2 processes are many - and much is now understood about the processes involved[3,7]. Transposition, on the other hand, is a novel mechanism, and most of the talk was devoted to explaining what was involved and the techniques used for studying the phenomenon. Review articles by Cohen[5] and by Kleckner[4] are available which summarize this process very well.

One example of transposition in action was given in some detail. Over the last years isolates of *Haemophilus influenzae* resistant to either tetracycline or to ampicillin have become reasonably common, whereas before this time they were virtually never encoun-

tered. Moreover the appearance of these resistant organisms has been reflected in an increased failure of the antibiotics in question to treat infections caused by these bacteria. A comparison of the tetracycline resistance plasmid from *H. influenzae* with ampicillin resistance plasmids from the same strain has shown that the 2 types of resistance plasmids are very similar, save that one carries ampicillin transposon (Tn3-like) and the other has one that specifies resistance to tetracycline (Tn10-like)[2]. Thus it seems probable that the emergence of these resistant strains of *H. influenzae* occurred in 2 stages: first the organism acquired a plasmid which specified no resistance traits but which was able to replicate stably in *H. influenzae*. Then this plasmid acquired either an ampicillin-resistance transposon, or a tetracycline resistance transposon as a separate event. Presumably the source of these transposons were members of the Enterobacteriaceae - since the 2 types of transposon involved are very prevalent on plasmids in these species. But exactly when and where the events occurred is quite unclear.

In summary: One can see that bacterial DNA - and this is particularly the case with respect to DNA which specifies antibiotic resistance - is organized at 3 hierarchical levels - that of the whole bacterial chromosome, that of the bacterial plasmid and that of the transposon. In practical terms these hierarchies of DNA are continually interacting. Bacteria infect man: plasmids infect bacteria: transposons infect plasmids. Nor is this a sequence that relates only to antibiotic resistance; but our studies on antibiotic resistance in bacteria do allow us to study evolution in action, and this is becoming increasingly possible at the molecular level.

1 E.S. Anderson, A. Rev. Microbiol. *22*, 131 (1968).
2 L.P. Ellwell, J.R. Saunders, M.H. Richmond and S. Falkow, J. Bacteriol. *131*, 356 (1977).
3 S. Falkow, Infectious Multiple Drug Resistance. Pion Ltd, London 1975.
4 N. Kleckner, Cell *11*, 11 (1977).
5 D.J. Kopecko, J. Brevet and S.N. Cohen, J. molec. Biol. *108*, 330 (1976).
6 E. Munch-Petersen and C. Boundy, Bull. Wld Hlth Org. *26*, 241 (1962).
7 M.H. Richmond, in: Progress in Nucleic Acid Research and Molecular Biology, vol. 13, p. 191. Ed. J.N. Davidson and W.E. Cohen (1973).

DNA rearrangements and their importance in the evolution of gene systems

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See the following publications:

1 Transposable Genetic elements as agents of gene instability and chromosomal rearrangements.
P. Nevers and H. Saedler, Nature *268*, 109 (1977).
2 The Role of IS-Elements in *E. coli*.
H. Saedler and D. Ghosal, 28. Colloquium, Mosbach 1977, p. 41. Springer-Verlag.
3 Tn 951: A new Transposon carrying the Lactose Operon.
G. Cornelis, D. Ghosal and H. Saedler, Molec. Gen. Genet. *160*, 215 (1978).

ABSTRACTS

Structure at the ends of bacteriophage Mu DNA

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Bacteriophage Mu exhibits genetic properties that are analogous in many details to those of established insertion mutants in procaryotic and eucaryotic chromosomes (for a review, see DNA insertion Elements, Plasmids and Episomes [1977], Cold Spring Harbor Monograph Series, edited by A.I. Bukhari, J.A. Shapiro and S.L. Adya). These properties, which include the ability to be transposed, and to delete DNA adjacent to the insertion site, seem to involve invariant DNA sequences in the insertion elements. In Mu these particular sequences must lie at the ends of the viral genome, and these ends are covalently bound to heterogenous bacterial DNA in vegetative, but presumably not in lysogenic Mu DNA.

We have analyzed the nucleotide sequences at the 2 ends of the Mu DNA using the Maxam and Gilbert method. In some cases, these ends were present in a genetic material derived from lysogenic Mu. They were included in plaque-forming *λ-lac*-Mu hybrid particles constructed by recombination between Mu lysogen and *lac λplac*5. In one case the Mu SE (or variable) end was present in a plasmid constructed with a vegetative Mu DNA fragment and pMB 9. Our analyses lead to 3 main conclusions. 1. They show that a short stretch of 5 identical bases is located at each Mu end, oriented as an inverted repeat. 2. They strongly suggest that identical Mu end sequences are present in lysogenic and vegetative DNA. 3. They demonstrate that the heterogenous bacterial DNA bound to vegetative Mu DNA is completely removed during lysogenization, thus implying that the transposition and deletion events are, at least in part, site specific.