

IS-Elements in Bacteria

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The first extrachromosomal genetic elements discovered in bacteria were temperate bacteriophages, which can exist either as extracellular virus, as chromosomes replicating autonomously within cells or integrated into the bacterial chromosome. Integration of viruses into host chromosomes has subsequently attracted considerable attention by tumor virologists. This may justify the discussion of other types of genetic elements in bacteria in a meeting on human leucaemia.

In addition to temperate bacteriophages, there are other extrachromosomal genetic elements in bacteria. Some of them are called plasmids. They lack the extracellular state, but exist either autonomously within the bacterial cytoplasm or integrated into the bacterial chromosome.

A third class of genetic elements has been described in recent years. It apparently lacks the ability to multiply autonomously and exists only integrated into the bacterial chromosome. Within this chromosome, however, it can be transposed to various positions. At present, three such elements, called IS1, (= insertion sequence) IS2 and IS3 are known. Their length is 0.8, 1.4 and 1.25 kilobases, respectively (1-5).

The presence of these elements can be detected by various effects which they show at the point of insertion:

- 1) Integration into the continuity of the gene causes the loss of gene function (6,7).
- 2) Insertion into a gene within an operon causes severe polar effects on genes distal to the mutated gene (6, 7, 8).
- 3) At least one representative of class IS2 carries a promoter. Genes linked to this promoter are expressed constitutively (9).
- 4) If two circular chromosomes, e. g. the *E. coli* chromosome and the F-factor, share an IS-element, e. g. IS2 or IS3, recombination within the IS-elements leads to the fusion of these two chromosomes. This mechanism accounts, at least in some instances, for the integration of the F-factor into the *E. coli* chromosome upon formation of Hfr strains or for the joining and disjoining of parts of bacterial R-factors (10, 11).
- 5) Two copies of the same IS-element, inserted in inverted position relative to each other and bordering between them a certain gene may form a transposon (12). The gene for tetracyclin resistance, carried on plasmid R6-5 and also on phage P22 may serve as an example, in which the IS-element is IS3 (13, 14).

The physical and biochemical characterization of IS-elements has been possible in bacteria, due to the relative ease with which bacterial and especially bacteriophage

DNA can be handled. However, elements with very similar properties have been characterized by genetic methods in higher organisms also. Most notable are the controlling elements in maize and mutable genes in *Drosophila* (15, 16). Should it turn out that similar elements have a more widespread occurrence, even among vertebrates, they may well deserve also the attention of those interested in the genesis of malignant tumors.

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References

1. E. Jordan, H. Saedler and P. Starlinger: O° - and Strong Polar Mutations in the gal Operon are Insertions. *Molec. Gen. Genetics* 102: 353 (1968).
2. J. A. Shapiro: Mutations caused by the Insertion of Genetic Material into the Galactose Operon of *Escherichia coli*. *J. Mol. Biol.* 40: 93 (1969).
3. P. Starlinger and H. Saedler: Insertion Mutations in Microorganism. *Biochemie* 54: 177 (1972).
4. H. J. Hirsch, P. Starlinger and P. Brachet: Two Kinds of Insertions in Bacterial Genes. *Molec. Gen. Genetics* 119: 191 (1972).
5. M. Fianndt, W. Szybalski and M. H. Malamy: Polar Mutations in lac, gal and phage consist of a few DNA Sequences inserted with either Orientation. *Molec. Gen. Genetics* 119: 223 (1972).
6. E. Jordan, H. Saedler and P. Starlinger: Strong-Polar Mutations in the Transferase Gene of the Galactose Operon in *E. Coli*. *Molec. Gen. Genetics* 100: 296 (1967).
7. S. L. Adhya and J. A. Shapiro: The Galactose Operon of *E. Coli* K12. I. Structural and Pleiotropic Mutations of the Operon. *Genetics* 62: 231 (1969).
8. M. H. Malamy: Some Properties of Insertion Mutations in the lac Operon. In: *The Lactose Operon*, ed. J. R. Beckwith and D. Zipser, Cold Spring Harbor Laboratory 1970.
9. H. Saedler and H. J. Reif: IS2, A Genetic Element for Turn-off and Turn-on of Gene Acticity in *E. coli*. *Molec. Gen. Genetics* 132: 265 (1974).
10. S. Hu, E. Ohtsubo, N. Davidson and H. Saedler: Electron Microscope Heteroduplex Studies of Sequence Relations among Bacterial Plasmids: Identification and Mapping of the Insertion Sequences IS1 and IS2 and R-Plasmids. *J. Bacteriol.* 122: 764 (1975).
11. S. Hu, E. Ohtsubo and N. Davidson: Electron Microscope Heteroduplex Studies of Sequence Relations among Plasmids of *E. coli*: Structure of F13 and Related F-Primes. *J. Bacteriol* 122: 749 (1975).
12. R. W. Hedges and A. E. Jacob: Transposition of Ampillicin Resistance from RP4 to Other Replicons. *Molec. Gen. Geneteics* 132: 31 (1974).
13. K. Ptashne and S. N. Cohen: Occurrence of Insertion Sequence Regions on Plasmid Deoxyribonucleic Acid as Direct and Inverted Nucleotide Sequence Duplications. *J. Bacteriol.* 122: 776 (1975).

14. B. Tye, K. Russel, Chan and D. Botstein: Packaging of an Oversize Transducing Genome Phage P22. *J. Mol. Biol.* 85: 485 (1974).
15. J. R. S. Fincham and G. R. K. Sastry: Controlling Elements in Maize. *Annual Rev. Genetics* 8: 15 (1974).
16. B. Rasmuson, M. M. Green and B. M. Karlsson: Genetic Instability in *Drosophila melanogaster*: Evidence for Insertion Mutations. *Molec. Gen. Genetics* 133: 237 (1974).