Microbiology

Proteins that bind the β -lactam antibiotics

from A.F.W. Coulson

A MEETING that is concerned more with the enzymes that form the targets for the β -lactam antibiotics than with the β -lactamases that destroy them, would not sensibly be called a ' β -lactamase workshop'. But the name was coined in 1975 for the first of the workshops; by the third*, held recently, the focus had changed.

The target enzymes can be identified in whole cells by their binding to ^{14}C -penicillin G. In *Escherichia coli* there are two classes of penicillin-binding protein (PBP). The low-molecular-weight proteins, PBP-4, -5 and -6, are not essential to the organism, are DD-carboxypeptidases and are believed to regulate the degree of cross-linking of the cell wall. The high-molecular-weight PBP-1a, -1b, -2 and -3 have already been shown to be essential to *E. coli*; real progress in understanding the behaviour of these membrane-bound proteins is now becoming possible through the cloning and sequencing of their genes.

The sequence of the PBP-3 gene, representing a protein of 588 amino acids, was reported a year ago by Y. Hirota (National Institute of Genetics, Mishima). PBP-3 displays both transpeptidase and transglycosylase activities, and the latter is not inhibited by penicillins. B. Spratt (University of Sussex) presented evidence that the transpeptidase activity is associated with the carboxy-terminal half of the molecule, whereas the amino-terminal half contains the transglycosylase activity.

J. Broome-Smith (University of Sussex) has sequenced the genes for PBP-1A, PBP-1B and PBP-5. 1A and 1B are highly homologous; otherwise the only extensive sequence similarities in this group occur in the region of the tetrapeptide -Ser-X1-X2-Lys-. Tetrapeptides of the same form also occur in low-molecular-weight DD-carboxypeptidases and in several examples of each of two types of β -lactamase. For β -lactamase it has been very thoroughly established that the serine residue is part of the active site, and is acylated by a β -lactam in the course of its hydrolysis. Other similarities in the sequences of these three groups of enzymes are also concentrated in the neighbourhood of the tetrapeptide sequence. It is clearly very tempting to suppose both that the serine residue is part of an active site with a similar role in the mechanisms of all the enzymes, and that all the genes are homologous, at least in parts.

A highlight of the meeting was the presentation of the first high-resolution X-ray crystal structure of one of the proteins that interact with penicillins: the

2.8 Å structure of a *Streptomyces* DD-carboxypeptidase (J. Kelly, University of Connecticut). The enzyme contains two regions of secondary structure — a six-strand β -sheet and a group of five stacked α -helices. To add to the progress that has been made in the last four years in extending the sequence-based classification of β -lactamases, R. Ambler (University of Edinburgh) reported a partial sequence of the Zn-containing β -II enzyme from *Bacillus cereus*, still the only member of class B. And J.O. Lampen (Rutgers University) presented a partial sequence of its gene.

The most interesting mechanistic study was that described by R.F. Pratt (Wesleyan

University, Connecticut) who showed that acyclic esters of the form $\text{Ar.CH}_2\text{.CO.NH.CH}_2\text{.CO}_2\text{R}$ are hydrolysed by β -lactamases — the first non- β -lactam substrates to be discovered. Transpeptidation can occur from these substrates to suitable amines, which implies that acyclic amides must also be substrates (J.R. Knowles, Harvard University).

The induction of penicillinase in bacilli has unusual features which have made it a long-standing problem, a solution to which may be at hand now that clones of the entire penicillinase operons are available (Lampen). It seems clear that the main oddities in the induction arise because the inducer modifies the cell wall giving rise to a 'second messenger' within the cell; the genetic control itself may be entirely conventional. The nature of the modification to the cell wall remains mysterious, particularly since it can be brought about by a variety of chemically very different agents.

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Astronomy

Quadrantid meteors

from David W. Hughes

It is not too easy to gather data on the Quadrantid meteoroid stream. January 3 or 4, depending on our phase in the leap-year cycle, is the only day of the year on which the Earth intersects the stream; the point on the celestial sphere from which the shooting stars appear to originate has a declination of $+48.5^\circ$, so Quadrantids are best seen from high latitudes in the Northern Hemisphere where winter makes visual and photographic conditions seldom satisfactory; and at least one year in four is hampered by moonlight. Moreover, the Quadrantid stream is very narrow, the time between half-maximum flux rates being about 12 hours, and if the maximum occurs when the radiant is low in the sky, the proportion of the flux that can be observed by any method is much reduced. This factor limits optimum observations of the shower to one year in every four.

Radar methods can overcome two of the problems, permitting the observation of meteors in daylight and through clouds. They, however, suffer from their own kind of 'bad weather', because radio propagation conditions in the ionosphere can vary considerably as a function of solar cycle. Another problem with radar is the identification of the shower meteors. This is usually accomplished simply by subtracting an assumed background rate from the total observed rate.

One goal of meteor stream investigations is to unravel the disintegration process of the parent comet and the subsequent evolution of the meteoroid stream. A knowledge of the particle number density

across the stream and around the stream orbit, and the way both of these vary as a function of particle size, would be very useful in that context. Hence the value of the determination by B.A. McIntosh, of the Herzberg Institute of Astrophysics, Ottawa, Canada, and M. Šimek, of the Astronomical Institute, Ondřejov, Czechoslovakia, of the long-term average cross-section of the Quadrantid meteoroid stream by analysing radar data obtained over nearly a quarter of a century (*Bull. astr. Inst. Czechoslovakia* 35, 14; 1984).

The Ondřejov and Ottawa radars are both pulsed systems and are similar in operation. Typical parameters are pulse length $10\mu\text{s}$, peak power 25 kW, repetition frequency 500 Hz. The antenna is fixed at an elevation of 45° and meteors within a line-of-sight distance of 400 km are recorded. Meteors are sorted into three duration classes, equivalent to median magnitudes of $+6$, $+1.6$ and -1.0 .

The practice of adding one year's data to the next is common with Quadrantid researchers but McIntosh and Šimek warn that it is not without problems. These become obvious when the combined data for the time interval 1958–81 are compared with the well-observed year of 1979. There are three basic numerical values which represent any flux curve: the time of maximum flux, the rate of rise and the rate of decay. The last two can be combined to give a stream width which is usually defined as the change of solar longitude that occurs during the time when the stream is more active than half its maximum activity. The

* β -Lactamase Workshop, Holy Island, Northumbria, 4–6 April.