

Flow of genetic material

Bernard Dixon

European Contributing Editor to Bio/Technology
and the Former Editor of New Scientist

Many microbes are specialists, and fastidious too. Nitrogen-fixing *rhizobia* live in nodules on leguminous plants such as peas. Food poisoning bacteria invade the intestinal tract, leaving our other tissues alone. Distemper virus attacks dogs, but not cats, elephants or humans. An exception is *Pseudomonas cepacia*, a bacterium that seems to turn up everywhere. It has been found in the soil and in contaminated wounds, in rotting onions and infected lungs. Primarily a soil inhabitant, it has even been known to cause endocarditis in heroin addicts.

Now, according to data in the current "Journal of General Microbiology" (139, 1767, 1993), this unusually versatile microbe may play a major role in facilitating a hitherto undocumented phenomenon: the transfer of genes between bacteria responsible for plant diseases and those that cause infections in humans and other mammals. The discovery has considerable implications — not least as regards the assessment of likely consequences when genetically modified microbes are released into the environment for agricultural and other purposes. Francesca Mariani and her colleagues at the University of Rome and elsewhere were led to *P. cepacia* almost by accident, when they were studying *Mycobacterium tuberculosis* and its close relatives. They were primarily interested in developing better methods of distinguishing species and strains within this group of bacteria, and of charting their spread. One possible approach was by means of insertion sequences (IS), DNA sequences very similar to transposons, small mobile pieces of DNA that can replicate and insert copies of themselves at random sites in the bacterial chromosome.

IS elements are of potential value in diagnosis and epidemiology because their presence can be unique to particular species or even strains within a species. This has proved to be so in the case of *M. tuberculosis*. However, while studying this bacterium, Mariani and her collaborators discovered a previously unknown IS-like sequence that appeared to be specific to it and to close relatives such as *M. bovis* (the attenuated version of which forms the TB vaccine known as BCG).

The totally unexpected twist to the story came when they examined the sequence itself. As with many other IS elements and transposons, this coded not only for the genes required to insert itself into the bacterial chromosome, but also for a gene specifying a particular protein. Francesca Mariani and her coworkers have not yet isolated this protein. But they have accessed

a database to compare the amino acid sequence, determined from the corresponding nucleotide sequence, with that of other, known proteins. They discovered that the sequence of the (as yet-hypothetical) protein from *M. tuberculosis* was very similar to that of proteins coded by IS elements from other bacteria, including *Agrobacterium tumefaciens*, which causes tumour-like galls on tobacco and other plants; *Rhizobium meliloti*, which fixes nitrogen in alfalfa root nodules; and *P. cepacia*. The sequences were sufficiently homologous for the research team to announce an entirely new family of transposable elements.

This sharing of genetic information strongly suggests that it has been transferred between the different bacteria, despite their disparate genera and lifestyles. In addition, the IS element could ferry other genes between one bacterium and another. Such "horizontal" gene flow has, of course, been increasingly recognized as a widespread phenomenon among bacteria. Originally believed to occur only within species, it is now known to take place between species and between genera, too. The new discovery indicates that genes can be ferried even between microbes as distinct from each other as the *Tubercle bacillus* and agents of plant disease.

But how **precisely** could fragments of DNA cross such barriers of genus and habitat? One possibility may have involved the transfer of genes between *M. tuberculosis* and related, non-pathogenic mycobacteria that occur in the environment. These, however, do not contain the newly described sequence. *P. cepacia*, on the other hand, is a highly plausible candidate as the prime mover. "As *P. cepacia* strains are associated with plant and human disease, especially pulmonary disorders". Mariani and her colleagues write "this organism would have had the opportunity to come into close contact with both the mammalian pathogens in the lung of humans and the environmental organisms". In addition, it is already known to be very active in the horizontal exchange of genetic information. Thus *P. cepacia* may well have played, and may continue to play, a crucial role in mediating the flow of genetic material between bacteria as diverse in evolutionary terms as it is possible to imagine.

And the implications for the release of genetically engineered organisms into the environment? Could, for example, genes inserted into *Rhizobium*, to boost their nitrogen fixing capacity, be ferried into *M. tuberculosis* and enhance its virulence? As yet, there is no concrete evidence of any such hazard. Indeed, it seems inherently unlikely, given the nature and purpose of the genes likely to be engineered in this way. Nevertheless, such possibilities can no longer be dismissed as of no practical consequence gene transfer of this sort is precisely the type of scenario that biotechnologists and their regulators are now going to have to take very seriously.

Adres dla korespondencji:

Bernard Dixon, 130 Cornwall Road, Ruislip Manor, HA4 6W Middlesex, Wielka Brytania.