Bacteria learn antibiotic resistance in the sludge

Henry Nicholls, BMN News

The sludge in wastewater treatment plants could be where bacteria 'learn' to overcome antibiotics through a natural process of genetic engineering, which might explain the rapid evolution of multidrug-resistant strains.

A natural genetic engineering device called the integron allows diverse species of Gram-negative bacteria to exchange and accumulate entire libraries of useful genes. The process is central to the evolution of antibiotic resistance, say microbiologists, and wastewater treatment plants, where different bacteria and antibiotics congregate, could be where the exchange is occurring.

Sludge, sludge, glorious sludge

Bacteria residing in the sludge of a municipal water treatment plant contain integron-specific DNA sequences, says Alfred Pühler, a microbiologist at the University of Bielefeld in Germany (http://www.uni-bielefeld.de). Such sequences are virtually absent from soil samples, he says, so their presence in this environment indicates that sludge is 'a specific location where genes are coming together and being distributed'.

Furthermore, analysis of effluents from the plant reveals that bacteria containing integron-specific sequences on plasmids are being released into the environment. 'You have to block the release of bacteria from wastewater treatment plants,' urged Pühler. Simply filtering the effluent, he suggests, could significantly reduce the abundance of drug-resistant bacterial strains in the environment.

Didier Mazel, a microbiologist at the Pasteur Institute in Paris, France (http://www.pasteur.fr) agrees that this sort of environment with 'abundant nutrients and high bacterial density' is perfect for genetic exchange. The integron device is 'the major system that is responsible for antibiotic resistance' in Gram-negative bacteria, he said. Found embedded within mobile genetic elements, such as plasmids or transposons, integrons trigger the transmission of resistance genes both within and between bacterial species.

Integrase and gene cassettes

At the center of the integron platform is a so-called integrase gene, which catalyzes the recombination between two nearby sites, one of which is known as a 'gene cassette'. This encodes one or more antibiotic resistance genes, and recombination inserts the gene cassette alongside a promoter within the integron, driving expression of the encoded product.

But the real power of the integron is its ability to stockpile gene cassettes from other mobile genetic elements and also from super-integrons, ancestral versions of this device that have been found meshed into the chromosomes of Gram-negative bacteria from very diverse lineages. By plundering this evolved genetic resource, bacteria can acquire genes that have come through eons of natural selection.

Because this system of gene exchange is so widespread, researchers aim to find ways of disrupting it, thereby sabotaging this means of information exchange. 'We hope to be able to hamper the recombination process,' said Mazel, whose research is now concentrating on the 3D structure of integrase. 'The recombination system in charge of integron cassette recombination is very peculiar,' he told *BioMedNet News* (http://news.bmn.com). It could be just five years until a specific inhibitor of this enzyme is found, he says.

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