New route of acquiring antibiotic resistance in bacteria is the most potent one to date

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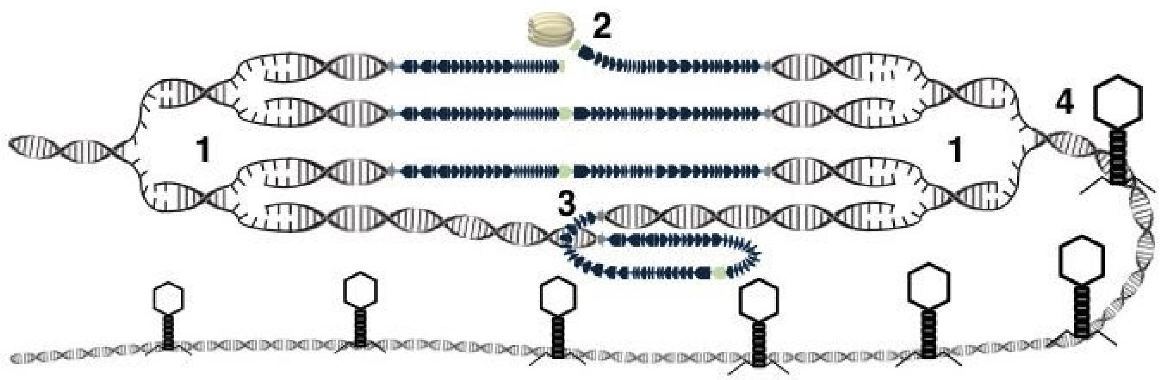

The induced prophage genome (blue) replicates in situ bidirectionally (1) and amplifies the adjacent bacterial DNA (gray). Phage terminase initiates in situ DNA packaging from a pac site (2), while prophage excision occurs (3) in parallel. Prophage excision produces infectious phage particles. Lateral-transducing particles are completed (4) when a headful capacity is reached. The DNA packaging machinery then proceeds to fill additional headfuls of bacterial chromosome for several hundred kilobases. Credit: Chen J, Quiles-Puchalt N, Chiang YN, et al. Genome hypermobility by lateral transduction. *Science*. 2018. [In Press]

Bacteriophages (or phages) are viruses that infect and parasitize bacteria. These phages can transfer DNA from one bacterium to another through a process known as genetic transduction. This is thought to be the major means by which bacteria evolve and acquire the antibiotic resistance and virulence factors that accelerate the emergence of new and progressively more pathogenic strains. Up to now, two mechanisms of genetic transduction were known: generalized and specialized transduction. For over 60 years, since their discovery by American scientist and Nobel laureate Joshua Lederberg, these two mechanisms have stood as the only mechanisms of genetic transduction.

In a paper published online in the journal *Science* on October 12, 2018, research teams led by NUS Medicine and the University of Glasgow report the discovery of a third mode of transduction. Termed lateral transduction, this new mode appears to be the most powerful means of transduction yet discovered, with the ability to transfer large sections of bacterial chromosomes (several hundred kilobases) between bacteria at extremely high frequencies.

When a phage infects a bacterial cell, it normally reproduces in one of two ways: (1) the lytic cycle, in which the phage reproduces and lyses the cell, resulting in the release of new phage particles; or (2) the lysogenic cycle, in which the phage DNA incorporates into the host genome and replicates together with the host genome. In (2), certain stimuli can provoke the phage DNA to cut itself out of the host genome (excision), assemble with proteins into new phage particles (packaging), undergo maturation and lyse the host cells. The released phages from both (1) and (2) can then infect other bacteria and transfer their DNA, which includes DNA from the host cell.

In contrast, the researchers, led by Assistant Professor John Chen of NUS Medicine, found that lateral transduction occurs when phages delay excision to late in their life cycle. Instead, the phages initiate DNA replication while they are still part of the host genome, resulting in multiple integrated phage genomes. DNA packaging can then initiate on some genomes, resulting in the packaging and transfer of chromosomal DNA to other bacteria, while other phage genomes excise and lead to normal phage maturation.

Assistant Professor Chen says, "Lateral transduction elevates the concept of mobile genetic elements well beyond that of defined DNA elements, by transforming sections of the genome into hypermobile platforms that are capable of transferring any genetic element within their boundaries at incredibly high frequencies."

The discovery of this highly efficient mode of gene transfer could help to explain the rapid evolution of bacteria that occurs, for example, in the development of multi-drug resistant strains.

Putting the discovery in context, Assistant Professor Chen observed that "phages are by far the most abundant biological entities on the planet, and the importance of genetic transduction as one of the principal drivers of microbial evolution has never been more apparent than with the discovery of lateral transduction."

More information: J. Chen el al., "Genome hypermobility by lateral transduction," *Science* (2018). science.sciencemag.org/cgi/doi … 1126/science.aat5867

"A common trick for transferring bacterial DNA," *Science* (2018). science.sciencemag.org/cgi/doi … 1126/science.aav1723

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