The 'Eat me cake' theory, or genetic cannibalism of the enemy: A cause of vanishing antimicrobial resistance

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of the enemy's genetic material makes it possible to develop defences and to multiply (Fig. 1). Indeed, the exogenous sequences contained in the genetic macromolecules are not welcome because they constitute a genetic parasitism costly in terms of multiplication of organisms, and it is generally accepted for genes, as quoted by Moran, 'use it or lose it' [4]. These unnecessary additional sequences weigh on the cost of reproducing micro-organisms.

Many of the antimicrobial resistance gene transfer mechanisms are conferred by exogenous sequences carried by plasmids, transposons or bacteriophages. These resistances, in an interesting way, are unstable [5]. Indeed, many resistances disappeared over time when the use of antibiotics, and therefore the pressure of antimicrobial selection, disappeared. One of the major reasons for the disappearance of these resistances is the cannibalisation of repli-

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con sequences, which allows bacteria to eliminate replicons by cannibalism following the model 'Eat me cake'. Indeed, clustered regularly interspaced short palindromic repeats (CRISPRs) are one of the defence modes for integrating sequences of the enemy [6]. Following integration, enemy sequences (from phages, transposons or plasmids) are recognised when the transcribed RNA of the DNA sequence, integrated into the chromosome of the bacterium, pairs with the single-stranded DNA of the enemy sequence, after which the enzyme Cas9 cuts the whole, thus destroying the enemy DNA. This has already been found for *Enterococcus faecalis*, in which the presence of resistance genes to vancomycin is antagonised by the presence of CRISPR [7]. As a matter of fact, as soon as the selection pressure disappears, the alien replicon sequence is destroyed by genetic cannibalisation, as microbes without defence against alien genetic sequences are no longer selected. Another mechanism that illustrates the 'Eat me cake' model is that of retroposons. Humans are composed of thousands of integrated retroviruses, including those that have allowed the existence of the placenta and those that play a role in embryogenesis, which differentiates us from the great apes [8]. This process is currently ongoing with the retrovirus causing AIDS-like disease in koalas. Following the endogenisation process, the progeny of koalas are no longer susceptible to the virus [9]. Finally, we describe the same mechanism in giant viruses integrating the sequence of the virophage in an operon that we named MIMIVIRE, allowing to resist its infectivity [10]. Thus, cannibalisation of enemy sequences in the 'Eat me cake' model plays a major role in the evolution and protection of populations, including humans, against foreign agents and explains the instability of antimicrobial resistance.

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