A new concern of nanowaste: A case study of bacterial pathogenic evolution

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Silver nanoparticles (AgNPs), own to its broad spectrum of antibacterial and antifungal activities, has been widely used in many commercial products, ranging from biomedical supplies, textile, to personal-care products (Patchin et al. 2016). It is estimated that over 400 t of AgNPs is produced globally each year (Vila et al. 2017). In general, a 5 to 95% of the total amount of AgNPs in the commercial products will be released into the swage-treatment plant (Syafiuddin et al. 2018). As a result, AgNPs is widely detected in a variety of environmental matrices. Therefore, AgNPs exposures in ecosystems will mostly be chronic exposures to low concentrations, and it is imperative to explore whether bacteria can develop adaptive response/resistance under this circumstance.

The main objective of this study was to elucidate the physiological changes of a model bacteria *E. coli* after chronic exposure to low dose of AgNPs. Additionally, how the capability of AgNPs-resistance/tolerance influenced bacterial sensitivity to various antibiotics was investigated. Our study provides insight into the hitherto little explored phenomenon of bacterial nano-resistance and understands whether the adaptive mechanisms are also relevant for bacteria developing resistance to antibiotics.

The results showed that *E Coli* decreased the susceptibility to AgNPs after 100 generations of exposure as evidenced by the change of minimal inhibition concentration (MIC) from 1.24 to 3.01 mg/L. This tolerance is due to the overexpression of Cu-related efflux pump (i.e., *cusABCF*). Importantly, the developed bacterial resistance also implicates in antibiotic tolerance (i.e., penicillin, ciprofloxacin, kanamycin, gentamicin), due to the adaptation to oxidative stress and associated upregulations of multidrug resistance genes. Together, this outcome will allow us to address the question concerning evolution mechanism of bacteria towards AgNPs, which also poses an important concern about the sustained use of AgNPs as a "miracle" biocide.

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