

Heavy metal-induced selection for antibiotic resistance: evidence from high-throughput profiling of resistome in nickel-contaminated soils

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Heavy metal contamination is assumed to function as a selection pressure in the proliferation of antibiotic resistance due to their shared mechanisms of resistance, however, our knowledge of the heavy metal-induced selection for antibiotic resistance is lacking in a long-term basis. Using high-capacity quantitative PCR array and Illumina sequencing, we investigated the responses of a wide spectrum of soil antibiotic resistance genes (ARGs) to 4-5 year nickel exposure (0-800 mg kg⁻¹) in two well-manipulated experimental sites. In total, 149 unique ARGs were detected in the two sites, with genes conferring resistance to multidrug and β -lactam as the most prevalent ARG types. The frequencies and relative abundance of ARGs tended to increase along the gradient of increasing nickel concentrations, with the highest values recorded in the treatments amended with 400 mg nickel kg⁻¹ soil. The abundance of mobile genetic elements (MGEs) showed increasing tendency with increasing nickel levels and was significantly correlated with ARGs, suggesting that nickel exposure might enhance the mobility potential of ARGs. Network analysis revealed significant interaction/association between ARGs and MGEs, with the integrase *intI1* gene having the most frequent interactions with other co-occurring ARGs. Structural equation models demonstrated that the impacts of nickel-induced selection on ARG patterns were mainly driven by nickel bioavailability and MGEs, rather than by bacterial communities. Taken together, we provide field-based evidence that long-term nickel exposure significantly increased the diversity, abundance, and mobility potential of soil antibiotic resistance, and highlight the health risk of multi-resistant ARGs selected by heavy metal in polluted environments.