Horizontal gene transfer is a major contributor to the evolution of bacterial genomes and can facilitate the dissemination of antibiotic resistance genes between environmental reservoirs and potential pathogens. Wastewater treatment plants (WWTPs) are believed to play a central role in the dissemination of antibiotic resistance genes. However, the contribution of the dominant members of the WWTP resistome to resistance in human pathogens remains poorly understood. Here we use a combination of metagenomic functional selections and comprehensive metagenomic sequencing to uncover the dominant genes of the WWTP resistome. We find that this core resistome is unique to the WWTP environment, with <10% of the resistance genes found outside the WWTP environment. Our data highlight that, despite an abundance of functional resistance genes within WWTPs, only few genes are found in other environments, suggesting that the overall dissemination of the WWTP resistome is comparable to that of the soil resistome.