

Plants may utilize bioactive chemical compounds which exude from their root to shape their associated beneficial microorganism in the rhizosphere to acquire resistance against pathogen infection [Fig. 1]. However, the underlying mechanism regulating this interaction has been poorly elucidated. The aim of the present study was to investigate the functional role of root exudate (from different host genotypes) in mediating belowground indirect plant defense. To elucidate the molecular mechanism underlying plant interaction with health-promoting microorganism, *Arabidopsis thaliana* (Col-0 and Ler-0 accessions) were grown for three weeks in field soil (non-sterile). Subsequently, the roots were exposed to *Fusarium oxysporum matthioli* (FOM). Sampling was done every five days after the infection for 25 days. The collected samples were subjected to both targeted (aliphatic and indole glucosinolates, plant hormones, and mycotoxins) and untargeted analysis by employing LC-MS/MS and GC-TOF/MS platforms as well as metabarcoding (Illumina MiSeq). Phenotypic characterization of the plants displayed that the Col-0 accessions had developed a resistance to FOM exposure whereas the Ler-0 ecotype was susceptible. The disease progression was also evaluated on a molecular level and resulted in the identification of beauvericin in both root and shoot tissues of the susceptible plants which likely was associated with promoting pathogenicity in FOM. The result from targeted and untargeted metabolomics as well as analysis of the root microbial community composition (bacteria and fungi) revealed the role of novel natural products in shaping the distinct member of the microbial community leading to diseases suppression.