

## Mapping the *Arabidopsis* metabolic landscape by untargeted metabolomics at different environmental conditions

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Metabolic genome-wide association studies (mGWAS), whereupon metabolite levels are regarded as traits, can help unravel the genetic basis of metabolic networks. Aiming to increase the discovery of true metabolite–gene associations, we applied abiotic stress to *Arabidopsis thaliana* using an integrative approach combining mGWAS and metabolite-transcript correlation-network analysis. 309 natural accessions were grown under two independent environmental conditions (control and stress) and subjected to untargeted LC-MS-based metabolomics; levels of the obtained hydrophilic metabolites were used in GWAS, followed by integration with network-derived metabolite-transcript correlations using a time-course stress experiment. Our two-condition-based GWAS for ~2,000 semi-polar metabolites resulted in the detection of numerous highly resolved mQTL, many of which environment-specific. We show increased discovery of causal genes for well-characterized secondary metabolites by applying GWAS under stress. We, moreover, discovered a large number of hitherto uncharacterized metabolite-gene associations, serving as a rich reservoir for further

gene-characterization efforts. Of these, we identified 93 key candidate associations between structural genes and metabolites. We then experimentally validated—using loss-of-function mutants—eight of the novel associations, two of them showing differential genetic regulation in the two environments studied. Our study thus demonstrates the power of combining large-scale untargeted metabolomics-based GWAS with time-course-derived networks, when both approaches are performed under different abiotic environments, to facilitate the identification of metabolite-gene associations. Additionally, it also provides new global insights into the metabolic landscape of *Arabidopsis* using a strategy that could readily be adapted for other plant species.

### Biography

Si Wu conducted MS-based untargeted metabolomics study to investigate the pathophysiology of complex metabolic disease – hypothyroidism and therapeutic effects of traditional Chinese medicine. She published four metabolomics-related scientific papers as the first author during the Master degree. She worked as an Intern at Agilent Technologies (Shanghai, P.R. China) to conduct Drug Quality Standard Test of Chinese Pharmacopoeia (2010 Edition). At present, she is a PhD candidate waiting for the defense at Max Planck Institute of Molecular Plant Physiology to carry on an integrative research of combining Genome Wide Association Study (GWAS) and network analysis to identify novel genes involved in secondary metabolism in *Arabidopsis*.

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