# Untargeted Metabolomics of Dried Blood Spots Using Mass Spectrometry in Glutaric Aciduria Type 1

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The disease course of patients with glutaric aciduria type 1 has improved through the implementation of newborn screening and early patient identification with a worldwide reduction in the number of patients presenting with an acute encephalopathic crisis. However, acute encephalopathic events remain high in some patient subsets including patients homozygous for the GCDH IVS-1 + 5g -t variant. Our study aims to further the understanding of the metabolic perturbations in GA1 contributing to disease properties and prognosis. To this end we performed untargeted metabolomics on the dried blood spots (DBS) of 17 patients with GA1 and 20 controls identified through Newborn Screening Ontario after 2000 using mass spectrometry. Untargeted metabolomics allows for the simultaneous profiling of thousands of metabolites for hypothesis testing and to help derive biochemical signatures.

Our results showed distinct clustering of metabolites between GA1 DBS and control DBS using principal component analysis. As expected, increased abundance of glutarylcarnitine and glutaric acid were found in GA1 DBS. We then used computational algorithms including Mummichog to perform functional analysis and identify enriched pathways. GA1 DBS showed significant enrichment in over 17 pathways including glutathione metabolism, lysine metabolism, lineolate metabolism and in the metabolism and degeneration of various amino acids. Our results show that there are numerous differences in metabolite abundances and biochemical pathways already identifiable in GA1 DBS at birth. Ongoing analysis and metabolite identification is being performed to further understand the metabolomic differences of different GA1 genotypes and distinct biochemical phenotypes.