**INTRODUCTION**

Lysinuric protein intolerance (LPI, OMIM 322790) is an autosomal recessive aminoacidopathy caused by a defective transport of certain neutral amino acids (arginine, lysine, ornithine; CAA) at the basolateral membrane of epithelial cells in the intestine and kidney. As a consequence, intestinal absorption and renal reabsorption of CAA are impaired with net loss of these compounds, coming from other metabolic pathways, into urine. Biochemical findings of human LPI such as massive urinary excretions of arginine, ornithine and orotic acid were already present when both animal and human subjects were kept on the special dietary regimen. Hyperlysinuria appeared only in homozygous animals. The homozygous mouse is viable, but shows renal involvement and stunted growth.

**RESULTS AND DISCUSSION**

A mouse was generated in which Slc7a7 gene function was disrupted, as a consequence, no Slc7a7 mRNA is present in null animals. The homozygous disruption of the Slc7a7 gene leads to a severe phenotype of null mutants. Biochemical findings of human LPI such as massive urinary excretions of arginine, ornithine and orotic acid were already present when both animal and human subjects were kept on the special dietary regimen. Hyperlysinuria appeared only in homozygous animals. The homozygous mouse is viable, but shows renal involvement and stunted growth.

The combinatorial metabolic differences is therefore greatly simplified, even where a metabolic pathway contributes to more than one metabolite (Figure 7). Advanced multivariate statistical analysis performed using SIMCA-P11 is a powerful and complementary approach to the later analysis (PCA). The scores and loadings plots display the results of the PCA, which were used to facilitate the acquisition of data over a wide dynamic range (up-to four orders) with accurate isotope patterns. Data processing was performed by multivariate statistical analysis utilizing a combination of Marklynx and UPLC/DAD software.

**CONCLUSION**

The metabolic basis underlying the malnourished and disordered phenotypes of null animals is the failure to transport CAA. Therefore, an animal model may represent a crucial tool for obtaining insights into the pathophysiology of this disorder and for testing innovative treatments of this disease.

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**RESULTS AND DISCUSSION**

Repulsion of UPLC oa-TOF MS data for the three genotypes facilitated the identification of discrete differences between the samples related to the LPI. The PCA data visualization whilst possible is extremely time consuming and thus employing an automated approach is advantageous.

**METHODS**

Metabolomic profiling of urine in knockout mice with lysinuric protein intolerance was performed on LC/MS from three genotypes (homozygous, heterozygous and wild type), for fast, high efficiency separations without the need for any external liquid chromatograph with 1.7 µ column particle size. This was coupled to an electroosmotic elution LC-TOF mass spectrometer with enhanced option on to thermospray interface. Novel on column SPE facilitated the acquisition of data over a wide dynamic range (up-to four orders) with accurate isotope patterns. Data processing was performed by multivariate statistical analysis utilizing a combination of Marklynx and UPLC/DAD software.

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