Background. Tangier disease (TD) is a rare autosomal recessive disorder characterized by a deficiency or absence of high-density lipoprotein caused by mutations in the adenotriphosphate-binding cassette transporter-1 gene (ABCA1). These lead to a defect in cellular cholesterol removal causing the deposition of cholesterol esters throughout reticuloendothelial system.

Methods. We enrolled a homozygous TD patient and the heterozygous father. Whole plasmatic extracts were processed and mass spectrometry analyses of peptide fragments were performed on MALDI TOF/TOF equipment. Trypsin digestion produces a constant set of peptide fragments distinctive of each starting protein (finger print). Peptide ions are automatically processed by MASCOT and GPS Explorer software, which provide us the identification of starting proteins. Peaks, indicative of different peptides, also subjected to mass/mass analysis by means of fragmentation in a collision chamber. Such second mass analysis provided aminoacid sequence of peptide and the identification of possible post-translational modifications.

Results. The very high sensitivity of the method allowed us to identify plasma proteins less peresented (<1.2 pg/ml). Apolipoprotein A-I, haptoglobin, alpha-2 macroglobulin, fibrinogen beta chain and isoform 1 of alpha-1 antitrypsin (C.I. 95%) resulted to be downregulated, while serotransferrin and Ig kappa resulted upregulated in the homozygous TD patient respect to the heterozygous. The same pattern was also observed by routine assays.

Conclusions. The downregulation of the acute phase proteins observed in this case was unexpected. Proteome analyses may help in identification of abnormal metabolic pathways eventually activated in TD.