Glycosaminoglycans and Fabry's disease

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Fabry's disease is an X-linked inherited disorder with an estimated incidence of one in 40 000 to one in 117000 and substantial morbidity and mortality worldwide. The numerous mutations identified regard the GLA gene coding for the enzyme α-galactosidase A. This lysosomial enzyme, normally breaks down neutral glycosphingolipids, particularly globo triaosylceramid and galactosylceramide. Mutations causing the total or partial enzyme inactivation lead to the storage of these molecules in different cell types. Over time, this buildup damages cells throughout the body, particularly blood vessels in the skin and cells in the kidneys, heart, and nervous system [1].
Glycosaminoglycans (GAGs) are linear, heterogeneous polysaccharides involved in numerous physiological and pathological processes. In plasma, the principal GAG, the chondroitin sulfate (CS), is bound to the bikunin, the small subunit of Inter-α-Trypsin Inhibitor [2]. It has been reported that this complex is implicated in some inflammatory processes and that bikunin, found in urine as Urinary Trypsine Inhibitor (UTI), could be an useful marker of renal disease.
The aim of this work was to evaluate eventual correlations between levels/structure of these molecules in plasma and urine and the presence/progression of Fabry's disease.
The study comprised 21 patients affected by Fabry's disease aged from 19 to 61 and 40 healthy volunteers homogeneous for age and gender.
Preliminary data shows a 35% increase of plasma GAGs in Fabry's patients. Moreover, urinary GAG levels are 29% higher in patients respect to controls, showing also a different distribution. In particular we found a reduction of UTI and an increase of both heparan sulfate and chondroitin sulfate. Structural analysis of urinary chondroitin sulfate isomers evidenced deep differences in the relative abundance of their constituting disaccharide units.
These results suggest that the biochemical pathways involved in the synthesis and metabolism of GAGs could be altered in Fabry's disease. Further studies will be directed to establish if GAGs can be used as markers both in the diagnosis and in the follow up of Fabry's disease.

References

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