Early Detection of Lysosomal Storage Disorders with Tandem Mass Spectrometry

Summary / Zusammenfassung
Lysosomal storage disorders (LSDs) are a group of rare genetic diseases characterized by inherited defects in functional expression of lysosomal enzymes and proteins. Patients with LSDs accumulate the substrates of deficient lysosomal enzymes inside the cells, tissues and blood. Owing to the complexity of the storage products, differences in their tissue distribution and rates of accumulation, the disease can cause pathologic changes in multiple organ systems (liver, spleen, kidney, bones and others) and can be confined to the nervous system. As effective treatment for some of these disorders becomes more of a reality, it is critical that patients are diagnosed as early as possible. Because of the strong correlation between age at diagnosis (and start of therapy) and life expectancy and quality, there are even initiatives to institute newborn screening for LSDs to identify presymptomatic individuals as candidates for therapeutic intervention, e.g. bone marrow transplantation, enzyme replacement therapy or substrate reduction therapy.

As a result of the wide range of clinical phenotypes, many of the LSDs are missed, incorrectly diagnosed or too late. Diagnosis of suspected patients is made by measuring the activity of the affected enzyme or determination of its accumulating substrate in tissue samples or body fluids.

In 2004, Michael H. Gelb's group published a method based on tandem mass spectrometry (TMS) that allows simultaneous analysis of five different LSDs (Ref.: Li et al. Clin. Chem. 50 (2004) 1785-1796). This multiplex assay is suitable for large sample numbers, even in newborn screening programs.

The aim of this study is to introduce TMS for diagnosis of LSDs in Switzerland. This method enables the detection of symptomatic and asymptomatic patients. This study allows assessment of epidemiological data and will be the basis for the decision whether LSD screening is feasible in the Swiss population.

Keywords / Suchbegriffe
LSD, Lysosomal storage disorders, tandem mass spectrometry, Fabry disease, Gaucher disease, Pompe disease, Niemann Pick disease type A & B

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Other Links to external Webpages / Andere Links zu externen Webseiten
http://www.kispi.unizh.ch/af/ForschungLehre/ClinicalChem/MassSpect_de.html

Funding Source(s) / Unterstützt durch
Wolfermann-Nägeli-Stiftung, Kilchberg

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Duration of Project / Projektdauer
Jan 2008 to Nov 2011