MASS Medical SPEC

Sophi™ Quantification of Carbohydrate-Deficient Transferrin RUO

The Carbohydrate-Deficient Transferrin (CDT) quantification is a Sophi™ affinity chip assay that determines relative levels of CDT with respect to the normal intact transferrin. It is known that severe alcohol consumption leads to liver damage and alterations in glycosylation of transferrin. That is why elevated abundance of CDT is declared to be indicative of long term and/or heavy alcohol abuse.

BACKGROUND

Transferrin is synthetized in the liver and is the most important iron carrier in the human body. Its carbohydrate-deficient form (CDT) is a widely recognized marker of heavy alcohol abuse. The transferrin molecule consists of a single peptide chain arranged in 2 globular domains, the N-terminal domain (1–336) and the C-terminal domain (337–679). The C-terminal domain contains 2 N-glycosylation sites located at asparagines 413 and 611, which are occupied mostly by complex biantennary glycans terminated with N-acetylneuraminic acid. Severe alcohol consumption leads to alterations in glycosylation of intact tetrasialotransferrin, which results in production of 2 transferrin isoforms that lack either one [disialotransferrin (DST)] or both [asialotransferrin (AST)] glycan structures. DST and AST are collectively named CDT. The CDT levels with respect to intact ("healthy") transferrin levels represent a highly sensitive and clinically specific marker of alcohol abuse. Due to the half-life of 2 to 4 weeks following abstinence, it can also serve as a useful relapse marker. **Sophi**™ mass spectrometer provides fast detection and quantification of transferrin isoforms because their molecular masses are different from the intact transferrin. Relative quantification of CDT levels provides information about the severity of liver damage and can be attributed to alcoholism using clinically known threshold values.

TEST

Serum samples (2uL) are applied and incubated on a **Sophi**™ affinity target array with an antitransferrin antibody for 60min. After the incubation, a series of washing steps is applied. After the deposition of a MALDI matrix a measurement is taken. The removal of sialic acids due to pathological deglycosilation result in different molecular masses of carbohydrate deficient transferrin variants compare to intact (tetrasialo) transferrin. These differences can be detected as different m/z values in mass spectrum. After the analysis is performed by **Sophi**™, the relative abundance of CDT is determined automatically by the software from the respective signals of the transferrin forms in mass spectrum. Following current clinical recommendations, relative value of 1.6% of CDT level is considered to be a threshold for long-term alcohol abuse.

CLINICAL USE

Determination of long-term alcohol abuse using liver transferrin deglycosilation damage as a clinical marker.

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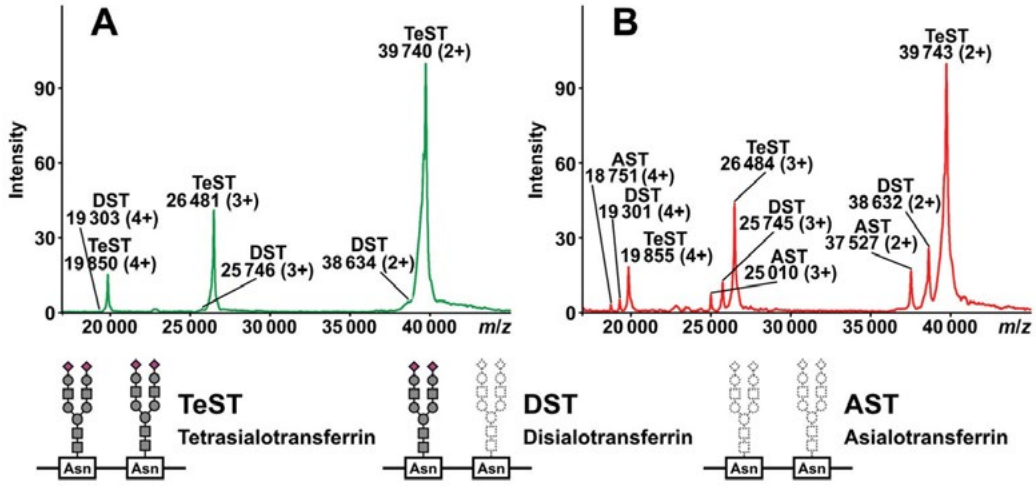
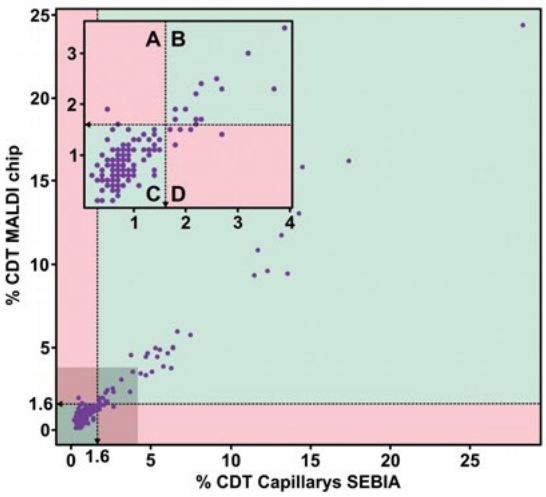
DATA EXAMPLE

Spectrum of transferrin from sample of
A/ Healthy patient (A)
B/ known alcoholic patient

Transferrin isoforms TeST (intact transferrin), DST, and AST differ in N-glycosylation site occupancy by biantennary doubly sialylated glycans. The presence of declyco DST and AST forms of transferrin in mass spectrum above the clinical threshold is considered to be a molecular marker of liver damage, most likely due to long-term alcohol abuse.





Plot representing validation of Sophi CDT assay against gold standard Sebia Capillarys CE assay using 179 patient samples.

A/ False-positive
B/ True-positive
C/ True-negative
D/ False-negative

Detailed information

Darebna et al.: Detection and Quantification of Carbohydrate-Deficient Transferrin by MALDI-Compatible Protein Chips Prepared by Ambient Ion Soft Landing, Clin Chem, 2018, 64(9):1319-1326.
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