MASS Medical SPEC

# Sophi™

# Rapid Human Haptoglobin Phenotyping RUO

**The Rapid Human Haptoglobin Phenotype test is a Sophi™ affinity chip assay that measures human haptoglobin alpha subunits in serum or plasma samples, which results in quick determination of the haptoglobin phenotype.**

## BACKGROUND

Haptoglobin (Hp), is a prominent plasma glycoprotein involved in the scavenging of free hemoglobin. Hp is composed of disuphide bridge linked α-chains and β-chains. The human gene for Hp, located on chromosome 16q22, consists of three structural alleles: Hp1F, Hp1S and Hp2. The presence of the Hp1 and Hp2 alleles gives rise to three major phenotypes: Hp1-1 phenotype is represented by a single α1β homodimer with a molecular weight of 86 kDa; the other homozygous phenotype is Hp2-2, which consists of cyclic Hp polymers containing 3 or more α2β subunits (170–900 kDa); The heterozygous Hp2-1 is assembled into linear homodimers and multimers from various numbers of α2β subunits joined with α1β subunit at each terminus (86–300 kDa). The prevalence of the three Hp genotypes varies dramatically across populations. The normal level of plasma Hp varies considerably ranging from 0.3 to 3 mg/ml, but in any given individual the Hp level remains constant and therefore the observation of marked concentration changes has clinical significance. The Haptoglobin protein of phenotype Hp1-1 is more efficient in protection against heme- and iron--driven oxidative damage to the vascular system and kidney. In several disease states, the Hp2-2 protein has been associated with reduced ability to protect against toxic free hemoglobin. For instance, Hp2-2 phenotype has been implicated as a risk factor in both type 2 diabetes and associated cardiovascular diseases. It has been reported that Hp2-2 has higher affinity to bind to apolipoprotein A1 (ApoA1) in the same location as lecithin-cholesterol acyltransferase (LCAT), subsequently decreasing LCAT activity and therefore limiting high density lipoprotein (HDL) maturation. This inhibits reverse cholesterol transport causing HDL to become proatherogenic. Another hypothesis exists, that Hp2-2 phenotype is an independent risk factor for the development of both focal and global Cerebral vasospasm (and the resulting delayed cerebral ischemia) and also predicts poor functional outcomes and mortality after subarachnoid hemorrhage. The risk of developing cardiovascular disease (CVD) in patients with diabetes has been shown to be connected with Hp2-2 phenotype while the vitamin E supplementation was found to significantly decrease the risk of CVD in Hp2-2 diabetic patients.

## TEST

The serum or plasma samples (1uL) are incubated on a **Sophi**™ target array with immobilized anti-human haptoglobin antibody. After 60 minutes incubation, a washing and reduction step follows before MALDI matrix is added and samples are measured by **Sophi** mass spectrometer. The α1 and α2 subunits of haptoglobin have different molecular masses and thus appear in mass spectrum at different m/z values. This allows to decide haptoglobin phenotype from the mass spectrum of the alpha subunits. After the analysis is performed by **Sophi**™, the phenotype is determined automatically by the software from the respective signals of the haptoglobin alpha units in mass spectrum.

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(under construction as of February 2024)

## CLINICAL RESEARCH USE

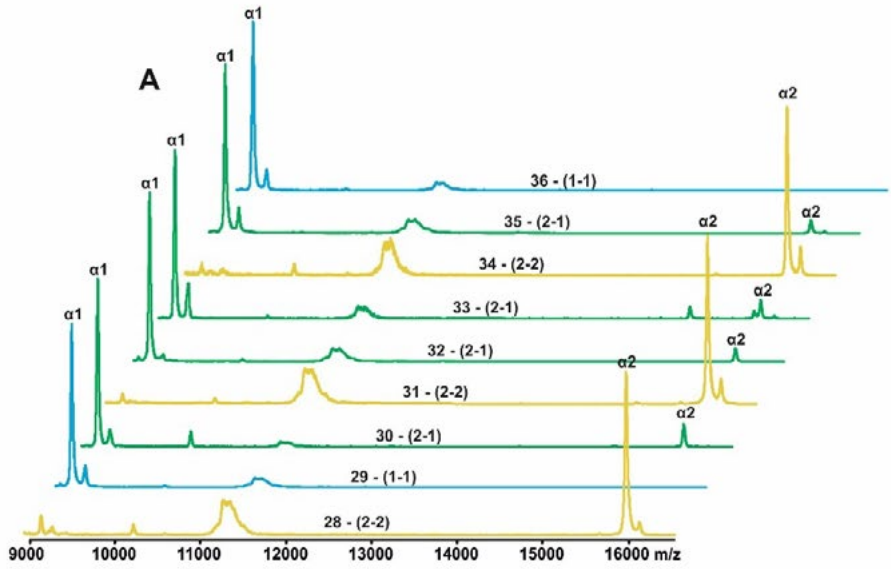
Determination of the haptoglobin phenotype can be used to predicts the development and outcomes of the following severe pathologies:

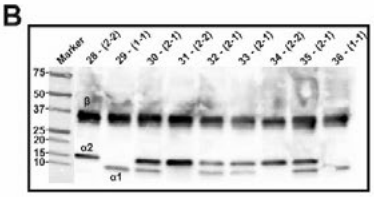
– Cardiovascular diseases
– Type 2 diabetes
– Aneurysmal subarachnoid hemorrhage
– Chronic kidney disease
– Global cerebral vasospasm/delayed cerebral ischemia

## DATA EXAMPLE

The following demonstrates an example of Haptoglobin phenotyping with **Sophi**™ affinity chip:

A) Shows results of analysis of 9 patient sera with different combinations of α1 and α2 subunits in mass spectrum, which determines the three phenotypes: 1-1, 1-2 or 2-2
B) Same samples were analyzed by SDS/Western blot for validation
C) Output table that shows determined Hp phenotype for individual samples

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| Analysis Name | alpha 1 int | alpha 2 int | Phenotype |
|---|---|---|---|
| Sample_28 | 1577 | 13602 | 2-2 |
| Sample_29 | 71605 | 0 | 1-1 |
| Sample_30 | 14806 | 1972 | 2-1 |
| Sample_31 | 675 | 10087 | 2-2 |
| Sample_32 | 78088 | 6277 | 2-1 |
| Sample_33 | 5279 | 580 | 2-1 |
| Sample_34 | 244 | 3255 | 2-2 |
| Sample_35 | 56063 | 4458 | 2-1 |
| Sample_36 | 23583 | 0 | 1-1 |

**Detailed information**

Pompach et al.: Planar Functionalized Surfaces for Direct Immunoaffinity Desorption/Ionization Mass Spectrometry, Clin Chem, 2016; 62(1):270-8. doi: 10.1373/clinchem.2015.244004

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