Information for „Nagalase-Bloodtest“

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1. **Summary**

- Nagalase is an endogenous enzyme in the metabolism of sugar.

- Tumor cells can form Nagalase

- **Gc-MAF** is a *Macrophage-Activating-Factor*.

- GcMAF is formed from Gc-Protein.

- The Nagalase formed from tumors can prevent the formation of immune-stimulating factor of GcMAF.

- Artificially produced Gc-MAF is used as immunostimulatory substance.

- The Nagalase test is performed to verify whether a GcMAF therapy will be useful "therapeutic indication" and to monitor the effect of the GcMAF-therapy.

- Further readings at a GcMAF therapy are important: vitamin D and calcium levels in the blood, the genetic variant of the vitamin D receptor and the serum levels of soluble uPA receptor.
2. **What is „Nagalase“?**

The so-called. "Nagalase" is an endogenous enzyme that plays a role in sugar metabolism. The scientifically correct name is "N-acetyl-Galaktosaminidase". Nagalase can split certain sugar molecules, splitting of the N-acetyl-galactosamine from large molecules.

Yamamoto and colleagues showed that tumors secrete increased Nagalase. Accordingly, it was also found that tumor diseases with an increased Nagalase value are linked in serum ("tumor markers"). But even in some other diseases increased Nagalase values were found.

The produce of Nagalase in tumors was attributed to a suppressive effect on the immune system. Medically and Immuno-suppressive effect means the Nagalase-mediated immune suppression in tumor diseases is thought to contribute the promoting growth of existing tumors and the formation of metastases.

The immunosuppressive effect of Nagalase is explained that Nagalase prevents the formation of immune-stimulating factor from Gc-MAF Gc protein. "MAF" stands for "macrophage activating factor". Macrophages are known "Scavenger cells" of the immune defense system.

3. **How the inactivation of GcMAF by Nagalase works**

Gc-MAF is formed of Gc-Protein.

By the enzyme "Nagalase" the sugar chain of the Gc-protein is completely eliminated. So the modified Gc protein can no longer be transferred to Gc-MAF

**In other words: The effect of Nagalase on Gc protein causes that Gc-MAF can not be formed anymore.**

the Nagalase formed by tumors is attributed to an immunosuppressive effect. This effect will lead to a suppression of an immune response.
4. „Nagalase-Test“: What is this?

There are test methods by which the activity of Nagalase can be determined in serum. The Nagalase is isolated from a serum sample and the enzyme activity is measured.

This method is referred to as „Nagalase-Test“.

Increased Nagalase levels in the blood have been reported in many diseases, but particularly in tumor diseases.

Increased Nagalase values are used to decide on a GcMAF therapy ("therapy indication").

A deprecation of Nagalase values is an indication of a successful therapy, especially in the therapy with Gc-MAF, counted ("Therapy monitoring").

5. I want to carried out a Nagalase test? How does it work?

For the test, a blood test (serum) is taken and returned.

A requestform for the actual bloodtest can be found in our clinics

6. What is the cost of the test and how the test will be billed?

Billing is for private patients according to the official rate of doctors (medical fee schedule).

Unfortunately, this test is currently not covered by statutory health insurance and must be paid, if necessary by the patient himself. The price for self-pay amounts to € 89, - €
7. Agglomerated GcMAF for treating diseases

After the macrophage activating effect of GcMAF had been described, methods have been developed to synthesize Gc-MAF and applicate as an immune-stimulating substance.

Here the therapeutic approach benefits from the fact that agglomerated Gc-MAF from the serum Nagalase can not be degraded.

Attempts have therefore developed treatment methods in which GcMAF is artificially prepared in the laboratory (in vitro), and then the patient is administered.

8. What other readings can be relevant at a GcMAF therapy?

Vitamin D-level and calcium serum

The best effect of GcMAF therapy depends on an optimal vitamin D level. Recommended values are between 30 and 70 ug / L.

It is recommended to determine the vitamin D value in the serum and if necessary to supplement treatment with the administration of vitamin D before starting the GcMAF therapy.

Genetic Gc-Proteins versions

The Gc protein genetic versions are described to what extent the playrole in optimizing a Gc-MAF therapy is still the subject of scientific discussion.
9. Literatur

Yamamoto et al.
Immunotherapy for prostate cancer with Gc-protein-derived macrophage-activating factor, gcMAF
Transl Oncol (2008a) 1: 65-72

Thyer et al.
A novel role for a major component of the vitamin D axis: vitamin D binding protein-derived macrophage activating factor induces human breast cancer cell apoptosis through stimulation of macrophages
Nutrients (2013) 5: 32577-2589

Korbelik et al.
The value of serum alpha-N-acetylgalactosaminidase measurement for the assessment of tumor response to radio- and photodynamic therapy
Br J Cancer (1998) 77(6): 1009-1014

Wang et al.
Schindler Disease: the molecular lesion in the alpha-N-acetylgalactosaminidase gene that causes an infantile neuroaxonal dystrophy

Reddi et al.
Serum alpha-N-acetylgalactosaminidase is associated with diagnosis/prognosis of patients with squamous cell carcinoma of the uterine cervix

Kisker et al.
Vitamin D binding protein-macrophage activating factor (DBP-maf) inhibits angiogenesis and tumor growth in mice

Saharuddin et al.
Tumor cell alpha-N-acetylgalactosaminidase activity and its involvement in GcMAF-related macrophage activation
Thyer et al.
Therapeutic effects of highly purified de-glycosylated GcMAF in the immunotherapy of patients with chronic diseases

Gregory et al.
Vitamin D binding protein-macrophage activating factor directly inhibits proliferation, migration, and uPAR expression of prostate cancer cells

Fabris et al.
Role of angiotensin-converting enzyme and vitamin D receptor gene polymorphisms in cancer anorexia-cachexia syndrome

Uto et al.
GcMAF: our next-generation immunotherapy

Nagasawa et al.
Association of the macrophage activating factor (MAF) precursor activity with polymorphism in vitamin D-binding protein

Kuchiike et al.
Degalactosylated/desialylated human serum containing GcMAF induced macrophage phagocytic activity and in vivo antitumor activity

Inui et al.
Clinical experience of integrative cancer immunotherapy with GcMAF
Yamamoto et al.
Prognostic utility of serum alpha-N-acetylgalactosaminidase and
immunosuppression resulted from deglycosylation of serum Gc protein in oral
cancer patients

10. Explanation of keywords

Bsm1
BSM1 denotes a genetic variant of the vitamin D receptor. For this variant, three forms are known: BB, Bb, bb.

DBP
Gc-Protein
A chemically defined sugar molecule.

Galaktosamin
http://en.wikipedia.org/wiki/N-Acetylgalaktosamine

Galaktose
A chemically defined sugar molecule.
http://en.wikipedia.org/wiki/Galactose

Galaktosidase
An enzyme that cleaves galactose.

Fok1
Fok1 refers to a genetic variant of the vitamin D receptor. For this variant, three forms are known: FF, Ff, ff.

Gc-MAF
Also often abbreviated as "GcMAF" is a Macrophage Activating Factor formed by removal of the sugar chain of Gc protein. The trisaccharide side chain of Gc protein is galactose and sialic acid, then N-acetylgalactosamine remains.

Gc-Protein
Gc protein is a serum protein which has the ability to bind vitamin D. For this reason it is also called vitamin D-binding protein (DBP). Gc protein possesses a three-sugar chain model these three sugars are a galactose, a sialic acid and a N-actely-galactosamine.
http://en.wikipedia.org/wiki/Vitamin_D-binding_protein
Immune suppression refers to the suppression of an immune response by different mechanisms, such as diseases, treatment with "immunosuppressive" drugs or certain environmental influences. The "Nagalase" formed by tumor cells will also be awarded an immunosuppressive effect.

**MAF**
Abbreviation for macrophage activating factor.
There are several factors who can activate macrophages; Gc-MAF is one of them.

**Makrophagen**
Macrophages (freely translated from the Greek: "Big Eater") are killing cells of the immune system and play a role in a defense reactions of the body, especially in immune response. [http://en.wikipedia.org/wiki/Macrophage](http://en.wikipedia.org/wiki/Macrophage)

**Nagalase**
The so-called "Nagalase" is an endogenous enzyme that is needed in sugar metabolism. The scientifically correct name is "N-acetyl-Galaktosaminidase". Nagalase can split certain sugar molecules, namely the so-called N-acetyl-galactosamine will split off from large molecules.

**Sialidase**
An enzyme that cleaves sialic acid.

**Sialin-acid**
11. Instructions for collecting samples for the Nagalase-test

The Nagalase test is performed on a serum sample, such as in the original work of Yamamoto et al. described under "Publications".

For the examination at least 1 ml serum is required.

By veins-puncture blood is removed from the patient's whole blood. From the whole blood obtained serum by coagulation and subsequent centrifugation is used for examination. The patient should be sober.