GcMAF Background Information

GcMAF (Gc Protein derived Macrophage Activating Factor) occurs naturally in our bodies and activates macrophages to destroy cancerous cells and foreign invaders such as bacteria and viruses. Serious illnesses like cancer, HIV and viral hepatitis destroy GcMAF and so neutralizes our immune system to defend itself. This allows the disease to progress uncontrolled.

We use a small sample of serum from **healthy human people** to produce large amounts of new second generation GcMAF in our specialized sterile laboratory called a Cell Processing Center (CPC). This highly active **Second Generation Gc-MAF** is injected intramuscularly (IM) or subcutaneously (SC) into the patient usually twice weekly, and in some cases 3 times weekly. Over a matter of weeks and months the immune system becomes strengthened through the activation of macrophages, and begins to eradicate cancer cells, viruses and bacteria. In addition to GcMAF injections, another form of GcMAF manufactured from high quality colostrum can be administered orally in the gut and sublingually in the mouth to activate macrophages in the lymphoid tissue.

General goals of GcMAF therapy are to:

- Improve well-being and quality of life (QOL)
- Return the patient to good health so that they are able to participate in regular lifestyle activities
- Achieve long term survival
- Enhance the effect of other therapies
- Repair the immune system
- Increase the number of monocytes (macrophages) and activate them to destroy cancer cells, viruses, bacteria and other pathogens in the body
- Increase the rate of maturation of dendritic cells (DCs)

GcMAF therapy overview

- **One course of High Dose GcMAF is usually 48 doses for 6 months (2 times weekly administration).**
- For advanced disease, High Dose GcMAF may be administered **3 times weekly**.
- Additional courses may be required depending on stage of disease and other factors specific to each patient.
- Treatment should be continued at the high dose as long as necessary while disease is present to destroy cancer cells, viruses, bacteria and other pathogens in the body.
- For serious diseases we recommend a combination of GcMAF injection and daily **Colostrum MAF** by oral and sublingual administration for the most effective treatment.
- Longer term maintenance doses of High Dose GcMAF may be important to reduce recurrence after all evidence of disease eradication.
- **Oral Colostrum MAF** may be a convenient long term option to maintain health.

Other important points

- Activating macrophages with High Dose GcMAF is an important part of any treatment program which can be used alone or in combination with most other therapies.
- GcMAF works especially well in synergy with targeted therapies which don't harm the immune system. Examples of targeted therapies include hormone therapies, monoclonal antibody drugs, small-molecule drugs, signal transduction inhibitors (HER2 inhibitors, BRAF inhibitors, EGFR inhibitors), angiogenesis inhibitors, immunotherapy drugs (such as drugs that target CTLA-4 protein).
- Second Generation GcMAF has the advantage of having no side effects so treatment should be continued as long as necessary while disease is present. This is a significant advantage over many conventional therapies which have cumulative toxicity that limits their use.
- GcMAF never stops working and will continue to activate macrophages while treatment is continued, either by GcMAF injections and/or oral administration of Colostrum GcMAF.
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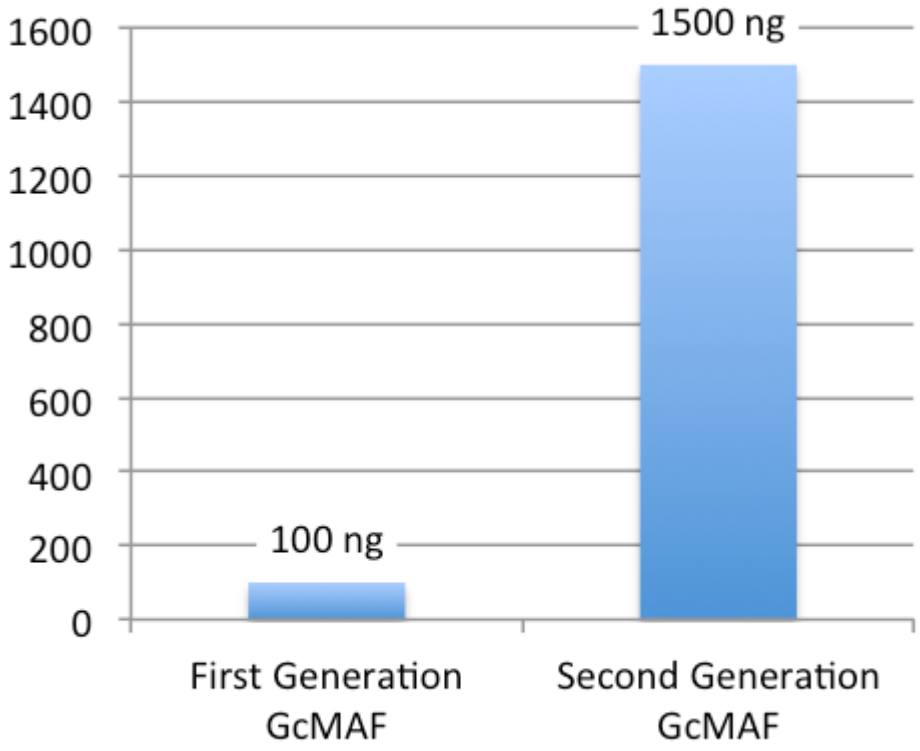
Our principle of treatment is, first do no harm.

Second generation GcMAF

Second generation Gc-MAF is produced using a new Patented process which was developed here in Japan by Saisei Mirai in collaboration with researchers from the University of Tokushima who have been studying GcMAF for over 20 years. Our GcMAF is made in our sterile cell processing facility using this new and improved 2nd generation method which is **10-15 times more concentrated and is more active and stable** than other GcMAF that is currently available. Importantly, this much higher concentration GcMAF has been clinically demonstrated to be largely free of any side effects in the great majority of patients and is much more stable because it is resistant to oxidation. Only low grade fever or eczema have been observed in about 1 out of 100 patients using GcMAF, but these were short-term effects.

First Generation GcMAF vs Saisei Mirai Second Generation GcMAF concentration



- **0.5 ml of High Dose GcMAF is approximately 1500 ng GcMAF**
- Gc-MAF is a natural immunotherapy product. Variation in GcMAF concentration is due to normal variation between serum samples. In the same way that Lymphocytes or Natural Killer cells vary in number between people and at any given time, so will the amount of GcMAF that can be produced from serum.
- Our GcMAF is produced under aseptic conditions in a specialized facility and sterile filtration is used in the production of all product.
- **Our new 2nd generation Gc-MAF has been safely used in hundreds of patients in our clinics in Japan, since April 2011.** Treatment in our clinics has been by Intramuscular (IM), Subcutaneous (SC), and Intratumoral (IT) injection.

Our specialized sterile Cell Processing Center (CPC) and team of highly skilled laboratory staff


Clean clothes


Security doors


Microscope work

Carbon dioxide incubator

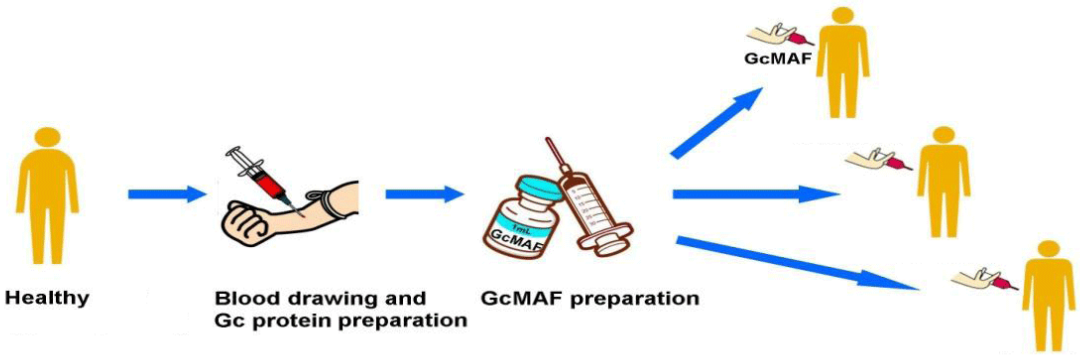
Centrifuge

Sterile cabinet

How is our second generation GcMAF made?

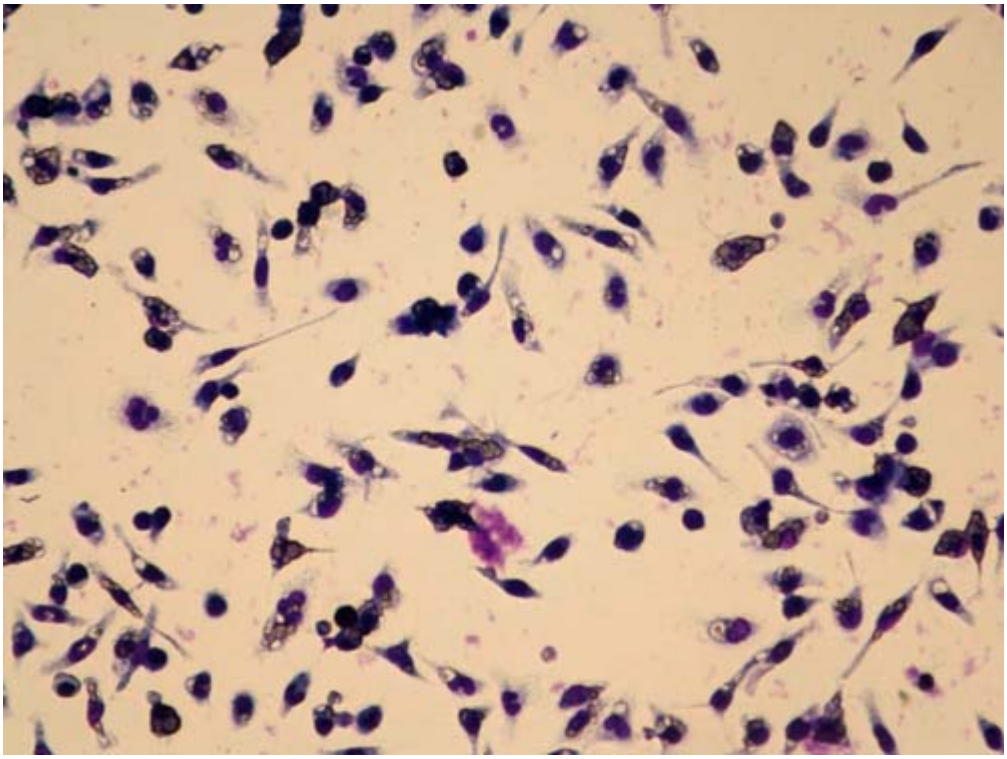
Second generation GcMAF is manufactured in our own sterile Saisei Mirai Cell Processing Center (CPC) from serum of healthy people which is carefully screened and the final product sterile filtered to ensure safety. See ***Tests of our GcMAF*** below for more details.

Diagram showing steps of our GcMAF preparation process



How is our second generation GcMAF tested for activity?

Our second generation GcMAF is tested for macrophage phagocytic activity using mouse macrophages and sheep red blood cells at the University of Tokushima. The red blood cells are opsonized which marks them for ingestion and destruction by activated macrophages, seen as purple areas in the clear cells. From this we calculate the Phagocytosis (ingestion) Index (PI).

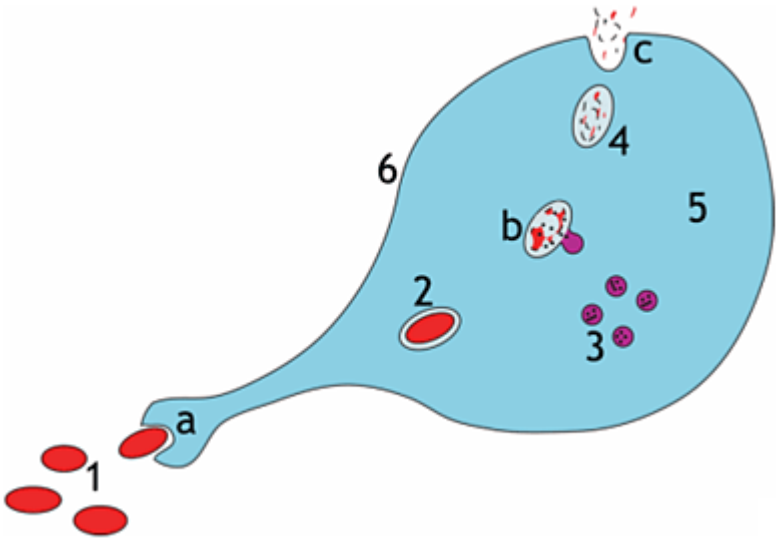


Macrophage phagocytic activity of second generation GcMAF. The purple color are macrophages activated by GcMAF phagocytizing (ingesting) opsonized red blood cells which are clear in color. (Photo courtesy, University of Tokushima)

What are macrophages?

Macrophages (Greek: big eaters) are cells produced by the differentiation of monocytes, a type of white blood cell, in tissues. Macrophages function in both non-specific defense (innate immunity) as well as help initiate specific defense mechanisms (adaptive immunity) of vertebrate animals. Their role is to phagocytose (engulf and then digest) cellular debris and pathogens, either as stationary or as mobile cells. They also stimulate lymphocytes and other immune cells to respond to pathogens. They are specialized phagocytic cells that attack foreign substances, infectious microbes and cancer cells through destruction and ingestion.

Steps of a macrophage ingesting a pathogen



a. Ingestion through phagocytosis, a phagosome is formed
b. The fusion of lysosomes with the phagosome creates a phagolysosome; the pathogen is broken down by enzymes
c. Waste material is expelled or assimilated (the latter not pictured)

Parts: 1. Pathogens, **2.** Phagosome, **3.** Lysosomes, **4.** Waste material, **5.** Cytoplasm, **6.** Cell membrane

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Vitamin D binding protein

Vitamin D binding protein is also known as Gc Protein. It is produced in our body, mainly in the liver, especially when we are exposed to the sun. This binding protein binds to 25 (OH) vitamin D in our body for transport and storage. There are different forms of Vitamin D BP, the most dominant being non-glycosylated 656 Da proteins. Vitamin DBP is the most important scavenger of extracellular G-actin, important in liver disease. Vitamin DBP activates macrophages through GaINAc- modified Gc Protein. Vitamin DBP has virtually no impact on the distribution, uptake, activation profile, or biological potency of the hormone vitamin D in our body, so too much is unlikely to be a problem. Vitamin D binding protein is the basic macrophage activating factor in our body.

Factors that influence Vitamin DBP levels

Liver disease decreases levels of Vitamin DBP (Gc Protein). Chronic liver disease will decrease levels less than acute liver failure. Trauma and surgery will decrease Vitamin DBP. Septic infections will consume Vitamin DBP faster than production can be increased.

Normal Vitamin DBP (Gc Protein) levels in serum are 350-500 mg/l. Levels of Gc Protein less than 80 mg/l yield positive and negative mortality predictive values of 85% and 43% respectively. Survivors had levels greater than 102 mg/l.

Macrophage activation factor (MAF)

What is macrophage activation factor?

Macrophage activation factor (MAF) are glycoproteins that increase macrophage activity and transform them into natural killer (NK) cells. Vitamin DBP (Gc Protein) is the primary MAF. The glycosylated Gc Protein is the best MAF.

NaGaLase (Alpha-N-acetylgalactosaminidase)

NaGaLase is an enzyme produced in trace amounts in normal healthy liver cells.

What harm can NaGaLase do?

Alpha-N-acetylgalactosaminidase (alpha-NaGaLase) is produced in large amounts by cancer cells. alpha-NaGaLase deglycosylates the trisaccharide of Gc Protein at step prior to the final isoform of MAF. alpha-NaGaLase from tumors induces an immunosuppressive state that allows the cancer to spread and eventually results in death by infection.

What good can NaGaLase do?

Endo-alpha-N-acetylgalactosaminidase is produced in small amounts by probiotic bifodobacterium. NaGaLase produced in the intestine by our probiotics serves a role in breaking down mucin glycoproteins in our food.

Where else is NaGaLase found?

NaGaLase is also produced by bacteria, virus infected cells and fungi.

Normal serum levels of NaGaLase

Normal levels of NaGaLase range between 0.38 to 0.63 nmole/min/mg protein. People with cancer have NaGaLase above 2.32 nmole/min/mg protein.

Radiation therapy decreases the number of cancerous cells capable of secreting alpha-NaGaLase. Radiation also increases Gc Protein activation to principle MAF. Radiotherapy and photodynamic therapy decreases NaGaLase activity.

Target diseases for GcMAF therapy

- Gc-MAF macrophage activation therapy is useful in the treatment of many diseases, such as cancer, HIV AIDS, Hepatitis B virus (HBV), Hepatitis C virus (HCV), Herpes Simplex virus (HSV), Tuberculosis, Pneumonia infection, Epstein-Barr virus (EBV), cystitis/urinary tract infection (UTI), Endometriosis, Selective IgA deficiency disorder and influenza virus.

- In healthy individuals the immune system may be able to overcome many kinds of diseases, however people with a compromised immune system will benefit from GcMAF therapy.
- In the great majority of people there are no side-effects with our **2nd generation Gc-MAF therapy,** or side-effects are very minor and extremely rare. Low grade fever and eczema has been observed in about 1 out of 100 patients using GcMAF, but these were short-term effects.
- Treatment in our clinics has been by Intramuscular (IM), Subcutaneous (SC), and Intratumoral (IT) injection.

In combination with other treatments

GcMAF can be safely used with a wide variety of other standard treatments and drugs to improve their effect. We refer to this as integrative medicine.

- In combination with anti-cancer drugs and radiation therapy (radiotherapy) is possible. For maximum effect and benefit from GcMAF, administer a few days apart from chemotherapy. **Radiation therapy does not have significant effects on Gc-MAF, so both can be used together at any time. In our clinical experience we have observed significant cancer killing effects from GcMAF combined with palliative radiotherapy in patients who have had significant prior treatment with chemotherapy.** See our Case Reports for more details on this multimodality integrative treatment.
- **Studies show that GcMAF has anti-angiogenic activity in addition to tumor killing activity through the activation of macrophages.**
- GcMAF can be combined with Sonodynamic Therapy (SDT), Photodynamic Therapy (PDT) or both (Sonophotodynamic Therapy, SPDT), Maitake Extract, Coley Vaccine (Coley Fluid), high dose IV Vitamin C, low dose Naltrexone (LDN), Alpha-Lipoic Acid, hyperthermia therapy, immunotherapies and cancer vaccines (such as autologous cancer vaccine).
- **GcMAF should be used in combination with at least 5,000 IU vitamin D3 daily.** Blood levels of vitamin D are often low in many kinds of diseases, such as cancer, HIV AIDS, etc. Normal vitamin D levels are necessary in order for GcMAF to work fully. Ask to have your blood **25 hydroxy-vitamin D** as well as **calcium** levels tested. If blood calcium levels become elevated, the dose of vitamin D3 may need to be reduced to achieve optimal balance.

Things to avoid

Gc-MAF can be safely used with a wide variety of drugs and other treatments however we recommend:

- Minimal use of steroids is desirable because of their immune suppressing effect, however steroids may be safely used with GcMAF if necessary and prescribed by your doctor.
- Radiation therapy is preferred over chemotherapy, if possible.

Treatment

- Treatment is by Intramuscular (IM) or Subcutaneous (SC) injection of GcMAF macrophage activating factor, 1-2 times per week (or as prescribed by the treating medical doctor). See ***Dosing recommendations*** below.
- Treatment in our clinics has also been by Intratumoral (IT) injection, although IM and SC injection is by far the most common means of administration.
- **Good aseptic technique with ethanol is required when using the vials.**

Dosing recommendations for Second Generation GcMAF

- Dosage and frequency of Gc-MAF administration is at the discretion of the treating doctor and/or the patient.
- No upper limit has been established for second generation GcMAF.

Cancer, HIV AIDS, Hepatitis, Tuberculosis:

For cancer patients, HIV AIDS, Hepatitis, Tuberculosis we suggest **1500 ng High Dose GcMAF once or twice per week.**

- **For maximum effect we recommend 0.5 ml twice weekly.**
- **One course of High Dose GcMAF is usually 48 doses for 6 months. Additional courses may be required depending on stage of disease and severity of symptoms.**

Macrophage activation is always necessary for the effective functioning of the immune system. Gc-MAF therapy should continue while there is disease present and for a period after to reduce the chance of recurrence.

Chronic Fatigue Syndrome (CFS)/Myalgic Encephalomyelitis (ME):

In Chronic Fatigue Syndrome (CFS) and Myalgic Encephalomyelitis (ME), a lower dosage of 100 ng Low Dose GcMAF once per week is commonly recommended. With Second Generation GcMAF we recommend using High Dose GcMAF for more effective treatment.

- **Recommended dose - 0.25ml High Dose GcMAF, twice weekly by intramuscular or subcutaneous injection. ***

- Some improvements in symptoms should be observed within 2 months.
- Minimum treatment course of 6 months should be expected, but each patient is different and additional courses may be required based on positive progress.
- Patients may need longer term maintenance doses of GcMAF therapy to stay well and symptom free until their immune system is fully recovered enough to cope with challenges.

- If patients are are already using 100 ng Low Dose GcMAF and the effects from the treatment are not pronounced, we recommend switching to Second Generation High Dose GcMAF.
- In our clinics in Japan, all of our patients, regardless of the disease, use second generation High Dose GcMAF.

*** These dosage recommendations apply only to Saisei Mirai Second Generation GcMAF.**

Autism Spectrum Disorders (ASD):

- **Recommended dose - 0.25ml High Dose GcMAF, twice weekly by intramuscular or subcutaneous injection. ***
- Some improvements in symptoms should be observed within 2 months.
- Minimum treatment course of 6 months should be expected, but each individual patient is different and additional courses may be required based on positive progress.
- Patients may need longer term maintenance doses of GcMAF therapy to stay well and symptom free until their immune system is fully developed enough to cope with challenges.
- See our Autism Spectrum Disorders (ASD) page for more details on Autism.

*** These dosage recommendations apply only to Saisei Mirai Second Generation GcMAF.**

GcMAF Therapy

If you wish to get GcMAF therapy, please contact us by email with details of your disease, current treatment and the quantities of GcMAF you require. Below are details about pricing and payment.

High Dose GcMAF 2.5 ml multi-dose vials (1500 ng/0.5 ml):