# What is GcMAF?

*A guide on the natural role of GcMAF in the immune system and its use in immunotherapy*

GcMAFplus

www.gcmafplus.com

# Introduction

GcMAF is a complex protein produced in all healthy humans. It is an essential part of how the immune system attacks and defends against pathogens, bacteria, viruses, toxins, inflammation and other cellular threats. GcMAF activates special white blood cells called macrophages to help identify and eradicate invasive cells. Macrophages are the first line of immune defence. Without activation, their performance is significantly limited, thus potentially proliferating illness.

Unfortunately your body will not always produce enough GcMAF on its own, especially if you are sick or immune-compromised. This is where supplementing GcMAF proteins identical to those produced by your body may help. Doing so you are giving your immune system what it needs to aggressively fight back. This is a very powerful, safe and effective type of immunotherapy which works with your body's natural processes rather than against them.

In this document we aim to provide you with more information surrounding GcMAF so you can make an informed choice if this approach is right for you. Please note that nothing in this document is intended to replace or supersede traditional medicine or advice, nor guarantee any type of health outcome. What this document serves to achieve is a summary of the 100+ scientific and medical research papers written about GcMAF, and its safe widespread use by hundreds of thousands of patients worldwide since the 1990's. We encourage you to view the linked scientific trials in this document and other research materials. If you would like to try GcMAF please visit our website www.gcmafplus.com where we have a range of different home-use products and additional information for your consideration.

## What is GcMAF?

GcMAF stands for Glycoprotein-derived Macrophage Activating Factor. It is a complex protein naturally produced by the sequential deglycosylation of Vitamin D Binding Proteins (VDBP) in Gut Associated Lymphoid Tissue (GALT). This is why GcMAF is also often referred to as VDBP, VDP, VDP-MAF and other similar derivatives. This small molecule plays a very important role in how the broader immune system defends and responds to disease and illness. The Macrophage Activating Factor (MAF) of GcMAF is central to this. By breaking down what GcMAF stands for, we can see how it all works:


The precursor to GcMAF is the Gc protein. Also known as Vitamin D Binding Protein (VDBP), Gc binds to vitamin D for transport and storage throughout the body. It is produced mostly in the liver and is naturally abundant in the blood, as well as other organs and bodily fluids. When Gc proteins are modified by N-Acetylgalactosamine (amino sugars) in the small intestine tissue (GALT), GcMAF is formed.


The 'MAF' part of GcMAF refers to the modified Gc protein's ability to activate special immune cells called macrophages. These are the immune system's first line of defence and central to regulating illness, disease and infection. MAFs are lymphokines or other receptor based signals that prime macrophages towards cytotoxicity to tumors, cytokine secretion, or clearance of pathogens. GcMAF is a very important MAF and responsible for the activation of a wide range of macrophages throughout the body.

## What functions is GcMAF known to perform?

The GcMAF protein has been shown through over 100 research studies to be capable of numerous beneficial important cellular functions. Below is a summary of 3rd party research conducted on this. We encourage you to visit the links and read the full study data for more information and specific details.

### Macrophage Activating Factor (MAF) for enhanced phagocytosis

GcMAF is most well known for its Macrophage Activating Factor (MAF) capability. Numerous studies have demonstrated GcMAF-activated macrophages displayed significantly enhanced phagocytosic activity (1), particularly towards tumors (2), cancers (3) and infections (4).

### Inhibits angiogenesis

Angiogenesis is the formation of new blood vessels. With respect to cancer/tumor cells, they need this to form a new independent blood supply in order to grow. Multiple studies found GcMAF to have specific antiangiogenic effects, independent from its MAF abilities. (5) (6)

### Promotes cell apoptosis

Apoptosis is the process of programmatic cell death. One study found GcMAF-activated macrophages were able to induce cell apoptosis on human breast cancer cells prior to phagocytosis (7) Another study found that GcMAF functioned positively by stimulating apoptosis on macrophages at the site of inflammation once they were no longer needed. (8)

### Decreases metastatic potential

GcMAF was demonstrated capable of inhibiting metastasis (spread of cancer cells) via studies on breast (9), colorectal (10), carcinoma (11) and other cancer types (12). This was found to be independent of MAF response.

### Increases mitochondrial energy

Mitchondria are the energy factory for your cells and body. One study on ME/CFS found GcMAF significantly increased neuronal cell viability and metabolism through increased mitochondrial enzyme activity (13).

### Normalizes endocannabinoid gene dysregulation

One study found that *"GcMAF treatment was able to normalize the observed differences in dysregulated gene expression of the endocannabinoid system of the autism group. GcMAF also down-regulated the over-activation of BMDMs from autistic children. "* (14) More research is needed in this area, but it is hypothesized that immune system dysregulation etiology in Autism, and specifically the role of cannabinoid receptor type 2 (CB2R) expressed on macrophages and microglial cells within this, may explain some of the findings with GcMAF.

### New neuron formation (neurogenesis)

One study found GcMAF helped promote neurogenesis (formation of new brain cells) displaying high levels of synthetic signal activity, and this could be used for further studies to *"treat neurodegenerative disorders from Parkinson's and Alzheimer's diseases to Myalgic Encephalomyelitis and ASD"*. (15) Another

study discovered GcMAF had a neuroprotective effect on neurotoxicity induced by the chemotherapy drug oxaliplatin (16) More research is needed in this area, but these studies hypothesise a link between the known roles of Vit D and vitD receptor (VDR) in adult neurogenesis (17) and the influence of GcMAF within this process.

## GcMAF as a therapeutic approach

It is important to distinguish that GcMAF is primarily the name for the naturally occurring protein, but it is also commonly used to describe the use of this protein as a replacement therapy. Unlike other treatment methods, GcMAF is not about introducing a foreign substance to the body. It is about giving the body back what it should be producing naturally in higher amounts to re-facilitate a healthy immune system. This is why it is categorised as an immunotherapy - a broader term for therapies designed to boost (or sometimes suppress) natural immune response. This is done by administering external GcMAF into the body to restore natural function and help fight back. The immune system is incredibly powerful, however sometimes it needs a helping hand to do the job it was designed to do. This is where supplementing additional GcMAF becomes a replacement therapy for those who can not make enough on their own to respond to a current health issue. It is also used in lower strength doses as a general immune booster and preventative approach for those who are not sick.

## Who can benefit from GcMAF therapy?

Due to its multifaceted roles boosting overall immune response, GcMAF is used for a very broad range of conditions. When looking at whether GcMAF is something you may benefit from, it is important to firstly assess whether the immune system is capable of regulating the issue you are experiencing. Most of the time this is clear, however due to the complex nature of the relationship between the immune system and other parts of the body, this is often not as clear, particularly with neurological-related conditions. Furthermore the presence of toxins, bacteria and other irregular cells may be manifesting symptoms in other parts of the body not necessarily associated with immune response, such as CFS, lyme or fibromyalgia.

Much of the research on GcMAF has been focused around various cancers and tumors. This is the main reason most people decide to use GcMAF. It is also extensively used to stimulate macrophage response against the invasive cells deriving from numerous pathogens and bacterial infections. As more is being discovered about the etiology of immune dysregulation in neurodegenerative and spectrum disorders, GcMAF is also increasingly being used to boost immune response in these areas, generally adjunct to

other therapies. The studies on GcMAF and osteoclasts (18) (19) as well as its general MAF properties, see it often used for specific bone and inflammatory disease such as osteoporosis and rheumatoid arthritis. Finally, even healthy people use GcMAF for general immune boosting and prevention purposes. For this, only low strength doses are required, but with the advent of colostrum-derived GcMAF such as used in our products, there are numerous lower concentration options now available.

## GcMAF scientific research papers

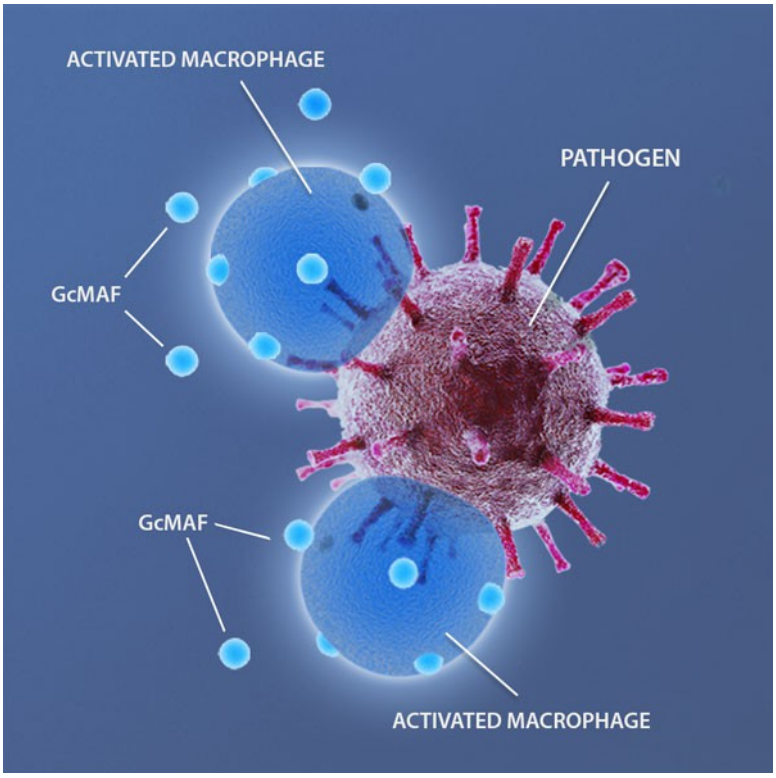
There have been hundreds of scientific research papers conducted by 150+ doctors and scientists regarding GcMAF. These have not only demonstrated it as a safe therapy, but also very effective for a very wide range of health conditions. Conducting a search for 'GcMAF' at the PubMed National Library of Medicine website, brings up 87 individual studies alone (view here). These cover the use of GcMAF on many types of cancers, tumors, viruses, ASD, auto-immune disorders, infections, MS, CFS, neuroimmune disorders, inflammation issues, lupus, osteoclast-related disease (rheumatoid arthritis) and others. There have also been numerous other studies published since the late 1980's in various printed scientific journals, academic institutions and privately from doctors, scientists and researchers. We encourage you to read these to make an informed decision if GcMAF is an approach you would like to take.

## Macrophages, phagocytosis and MAF

Macrophages and the agents which activate them (MAFs), are central to how GcMAF works. Macrophages are a type of white blood cell that attack, eat, and destroy harmful cells through a process known as phagocytosis. They play an incredibly important role in your immune system's response to many types of cellular invaders such as viruses, pathogens, toxins, bacteria and cancers/tumors. Macrophages reach their target when they receive a call for help. This call for help usually comes in the form of chemical signaling from entities such as Helper T Cells. When the macrophages receive those signals, they travel to the area they came from and begin their cleanup work, performing phagocytosis on the unwanted cells. The name macrophage comes from the Greek word meaning *'big eaters'*. This is quite literally what they do on a cellular level.

There are many types of macrophages responsible for regulating cells in different parts of the body. Many of these reside in the blood and stem from a large white blood cell called a monocyte. Both monocytes and macrophages have the ability to be 'activated'. Activated macrophages undergo many changes and are larger, have increased metabolism, increased levels of lysosomal proteins, and a greater ability to phagocytosis and kill microbes. GcMAF is one such 'Macrophage Activating Factor' and very important for

activating many types of macrophages throughout the body.



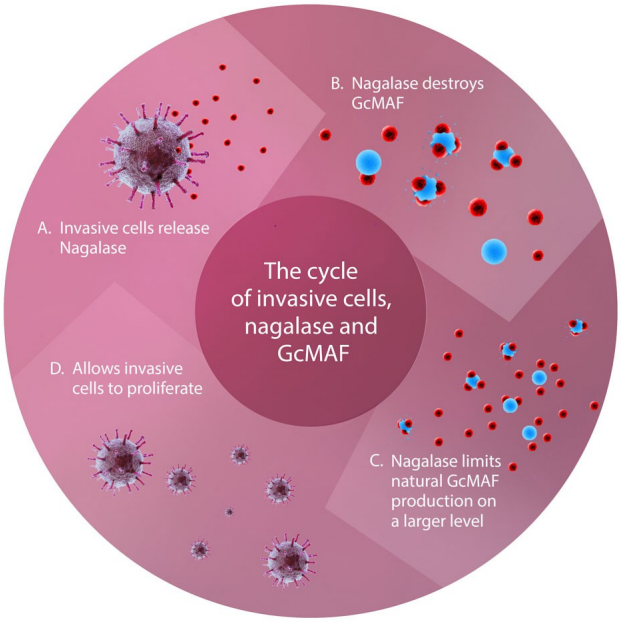

Additionally, macrophages also help your immune system adapt so that it can tackle new cellular threats as they emerge at a later date. After they're done eating a pathogen, they produce something called an antigen. They then take this antigen to a relevant helper T cell, work it into the cell membrane, and create something called an MHC Class II molecule. Eventually, this results in the production of antibodies against the pathogen that started the process. If the same infection makes itself known again, the macrophage's work has made it easier for the body to fight it. The body will know what a processed version of the infection's antigen looks like, so the immune system remains on high alert for unprocessed versions. When unprocessed versions arise, they are recognized quickly, and the immune system tackles it more effectively. As a result, you're less likely to develop the same symptoms that come with an initial infection.

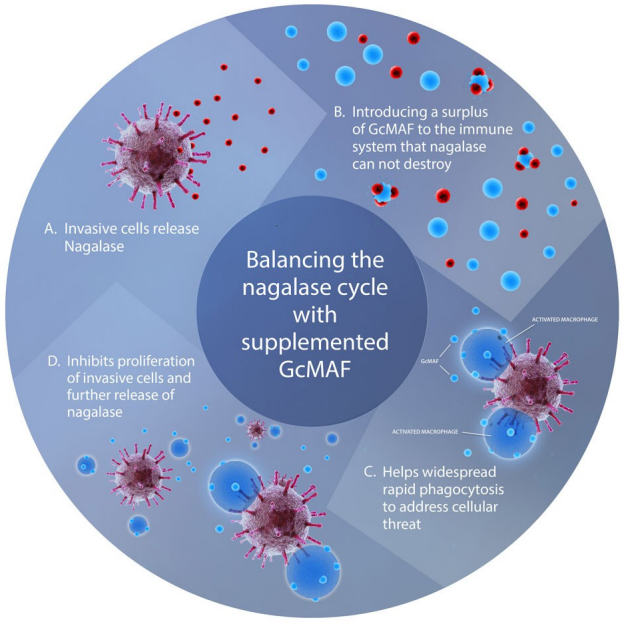
## Relationship between nagalase and GcMAF

GcMAF is intrinsically linked to an enzyme known as nagalase (α-N-acetylgalactosaminidase). If you have already done some research around the GcMAF space it is likely you have come across this before. The nagalase enzyme inhibits Gc proteins (Vit D biding proteins) being converted into GcMAF capable ones. This severely compromises the immune system's ability to defend against cellular threats due to significantly decreased macrophage activity. Elevated nagalase levels are associated with numerous

systemic conditions, cancers, tumors, immune disorders and even ASD. The presence of high nagalase is a good indicator that something is wrong, and that the body is unable to produce enough of its own GcMAF.

As nagalase-producing conditions advance, more nagalase is released, which then further reduces the production of new GcMAF and overall macrophage activity. This creates a cyclical effect, proliferating the effects of the illness as the threat grows and the immune system becomes less capable of regulating it. The only way to override this cycle is to supplement external GcMAF to create a surplus of what is available to the immune system verse what nagalase is destroying. The diagram below illustrates this.




GcMAF is not intended to have to be used forever. The goal is to supplement sufficient levels, generally for between 3-12 months, to help re-balance the cycle to a stage where the threat is addressed and the body can produce enough GcMAF on its own without the presence of nagalase. Many patients who use GcMAF will do a blood test for nagalase levels before, during and after treatment. This is not something we can recommend a particular place to test with, however there are numerous options in a lot of countries and online which you can independently Google to find out more.

## Using GcMAF alongside other treatment methods

The way GcMAF naturally operates within the immune system means it is effective and perfectly safe to use adjunct to almost all other traditional and non-traditional treatment methods. It works particularly with targeted therapies which don't harm the immune system. Patients taking GcMAF will often use it alongside other conventional treatments such as chemo, radiation, monoclonal antibodies, angiogenesis

inhibitors, hormone therapies etc. We also have many customers who use it with other alternative medicines such as C60, CBD oil, herbal supplements and a whole host of other non-traditional methods. GcMAF will work independently of these, often helping support the immune system to better deal with any negative effects from other therapies.

The only exceptions to this, due to decreasing the efficacy of GcMAF are:

**Any type of immunosuppressant drug:** These are drugs which suppress the immune system instead of boosting it like GcMAF does. Using together will decrease the efficacy of both and lead to possible complications, especially if treating a condition related to an overactive immune system.

**Most opioid-based pain medications:** There has been evidence the effects of most opioid-related pain medications may counteract GcMAF. Although not harmful, using GcMAF alongside these will greatly reduce its efficacy. The exception to this is buprenorphine which does not have the same type of interaction with GcMAF and may be an option.

**Minimize the use of steroid medications:** Due to their immune suppressing effects, if you are on high strength doses of a steroid medication, this may decrease the efficacy of GcMAF. Whilst it is safe to use both together, it is still worth noting the effectiveness will be reduced.

** Please do not cease taking these medications just because you are thinking about using GcMAF without first consulting your doctor or physician.*

We often get asked if it is ok to use other transdermal/absorption enhancers such as DSMO and hyularon with GcMAFplus products. Due to the enhanced transdermal formula in our creams and ease of sublingual absorption via our sprays, there is no need to use any other enhancers for this.

## What else to take to support GcMAF

To specifically support supplemented GcMAF, there are a few important things to do to ensure you receive maximum benefit. Whilst there are thousands of other supplements, therapies, medicines, treatments etc. to help different health issues, below are highly recommended when it comes to specifically maximizing the effects of the GcMAF.

a) **Vitamin D.** Make sure you are receiving at least 5000IU vitamin D a day. This can be obtained from supplements, foods or better still, getting some sun each day. This is very important because vitamin D is needed to transport and make new GcMAF. Ensuring the body has sufficient levels to do this will help

support the GcMAF you are supplementing and promote production of new GcMAF.

b) **Vitamin K2.** K2 specifically supports vitamin D, particularly to help minimize potential adverse effects if you are taking very high levels of it. The recommended levels of K2 per day are 90 mcg for women and 120 mcg for men, and can be obtained by supplements or foods rich in K2 like green leafy vegetables.

c) **Sleep, diet, exercise & hydration.** It goes without saying that these are all fundamental for good health, particularly for the immune system. Anything you can do to help your immune system and general health will also increase the efficacy of GcMAF.

## Side-effects & safety

Through many scientific studies and 30+ years use by hundreds of thousands of people, GcMAF has been shown to be very safe and without serious side-effects. When considering safety, it is important to remember GcMAF is naturally produced in the body. We are simply supplementing what the body should be producing naturally. It is not like other medicines which are foreign to the body and pose additional risks when introduced. However in rare cases, some patients do report initial minor detox-related side effects, normally from higher strength doses. These symptoms generally manifest as a runny nose, fatigue, nausea and lethargy - similar to a mild cold. This is the result of heightened immune detox activity resulting from the sudden increase in macrophage activation. Generally such symptoms will only last a few days at the start of treatment and there is no need to stop. However if they present discomfort, you may wish to discontinue use for a few days to let them reside and then continue normal use again.

GcMAF has also been demonstrated to be perfectly safe for children too. You may wish to start them on lower doses to minimize the potential for the aforementioned mild detox-related symptoms, although this is not necessary. You can not overdose on GcMAF either.  The body will simply use what it needs and put aside the rest. However, this doesn't mean you should use more than the recommended dosages. Doing so may increase the risk of unwanted detox-related symptoms, and it is very expensive, so using too much is superfluous and a waste of money.

## A brief history on GcMAF and how it was made

The GcMAF protein and its role in the body was first identified in the late 1980's by Japanese Philadelphia-based biological researcher Dr. Nobuto Yamamoto. In the early days the production techniques used to make GcMAF and what we knew about it in general,  were a lot different to today. Due to being a naturally occurring protein made in the body, GcMAF can not be patented. As more scientists and medical

professionals came onboard, the research surrounding GcMAF and better ways for making it were improved. The evolution of GcMAF is broken down into 3 main 'generations'.

### 1st Generation GcMAF

In the early days, the first GcMAF was isolated from human serum (blood), sterilized and added to other compounds to make a liquid for intravenous injection. This was a very low concentrate (amount of GcMAF per dose) and unstable at room temperature, so it had to be kept refrigerated at all times. There were also obvious safety and ethical concerns due to the way it was made from serum too.

### 2nd Generation GcMAF

The next evolution was also derived from human serum, but was a higher concentrate and more stable formula. Still, using serum and only available as an injectable formula, this presented the same obstacles to widespread use of GcMAF around the world.

### 3rd Generation GcMAF

Advancements in research and laboratory techniques culminated in an alternative to using human serum to produce GcMAF. It was discovered that bovine colostrum could be used as a base and processed through various stages in a lab to produce the same bioidentical GcMAF. This had much higher concentration levels and was more more stable at room temperature than previous generations. It also was much safer and could be used in other administration formats that did not have to be injected.

## Our colostrum-derived GcMAF formula

In 2011 we tasked our scientists to come up with a non-serum GcMAF formula. We identified the immense benefits of GcMAF, but knew it was being held back by numerous safety, legal and ethical concerns. Because the only GcMAF at the time was produced using human serum, this opened up a very real possibility that contaminated or infected samples could be used and subsequently injected into patients. As an alternative, our team of industry leading scientists and researchers discovered raw bovine colostrum contained suitable glycoproteins which could be converted into bioidentical GcMAF. We found that by extracting these, and then processing them through multiple stages, that they could be molecularly altered to form GcMAF. Independent tests demonstrated the formula to be bioidentical to GcMAF made in the human body and capable of the same macrophage activation factor. Furthermore, the formula was a very high concentrate and ultra-stable at even extreme room temperatures without degradation. More importantly it was a much safer way to make GcMAF without the inherent risks using serum. This really

was a big step forward.

It is important to note that colostrum on its own does not contain GcMAF. The glycoproteins naturally found in colostrum have to be extracted and processed in a lab to molecularly alter their structure to form genuine GcMAF. Although colostrum contains many vitamins, nutrients and glycoproteins which are extremely good for you, it does not contain GcMAF, nor is it capable of macrophage activation. Please be aware of this when it comes to the myriad of colostrum powders, yogurts, kits and supplements on the market which claim to contain GcMAF. All GcMAFplus products contain GcMAF proteins derived from a colostrum base, but not colostrum itself. There is a big difference.

## About GcMAFplus products

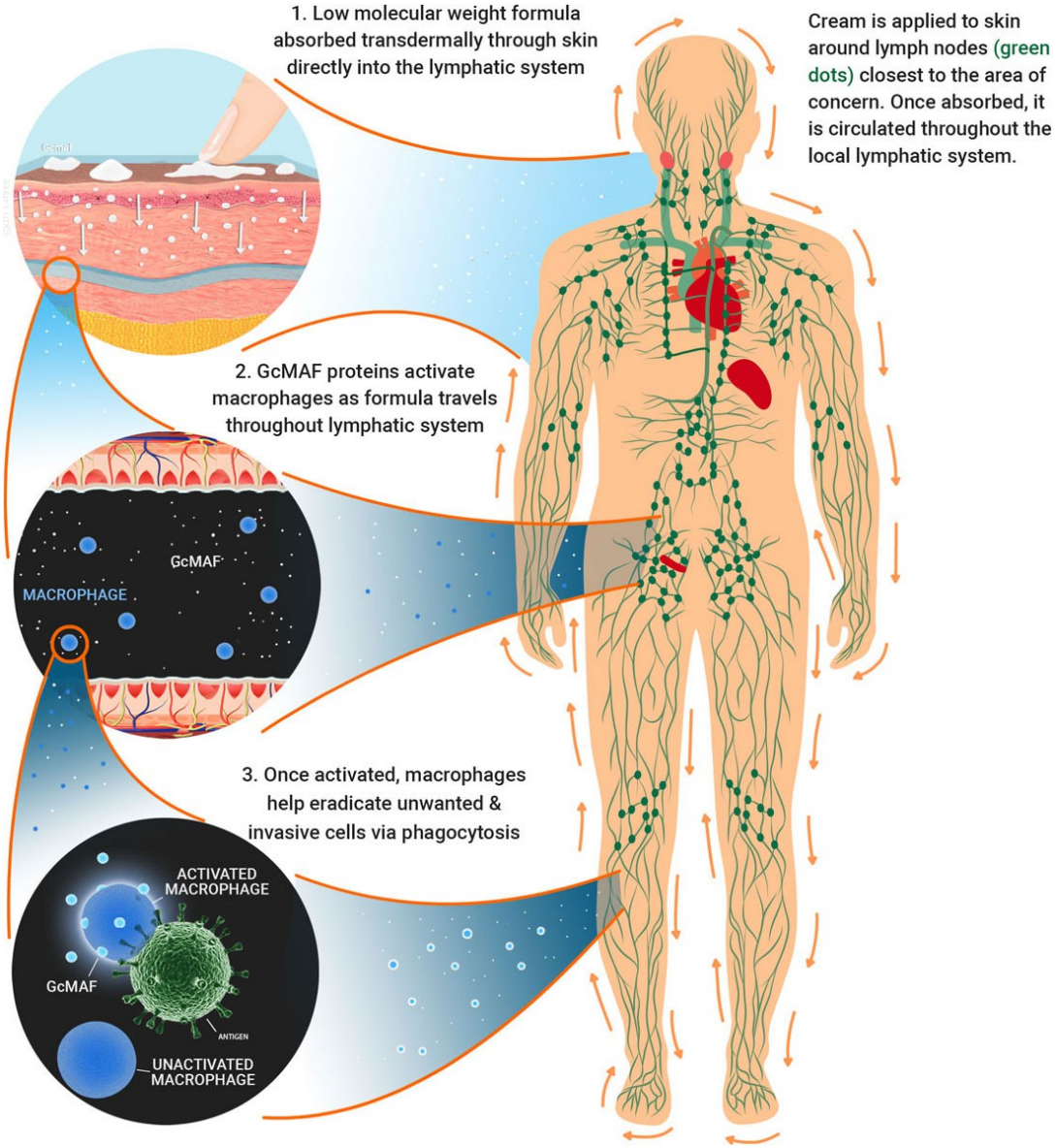

All GcMAFplus products are made in an ISO22716 GMP certified laboratory in Australia. They contain our colostrum-derived GcMAF formula which is added to other supporting ingredients to make up our sublingual spray and transdermal cream ranges. Compared to injectable serum-derived alternatives, our products are a much safer and easier way to administer GcMAF at home.

GcMAFplus products come in a range of different strengths which are suitable for all types of applications. This includes our lower strength products which can be used for general immune maintenance, all the way up to our highest strength products which are suitable for more aggressive conditions. Both the sprays and creams are stable at room temperature, and only need to be refrigerated between use after opening. Doing so they will last for over 12 months before expiry.

All GcMAFplus products are tested and verified to be free from impurities and are biologically active and MAF-capable. This is important because not all GcMAF manufacturers do this, nor do all manufacturers even make their products in a clinical facility.

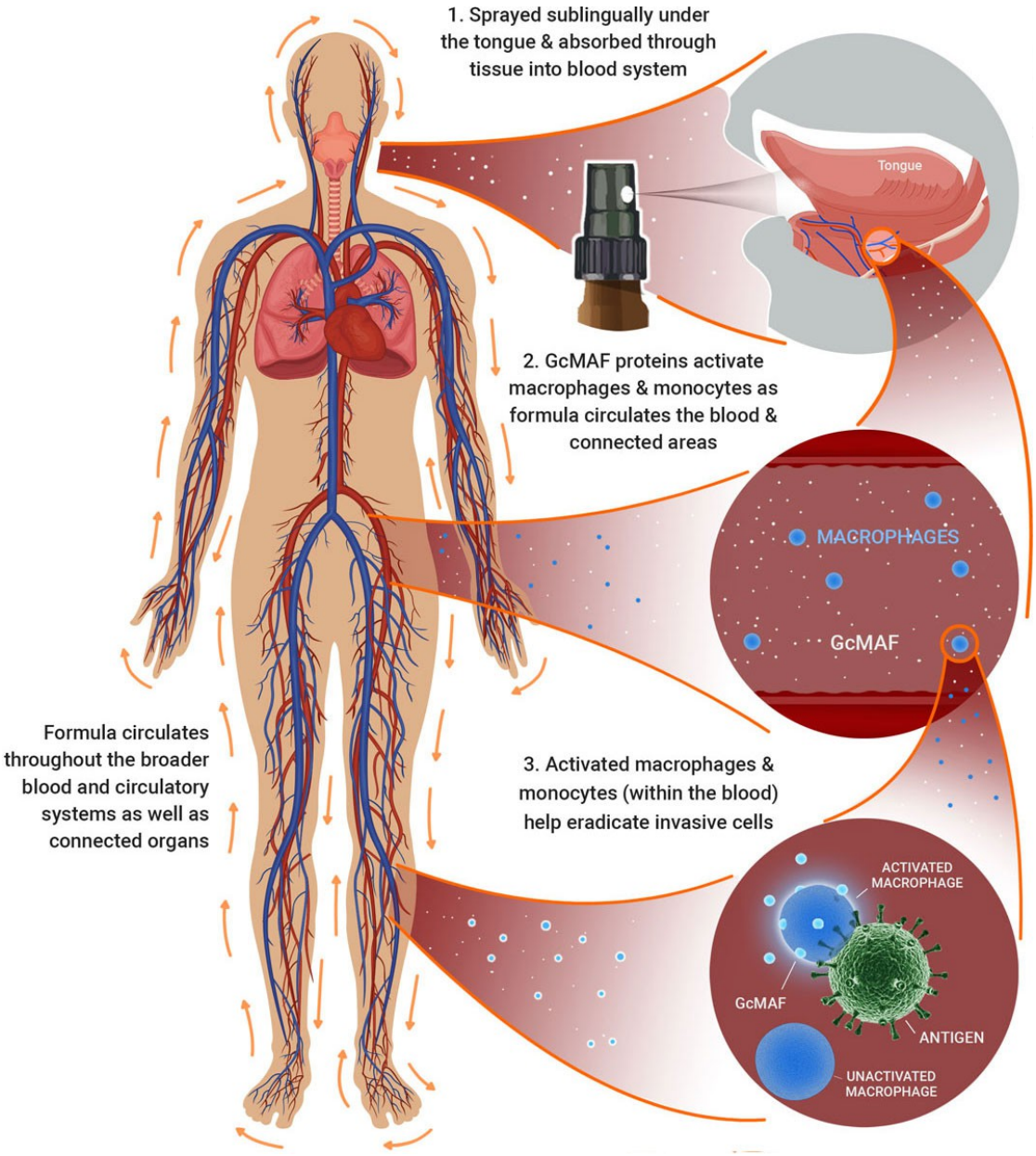
## Transdermal skin creams

All GcMAFplus creams feature a proprietary low-molecular weight transdermal formula that allows it to be readily absorbed through the skin into the lymphatic system. The inclusion of hyularon and other compounds facilitates rapid passing through all 7 protective layers of the epidermis. As well as GcMAF, all our creams contain other ingredients designed to support general wellbeing. Simply apply a small amount of cream to lymph nodes closest to your region of concern, or on the lower neck for non-topical issues. Our creams are a particularly effective way to deliver GcMAF directly to the macrophages which are responsible for regulating skin, lymphatic, tissue, gut, and other topical conditions.  The diagram below demonstrates how they are designed to work.



## Sublingual sprays

Our sprays are the most popular product format. They contain pure GcMAF proteins suspended in a neutral saline solution (salt water). Designed to be taken sublingual, the formula is sprayed under the tongue and absorbed through the thin layer of tissue into the capillaries. This is a very easy and effective way to deliver GcMAF into the blood system. For this reason our sprays are particularly suited for use on viruses, infections, blood-borne problems, neurological disorders, mouth/face issues, and other non-topical conditions such as lyme, CFS, fibromylagia etc. They are also a good option when used once a day for general immune boosting and wellbeing purposes.



## Treatment duration

Our products are generally designed to be used twice daily (morning and evening) for at least 2-3 months. For very aggressive issues you may wish to use them 3 times a day, or for general immune boosting and preventative purposes once per day is sufficient. We recommend an initial minimum period of 2-3 months because it can often take this long for the immune system to begin responding, particularly if you are immune-compromised or display high nagalase levels. For more aggressive issues it is likely you will need to continue for longer, sometimes for up to 12 months or until the issue is fully resolved. Every person and their individual health circumstances are different. This greatly influences the expected time and outcome.

GcMAF is not intended as a therapy you have to keep doing for the rest of your life to maintain results. It is about initially giving the body more of what it needs to deal with the threat at hand, and then support rebuilding the natural capacity of the immune system to deal with future threats. For more serious issues we do not recommend just stopping treatment once the issue is resolved. It is best to continue with the current dose and frequency for a further 1-2 months to ensure this natural capacity is fully restored. After this you may discontinue treatment altogether, or continue with a lower strength dose once per day for ongoing preventative and immune maintenance purposes if you wish.

If you decide to purchase our products, we strongly recommend following the specific instructions as documented on our website here. Doing so will ensure you get the best results.

## A final word

In recent times there have been huge advancements in the broader immunotherapy space. As science learns more about the full extent of what the immune system is capable of, it just makes sense to work with what the body does best naturally. Since the late 1980's GcMAF has been pushing the boundaries of what immunotherapies have been considered capable of achieving. As a naturally occurring protein, GcMAF can not be patented. This has led to GcMAF (like many other alternative medicines) receiving its fair share of scrutiny, particularly from big pharma and the like. It is a shame, because all this does is further hold back more advancement on the hundreds of scientific research papers demonstrating how important this tiny molecule really is. Whilst traditional medicine is certainly very important, there is always room for alternatives and the opportunity of choice when it comes to our health. GcMAF is well documented, very safe and works hand-in-hand as an adjunct to other traditional medicines. With new trials and research papers being published every year, and more and more people turning to its use, the future for GcMAF is indeed looking very bright.

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