GcMAF Science

GcMAF has published science attributing 12 actions in the body and 11 of them support the body in overcoming cancer.

Actions Attributed to GcMAF

1. Activates Macrophages [white blood cells] that eat cancer cells (1).
2. Inhibits cancer cell-induced blood supply to tumors (2).
3. Inhibits cancer cell proliferation and metastatic potential (1).
4. Turns cancer cells back into healthy cells [reverts phenotype] (1).
5. Induces apoptosis [suicide of cancer cells] (1).
6. Suppresses HER2 oncogene expression in human breast cancer (3).
7. Repairs and grows new human neurons [neurogenesis] (4) (5).
8. Increases cellular energy [mitochondrial level] (5).
9. Normalizes endocannabinoid gene expression (6).
10. Induces the synthesis and release of Nitric Oxide by activated macrophages (7).
11. Counteracts the neuronal damage induced by Oxaliplatin [Chemotherapy] (8).
12. Activates osteoclasts, which are responsible for the resorption of bone (9).

Conditions Treated with GcMAF

1. Amyotrophic lateral sclerosis (10)
2. Autism (11) (10)
3. Brain Cancer (12)
4. Breast cancer (12) (10) (13) (14)
5. Bladder cancer (12)
6. Chronic Fatigue Syndrome (10) (15)
7. Colorectal cancer (12) (13)
8. Head/Neck squamous cell cancer (12)
9. HIV / AIDS (16)
10. Larynx cancer (12)
11. Liver cancer (17)
12. Lung cancer - non-small cell (18)
13. Lymphoma follicular (12)
14. Lymphoma (12)
15. Melanoma (13)
16. Multiple Myeloma (10)
17. Multiple Sclerosis (10) (19)
18. Ovarian cancer (12)
19. Pancreatic cancer (20)
20. Prostate cancer (10) (12) (17) (21) (22)
21. Renal carcinoma (13)
22. Serious Infection (15)
23. Squamous cell cancer (12)
24. Thymic cancer (17)
25. Thyroid cancer (13) (23)
26. Tongue squamous cell cancer (12)

The Old Theory of GcMAF

The commonly accepted theory was that the enzyme Nagalase, which is produced by viruses and cancer cells, deactivates GcMAF and suppresses the immune system. So by making GcMAF outside the body and injecting it, we rebuild the immune system and support the body in overcoming cancer and numerous other diseases.

What is GcMAF?

GcMAF is a carrier protein which is produced by the combined action of two enzymes upon Vitamin D-binding protein.

- Vitamin D-binding protein (Gc Protein) is found in plasma (blood) and to a lesser degree in colostrum and milk. So GcMAF can be made from plasma or colostrum.
- The enzymes (sialidase & beta-galactosidase) remove two sugar molecules (galactose & sialic acid) and expose the sugar **GalNAc** (N-Acetylgalactosamine).
- Active GcMAF is identified by looking for the exposed **GalNAc** residue. (electrophoresis Western blot with Helix pomatia agglutinin lectin).

IMPORTANT NOTE: Vitamin D-binding protein (Gc Protein) binds to the Chondroitin Sulfate (**GalNAc** and glucuronic acid) found in plasma and milk, and the process of making GcMAF does not have a purification process to remove any Chondroitin Sulfate, so GcMAF has Chondroitin Sulfate bound to it (24).

GcMAF Theory Inconsistencies

In 2008, it was shown that some humans are genetically unable to produce one single molecule of GcMAF, but despite this fact, the risk of cancer in these individuals is decreased rather than increased (25). And in 2009, it was shown that there was no significant depletion of internal GcMAF in cancer patients and that the internal GcMAF was actually much higher than the amount of GcMAF being administered in the immunotherapy of cancer (26). These observations clearly disprove the theory that cancer patients have decreased production of internal GcMAF, or that decreased levels of GcMAF create immunodeficiency. So how can it be that several research groups and many clinical case reports have reported consistently positive results, utilizing small doses of GcMAF?

In order to solve the inconsistencies, an alternative theory was proposed, that the chondroitin sulfate attached to GcMAF is responsible for the biological action attributed to GcMAF (24).

How Does GcMAF Actually Work?

GcMAF binds to a variety of cells that include the immune system, but a GcMAF cellular receptor has never been found or described in molecular detail (24).

- Gc Protein instead binds in chains (oligomer) with Chondroitin Sulfate on the cell surface (24).
- Chondroitin Sulfate is composed of a chain of alternating sugars (**GalNAc** and glucuronic acid).
- The biological and clinical effects of GcMAF are actually due to the Chondroitin Sulfate (with its **GalNAc** which is the supposed active site of GcMAF) and its association with lipophilic compounds (27) (28).

What is Nagalase?

Nagalase was believed to cause immunodeficiency through deactivating GcMAF, but if this were true, then the small amounts of GcMAF injected, would be immediately degraded by the Nagalase already present. And what about autistic children, with elevated Nagalase, who do not show signs of immunodeficiency. If however, we interpret Nagalase as a marker of chronic inflammation, then we can understand its association with cancer and Autism; and further understand how chrondroitin sulfate, attached to the GcMAF, with its anti-inflammatory properties, has the effect of lowering Nagalase (27).

GcMAF Made Better

In 2015 Rerum® was released. This product was based on animal-sourced Chondroitin Sulfate and its efficacy as a replacement for GcMAF was established with Autism and Cancer clinical case reports (29) (30). Then in 2018 Rerum® was superseded by imuno®.

imuno® is based on vegan, ultra-pure, homogeneous, low-molecular-weight Chondroitin Sulfate, complexed with ultra-pure Phosphatidylcholine and Vitamin D3. imuno® was designed as a substantial improvement over GcMAF and Rerum® and empowered with all their biological effects and more. On one side, we have the known health effects of its components, that are amplified by their assembly in a multi-molecular structure held together by a higher number of non-covalent bonds and on the other side, the physical-chemical features of the emulsion enable imuno® to function in a manner superimposable to that of Freund's adjuvants (31). The key benefits of this new formula are…

- Immune stimulating (32)
- Anti-inflammatory (32)
- Anti-cancer (31)
- Neuroprotective (32)
- Improves Mitochondrial Function
- Endocannabinoid Rebalancer (valid alternative to CBD) (32)
- Enhanced delivery (nano-emulsion)

Recent clinical case studies demonstrate that imuno® is far more potent than GcMAF and Rerum®. According to Bradstreet et al. (11), improvement of symptoms of Autism following GcMAF treatment were observed on average, after 100 +/- 32 days with doses ranging from 4 to 100 mg per week, whereas recently with imuno®, it was observed that with a much lower dose some of the most representative symptoms of autism were completely normalized after eight weeks of treatment and other showed a trend towards normalization (32).

As far as imuno® and cancer is concerned, in a paper that will be soon published, medical doctors demonstrate complete remission of multiple myeloma with 0.2 mL per week of imuno®.

imuno® = GcMAF made better

For the latest science on imuno® visit https://imuno.org

References

1. *Multifaceted immunotherapeutic effects of vitamin D-binding protein-derived macrophage activating factor (GcMAF) on human breast cancer and neuroblastoma cells.* **Ruggiero M, Pacini S, Morucci G, Branca J, Ward E, Smith RJ, Thyer L and Gulisano M.** Milan, Italy : Frontiers. Translational immunology and immune intervention., 2013 Aug 22-27. 15th International Congress of Immunology (ICI). p. https://flore.unifi.it/handle/2158/820904.

2. *Effect of paricalcitol and GcMAF on angiogenesis and human peripheral blood mononuclear cell proliferation and signaling.* **Pacini S, Morucci G, Punzi T, Gulisano M, Ruggiero M, Amato M, Aterini S.** Jul-Aug 2012, Journal of Nephrology, pp. 577-581, https://doi.org/10.5301/jn.5000035.

3. *Glycosylated Oleic Acid/Vitamin D Binding Protein Suppresses HER2 Oncogene Expression In Human Breast Cancer.* **Ruggiero M, Branca J, Noakes D, Gulisano M, Morucci G, Thyler L, and Pacini S.** Porto Carras, Sithonia, Greece : Anticancer Research, 2014 October 6-10. Abstracts of the 9th International Conference of Anticancer Research. pp. 5845-5847, https://flore.unifi.it/handle/2158/918539.

4. *Vitamin D binding protein-derived macrophage activating factor stimulates proliferation and signalling in a human neuronal cell line.* **Morucci G, Fiore M, Magherini S, Branca J, Gulisano M, Thyer L, Ruggiero M, and Pacini S.** 2013, Italian Journal of Anatomy and Embryology, pp. 143. http://dx.doi.org/10.13128/IJAE-14897.

5. *Effects of Gc-Macrophage Activating Factor in Human Neurons; Implications for Treatment of Chronic Fatigue Syndrome.* **Smith R, Thyer L, Ward E, Meacci E, Branca J, Morucci G, Gulisano M, Ruggiero M, Pacini A, Paternostro F, Lorenzo D, Noakes D, and Pacini S.** 6 Nov 2013, American Journal of Immunology, pp. 120-129, https://doi.org/10.3844/ajisp.2013.120.129.

6. *The in vitro GcMAF effects on endocannabinoid system transcriptionomics, receptor formation, and cell activity of autism-derived macrophages.* **Siniscalco D, Bradstreet JJ, Cirillo A, Antonucci N.** 17 April 2014, Journal of Neuroinflammation, pp. 1-11. https://doi.org/10.1186/1742-2094-11-78.

7. *Intra-tumoural nitric oxide release by macrophages activated by Gc-protein-derived Macrophage Activating Factor (GcMAF).* **Ruggiero M, Gulisano M, Branca J, Morucci G, Noakes D, and Pacini S.** Anacona : Italian Journal of Anatomy and Embryology, 2014 Sept 18-20. 68° Congresso della Società Italiana di Anatomia e Istologia. pp. 170. https://doi.org/10.13128/IJAE-16011.

8. *Gc-protein-derived macrophage activating factor counteracts the neuronal damage induced by oxaliplatin.* **Morucci G, Branca JJ, Gulisano M, Ruggiero M, Paternostro F, Pacini A, Di Cesare Mannelli L, Pacini S.** Feb 2015, Anti-cancer drugs, pp. 197-209. https://doi.org/10.13128/IJAE-15974.

9. *Baculovirus-expressed vitamin D-binding protein-macrophage activating factor (DBP-maf) activates osteoclasts and binding of 25-hydroxyvitamin D(3) does not influence this activity.* **Swamy N, Ghosh S, Schneider GB, Ray R.** 2001, Journal of Cellular Biochemistry, pp. 535-546. https://www.ncbi.nlm.nih.gov/pubmed/11255236.

10. *Therapeutic Effects of Highly Purified De-Glycosylated GcMAF in the Immunotherapy of Patients with Chronic Diseases.* **Thyer L, Ward E, Smith R, Branca J, Morucci G, Gulisano M, Noakes D, Pacini S.** 3, 20 Aug 2013, American Journal of Immunology, Vol. 9, pp. 78-84. https://doi.org/10.3844/ajisp.2013.78.84.

11. *Initial Observations of Elevated Alpha-N-Acetylgalactosaminidase Activity Associated with Autism and Observed Reductions from GC Protein—Macrophage Activating Factor Injections.* **Bradstreet J, Vogelaar E, Thyler L.** Dec 2012, Autism Insights, pp. 31-38, http://dx.doi.org/10.4137/AUI.S10485.

12. *GC protein-derived macrophage-activating factor decreases α-N-acetylgalactosaminidase levels in advanced cancer patients.* **Thyer L, Ward E, Smith R, Branca JJ, Morucci G, Gulisano M, Noakes D, Eslinger R, Pacini S.** 29 Jul 2013, OncoImmunology, pp. e25769-1-7. https://doi.org/10.4161/onci.25769.

13. *Clinical Experience of Cancer Immunotherapy integrated with Oleic Acid complexed with de-glycoslated Vitamin D Binding Protein.* **Ward E, Smith R, Branca J, Noakes D, Morucci G, Thyer L.** 8 Mar 2014, American Journal of Immunology, pp. 23-32, https://doi.org/10.3844/ajisp.2014.23.32.

14. *Case Report: A Breast Cancer Patient Treated with GcMAF, Sonodynamic Therapy and Hormone Therapy.* **Inui T, Makita K, Miura H, Matsuda A, Kuchiike D, Kubo K, Mette M, Uto Y, Nishikata T, Hori H, Sakamoto N.** Aug 2014, Anticancer Research, pp. 4589-4593. http://ar.iiarjournals.org/content/34/8/4589.full.

15. *Oral Colostrum Macrophage-activating Factor for Serious Infection and Chronic Fatigue Syndrome: Three Case Reports.* **Inui T, Kubo K, Kuchiike D, Uto Y, Nishikata T, Sakamoto N, Mette M.** Aug 2015, Anticancer Research, pp. 4545-4549, http://ar.iiarjournals.org/content/35/8/4545.long.

16. *Macrophages of the mucosa-associated lymphoid tissue (MALT) as key elements of the immune response to vitamin D binding protein-macrophage activating factor.* **Pacini S, Punzi T, Morucci G, Ruggiero M.** Nov 2011, Italian Journal of Anatomy and Embryology, pp. 136. https://doi.org/10.13128/IJAE-10160.

17. *Clinical experience of integrative cancer immunotherapy with GcMAF.* **Inui T, Kuchiike D, Kubo K, Mette M, Uto Y, Hori H, Sakamoto N.** Jul 2013, Anticancer Research, pp. 2917-2919. http://ar.iiarjournals.org/content/33/7/2917.full.

18. *Case Report: A Non-small Cell Lung Cancer Patient Treated with GcMAF, Sonodynamic Therapy and Tumor Treating Fields.* **Inui T, Amitani H, Kubo K, Kuchiike D, Uto Y, Nishikata T, Mette M.** Jul 2016, Anticancer Research, pp. 3767-3770, http://ar.iiarjournals.org/content/36/7/3767.long.

19. *Case Report: GcMAF Treatment in a Patient with Multiple Sclerosis.* **Inui T, Katsuura G, Kubo K, Kuchiike D, Chenery L, Uto Y, Nishikata T, Mette M.** Jul 2016, Anticancer Research, pp. 3771-3774, http://ar.iiarjournals.org/content/36/7/3771.long.

20. *Clinical experience of immunotherapy based on oleic acid bound to glycosylated vitamin d-binding protein in localised and metastatic adenocarcinoma of the pancreas.* **Thyer L, Branca J, Taubmann M.** 6-10 Oct 2014, Anticancer Research, pp. 5847-5849, https://flore.unifi.it/handle/2158/918546.

21. *Immunotherapy for Prostate Cancer with Gc Protein-Derived Macrophage-Activating Factor, GcMAF.* **Yamamoto N, Suyama H, Yamamoto N.** Philadelphia : Elsevier, Jul 2008, Translational Oncology, pp. 65-72, https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2510818/.

22. *Vitamin D Binding Protein-Macrophage Activating Factor Directly Inhibits Proliferation, Migration, and uPAR Expression of Prostate Cancer Cells.* **Gregory K, Zhao B, Bielenberg D, Dridi S, Wu J, Jiang W, Huang B, Pirie-Shepherd S, Fannon M.** 10, 18 Oct 2010, PLoS ONE, Vol. 5, pp. e13428-1-11. https://doi.org/10.1371/journal.pone.0013428.

23. *The use of Gc protein-derived macrophage activating factor for management of thyroid cancer.* **Chaiyasit K, Toshio I, Wiwanitkit V.** Bangkok : s.n., 15 Feb 2016, Journal of Cancer Research and Therapeutics, pp. 1041, https://doi.org/10.4103/0973-1482.151448.

24. *Is chondroitin sulfate responsible for the biological effects attributed to the GC protein-derived Macrophage Activating Factor (GcMAF)?* **Ruggiero M, Reinwald H, Pacini S.** 17 July 2016, Medical Hypotheses, pp. 126-131. https://doi.org/10.1016/j.mehy.2016.07.012.

25. *The Gc2 Allele of the Vitamin D Binding Protein Is Associated with a Decreased Postmenopausal Breast Cancer Risk, Independent of the Vitamin D Status.* **Abbas S, Linseisen J, Slanger T, Kropp S, Mutschelknauss EJ, Flesch-Janys D, and Chang-Claude J.** 6, Heidelberg : American Association for Cancer Research, Jun 2008, Cancer Epidemiology, Biomarkers & Prevention, Vol. VII, pp. 1339-1343. https://doi.org/10.1158/1055-9965.

26. *Glycosylation status of vitamin D binding protein in cancer patients.* **Borges, Douglas S. Rehder Randall W. Nelson Chad R.** Tempe : Wiley-Blackwell, 23 Sept 2009, Protein Science, Vol. XVIII, pp. 2036-2042. https://doi.org/10.1002/pro.214.

27. *Gc Protein-Derived Macrophage Activating Factor (GcMAF) and Autism: Do Clinical Results Require a Novel Interpretation?* **Ruggiero, M.** Schwarzenbruck : American Journal of Immunology, 13 Oct 2016, American Journal of Immunology, pp. 77-82. https://doi.org/10.3844/ajisp.2016.77.82.

28. *A Novel potential Adjuvant for Cancer Vaccines.* **S, Ruggiero M and Pacini.** 1, 29 Sept 2018, Madridge Journal of Vaccines, Vol. 2, pp. 58-62. https://doi.org/10.18689/mjv-1000112.

29. *Clinical Observation of a Novel, Complementary, Immunotherapeutic Approach based on Ketogenic Diet, Chondroitin Sulfate, Vitamin D3, Oleic Acid and a Fermented Milk and Colostrum Product.* **Michael Schwalb, Margit Taubmann, Steve Hines, Heinz Reinwald and Marco Ruggiero.** 4, s.l. : Science Publications, 21 Nov 2016, American Journal of Immunology, Vol. XII, pp. 91-98, https://doi.org/10.3844/ajisp.2016.91.98.

30. *Clinical Case Report of a Novel Immunotherapeutic Approach to Autism Spectrum Disorders based on an emulsion of Chondroitin Sulfate, Vitamin D3 and Oleic Acid.* **Nicola Antonucci, Stefania Pacini and Marco Ruggiero.** 3, s.l. : Science Publications, 7 Aug 2017, American Journal of Immunology, Vol. XIII, pp. 180-185, https://doi.org/10.3844/ajisp.2017.180.185.

31. *Rationale for the design of a novel tool for immunotherapy.* **Ruggiero M, Pacini S.** Switzerland : s.n., 27 Aug 2018, Integrative Cancer Science and Therapeutics, pp. 1-5, https://doi.org/10.15761/ICST.1000285.

32. *Clinical Experience of Integrative Autism treatment with a Novel type of Immunotherapy.* **Antonucci N, Pacini S, Ruggiero M.** 1, Italy : s.n., 22 Feb 2019, Madridge Journal of Vaccines, Vol. III, pp. 71-76, https://doi.org/10.18689/mjv-1000116.