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論　文　内　容　要　旨

報告番号	甲　先　第　２４２　　号	氏　　名	乾　利夫
学位論文題目	Clinical Experience of Integrative Cancer Immunotherapy with GcMAF （GcMAF含有ヒト血清を用いたがん、AIDSなど感染症における臨床効果の検討、及び有効性の高い総合治療プロトコルの開発）		

内容要旨

Background:

Immunotherapy has become an attractive new strategy in the treatment of cancer. The laboratory and clinical study of cancer immunotherapy is rapidly advancing. However, in the clinical setting, the results of cancer immunotherapy are mixed. We therefore contend that cancer immunotherapy should be customized to each individual patient based on their immune status and propose an integrative immunotherapy approach with Gc protein derived macrophage activating factor (GcMAF)-containing human serum. GcMAF occurs naturally in our body. It has various functions, such as macrophage activation and antitumor activities. Recently immunotherapy has become an attractive new strategy in the treatment of cancer. Our Standard protocol of our integrative cancer immunotherapy is as follows. 0.5 ml GcMAF-containing human serum is administered intramuscularly or subcutaneously once or twice per week for the duration of cancer therapy until all cancer cells are eradicated. GcMAF based immunotherapy can be combined with many other therapies such as Hyper T/natural killer (NK) cell therapy which is administered intravenously once per week for six weeks and high-dose vitamin C therapy which is administered intravenously twice per week. It is also possible to use oral medicine such as alpha lipoic acid (600 mg). which is administered orally daily and vitamin D_3 (5,000-10,000 IU) which is administered orally daily.

Sonodynamic therapy (SDT) using low-intensity ultrasound is also a novel therapeutic modality. Ultrasound has been demonstrated to activate a number of sono-sensitive agents allowing for the possibility of non-invasive targeted treatment for both superficial and deep-seated tumors.

GcMAF immunotherapy has been steadily advancing in the last two decades. In 2014, Saisei Mirai developed a new form of macrophage-activating factor (MAF) made from colostrum in collaboration with Tokushima

University. This new form, referred to as colostrum MAF, is manufactured using bovine colostrum instead of human serum and showed high macrophage phagocytic activity. GcMAF-based immunotherapy has a wide application for use in treating many diseases via macrophage activation or for use as a supportive therapy.

Results:

Saisei Mirai have treated over more than 1,000 patients with GcMAF. Among them we present here the case of patients with breast cancer (left side, with skin invasion), with pancreatic cancer, multiple liver metastasis and rheumatoid arthritis, chronic fatigue syndrome (CFS), with thymic carcinoma with lung metastasis, prostate cancer with multiple bone metastases, and metastatic liver cancer after sigmoidectomy and bilateral oophorectomy, with atopic dermatitis, with alopecia totalis, with colon cancer stage 2, with multiple sclerosis (MS). The results of this integrative immunotherapy look hopeful. We also plan to conduct a comparative clinical study to clarify its efficacy to that of several integrative immunotherapies using different Gc protein subtypes, different concentrations of GcMAF, and different macrophage status to find the relationship between each therapy and the curative effect of GcMAF-containing human serum. We aim to determine the optimal combination of the integrative immunotherapy from the results of these clinical and analytical studies. This type of integrative immunotherapy can be of benefit to patients and is a promising treatment. We expect that the described immunotherapy using second-generation GcMAF will play a central role in future treatments against human cancer, both alone and in combination with other therapies, such as sonodynamic and photodynamic therapy.

As indicated in our case study of infection in a terminally ill cancer patient, GcMAF-based immunotherapy was proven quite effective as it could play a critical role in combination with, or even without, antibiotics in patients with cancer and infections.

With regards to CFS, we highlighted case reports of two patients with CFS who had very good effects from oral colostrum MAF. It suggests oral colostrum MAF can be used to achieve much better outcomes for patients with CFS, including additional benefits such as skin repair, decreased freckles, blotches, and hair regrowth.

The treatment with colostrum MAF has been shown to be non-toxic, improving quality of life (QOL), prolonging life and curing the infection, which addresses the major goals of palliative care.

Case studies with atopic dermatitis, alopecia totalis, multiple sclerosis (MS) demonstrate that oral colostrum MAF can be used for serious desease without adverse effects.

Conclusion:

The results of our integrative immunotherapy look hopeful. We also plan to conduct a more comparative clinical study.

We demonstrate that colostrum MAF shows promising clinical results in patients with infectious diseases and for symptoms of fatigue, which is common in many chronic diseases.

We propose integrative cancer immunotherapy based on GcMAF or oral colostrum MAF as a promising candidate for a patient-friendly cancer immunotherapy and an amazing medicine.

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論文審査の結果の要旨

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学位論文題目

Clinical Experience of Integrative Cancer Immunotherapy with GcMAF

（GcMAF含有ヒト血清を用いたがん、AIDSなど感染症における臨床効果の検討、及び有効性の高い総合治療プロトコルの開発）

審査結果の要旨

手術療法、放射線療法、化学療法に続く、第4の癌治療法として免疫療法が近年注目されている。GcMAFはマクロファージ活性化因子であり、マクロファージ貪食活性化能、スーパーオキシド産生能、血管新生阻害作用、抗腫瘍活性を有することが知られており、癌や非定型抗酸菌症などの難治性疾患の治療にも有効であると考えられる。血清から高濃度のGcMAFを生成する方法を確立しており、それを第2世代血清GcMAFと定義して以下の治療プロトコルを標準として、進行癌や非定型抗酸菌症などの難治性疾患に対して血清GcMAFを用いた免疫療法を中心とした統合的アプローチを行った。統合的アプローチは、１）血清GcMAF：1回0.5/1.0ml筋注・週1/2回、２）ビタミンD：1日10,000IU・内服、３）高濃度ビタミンC：1回50g/75g点滴・週1/2回、４）αリポ酸：1日600mg内服をセットとする。代表的な有効例を以下に示す。

症例1.　71歳男性。初診時診断　胸腺癌、肺転移。血清GcMAF　48回投与、濃度ビタミンC　56回投与。治療開始1年後、腫瘍の進行を認めていない。

症例2.　74歳男性。初診時診断　前立腺癌、多発性骨転移。血清GcMAF　24回投与、高濃度ビタミンC　39回投与、ハイパーサーミア　19回施行。治療開始9ヶ月後の骨シンチで転移巣消失。

症例3.　72歳女性。初診時診断　S状結腸癌術後、卵巣転移術後、転移性肝癌。血清GcMAF　48回投与、高濃度ビタミンC　66回位投与、放射線　55Gy。治療開始1年後、PET-CTにて局所再燃、転移を認めず。

症例4.　76歳女性。初診時診断　肺非定型抗酸菌症。血清GcMAF　41回投与、高濃度ビタミンC、239回位投与。治療開始3年後、胸写で陰影消失。

以上の結果より、本統合的治療法は副作用も少なく、手術療法、放射線療法、化学療法、温熱療法などと組み合わせることにより、より高い治療効果を実現できると考えられる。

以上本研究は，進行癌や非定型抗酸菌症などの難治性疾患に対する血清GcMAFを用いた統合的アプローチの臨床成果に関するものであり，本論文は博士（工学）の学位授与に値するものと判定する。