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Research Article

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The Cellular Expression Dynamics of Endogenous Gp70 TAA Antigens in Cancer Cells and Their Biomarkers and Immunopotential for Clinical Relevance of Drug Combinations

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Abstract

Cancer cells do not want to die. After the transformation of normal cells into malignant cancer cells they absorb more glucose from outside than the normal cells. With this induction more glycoproteins are synthesized. This glycoprotein becomes specific membrane antigens which are also shed into systemic circulation. These become the bio makers for cancer diagnosis. This is one of the reasons to regulate sugar intake by the cancer patients. Both oncogenic viruses and chemical carcinogens like methyl-cholanthrene can induce malignancy in normal cells. MST cells line is a virus induced cancer cell line. MST displays on its surface viral antigens, p30 and gp70 mainly. These antigens can induce in vitro the T cells, These T cells can be employed for successful cancer therapy. P30 on a cell membrane or insoluble p30 might be considered an effective immunogen. The cell cultured and procured growing T-cells are efficient effector cells to eliminate in vivo the established tumours either viral induced or chemically induced. Cancer cells survive even after radiation and chemotheraphy.

About 15% of residual cells remain alive at the primary site of tumour. These cells comprise the resistant cells, cancer stem cells, and cells which acquired the metastatic potential. In addition, the fibroblast cells in the outer boundary of the tumour also are transformed into malignant cells by the interaction and molecular talk between tumour cells and fibroblasts. So far the resistant capacity of metastatic cancer cells was construed as a trait due to multi-drug resistance gene. Recent investigations have unraveled the secret behind resistance, as due to over-expression of non-mutated sequences of cancer cells DNA and the epigenetic expression and coating of tumour associated antigens (TAA) over their cell surface. When secondary cancers are produced through metastasis the gp70 protein/antigens were attributed for the drug resistance as such gp70 cells among 30 percent of patients, show or document resistance by spitting out the chemo-drugs and even radiation therapy is of no use to them. (Prudent Proxies: K. Ramalingam 2018), The research domain in therapeutic cancer is now elaborated due to the contribution of non-mutated gene sequence towards the synthesis of tumour associated antigens (TAA) as shown in the case of Autoimmune SLE in murine model and in breast and colorectal cancers.

Keywords: GP70; Tumour Associated antigen: (TAA), Auto Immune Disease SLE (Systemic Lupus Erethematoses) CTLS.

1. Introduction

Until 1980s it was believed that the immunologic self-recognition ie auto-imma responses is rare and invariably is not producing any pathogenic diseases. Later reports however revealed that if any antigen by its localization and/or its physico-chemi character forms, upon reaction with auto-antibodies or self-reactive immune CTLS and macrophages, inflammation and auto-immune diseases are the outcomes auto-immune response IgGs are more pathogenic than IgM auto antibodies. Why cancer cells multiply and grow without any regulation raises the ques some endogenous factors may be operating in them and expression of certain antigens will silence the immune system and its regulation. Immune unresponsiveness or suppression is a known fact in cancer patients. The synthesis of endogenous antigens or the acquired exogenous antigens in the lifetime of an individual will reduce the anti-tumour responses. Cancer growth itself may be construed as a critical auto-immune response driven by such factors as genetic or environmental which play the etiological role[1]. Studies on murine SLE (Systemic Lupus Erethematoses) have revealed that it is a complicated multiple auto immune response of spontaneous origin. These studies also reported that in the older auto immune mice the total serum gp70 is increased and its immune complex (IC) that is gp70 complexed IgG (Pathogenic) is increased with age and caused the glomerulonephritis disease as evidenced by the presence of IgG complexed gp70 immune complex (IC) in the diseased kidneys. In all auto immune diseases in general and in SLE in particular, bone marrow and spleen cells demonstrated higher IgGs, higher anti-DNA antibodies and developed gp70 anti-gp70 antibody complexes in the sera [2].

GP70 is an endogenous tumour associated antigen (TAA) and its expression has been well documented in BALB/c derived colonic cancer CT26. Experiments have revealed that tumour cells grow in gp70 sufficient mice while its 50% deficiency controlled the tumour growth and evinced well marked T cell response. That is, in mice deficient of gp more robust gp70-specific CTL response and increased T cell avidity to the antigen were demonstrated. Tumour Associated Antigen (TAA), are mostly derived from non-mutated self-genes/proteins which results in deletion of CTL with high avidity for TAAS. GP70 mRNAs are detected in murine tumour cells such as ATI mammary carcinoma, A20 lymphoma, B16 and S91 melanoma. In all these cells gp70 represents a bonafide TAA. The gp70 is an ideal antigen for the study of anti-tumour immune response directed against TAAS.

The clues obtained in the light of above notes on murine gp70 are as follows:

1) To avoid cancer in human, immune mechanisms and activation of immune cells which regulate cancer are important
2) Successful anti-tumour CTL response can be elicited in the absence of endogenous TAA expression in the normal tissues.
3) Ageing could increase the levels of gp70 tumour specific antigens in vital tissues and the poor immune defense in gp70 over expressed cells could cause carcinogenic transformation, as the gp70 non mutated self-antigen can generate anti DNA antibodies to attack the cell DNA and cause DNA lesions like SNVs. deletions, Translocation and/or frame shift mutations.
4) T cell recognition and its tolerance to other TAAs decrease when gp70 over expression increase parallel to the ageing mechanism/ process in the body.

How these surface expressed gp70 tumour associated antigens can be eliminated such that their pathological implications of immuno suppression may be circumvented. The answer to this question is only a 'yes' because it is not outside the realm of cancer biology. As breast, colo rectal and lung cancer cells over express the gp70 TAA, these cells can be excised and grown in culture. The hosts specific T-lymphocytes with specificity for these TAA over expressed cancer cells may be cultivated and cloned for permanent growth. Such cell lines which are limitless in numbers undergoing culture can be injected into the tumour/ cancer or neoplasms of spontaneous autochthonous nature in human's patients who are endowed with genetic overexpression of such epigenetic antigens. Such trials in rats/mice and guinea pigs are successful dramatically. This can be accomplished in humans also by the culture of gp70 TAA expressed cells and the cultured T cell lines in vitro for trial and such cyto-toxic T cells may be infused into the patient and eliminate in vivo the cancers [3]. GP70 is a tumor-associated antigen (TAA) which shows different levels of expression in tumor types and plays a role in tumor immunogenicity, tumor progression, and therapeutic responsiveness. The above note focuses on the dynamics of expression of endogenous GP70 in cancer cells, its regulation, and its role in tumor biology, such as immune recognition and its possible role in therapeutic Engineering. Studies on development have demonstrated that the GP70 expression is highly regulated and can be transiently expressed in tissue differentiation in cells, especially in lymphoid and epithelial tissues. Though it is mostly silent in normal tissues, some tumor types have been reported with GP70 Over expressed like colorectal carcinoma, melanoma and osteosarcoma. GP70 is a tumor-associated antigen with the ability to induce immune response since; CD8 + cytotoxic T lymphocytes and CD4 + helper T cells recognize it [4-6]. The GP70 increases tumor immunogenicity by their

- Antigenic peptides and by
- Enhancing the penetration of immune cells in tumor tissues.
- Cancers that express GP70 can usually be more responsive to immunotherapy (Endogenous Retrovirus Studies, 2021).
- GP70 is a promising target of immunotherapy in cancer because it is expressed specific to tumors. It can proceed to discoveries like..
- DNA-based vaccines
- Peptide vaccines
- Therapies based on dendritic cells.
- These discoveries have shown the capability of causing tumor specific immune response and prevent tumor growth in experimental models.
- The expression of GP70 has the promise because:
- Being a diagnostic biomarker- it helps to detect cancers
- It serves as a prognostic indicator
- Its expression pattern can be used to stratify patients into specific therapies.

2. Conclusion

The phenolic compounds from plants Salvia miltiosorrhiza, Ilex pubescens, Artemesia capillaries revealed inhibition of cox-2 enzyme and the consequent prostaglandin synthesis and /or also the free radical Scavenging mechanism. In ginger, the Compounds-dehydrogingerdione and gingerdione were reported to inhibit the prostaglandin synthesis. According to recent research investigations the above note on TAA and gp70 primed. immune cell based therapy against cancer has been considered redundant since only 70 percent Cancer cells only will be killed and the rest 30 percent will revive the cancers [6-10]. CAR-T cell therapy which engineers genetically the T-Cells and tumours infiltrating Lymphocytes (TIL) have seen promising outcomes against blood cancers and some solid tumours. Similarly natural killer Cells CAR-NK Therapy is also a faster, safer, and potentially universal approach to target Cancers, Engineered Mac cells have also been employed to destroy cancer cells, overcoming certain limitations of CAR-T in solid cancers. However CAR T-cell therapy has its own limitations since it does not work for all Cancer patients. However some terminal cancer parents have outlived their terminal cancer prognosis by the CAR-T Cell based therapy. However in general, metastatic Cancers are considered incurable but prolong the remission duration [11].

Several criteria can extend safe period of remission in cancers. via,

- Combination of immuno therapy with chemotherapy and radiation therapy.
- Biomarker oriented immuno therapy will benefit broader range of cancer types and patients.
- Tumour mutational burden "determinant.
- Cold Tumours with low immune cell to infiltration responds well to cell therapy
- Metastatic vs non-metastatic condition. There is no personalized treatment for the former and one-size-fits-all will not suit.
- Viral mimicry drugs are promising compared to standard immuno therapy. Though viral mimicry drugs offers benefits, success it's also only up to 70 percent.

How to switch off the reminder 30 percent revival is a elusive question or strategy. The answer to this lies in the actions of natural sources of phytoadjuvant chemicals and Supplements vitamins which can switch off the epigenetic expressions. Age old integrated viral proteins like gp70 or the newly integrated corona viral proteins.(Neoantigens)

Recovery from the assault of cancer disease and the side effect of conventional therapy construe some lacunae on the part of both the drugs and the disease. There is one specific lacuna is the absence of integrated therapy. Combination of therapy i.e., Conventional chemotherapy plus hormone adjuvants, and combined drugs therapy all denotes the above lacuna of absence of integration of complementary / alternative therapies. In our observations of some case studies of the Combined dietary Constituents alongside chemo therapy revealed prolonged remission duration as compared to the stipulated duration i.e.,5 years one case study (Breast Cancer). Alongside Case (Breast cancer) Conventional therapies, the diets prolonged the survival beyond 5 years now up to 8 years. Likewise in another case study of throat / esophageal cancer subsequent to radiation, the Sidha drugs (indigenous) given to the patient made him to swallow solid foods and the inflammation and the internal wounds disappeared in his case and he is still alive after his death prediction.

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