Urgent Necessity for Standardized and Evidence Based Plant Immunomodulators (Such As Rice Bran Arabinoxylan Concentrate/MGN-3) for the Tumor Research

Abstract

Biological targeting therapies can inhibit the cascade of cell proliferation and enhance the sensitivity of malignant tumor cells against natural immune effector cells. Clinical observations suggest that their combination with evidence based and standardized plant immunomodulators (such as arabinoxylan concentrate using Biobran/MGN-3) can induce astonishing results.

Since the escape of tumor cells from T lymphocytes is well known, growing interest is focusing on the Pathogenic Associated Molecular Pattern (PAMP) molecules which are able to stimulate the so called type-1 natural antitumor mechanisms in a MHC unrestricted manner. However, PAMP molecules exist only in the nature (bacteria and plants). The chemistry is not able to produce them. Bacteria are toxic. Therefore growing interest developed for the PAMP like molecules in the plants. Unfortunately, in terms of PAMP like molecules standardized plant immunomodulators (such as arabinoxylan concentrate in Biobran/MGN-3) are registered world over as food supplement and therefore their further clinical research in various oncological centers is inhibited.

Keywords: MEK-inhibitor; Immunomodulatory treatment; Tumor disease; Rice bran arabinoxylan; MGN-3

Review Article

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Introduction

In the last time a case report was published that a MEK (Mitogen activated Extracellular signal regulation Kinase) inhibitors which can down regulate the receptor tyrosine kinase mediated signaling pathway [1-3] given in a combination with a standardized and evidence based plant immunomodulators was able to induce complete remissions of lung, liver and brain metastases [4]. Since these therapy modalities can't result in similar astonishing clinical responses if they are applied separately [5] the hypothesis arouse that without standardized and evidence based plant immunomodulators the further tumor research is impeded.

In the last decades the immunology exhibited an enormous progress. However, the clinical research of malignant tumors for a long time was not able to profit too much from this development. In the last years, new biological therapeutic efforts with targeting strategy opened new perspectives for the tumour immunology. Growing evidences suggest that inhibition of Growth Factor signaling or blocking several mechanisms can also improve the tumour-induced disturbance of the immune regulation. Despite the improved outcomes with monoclonal antibodies-related targeting therapies, durable responses are uncommon [5]. Recently, it was also found that these new biological therapeutic efforts with targeting strategy can enhance the expression of stress related ligands (MICA, MICB , ULBP1 etc.) on tumour cells resulting in their increased sensitivity to natural effectors [6-7]. There is now a logical conclusion that the monoclonal targeting therapy and natural effectors activating immunomodulatory treatment together may open new perspectives in the tumor research.

Pathogenic Associated Molecular Pattern (PAMP) Molecules in Plants are Promising Therapeutic Tools in the Treatment of Malignant Tumors

Since more than 100 years it was repeatedly observed that bacteria are able to improve the immune defense against tumors. Today, it is well known that the so called Pathogenic Associated Molecular Pattern (PAMP) molecules are responsible for this beneficial effect. As it is also well known, PAMP molecules exist on membrane of bacteria which are able to bind Pattern Recognition Receptors (PRR) on phagocytic cells inducing an activation of the cascade of effector cells which are potent inhibitors of tumor growth. However, the use of bacteria or their active components in tumor treatment was always very limited since they are toxic and the attempts to diminish their toxicity caused damages in the structure of their PAMP molecules. Namely, always more data support that not the chemical composition but the configuration of PAMP molecules is important for their biological

effects. Consequently, the chemistry is not able to produce PAMP configurations but fortunately plants have also PAMP like molecules which are mostly not toxic substances. We need in term of PAMP like molecules standardized, immunological and clinical evidence based plant immunomodulators. The first plant immunomodulator which can correspond to these requirements is a standardized Rice Bran Arabinoxylan Concentrate (BioBran/MGN-3) which also as food supplement is registered in spite of the immunological and clinical (based on randomized double blind trial) evidences [8-22]. Unfortunately, oncological centers are not ready to carry out further investigations with food supplements and arabinoxylan concentrate can't take part on further controlled clinical trials. Therefore we must create a social network for the acceptance of evidence based immunomodulatory therapy with plant origin.

The tumor research needs urgently effective immunomodulators since in the least years new perspectives are opened by targeting of important steps in biological regulation. Growing evidence suggests that a similar polarity exists in the innate immunity and in the neuroendocrine system. However, until now the role of their disturbed regulation observed in the tumour disease was only by the immunological research discussed. Indeed, available information suggests that tumor-associated (type-2) immune cells affect chronic inflammation, promote cell proliferation by producing growth factors, stimulate angiogenesis and inhibit the so called type-1 cells which are potent inhibitors of tumor growth [23-24]. In this tumor-induced disturbance of natural immune system the neuroendocrine system takes also part. Therefore the research of the relationship between immune and neuroendocrine regulation will be also very exciting and promising.

Conclusion

The evidence based and standardized plant immune-modulators must be more available for the tumor research since their combination with the new biological targeting therapy modalities may open new perspectives in the tumor treatment.

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