
Title: Standardized Plant Immunomodulators Containing Pathogenic Associated Molecular Pattern (PAMP)-Like Molecules are Essential in Tumor Research. Manipulation of the Regulatory Axis in the Innate Immune System together with the Neuroendocrine System may Open New Perspectives in the Tumor Therapy

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Proposal

It is well documented that cancer cells are characterized by loss or down regulation of HLA-class-I molecules which are not reversible and reparable. It leads to a definitive escape of tumor cells from T cell lyse. Consequently, growing attention is focusing on the effector cells of innate immune system which are able to kill tumor cells in a non-MHC restricted manner. However, parallel with the tumor progression this for the tumor defense important MHC unrestricted type-1 innate immune cells are down regulated. Type-1 cells producing proinflammatory cytokines and IL-12 activate cytotoxic effector cells which are potent inhibitors of tumor growth. Available information suggests that the tumor-associated natural non-MHC restricted immune cells belong to the prototypic type-2 population which generating IL-4 and IL-10, inhibits the type-1 natural system, affects inflammation, promotes cell proliferation by producing growth factors, can stimulate angiogenesis. A successful immunomodulatory treatment must be associated with an activation of type-1 cells and with inhibition of type-2 cells. Pathogenic Associated Molecular Pattern (PAMP) molecules can bind Pathogenic Recognition Receptors (PRR) on membrane of type-1 cells. Because of the importance of their configurations PAMP molecules cannot be manufactured by chemistry. They occur only in the nature, namely in bacteria or in plants. Bacteria are toxic. Therefore in term of PAMP-like molecules standardized and evidence based plant immunomodulators can open new perspectives in tumor therapy. If the plant immunomodulator-induced activation is combined with an inhibition of Growth factor receptor mediated signaling pathway, which is also an important tool of type-2 cells to inhibit the type-1 anti- tumor natural system, on base of several case reports astonishing clinical responses were observed. Our clinical observations suggest that we must learn to manipulate the regulatory axis of natural immune balance together with the neuroendocrine system and it can open new perspectives in the tumor therapy.
