The concept that the immune system can recognize and control tumor growth can be traced back to 1893 when William Coley used live bacteria as an immune stimulant to treat cancer, but the enthusiasm for cancer immunotherapy has been moderate due to limited clinical efficacy. This limited efficacy is due to the ability of tumor cells to avoid recognition and elimination by the immune system, allowing them to become established in the host [1]. Over the past few decades, tremendous progress has been made in the understanding of how cancer evades the immune system, which in turn offers new ways to stop cancer immune evasion in favor of eliminating cancer cells.

TLP complexes (proteins released from tumors) show antigenic activity that may be applied for diagnostic aims and represent a target for immunotherapy. TLP antigens are proteins found in many cells, and one of the main components was first isolated from lung cancer tissues [1]. From this protein, it was obtained an epitope on whose basis it was possible to develop a rabbit anti-TLP serum [2]. In fact, the antibodies developed against these antigens are able to mark lung carcinoma tissues and to recognize the specific sequences previously found in TLP [1]. In addition, TLP was found in sera from patients with lung and colorectal cancer, in lung and colorectal cancer tissues and cell lines [2] and detected in DHD-K12 cell line in vitro and in vivo, in metastases induced by DHD-K12 cell injection in rats [3]. Furthermore, TLP exerts specific mitogenic activity as its intradermic inoculation results in lymphocyte blastogenesis [4].

TLP can be detected in human sera using an ELISA assay. It is worthy of note the possibility to apply a kit able to measure sera TLP values as diagnostic tool for lung cancer. Indeed, the identification of TLP in sera from healthy subjects may result in an early diagnosis, thus providing the possibility to exert preventive strategies including, among others, the intervention through the modification of life styles, and the consumption of nutraceutical supplements that may contrast the molecular mechanisms underlying the onset and the progression of lung cancer.

- vaccine
- life style

These 2 ways are not in contrast between them, but they should be done together. In fact, there is a plethora of phytocomplexes able to produce molecular mechanisms. Camellia sinensis consumption seems to exert preventive role on carcinogenesis. These activities are, at least in part, due to the several effects of (−) epigallocatechin gallate (EGCG). The mechanisms underlying the chemopreventive effects concern the affection of carcinogen-metabolizing enzymes, of cell-signaling pathways apoptosis induction, arrest of cell-cycle, transcription factors activation inhibition.

EGCG (1–40 μM) reduces human lung cancer cells proliferation upregulating p53 expression, resulting from the augment of p53 phosphorylation at Ser15 and Ser20 and the induction of its transcriptional activity [5]. Another protein involved in EGCG chemopreventive activity is HIFα [6].

Furthermore, EGCG shows cytotoxicity against drug-sensitive and drug-resistant SCLC cells In both cell lines, DNA fragmentation and S-phase cell-cycle arrest were observed [7]. In particular, this flavonoid was shown to inhibit cell proliferation in erlotinib-sensitive and resistant cell lines, in addition to producing the same effect in H460 xenografts [8].

Green tea, EGCG and GTP exert preventive and therapeutic activities towards lung cancer in animals. Indeed, the oral administration of EGCG to nude mice augmented H1299 cells apoptosis through several mechanisms including the induction of oxidative DNA damage [9]. Theaflavin and EGCG inhibit proliferation at different stages of experimental lung carcinogenesis in the mouse model of benzo(a)pyrene [B(a)P]-induced lung carcinogenesis [10]. Furthermore, the administration of GTP and black tea polyphenols to Swiss albino mice decreased the
incidence of lungs diethylnitrosamine-induced alveo-
genic tumors, as result of Akt expression, cox and nuclear

Pomegranate (Punica granatum L., Punicaceae), is an
edible fruit whose juices and extracts are rich in hydroz-
able tannins such as punicalagin and punicalin. A pome-
granate fruit extract (PFE) reduced cell-viability of
human lung cancer A549 cells without affecting normal
human bronchial epithelial cells. In particular, this vegetal
extract, in A549 cells, produced cells arrest in G0–G1
phase and reduced the expressions of cyclins, cyclin-de-
dependent kinases. The molecular mechanisms underlying
this activity include the inhibition of MAPK, PI3K, phos-
phorylation of Akt, NF-κB and markers of cell-prolifera-
tion [12].

In the same work, it has been observed that PFE oral
administration to nude mice with implanted with human
lung cancer A549 cells resulted in a reduction of tumor
growth, and delayed solid tumors formation. Also in the
experimental models of lung cancer induced by B(a)P and
N-nitroso-tris-chloroethylurea (NTCU), PFE oral admin-
istration inhibited cancer growth and progression, and
angiogenesis, through several mechanisms including
NF-κB, MAPK, PI3K, Akt phosphorylation inhibition
[13].

Other plants extract able to inhibit cancer cells prolif-
eration are those obtained by Urtica dioica L., [14] Arte-
misia annua, [15] among others. In addition, for several
plants, such as Hedyotis diffusa Willd., the direct anticanc-
er effect occurring through several mechanisms in associa-
ted to the ability to activate immunity [16]. Also several
flavonoids, such as, vitexin, nobiletin were shown to
inhibit lung cancer cells proliferation affecting a plethora
of molecular networks [17, 18]. The same observation
may be exerted for many other classes on natural compo-
sounds such as stilbens including resveratrol and piceat-
annol, ellagitannins such as geraniin, Sanguiin H6, Oeno-
thein B, phytosterols such as beta sitosterol, daucosterol
whitaferin A [20-25].

In conclusion, the investigation of the anticancer activ-
ities of several plants extracts has provided some
evidence for the potential clinical application. Many
vegetal extracts and natural compounds act as anticancer
agents exerting a cytotoxic effect against some cancer
cells and increasing host immunity, potentially increasing
organism ability to fight cancer [26].

Conflict of Interest Statement
The authors declares no conflict of interest

Acknowledgments
The authors thank for their support: Foundation T&L
de Beaumont Bonelli for Cancer Research Napoli, Italy.

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To cite this article: Micucci M, Tarro G. Tumor Liberated Protein (TLP) as Potential Target for Immunotherapy Associated to Nutraceutical Supplements. Japan Journal of Medicine. 2019: 2:2.