Diagnostic and Prognostic Value of Lectins on Tumor

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Abstract Glycoconjugates, as a active species of substances, widely lie in human bodies. It is universally recepted that the oligosaccharides of glycoconjugates are markers of recognition in molecules and cells. They play an important role on recognition in human bodies. Many biochemical reactions are switched on through the recognition. It is well known that the N-oligosaccharides of glycoproteins are found to change in some malignant tumors, for example alpha fetoprotein(AFP) in primary liver carcinoma. Therefore, the oligosaccharides can be used as diagnostic and prognostic markers of tumors. Lectins are nature probes which can recognize different sorts of N-oligosaccharides and their core structures, detect distribution of oligosaccharides. The objective of this review is to present the diagnostic and prognostic value of lectins on tumors.

Key Words lectin; cancer; diagnosis; prognosis

Lectins are protein or glycoprotein substances, usually of plant origin, of non-immunoglobulin nature, capable of specific recognition of and reversible binding to carbohydrate moieties of complex glycoconjugates without altering any covalent structure of the recognized glycosyl ligands. This group includes monovalent lectins (i.e. bacterial and plant toxin). Plant lectins have a lot of biological functions. They can bind to sugar moieties in cell walls or membranes and change the physiology of the membrane to cause agglutination, mitosis, or other biochemical changes in the cell. They have become important tools in glycosciences.

Classification of Lectins

Hundreds of plant lectins have been separated and purified since Stillmark found ricin in 1888. Many lectins are available now. They are classified into seven kinds in terms of saccharide-specificity: (1)Mannose-specific-lectin or Gluctose-specific-lectin; (2)Galactose-specific-lectin; (3) Fucose-specific-lectin; (4) N-acetylgalactosamine-specific-lectin; (5)N-acetylglucosamine-specific-lectin; (6)Sialic-acid-specific -lectin; (7)complex-structure-specific-lectin. There are some other classifications. However, this classification is practically useful. The follow exhibits usual lectins each kind in table 1.

Application of Lectins on Tumor Diagnosis and Prognosis

The oligosaccharides of glycoconjugates in cell membranes and cytoplasm can be regarded as lectin-binding receptors. These receptors are relatively stable in normal. The quantity and qualitative of lectin-binding receptors may vary, for example, sialylation, glycosylation, fucosylation and so on, when cells become malignant. These changes can be detected by saccharide-specificity of lectin with some methods: lectin histochemistry, lectin affinity chromatography, lectin blotting and so on. Lectin-binding reactivity may be a useful marker in tumor diagnosis and prognosis.

Table 1 The classification of lectins

Classification	Lectin			
D-Mannose or D–Gluctose	ConA	LCA	PSA	
D-Galactose	PNA	Jacalin	MAL Ⅰ	
L-Fucose	AAL	LTL	UEA Ⅰ	
N-acetylgalactosamine	SBA	DBA	RCA	HPA
N-acetylglucosamine	DSL	LEL	STL	
Sialic acid	SNA	MAL Ⅱ		
complex structures	PNA-E	PNA-L		

Lung Cancer The worldwide incidence of adenocarcinoma of the lung is rising. Unfortunately, no significant prognostic marker beyond the classical TNM staging can be used to stratify these patients for appropriate therapy. Schumacher and colleagues found that in a multivariate analysis Helix pomatia agglutinin (HPA) was a significant independent prognostic factor on survival by lectin histochemistry, having a relative risk of mortality of 8.75 next to stage and gender. HPA binding was the primary marker- based predictor of prognosis in their patient population and allows to stratify patients with adenocarcinomas of the lung into a low- and a high- risk group. The precise structure of the HPA binding oligosaccharide associated with metastasis has not been identified, however, using the appropriate methodology, HPA binding to the cells of primary adenocarcinomas of the lung is a significant independent prognostic factor.[1]

Breast Cancer Axillary lymph node metastases at the time of diagnosis of breast cancer is the most accurate predictor of long-term prognosis. It was found that there was a strong association between HPA binding in primary breast cancer cells and axillary lymph node metastases by lectin histochemistry, but no association with tumour size, histological grades, S-phase fractions, or the age of patients at diagnosis. It is proposed that HPA recognises a glycoprotein that is associated with metastasis (to axillary lymph nodes and elsewhere) and poor prognosis in breast cancer.[2] Blamey studied formalin fixed, paraffin embedded tissue from 100 consecutive cases of breast carcinoma for binding with HPA and Ulex Europeus (UEA Ⅰ) lectins. Correlating staining with lectins and follow-up details of patients showed that UEA Ⅰ is related to disease-free interval and survival, and HAP related to lymph node stage, time to loco regional recurrence and to survival. The study demonstrates that a simple assessment of lectin binding can provide prognostic information in breast cancer. [3] Metastasis formation is a major clinical problem in cancer treatment, and no significant progress in the treatment of metastatic has been made. Other research showed the binding of the lectin HPA was associated with a poor prognosis in breast cancer patients. HPA-positive and-negative human breast cell lines were transplanted into severe combined immunodeficient (SCID) mice. HPA-positive breast cancer cell lines (MCF-7 and T47D) metastasized in SCID mice, whereas the HPA-negative ones (BT20, HS578T and HBL100) did not. The research manifested that HPA binding is a good indicator of the metastasis of human breast cancer cells in SCID mice.[4]

Colon cancer A lectin-gold cytochemical study with Sambucus nigra and Maackia amurensis lectins manifested alpha 2,6-linked sialic acid residues expressed in neoplastic but not in normal human colonic mucosa. Expression of binding sites for Sambucus nigra I lectin was associated with the occurrence of histologic features of malignancy. [5] Seelentag found that PHA-L staining in human colorectal carcinoma sections provides an independent prognostic indicator for tumor recurrence and patient survival and is associated with the presence of lymph node metastases.[6] There is different expression of T glycoepitope (Thomsen-Friedenreich antigen) in normal and cancerous groups. The glycoconjugate expression was demonstrated by lectin histochemistry, using PNA lectin. The results show that specific and different glycochemical staining patterns could be identified between benign and malignant epithelium.[7]

Prostate cancer Some found that the M. amurensis agglutinin-bound fraction of free serum PSA increase in prostate cancer patients compared to benign prostate hypertrophy patients, using lectin affinity column chromatography. The binding of PSA to M. amurensis agglutinin, which recognizes α-2, 3-linked sialic acid, was also confirmed by surface plasmon resonance analysis. These results suggest that the differential binding of free serum PSA to M. amurensis agglutinin lectin between prostate cancer and benign prostate hypertrophy could be a potential measure for diagnosis of prostate cancer.[8] Arenas found that the main differences in lectin labeling pattern between prostatic carcinoma and benign prostatic hyperplasia (BPH) were that the latter specimens showed more marked staining with PNA, DSA, DBA, SBA, UEA–I and AAA, and lesser staining with WGA and HPA.[9]

Cutaneous malignant melanoma Thies and collegues proved that Kaplan-Meier analysis of time to first metastasis revealed a positive correlation between HPA binding and metastasis. HPA positivity is an independent predictor for metastasis.[10] And

other study showed that since Mistletoe lectin I (ML-I)is specific for galactose, high density galactose expression in malignant melanoma is a predictor of poor prognosis.[11]

Oral squamous cell carcinoma By lectin histochemistry of oral squamous cell carcinoma with Phaseolus vulgaris leukoagglutinin (L-PHA), which potentially binds to N-glycosidic carbohydrates with beta 1-6 linked lactosamin antennae, Tanda manifested that the incidence of the metastasis to regional lymph nodes in the L-PHA staining positive cases was significantly higher than that in the negative cases. The expression of L-PHA-binding oligosaccharides in oral squamous cell carcinoma may be responsible for their metastatic potential to regional lymph nodes, possibly including their ability to escape macrophage recognition.[12]

Leukemia Patients with diffuse large B-cell lymphoma (B-DLCL) were analyzed by lectin histochemistry and lectin blotting method. Phaseolus vulgaris-L (L-PHA) binding reactivity positive showed that the survival of patients was significantly shorter than negative patients. L-PHA-binding reactivity may be a useful marker for the evaluation of survival of patients with B-DLCL.[13]

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