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# Phycolectins: characteristics and prospective application

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Carbohydrates of glycoproteins and glycolipids function as bio-informative elements in biological fluids or on cell surfaces because of their structural diversity, and play important roles in fundamental biological phenomena including development, aging and canceration. On the other hand, lectins are bio-molecules targeting for carbohydrates and serves as recognition molecules within a cell, between cells and between organisms through the binding to some definite carbohydrate structure. Thus, lectins are defined as carbohydrate-binding proteins or glycoproteins that agglutinate cells or precipitate glycoconjugates, and are present in a wide range of organisms from virus to humans. Consequently, diverse physiological roles have been demonstrated for lectins of various organisms. Some of lectins are also available as clinical and biochemical reagents or are the candidates for medicine, owing to their capability to discriminate between carbohydrate structures as well as their interesting biological activities. Along with this line, various biological sources have been targeted for the discovery of novel lectins.

Nowadays we know that marine algae are also good sources of lectins for basic research and application. About 200 species of marine algae have so far been reported to contain lectins (hemagglutinins), and algal lectins, we call phycolectins , have been isolated from 40 species. Among them, we isolated and characterized lectins from 11 Chlorophyta species, 10 Rhodophyta species and a Cyanophyta species, and detected various biological activities including cell agglutination, mitogenic activity for lymphocytes, anti-virus and anti-anticoagulant activities, inhibition of tumor cell-growth, platelet-aggregation and embryo developments of marine invertebrates, and cytotoxicity against microalgae. Biochemical studies showed that many of phycolectins have common characteristics of low molecular weights, monomeric molecules, no metal requirement for hemagglutination, thermostablity, and having affinity for glycoproteins but not for monosaccharides. In general, there is no similarity in N-terminal sequences between lectins from algae and other biological groups, although the sequences are homologous at least within the same genus of algae

As lectins are assumed to cause their activities through their binding to glycoconjugates

on cell surfaces, it is important to define their carbohydrate-binding specificity. With respect to this, no monosaccharide-binding phycolectins bind to glycoproteins or glycopeptides, preferentially those bearing asparagine-linked sugar chains (N-glycans). Then we further examined the oligosaccharide-binding specificity of phycolectins in details by a centrifugal ultrafiltration method with 44 kinds of oligosaccharides. The results revealed the uniqueness of them, including those strictly specific for high-mannose type N-glycans, complex type N-glycans, forsmans antigen sugar chain, or sialyl Lewis X. The high-mannose type N-glycan specific phycolectins are subdivided into two types, either of which has the decreased binding activity or binds only with high-mannose type N-glycans bearing the non-reducing terminal a-1, 2 linked mannosyl residue(s). With the highly selective binding nature, the phycolectins should be useful as novel proves for carbohydrate structures including the markers of cancer.

The information on the molecular structures of phycolectins has been recently increasing, determined the primary structures of lectins from 5 algal species. The monomeric lectins from the red algae, *Eucheuma serra* (268 amino acids), *E. amakusaensis* (268 amino acids), and a freshwater blue-green alga *Oscillatori agardhii* (132 amino acids), all of which belong to high-mannose type specific phycolectins, showed the highly similarity among their primary structures which have the tandem repeats of homologous sequences of the N-terminal 67 amino acids. The crystal structure of an *E. serra* lectin is constructed from two b-barrels, suggesting the presence of four carbohydrate-binding sites per a polypeptide chain. The lectin inhibited the growth in vitro of 37 human cancer cell lines at IC50 of 1~10 $\mu$M, whereas it was mitogenic for human and murine lymphocytes in the dose-dependent manner. The lectin significantly suppressed the colon carcinogensis without any toxicity when it was orally administered to mice, which had been given 1,2-dimethylhydrazine as a carcinogen. Thus the lectin should be useful as a supplement for cancer prevention as well as the prove for high-mannose type N-glycans.

Three isoagglutinins of the red alga, *Hypnea japonica* were commonly monomeric polypeptides composed of 90 amino acid residues including two intrachain disulfide bonds, and differed from one another in amino acids at three positions. About 43% of total residual numbers were consisted of three kinds of amino acids; Ser, Gly and Pro. The hemagglutinating activities did not change even after heating at 100°C for 30 min, but were lost by reduction and alkylation of the disulfide bonds. Surprisingly the agglutinins contained a motif similar to the alignment of nine COOH-terminal conserved amino acid residues including two half-cystine within carbohydrate recognition domains (CRDs) of C-type animal lectins. However, some of residues

involving in binding to carbohydrate and/or calcium ions in the CRDs were substituted with other amino acids in the algal agglutinins. The substitution might be related at least to no monosaccharide and metal binding property of the agglutinins. Thus the carbohydrate-binding property of the agglutinins are yet unknown, however, they showed diverse biological activities as described before. A Spanish group also determined the similar sequence of a hemagglutinin (91 amino acids) of a red alga, *Bryosamnion triquetrum*. Therefore, the low-molecular weight peptidic agglutinins may be widely distributed in Rhodophyta.

As described above, phycolectins may be considered as a new lectin category, promising their application as clinical and biochemical reagents and for medicinal purpose for human health.