



## Lectins As Indicators of Disease

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# Lectins as Indicators of Disease

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An increasing number of diseases are known to be associated with changes in the glycosylation profiles of specific glycoproteins. Since glycosylation patterns reflect the internal and external environment of the cells in which proteins are glycosylated they can be sensitive indicators of alterations in cell function brought about by disease. Glycosylation changes are therefore becoming widely used as markers both for initial diagnosis and for following disease activity. Glycoproteins in which alterations have been described include the serum glycoproteins IgG, transferrin,  $\alpha$ 1-acid glycoprotein and fibrinogen and the tumor products  $\alpha$ -fetoprotein and chorionic gonadotropin.

The specific sugar binding properties of lectins enables them to be used to compare the glycosylation profiles of normal and diseased cells. For example, changes in cell membrane glycoproteins which accompany malignant transformation alter the lectin binding patterns of these cells. This can be used to predict the invasive potential of tumors and allow their differential diagnosis. Also, the

distribution of glycoproteins on cell surfaces may change with disease, and their localization in normal and diseased cells can be compared using lectins conjugated to biotin<sup>(1)</sup>. A potential therapeutic use of lectins involves conjugating them to chemotherapeutic agents directed at tumor glycoproteins.

Lectins can also be used to determine the increased percentage of incompletely galactosylated IgG (IgG0) in serum and synovial fluid from patients with rheumatoid arthritis. This increase correlates with increased severity of the disease<sup>(2)</sup> and may be used at onset to predict the likely outcome of the disease<sup>(3)</sup>.

Although in many cases the role of abnormal glycosylation in disease pathogenesis currently remains obscure, the extensive use of lectins to investigate these changes is allowing new insights into the biological and pathological significance of glycosylation. In addition, a new range of diagnostic tools and therapeutic reagents is being developed and is summarized here.

## Disease

Carcinomas

Thyroid cancer

Sex cord- stromal tumours (SCST)

Warthin's tumour (Parotid gland)

Colorectal Cancer

## Reference

- Hsu, S.M. and Raine, L. (1982) Versatility of biotin-labeled lectins and avidin-biotin-peroxidase complex for localisation in tissue sections. *J. of Histochem. and Cytochem.* **30**, 157-161
- Zabel, P.L., Noujaim, A.A., Shysh A. and Bray J. (1983) Radioiodinated peanut lectin: a potential radiopharmaceutical for immunodetection of carcinoma expressing the T antigen. *Eur. J. of Nuclear Medicine* **8**, 250-254
- Hanson, J.E.S., Larsen, V.A. and Bog Hansen, T.C. (1984) The microheterogeneity of  $\alpha$ 1 acid glycoprotein in inflammatory lung disease, cancer of the lung and normal health. *Clin. Chim. Acta.* **138**, 41-48
- Vijaykumar, T., Augustine, J., Mathew, L., Aleykutty, M.A., Nair, M.B., Remani, P. and Nair, M.K. (1992) Tissue binding pattern of plant lectins in benign and malignant lesions of thyroid. *J. Experimental Pathology* **6**, 11-23
- Bychkov, V., Deligdisch, L., Talerma, A. and Reddy, V.B. (1992) Lectin histochemistry of sex cordstromal tumors and small cell carcinoma of the ovaries. *Gynecologic and Obstetric Investigation.* **34**, 115-118
- Hsu, S.M. and Raine, L. (1982) Warthin's tumor-epithelial cell differences. *American J. of Cell Physiol.* **77**, 78-82
- Kuroki, T., Kubota, A., Miki, Y., Yamamura, T. and Utsunomiya, J. (1991) Lectin staining of neoplastic and normal background colorectal mucosa in nonpolyposis and polyposis patients. *Diseases of the colon and rectum* **34**, 679-684

## Disease

Colon cancer

Lung Carcinoma

Oral cavity Squamous cell carcinoma

Nasopharyngeal carcinoma

Liver Diseases

## Reference

- Boland, C.R., Chen, Y.F., Rinderle, S.J., Resau, J.H., Luk, G.D., Lynch, H.T. and Goldstein, I.J. (1991) Use of lectin from *Amaranthus caudatus* as a histochemical probe of proliferating colonic epithelial cells. *Cancer Res.* **51**, 657-665
- Itzkowitz, S., Yuan, M., Montgomery, C.K., Kjeldsen, T., Takahashi, H.K., Bigbee, W.L. and Kim, Y.S. (1989) Expression of Tn, sialosyl-Tn and T antigens in human colon cancer. *Cancer Res.* **49**, 197-204
- Rosen-Levin, E., Patil, J.R., Watson, C.W. and Jagirdar, J. (1989) Distinguishing benign from malignant pleural effusions by lectin immunocytochemistry. *Acta-Cytol.* **33**, 499-504
- Alvarez-Fernandez, E. and Carretero-Albinana, L. (1991) Expression of blood group antigens by normal bronchopulmonary tissues and common forms of pulmonary carcinomas. *Arch. of Path. and Lab. Medicine* **115**, 42-49
- May, D.P.J. and Sloane, P. (1991) Lectin binding to normal mucosa, leucoplakic and squamous cell carcinoma of the oral cavity. *Med. Lab. Sci.* **48**, 6-18
- Chew, E.C., Yuen, K.E. and Lee, J.C. (1991) Lectin histochemistry of normal and neoplastic nasopharyngeal epithelium. *Anti Cancer Res.* **11**, 697-704
- Baumah, P.K., Cornell, C., Cassells-Smith, A.J. and Skillen, A.W. (1987) Differential reactivity of alpha-fetoprotein with lectins and its usefulness in the diagnosis of liver disease. *Clin. Chim. Acta.* **168**, 69-73

# Lectins as Indicators of Disease

	<p>Nikolic, J.A., Stajic, M., Cuperlovic, M., Hajdukovic, L. and Golubovic, G. (1990) Serum alpha fetoprotein levels and microheterogeneity in patients with different liver diseases. <i>J. Hepatol.</i> <b>11</b>, 252-256</p> <p>Wu, J.T. (1990) Serum alpha-fetoprotein and its lectin reactivity in liver diseases: a review. <i>Ann. Clin. Lab. Sci.</i> <b>20</b>, 98-105</p> <p>Du, M.Q., Hutchinson, W.L., Johnson, P.J. and Williams, R. (1991) Differential alpha-fetoprotein lectin binding in hepatocellular carcinoma. Diagnostic utility at low serum levels. <i>Cancer</i> <b>67</b>, 476-480</p> <p>Taketa, K., Ichikawa, E., Yamamoto, T., Matsuura, S., Taga, H. and Hirai, H. (1990) <i>Datura stramonium</i> agglutinin reactive alpha-fetoprotein isoforms in hepatocellular carcinoma and other tumours. <i>Tumour Biol.</i> <b>11</b>, 220-228</p> <p>Taketa, K., Sekiya, C., Namiki, M., Akamatsu, K., Ohta, Y., Endo, Y., and Kosata, K. (1990) Lectin reactive profiles of alpha-fetoprotein characterising hepatocellular carcinoma and related conditions. <i>Gastroenterology</i> <b>99</b>, 508-518</p> <p>Sekine, C., Aoyagi, Y., Suzuki, Y. and Ichida, F. (1987) The reactivity of alpha-1-antitrypsin with <i>Lens culinaris</i> agglutinin and its usefulness in the diagnosis of neoplastic diseases of the liver. <i>Br. J. Cancer</i> <b>56</b>, 371-375</p>
Prostatic cancer	<p>Abel, P.D., Keane, P., Leathem, A., Tebbutt, S. and Williams, G. (1989) Change in glycoconjugate for the binding site of the lectin <i>Ulex europaeus</i> 1 following malignant transformation of prostatic epithelium. <i>Br. J. Urol.</i> <b>63</b>, 183-185</p>
Pancreatic cancer	<p>Ching, C.K. and Rhodes, J.M. (1990) Identification and partial characterisation of a new pancreatic cancer related serum glycoprotein by SDS-PAGE and lectin blotting. <i>Gastroenterology</i> <b>95</b>, 137-140</p> <p>Ching, C.K. and Rhodes, J.M. (1989) Enzyme-linked PNA lectin binding assay compared with CA19-9 and CEA radioimmunoassay as a diagnostic blood test for pancreatic cancer. <i>Br. J. Cancer</i> <b>59</b>: 949-953</p>
Breast cancer	<p>Fernandes, B., Sagman, N., Auger, M., Demetrio, M. and Dennis, J.W. (1991) Beta 1-6 branched oligosaccharides as a marker of tumour progression in human breast and colon neoplasia. <i>Cancer Res.</i> <b>51</b>, 718-723</p> <p>Leathem, A., Doka, I. and Atkins, N. (1983) Lectin binding, to normal and malignant breast tissue. <i>Diagn. Histol. Pathol.</i> <b>6</b>, 171-180</p> <p>Fukotomi, T., Habishi, M., Tsugane, S., Yamamoto, Nanasawa, T. and Hirota, T. (1989) Prognostic contributions of <i>Helix pomatia</i> and carcinoembryonic antigen staining using histochemical techniques in breast carcinomas. <i>Jpn. J. Clin. Oncol.</i> <b>19</b>, 127-134</p> <p>Leathem, A.J. and Brooks, S.A. (1987) Predictive value of lectin binding on breast-cancer recurrence and survival. <i>Lancet</i> <b>i</b>, 1054-1056</p> <p>Leathem, A.J. (1990) Biological, biochemical and morphological markers of breast disorders and of breast cancer. <i>Acta. Histochem. suppl</i> <b>40</b>, 51-58</p> <p>Brooks, S.A. and Leathem, A.J. (1991) Prediction of lymph node involvement in breast cancer by detection of altered glycosylation in the primary tumour. <i>Lancet</i> <b>33</b>, 71-74</p> <p>Fukutomi, T., Hirohashi, S., Tsuda, H., Nanasawa, T., Yamamoto, H., Itabashi, M. and Shimosato, Y. (1991) The prognostic value of tumour associated carbohydrate structures correlated with gene amplification in human breast carcinomas. <i>Jap. J. of Surgery</i> <b>21</b>, 499-507</p>
Ovarian cancer	<p>Sasano, H., Saito, Y., Nagura, H., Kudo, R., Rojas, M. and Silverberg, S.G. (1991) Lectin histochemistry in mucinous and serous ovarian neoplasms. <i>J. Int. J. of Gynecological Pathology</i> <b>10</b>, 252-259</p>
Chorio-carcinoma	<p>Imamura, S., Armstrong, E.G., Birken, S., Cole, L.A. and Canfield, R.E. (1987) Detection of desialylated forms of human chorionic gonadotropin. <i>Clin. Chim. Acta.</i> <b>163</b>, 339-349</p>
Hodgkin's disease	<p>Sarker, A.B., Akagi, T., Jeon, H.J., Miyake, K., Murakami, I., Yoshino, T., Takahashi, K. and Nosse, S. (1992) Bauhinia purpurea- a new paraffin section marker for Reed-Sternberg cells of Hodgkin's disease. A comparison with Leu-M1 (CD15), LN2 (CD 74), peanut agglutinin and Ber-H2 (CD30). <i>American J. of Path.</i> <b>141</b>, 19-23</p>
Cervical cancer	<p>O'Brien, M.E., Souberville, B.E., Cowan, M.E., Allen, C.A., Leusley, D.M., Mould, J.J., Blackledge, G.R. and Skinner, G.R. (1991) Glycoprotein patterns in normal and malignant cervical tissue. <i>Cancer Letts.</i> <b>58</b>, 247-254</p>
Diabetes	<p>Mukherjee, N., Biswas, T.K., Mitra, S., Gupta, N. and Sarkar, M. (1991) Immunochemical correlation in diabetes mellitus, a preliminary report on the lectin-agglutinin test. <i>J. of the Association of Physicians of India</i> <b>39</b>, 172-174</p>

## Disease

Cystic fibrosis

Rheumatoid arthritis (RA),  
Juvenile arthritis (JA),  
and Tuberculosis (TB)

Severe burns

## Reference

- Thiru, S., Devereux, G. and King, A. (1990) Abnormal fucosylation of ileal mucus in cystic fibrosis: IA histochemical study using peroxidase labelled lectins. *J. Clin. Pathol.* **43**, 1014-1018
- Sumar, N., Bodman, K.B., Rademacher, T.W., Dwek, R., Williams, P., Parekh, R.B., Edge, J., Rook, G.A.W., Isenberg, D.A., Hay, F.C., Roitt, I.M. (1990) Analysis of glycosylation changes in IgG using lectins. *J. Immunol. Meths.* **131**, 127-136
- Roitt, I.M., Dwek, R.A., Parekh, R.B., Rademacher, T.W., Alavi, A., Axford, J.S., Bodman, K.B., Bond, A., Cooke, A., Hay, F.C., Isenberg, D.A., Lydyard, P.M., Mackenzie, Rook, G., Smith, M. and Sumar, N. (1988) The role of antigen in autoimmune response with special reference to changes in carbohydrate structure of IgG in Rheumatoid Arthritis. *J. Autoimm.* **1**, 499-506
- Young, A., Sumar, N., Bodman, K.B., Goyal, S., Sinclair, H., Roitt, I., and Isenberg, D. (1991) Agalactosyl IgG: an aid to differential diagnosis in early synovitis. *Arth. Rheum.* **34**, 1425-1429
- Mallet, B., Franc, J.L., Miquel, M. and Arnaud, C. (1987) Effects of severe burns on glycan microheterogeneity of four acute phase proteins. *Clin. Chim. Acta.* **167**, 247-257

# Lectins as Indicators of Disease

Lectins in Pregnancy	Horvat, B. (1993) Galactose binding lectins as markers of pregnancy-related glycoproteins. <i>Histochemistry</i> <b>99</b> , 95-101
Cell surface markers	Fujimoto, H., Muramatsu, T., Urushihara, H. and Yanagisawa, K.O. (1982) Receptors to <i>Dolichos biflorus</i> agglutinin. A new cell surface marker common to teratocarcinoma cells and preimplantation mouse embryos. <i>Differentiation</i> <b>22</b> , 59-61
Lectins in identification of <i>Neisseria gonorrhoeae</i>	Schaefer, R.L., Keller, K.F. and Doyle, R.J. (1979) Lectins in diagnostic microbiology: use of wheat germ agglutinin for lab. differentiation of <i>Neisseria gonorrhoeae</i> . <i>J. of Clin. Microbiol.</i> <b>10</b> , 669-672
Localisation of origin of cyst wall in <i>T.gondii</i>	Derouin, F., Beauvais, B., Larviere, M. and Guillot, J. (1981) Binding of fluorescein-labelled lectins on trophozoites and cysts of three strains of <i>Toxoplasma gondii</i> . <i>Comptes Rendes des Seances de la societe de biologis et de ses Filiales</i> <b>175</b> , 761-768
Glycoconjugate detection in developing endolymphatic sac	Yamashita, H., Bagger, Sjoback, D., Wersall, J. and Sekitani, T. (1991) Glycoconjugates in the human fetal endolymphatic sac (ES) as detected by lectins. <i>J. of Laryngology and Otology</i> <b>105</b> , 711-715
Lectins as markers of monocyte lineage	O'Keefe, D. and Ashman, L. (1982) Peanut agglutinin : a marker for normal and leukaemic cells of the monocyte lineage. <i>Clin. and Experimental Immunol.</i> <b>48</b> , 329-338
Inflammatory cells	Niikawa, S., Hara, A., Ando, T., Sakai, N., Yamada, H. and Shimokawa, K. (1992) Lectin cytochemistry combined with silver staining of argyrophilic nucleolar organiser regions in human gliomas. <i>Neurologia Medico-Chirurgica</i> <b>32</b> , 653-658
Lectins in development	Hausman, G.J.H., Wright, J.T. and Thomas, G.B. (1991) Vascular and cellular development in fetal adipose tissue : lectin binding studies and immunocytochemistry for laminin type IV collagen. <i>Microvascular Research</i> <b>41</b> , 111-125
Human junctional epithelium; new marker	Bampton, J.L., Shirlaw, P.J., Topley, S., Weller, P. and Wilton, J.M. (1991) Human junctional epithelium : demonstration of a new marker, its growth in vitro and characterisation by lectin reactivity and keratin expression. <i>J. of Investigative Dermatology</i> <b>96</b> , 708-717

## REFERENCES

1. Hsu, S.M. & Raine, L. (1982) Versatility of biotin-labeled lectins and avidin-biotin-peroxidase complex for localisation in tissue sections. *J. of Histochem. and Cytochem.* **30**, 157-161
2. Parekh, R.B., Eisenberg, D., Ansell, B., Roitt, I., Dwek, R.A. & Rademacher, T.W. (1988) *Lancet* **1**, 966-969
3. Young, A., Sumar, N., Bodman, K.B., Goyal, S., Sinclair, H., Roitt, I., & Isenberg, D. (1991) Agalactosyl IgG: an aid to differential diagnosis in early synovitis. *Arth. Rheum.* **34**, 1425-1429



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