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Peanut lectin histochemistry of 120 mammary carcinomas and its relation to tumor type, grading, staging, and receptor status*

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Summary. Peanut lectin (PNL) is known to bind β-D-galactosyl-(1-3)-N-acetyl-D-galactosamine, which provides antigenetic determination of the Thomsen-Friedenreich antigen (TFAg). The aim of this study was to analyse the expression of peanut lectin binding sites in mammary carcinomas and to correlate these with tumor type, histological grading, staging and biochemical receptor status. The series comprised 120 invasive mammary carcinomas and 14 cases with normal breast tissue or benign epithelial proliferations as controls. In controls mainly luminal or apical PNL-binding was discovered, however, in all except three carcinomas a cytoplasmatic localisation of TFAg with three major patterns was found: diffuse, granular-globular and vacuolar reactions. The quantitative-qualitative evaluation of the PNL-staining revealed a statistically significant correlation between globular-vacuolar PNL-reaction and tumor type with a higher percentage of this type of reaction in invasive lobular carcinomas as opposed to tubular and invasive ductal carcinomas. Furthermore a statistically significant relationship was disclosed between PNL-histopositivity and estrogen positive – progesterone positive cases. However, the findings of contradictory PNL-status and hormone-receptor status illustrates clearly the difficulty of predicting the biochemical receptor status. No correlation was found between PNL-histochemistry, histological grading, and pathological staging. The practical implications of PNL-histochemistry of mammary carcinomas are discussed.

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Abbreviations used in the text: PNL = peanut lectin, PO = peroxidase, ILC = invasive lobular carcinoma, IDC = invasive ductal carcinoma, NOS = not otherwise specified, E = estrogen, P = progesterone.

Key words: Peanut-Lectin – Histochemistry – Mammary cancer – Human

Peanut-lectins (PNL) are glycoproteins that have the ability to bind the disacharide β-D-galactosyl-(1-3)-N-acetyl-D-galactosamine, which is purported to be the antigenetic structure of the so-called Thomsen-Friedenreich antigen (TFAg) (Lotan et al. 1975; Springer et al. 1979). This TFAg is normally present on a number of cells and tissues in its sialic-acid covered form (Cooper 1982; Klein et al. 1978; Newman et al. 1975; Reisner et al. 1979; Uhlenbruck et al. 1977). Treatment of these cells with neuraminidase uncovers this previously cryptic antigen.

It has been shown that one can identify β-D-galactosyl-(1-3)-N-acetyl-D-galactosamine in tissue sections by using labelled PNL. Since the report of Springer et al. (1975), that breast carcinomas like normal epithelium, will express TFAg there has been increasing interest in TFAg in human mammary carcinomas (Seitz et al. 1983). Howard et al. (1981) and Klein et al. (1979 b) have subsequently revealed that both normal breast epithelium and breast carcinomas have PNL-binding sites – thus indicating the presence of TFAg. These authors demonstrated a predominantly intracytoplasmaic localisation of PNL-binding sites in carcinomas as opposed to the PNL-staining of the glycocalyx in the normal breast tissue. In addition, Newman et al. (1979) found a correlation between the number of PNL-binding sites and the degree of differentiation of mammary carcinomas. Recently, Klein et al. (1981) proposed that PNL-associated secretory phenomena of breast carcinomas are the final product of a synthetic pathway, which is modulated by steroid hormones. The presence of PNL-binding sites in carcinoma cells thus implies retention of the regulatory controls of mammary epithelium. Additional proof is needed to validate this hypothesis which would carry great practical implications. Furthermore, the relationship of PNL-binding to other morphological and biochemical variables appears to be important. This report examines the correlation between data obtained by studying the PNL-binding property of 120 breast carcinomas with data generated by the analysis of tumor type, histological grading, staging, and biochemical receptor status. Our objective was to define the relationship of PNL-histochemistry to the other variables in breast carcinomas.

Materials and methods

Material

One hundred and twenty invasive breast carcinomas were selected from the Gynecopathology files of the hospital for Gynecology and Obstetrics of the University of Mainz. All patients were operated on according to the method of Patey with removal of axillary and infraclavicular lymph nodes. These were divided into 9 stage I($T_{1-2}N_0M_0$), 39 stage II($T_{1-2}N_{0-1}M_0$), 52 stage III($T_{3-4}N_{0-3}M_0$ or $T_{1-4}N_{2-3}M_0$) and 20 stage IV($T_{1-4}N_{0-3}M_1$) cases as determined by preoperative clinical evaluation and pathological examination of the specimen. The only criterion for selection within this analysis was that material fixed with Bouin solution

was available. Tissue from 15 cases with fibrocystic disease and/or varying degrees of epitheliosis and adenosis were used as controls.

Histology

Haematoxylin-eosin and PAS-stained sections of all cases were examined. The benign lesions and the carcinomas were classified according to the criteria given by Azzopardi (1978), Bässler (1978), Dixon et al. (1982), Fechner (1975), Fisher et al. (1975), McDivitt (1978), van Bogaert and Maldague (1980), Martinez and Azzopardi (1979). All the cases were classified, histologically graded using the criteria of Bloom and Richardson (1957) and analysed for PNL-binding without prior knowledge of receptor content.

PNL-staining

PNL coupled to peroxidase was obtained from MEDAC (Hamburg/West Germany). Vibrio cholera neuraminidase, 1 IU per ml was obtained from Calbiochem Behring, Marburg in West Germany. 5 µm thick sections were dewaxed, rehydrated and equilibrated with phosphate buffered saline (PBS), pH 7.2. The sections were covered with neuraminidase (1 IU per ml) at room temperature for 30 min. After washing them three times with PBS, both the treated and untreated slides were covered with PNL at room temperature for 3 h with a dilution of approximately 1:200. The slides were drained and washed three times in PBS. Next, slides were stained with 25 mg diamino-bencidine-tetrahydrochloride, solved in 100 ml 0.05 M tris buffer, pH 7.6 with 0.001 H_2O_2. The slides were covered with 1% OsO_4 for 20 min and counterstained with haematoxylin. Sections were mounted in Eukitt.

Controls were carried out by: (1) substituting PBS for PNL in the first step, (2) using PNL that had been absorbed by type 0 red blood cells treated with neuraminidase, or (3) PNL absorbed by 0.3 M galactose. Red blood cells and lymphocytes were used as an inbuilt positive control in each slide treated with neuraminidase.

Assay of steroid hormone receptors

Of all 120 cases a dextran-coated charcoal absorbtion technique was used to determine the steroid receptor content (Schmidt-Gollwitzer 1979; EORTC Breast Co-operativ Group 1980). A content of 10 nmol receptor/mg protein or more was named estrogen receptor positive (E+) or progesteron receptor positive (P+), values below 10 nmol receptor/mg protein negative (E- or P-).

Statistical methods

Differences in frequency were tested with the Chi-Square-Test (Claus and Ebner 1977). The results were taken for significant if the probability of error (p) was lower than 5%. When the total number was lower than 40 and when the expected frequency was lower than 5, the continuity correction according to Yates was carried out.

Results

Normal breast tissue and benign proliferative lesions

There were 15 cases which were assessed as being either normal or as showing areas of adenosis and/or epitheliosis. Normal lobules were often PNL-negative (Fig. 1). Binding of PNL was detected mainly along the apical cell membrane of ductal and lobular cells. Some staining of secreted material could also be seen. Pretreatment of the sections with neuraminidase resulted in an increase in PNL-binding. However cytoplasmatic reaction was not clearly evident; only a few cells with irregular distribution throughout the

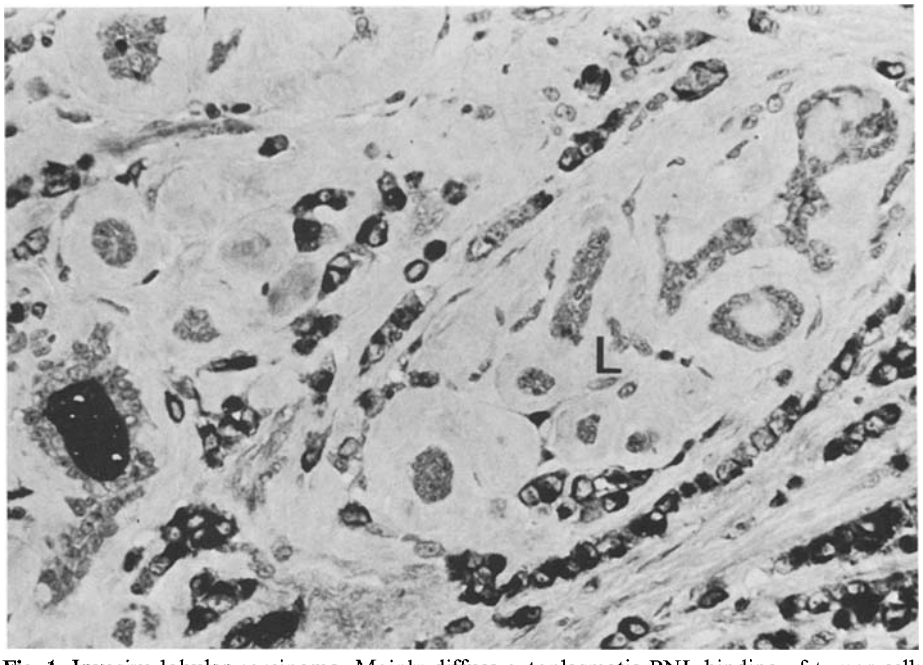

Fig. 1. Invasive lobular carcinoma. Mainly diffuse cytoplasmatic PNL-binding of tumor cells contrasting to the PNL-negative hyalinized lobule (*L*). PO-PNL, × 330

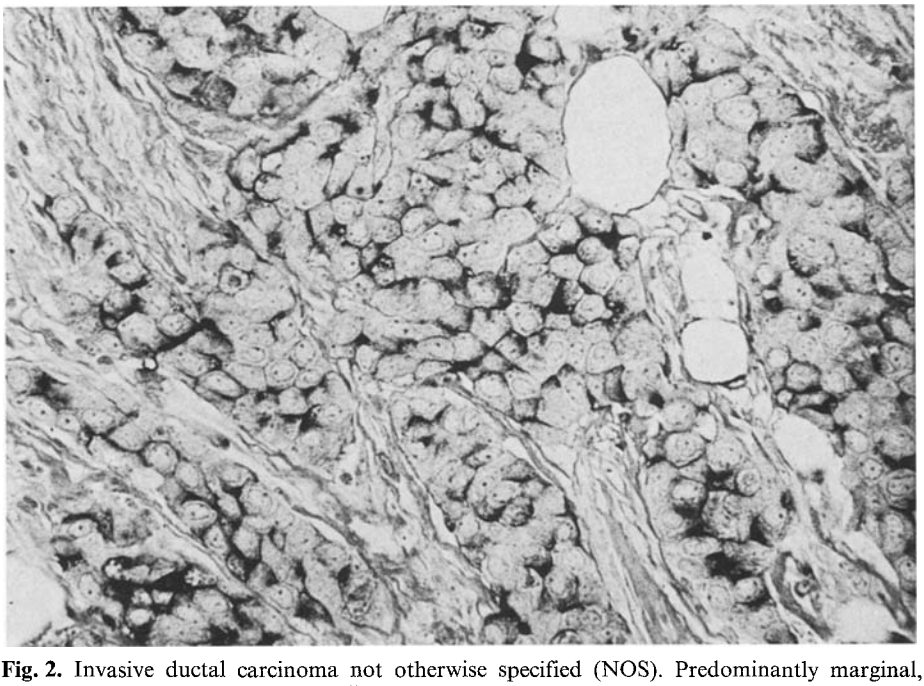

Fig. 2. Invasive ductal carcinoma not otherwise specified (NOS). Predominantly marginal, cell membrane orientated PNL-binding. PO-PNL, × 330

section were suspicious of homogenous cytoplasmatic reaction. A similar PNL-staining was obtained in areas with adenosis and epitheliosis.

Breast carcinomas

Of the 120 carcinomas examined 117 (97.5%) showed PNL-labelling. Four patterns of staining could be seen:

1. Diffuse staining with various modifications: involvement of a part of the cytoplasm or staining of the whole cytoplasm (Fig. 1 and 2).
2. A granular-globular staining with similar cytoplasmatic distribution patterns as in (1) (Fig. 3).
3. A vacuolar reaction consisting of several variations: a several small vacuoles; b a single large vacuole (Fig. 4); c the so called targetoid pattern (Fig. 4).
4. combinations of (1) to (3).

The staining pattern varied from case to case and even within individual carcinomas. Treatment of sections with neuraminidase resulted in an increase in PNL-binding in tubular and cribriform carcinomas but only to a lesser degree or not at all in lobular and ductal carcinomas.

A clear relationship could be shown both qualitatively and quantitatively between patterns of PNL-staining and type of carcinoma.

Twenty-seven out of 120 cases were classified as invasive lobular carcinomas (ILC) or as one of their variants. In most of these cases it was possible to observe a great number of globules, vacuoles, and targetoid reactions, stained with PNL (Fig. 4). The other staining patterns were also established but were likewise rare.

Thirty-eight cases in this series come into the category of invasive ductal carcinoma (IDC) of no special type (NOS). The PNL-staining pattern was usually of the combined type. It consisted mainly of type (1) and (2). Seldom could larger globules or vacuoles be seen as well.

The lectin pattern of 15 cases of tubular carcinomas was quite similar to normal ducts with a reaction at the apical-luminal cell border (Fig. 5). In most instances some intracytoplasmatic substance also reacted with PNL in contrast to benign lesions, a greater amount of cells showed granular or diffuse cytoplasmatic reactions with up to 20% of tumor cells. In 20% of cases intracytoplasmatic globular and/or vacuolar reactions, that were typical for lobular carcinomas, were found (Fig. 4).

Cribriform carcinomas revealed a similar staining pattern to tubular carcinomas with regard to the apical-luminal reaction. Apocrine carcinomas showed a polar reaction orientated at the cell-membrane with some positive granules or globules near the cell surface.

The quantitative evaluation of PNL-histochemistry of breast carcinomas and its relation to other variables is shown in Tables 2–6.

Of the 120 carcinomas 117 (97.5%) showed PNL-binding to tumor cells; only 3 cases were completely negative. In 55% of the tumors the number of PNL-positive cells was beyond the 25% percentage level. In predicting classification functions of mammary carcinomas this percentage figure was

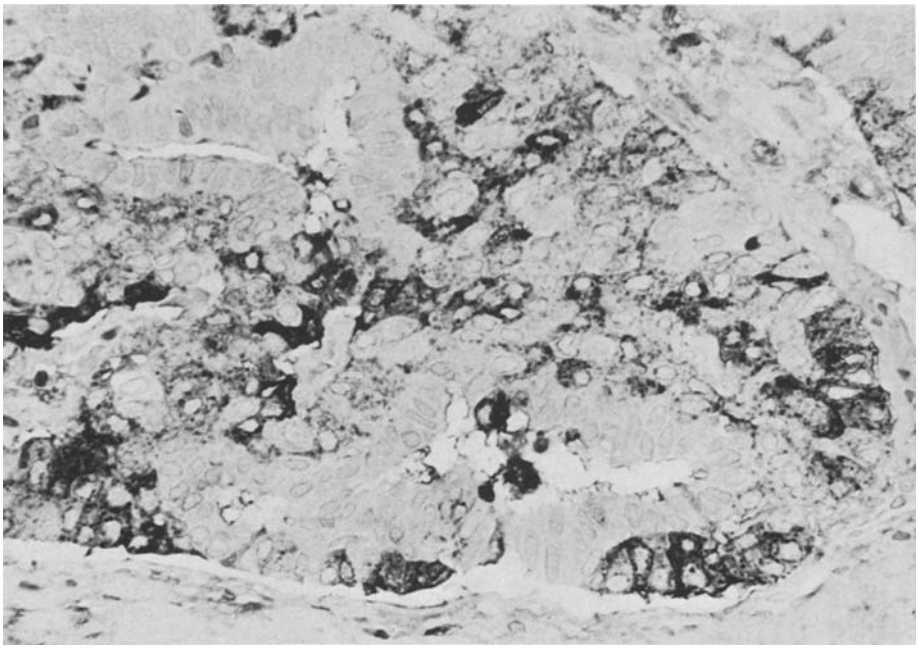

Fig. 3. Invasive ductal carcinoma with predominantly granular PNL-binding in the cytoplasm of about 40% of tumor cells. PO-PNL, × 330

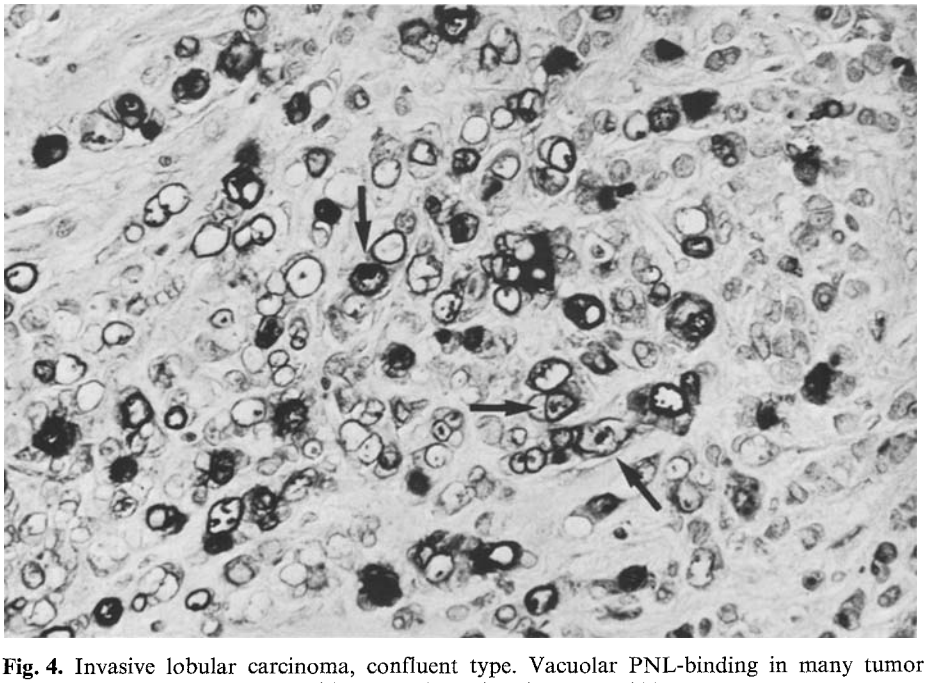

Fig. 4. Invasive lobular carcinoma, confluent type. Vacuolar PNL-binding in many tumor cells, occasionally with a targetoid pattern (*arrow*). PO-PNL, × 330

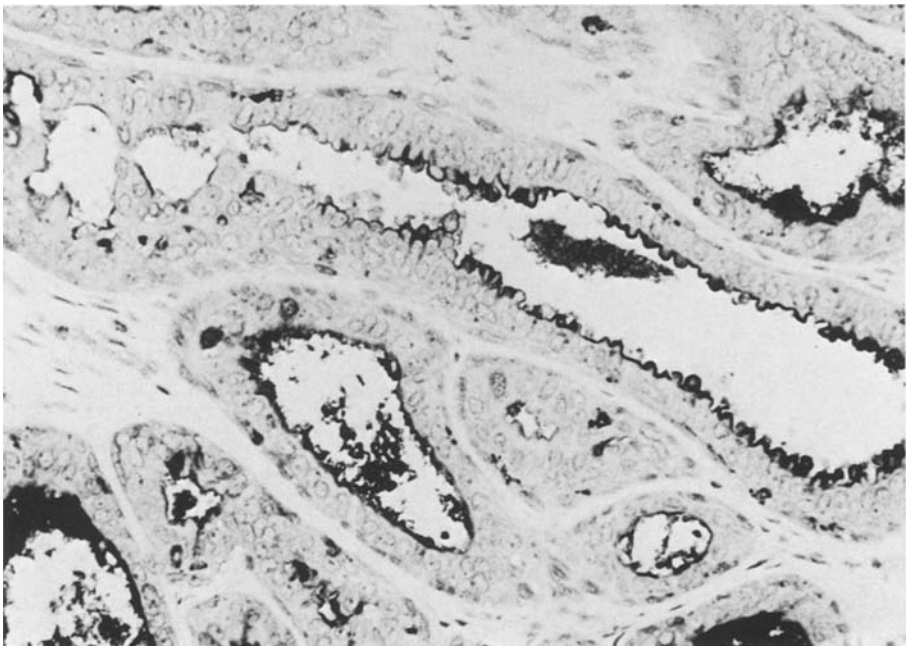

Fig. 5. Tubular carcinoma with apical-luminal PNL-staining. PO-PNL, × 330

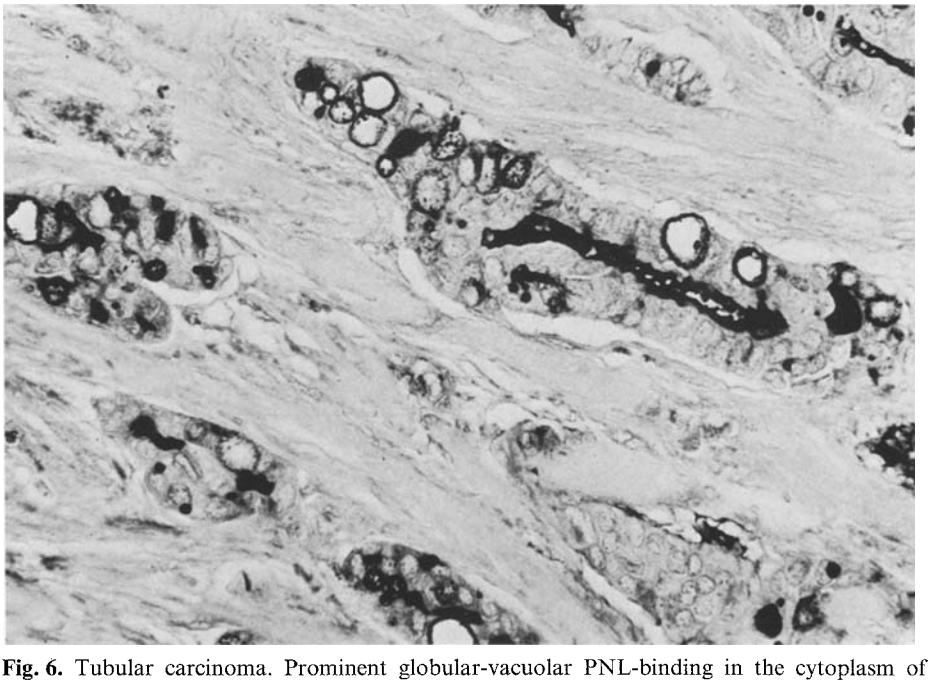

Fig. 6. Tubular carcinoma. Prominent globular-vacuolar PNL-binding in the cytoplasm of tumor cells in addition to apical-luminal staining. PO-PNL, × 330

Table 1. Types of PNL-staining in human mammary cancer

1. *diffuse* staining
   a) a *part* of the cytoplasm; **b)** the *whole* cytoplasm
2. *granular-globular* staining
   a) a part of the cytoplasm; **b)** the whole cytoplasm
3. *vacuolar* reactions
   a) *several small* vacuoles; **b)** *single large* vacuole; **c)** *targetoid* pattern
4. *combinations* of 1 to 3

Table 2. PNL-histochemistry and tumor type

Tumor type	PNL-histochemistry						*N*
	<5%[a]		6–25%		>25%		
Invasive Lobular Carcinoma	2	7%	8	30%	17	63%	27
Invasive Ductal Carcinoma (NOS)	8	21%	12	32%	18	47%	38
Tubular Carcinoma	3	20%	2	13%	10	67%	15
Other types[b]	7	18%	14	36%	18	46%	39
Sum.	20	17%	36	30%	63	53	119

[a] Including 3 cases without any PNL-binding
[b] This group contains the following subunits: infiltrating comedocarcinoma, cribriform carcinoma, apocrine carcinoma, lipid-rich carcinoma, carcinoma of uncertain type, mixtures of ILC and IDC

Table 3. Percentage of globular-vacuolar reactions of PNL-positive tumor cells in relation to tumor type

Tumor type	% globular-vakuolar						*N*
	<5%[a]		6–25%		>25%		
Invasive Lobular Carcinoma	4	15%	8	30%	15	55%	27
Invasive Ductal Carcinoma (NOS)	29	76%	9	24%	0	0%	38
Tubular Carcinoma	6	40%	6	40%	3	20%	15
Sum.	39	49%	23	29%	18	22%	80

[a] Including 3 cases without any PNL-binding

found to be relevant – especially in relation to tumor type and in predicting the receptor status.

As can be seen in Table 2 ILC and tubular carcinomas have a higher number of PNL-positive tumor cells. Among the different staining patterns, the globular-vacuolar type of staining shows a close relationship to the type of carcinoma.

Table 4. Relationship between PNL-binding and histological grading

Grading	PNL-binding tumor cells			N
	<5%[a]	6–25%	>25%	
I	5 15%	10 30%	19 55%	34
II	10 16%	22 34%	32 50%	64
III	4 18%	9 41%	9 41%	22
Sum.	19 16%	41 34%	60 50%	120

[a] Including 3 cases without any PNL-binding

Table 5. Relationship between PNL-histochemistry and staging

Stage	PNL-binding tumor cells			N
	<5%[a]	6–25%	>25%	
I	0 0%	3 33%	6 67%	9
II	11 28%	11 28%	17 44%	39
III	2 4%	20 38%	30 58%	52
IV	6 30%	3 15%	11 55%	20
Sum.	19 16%	37 31%	64 53%	120

[a] Included are 3 cases without any PNL-binding

Table 6. Relationship between PNL-histochemistry and hormone receptor status in 120 breast carcinomas. More than 10 nmol receptor/mg protein is named positive (E+ or P+)

Receptor status		PNL-binding tumor cells		N
		<25%	>25%	
Estrogen + Progesterone +		22 34%	42 66%	64
Estrogen + Progesterone −		10 43%	13 57%	23
Estrogen − Progesterone +		4 50%	4 50%	8
Estrogen − Progesterone −		16 64%	9 36%	25
Sum.		52 43%	68 57%	120

Table 3 lists the percentage of occurrence of globular-vacuolar PNL-reaction in relation to the number of PNL-positive tumor cells. There was a statistically significant (Chi-square 35.2, p lower 0.1%) higher percentage of globular-vacuolar (over 25%) reactions in ILC as compared to IDC and tubular carcinomas. Significant differences were also found between

IDC (NOS) and tubular carcinoma on the one hand and ILC on the other hand (Table 3).

These figures given for tubular carcinoma lie between those of lobular and ductal carcinomas.

Although the PNL-binding appears to be independent of histological grading, there is a tendency to show the occurrence of a greater number of PNL-positive tumors at 25% level with grading I and II (Table 4). No correlation between PNL-binding and pathological staging could be detected (Table 5).

The estrogen (E) and progesteron (P) receptor content was determined for all 120 carcinomas. Values of 10 nmol receptor/mg protein or more were named positive (E+ or P+), values under 10 negative (E- or P-). The relationship between PNL-histochemistry and receptor content is presented in Table 6. Of 64 E+P+ cases, 42 (65.6%) revealed a PNL-positive reaction at a 25 percentage level (e.g. the number of PNL-positive tumor cells exceedes 25% of the cell population), whereas only 36% of E−P− cases showed PNL-positivity at the same level. The differences between these groups are statistically significant (p lower 0.05).

No such relationship could be found in the E+P− and in the E−P+ group. However even in the E+P+ and E−P− groups a large number of cases with controversal hormone receptor and PNL-status was found. 22 of 64 E and P positive cases (34%) proved to be negative in PNL-staining. Further 9 of 25 E and P negative cases (36%) revealed a PNL-positivity, 5 of them with more than 50% PNL-positive tumor cells.

Discussion

The TFAg is a precursor of the MN blood group antigens (Springer et al. 1975). The immunodominant determinant of this antigen is the terminal β-D-galactosyl-(1-3)-N-acetyl-D-galactosamine. This disacharide is the binding site of peanut-lectin (PNL). Several authors have shown that PNL-binding sites are expressed patchily on the luminal surface of normal breast epithelium and in the secreted intraluminal material, but that they are mainly expressed intracytoplasmatically in breast carcinomas (Springer et al. 1975; Newman et al. 1979; Howard et al. 1981; Klein et al. 1979; Stegner et al. 1981; Seitz et al. 1983). This report on 120 breast carcinomas presents a detailed investigation of the relationships between PNL-histochemistry, tumor type, histological grading, pathological staging, and biochemical receptor status. Overall this study uncovered a notable correlation between PNL-binding on the one hand and tumor type and receptor status on the other. It was not possible to show a relationship between PNL-histochemistry, the histological grade and the pathological staging of the tumors.

In accordance with previous studies (see literature above) we found that in normal breast epithelium PNL-binding was localized predominantly at the apical-luminal surface and in intraluminal material. Overall, there was a great increase in unmasked PNL-binding sites in carcinomas, when com-

pared with normal breast tissues. Only 2.5% of breast carcinomas were completely devoid of any PNL-binding.

Expression of 3 types of cytoplasmatic staining patterns for PNL were disclosed (Table 1): these consisted of a diffuse, granular to globular, and vacuolar reaction, covering an area that might extent over a part to the whole of the cytoplasm. In some tumors a linear reaction at the cell periphery was mainly found (membrane?, glycocalix?).

Carcinomas with a tubular and/or cribriform differentiation generally showed an increase in the number of PNL-binding sites after pretreatment of sections with neuraminidase in contrast to ILC and IDC (NOS), thus demonstrating the presence of some sialic-acid masked disacharides.

A comparison of PNL-histochemistry with tumor types showed that only the lobular-vacuolar PNL-pattern revealed a tumour type specificity at a 25% discriminating point. Preferential lobular-vacuolar PNL-pattern occured in ILC and to a lesser degree in tubular carcinomas. These findings are in aggreement with results obtained by conventional AB/PAS stains in lobular carcinomas (Gad and Azzopardi 1975; Martinez and Azzopardi 1975). However, in contrary to the latter, the PNL-histochemistry is far more sensitive: 97.5% PNL-positivity as opposed to 65% of PAS-positivity in our material. A similar figure of 54% of PAS-positivity of 904 breast carcinomas was reported by Fisher et al. (1975). These differences between PAS- and PNL-staining results are probably attributable to the fact that a number of β-D-galactosyl-(1-3)-N-acetyl-D-galactosamine containing glycoproteins can only be detected by the more sensitive PNL-histochemistry (Klein et al. 1979b).

On the strength of their morpho-functional findings Eusebi et al. (1979) suggested that tubular and lobular carcinomas can be regarded as two distinct variants of the same entity. Our findings in PNL-histochemistry, together with the negative CEA-IH in both tubular and ILC (Böcker et al. to be published), is regarded as a further evidence in favour of this concept.

Some authors suggested the use of PNL-binding properties in predicting the steroid receptor status (Klein et al. 1981). It became evident in the present analysis, that a figure of 25% of PNL-positive cells was the most relevant discriminating point for the biochemical receptor status of breast carcinomas. A comparison of PNL-positivity of breast carcinomas at this 25% level with the receptor status revealed that out of 64 E+P+ carcinomas 42 (66%) showed PNL-positivity in contrast with only 9 of 25 E−P− cases (36%). Corresponding figures (68% versus 23%) were reported by Klein et al. (1981). However in contrast to the findings of these authors we detected no differences in our E+P− and E−P+ cases regarding PNL-positivity. Thus it is tempting to suggest that there might be a correlation between hormone receptor status and the expression of PNL-receptors (binding sites). However it is far from certain that PNL-associated secretory phenomena are a proof of a hormone modulated breast carcinoma. Much more information is still needed to determine which is the basic mechanism controlling these phenomena. It cannot be excluded that hormone receptors and PNL-associated secretory phenomena are merely expressions of differ-

entiation processes independent of each other. The large number of carcinomas with controversial biochemical receptor status and PNL-positivity may speak in favour of such a hypothesis.

The histological grade of the tumor has previously been proved to be a predictive factor for the receptor content. If it is accepted, that high grading is a sign of poor differentiation, low percentages of steroid receptor- and PNL-positivity should result. The later agrees with our finding that grade I and II carcinomas showed a higher percentage of PNL-positivity than grade III tumors, however the figures were not statistically significant. No correlation was apparent between PNL-binding sites and pathological staging.

In conclusion, the present study discloses that PNL-histochemistry shows different expressions of binding sites in lobular and ductal carcinomas. There is a statistically significant relation between PNL-positivity at 25% level and the receptor status. However, the results of PNL-histochemistry resulted in classification functions that correctly predicted the hormone receptor status in 60–65% of the cases at the most. In addition, the findings of controversal PNL-status and hormone receptor status illustrates the difficulty of lectin binding in biological terms. The nature of these differences and their possible significance has yet to be explored.

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References

Azzopardi JG (1979) Problems in breast pathology. WB Saunders Comp London, Philadelphia, Toronto

Bässler R (1978) Pathologie der Brustdrüse. Springer, Berlin, Heidelberg, New York

Bloom HJG, Richardson WW (1957) Histological grading and prognosis in breast cancer. Brit J Cancer 11:359–377

van Bogaert J-J, Maldague P (1980) Infiltrating lobular carcinoma of the femal breast: Deviations from usual histopathologic appearance. Cancer 45:979–984

Claus G, Ebner H (1977) Grundlagen der Statistik für Psychologen, Pädagogen und Soziologen. Verlag Harri Deutsch, Frankfurt a M

Cooper HS (1982) Peanut lectin-binding sites in large bowel carcinoma. Lab Investig 47:383–390

Dixon JM, Anderson TJ, Page DL, Lee D, Duffy SW (1982) Infiltrating lobular carcinoma of the breast. Histopath 6:149–161

EORTC Breast Co-operativ Group (1980) Revision of the Standards for the Assessment of Hormone Receptors in Human Breast Cancer. Europ J Cancer 16:1513

Eusebi V, Pich A, Machiorlati E, Bussolati G (1977) Morphofunctional differentiation in lobular carcinoma of the breast. Histopath 1:301–314

Fechner RE (1975) Histologic variants of infiltrating lobular carcinoma of the breast. Human Pathol 6:373–378

Fisher ER, Gregorio RM, Fisher B (1975) The pathology of invasive breast cancer. A syllabus derived from the findings of national surgical adjuvant breast project (protocol No 4). Cancer 36:1–83

Fisher ER, Gregorio RM, Fisher B (1975) The pathology of invasive breast cancer. A syllabus derived from findings of the national surgical adjuvant breast project (protocol No 4). Cancer 36:1–84

Gad A, Azzopardi JG (1975) Lobular carcinoma of the breast: a special variant of mucin secreting carcinoma. J clin Pathol 28:711–716

Howard DR, Batsakis JG (1980) Cytostructural localisation of a tumor-associated antigen. Science 210:201–203

Howard DR, Ferguson P, Batsakis JG (1981) Carcinoma-associated cytostructural antigen alteration detected by lectin binding. Cancer 47:2872–2877

Klein PJ, Citoler RA, Newman RA, Uhlenbruck G, Schäfer H-E, Fischer R (1979a) Die Bedeutung von Lectin-Receptoren für das Carcinoma lobulare in situ (CLIS) der Mamma. Verh Dtsch Ges Path 63:591–596

Klein PJ, Newman RA, Müller P, Uhlenbruck G, Citoler P, Schäfer HE, Lennartz KJ, Fischer R (1979b) The presence and significance of the Thomsen-Friedenreich antigen in mammary gland. II. Its topochemistry in normal, hyperplastic and carcinoma tissue of the breast. J Cancer Res Clin Oncol 93:205–214

Klein PJ, Newman RA, Müller P, Uhlenbruck G, Schäfer HE, Lennarzt KJ, Fischer R (1978) Histochemical methods for the demonstration of Thomsen-Friedenreich antigen in cell suspensions and soft tissue sections. Klin Wochenschr 56:761–765

Klein PJ, Vierbuchen M, Schulz K-D, Würz H, Citoler P, Uhlenbruck G, Ortmann M, Fischer R (1981) Hormonabhängige Lectin-Bindungsstellen. II. Lectin-Rezeptoren als Indicator einer Hormonsensibilität von Mammacarcinomen. In: Uhlenbruck G, Wintzer G (eds) Symposion Carcinoembryonales Antigen (CEA) und andere Tumormarker, Tumor Diagnostic Verlag, Leonberg

Lotan R, Skutelsky E, Danon D, Sharon N (1975) The purification, composition, and specifity of the anti-T lectin from peanut (Arachis hypogeae). J Biol Chem 250:8518–8523

Martinez V, Azzopardi JG (1979) Invasive lobular Carcinoma of the Breast: incidence and variants. Histopathology 3:467–488

McDivitt RW (1978) Breast carcinoma. Human Pathol 9:3–21

Newman RA, Klein PJ, Rudland PS (1979) Binding of peanut lectin to breast epithelium, human carcinomas, and a cultured rat mammary stem cell: use of lectin as a marker of mammary differentiation. JNCI 63:1339–1342

Newman RA, Klein PJ, Uhlenbruck G, Citoler P, Karduck D (1979) The presence and significance of the Thomsen-Friedenreich antigen in breast cancer. I. Serological Studies. J Cancer Res Clin Oncol 93:181–188

Reisner Y-B, Rosenthal E, Sharon N, Ramot B (1979) Interaction of peanut agglutinin with normal human lymphocytes and with leucemic cells. Proc Natl Acad Sci USA 76:447

Schmidt-Gollwitzer M, Eiletz J, Genz T, Pollow K (1979) Determination of estradiol, estrone and progesterone in serum and myometrium: Correlation with the content of sex steroid receptors and 17β-hydroxysteroid dehydrogenase activity throughout the menstrual cycle. J Clin Endocrinol Metabol 49:370

Seitz RC, Fischer K, Stegner H-E, Poschmann A (1983) Detection of metastatic breast carcinoma cells by immunofluorescent demonstration of Thomsen-Friedenreich (TF)-antigen. Cancer (in press, accepted July 1983)

Springer GF, Desai PR, Banatwala I (1975) Blood group MN antigens and precursors in normal and malignant human breast glandular tissue. J Natl Cancer Inst 54:335–339

Stegner H-E, Fischer K, Poschmann A (1981) Immunhistochemical localisation of Thomsen-Friedenreich antigen in normal and malignant breast tissue using peroxidase-antiperoxidase technique, Tumor Diagn 3:127–130

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