Diffuse Lymphocyte-predominant Hodgkin's Disease (Diffuse Paragranuloma)

A Variant of the B-cell–Derived Nodular Type

M.-L. Hansmann,* H. Stein,† F. Dallenbach,† and C. Fellbaum‡

From the Department of Pathology, University of Kiel*, Kiel; the Department of Pathology, Free University of Berlin, Berlint; and the Department of Pathology, Technical University of Munich, School of Medicine, Munich,‡ Federal Republic of Germany

Lymph node sections from 10 cases of mixed nodular/diffuse and 10 cases of completely diffuse lymphocyte-predominant Hodgkin's disease (LPHD) were immunophenotyped. The results obtained were compared with those of nodular LPHD (nodular paragranuloma). In conventional stains, nodular/diffuse LPHD differed from diffuse LPHD in the presence of nodularity, which can be best demonstrated with silver impregnation. Immunobistologic analysis showed a correlation of the difference in nodularity with the presence or absence and pattern of follicular dendritic cell (FDC) meshwork, ie, a relatively sharply defined and large spherical meshwork was present in nodular areas of nodular/diffuse LPHD, whereas FDCs were either absent or present in a diffuse, ill-defined mesbwork, usually of small size, in the diffuse zones of nodular/diffuse LPHD and in diffuse LPHD. The amount of FDC meshwork corresponded roughly to the number of reactive B cells and T cells, meaning that in diffuse areas significantly fewer B cells and more T cells were observed than in nodular areas. The immunohistologic analysis also showed that the antigen profile (positivity with the monoclonal Bcell marker L26 in the majority [14/20] of cases and negativity for CD15 in all but one of 20 cases) of the tumor cells in both nodular/diffuse LPHD and diffuse LPHD were comparable while it was different from the antigen profile ($L26^-$ and $CD15^+$) in most cases of nodular sclerosis and mixed cellularity types of HD. This suggests that the considered subtypes of LPHD differ mainly in FDC pattern, but not in origin and nature of the tumor cells. This further justifies assignment of the above-mentioned LPHD subtypes to the category paragranuloma (LPHD). (Am J Pathol 1991, 138:29-36)

The classification of Hodgkin's disease (HD) into four types is a result of the Rye Conference.¹ This classification has since been commonly accepted and applied. Further studies suggest that the inclusion of only one lymphocytepredominant (LP) type of HD in the Rye classification does not reflect the true phenotypic spectrum of lymphocytepredominant HD (LPHD) but rather represents a pragmatic compromise. The paragranuloma, ie, LPHD, originally included in the Jackson and Parker classification,² was divided into a nodular and a diffuse type in the classification of Lukes et al.³ The nodular variant has been investigated in detail and many arguments in favor of a B-cell neoplasia have been raised.⁴⁻⁹ Until now, however, there have been no immunohistologic studies concentrating on the diffuse variant of paragranuloma. In addition, a third variant of LPHD essentially belonging to the mixed cellularity type of Hodgkin's disease (MCHD) has been described by Lennert and Mohri.¹⁰ According to morphologic data and immunohistochemical studies,¹¹ this variant belongs to MCHD rather than to paragranuloma.

The question of which cellular components of the paragranulomas form the basis of the histologic difference between nodular/diffuse paragranuloma and diffuse paragranuloma was the subject of this study. To elucidate this question, we investigated cases of paragranuloma showing a mixture of nodular/diffuse areas within one lymph node, as well as completely diffuse variants. The cellular components were analyzed by immunohistochemical methods using antibodies specific for lymphocytes, follicular dendritic cells (FDC), L&H cells,¹ and Hodgkin and Sternberg–Reed (HSR) cells. Studies such

Supported by the Deutsche Forschungsgemeinschaft (Project 1284/1-4), and the Deutsche Krebshilfe Dr. Mildred Scheel-Stiftung.

Accepted for publication August 22, 1990.

Address reprint requests to M.-L. Hansmann, MD, Department of Pathology, University of Cologne, Joseph-Stelzmannstr. 9, D-5000 Cologne, Federal Republic of Germany.

as this were hampered in the past by the fact that only paraffin sections, and no frozen sections, of diffuse paragranuloma and nodular/diffuse paragranuloma cases were available. The present study was made possible by the recent generation of two new monoclonal antibodies (MAbs), 2G7¹² and 1F8,¹² recognizing a formalin-resistant epitope on the CD21 molecule that is strongly and nearly solely expressed on FDCs,¹³ and the MAb L26, strongly reactive with the B-cell-associated antigen CD20, which is expressed on B blasts and tumor cells in most cases of nodular paragranuloma.¹⁴⁻¹⁶

Materials and Methods

Paraffin sections from 20 cases of paragranuloma were stained with hematoxylin and eosin (H&E), Giemsa, periodic acid-Schiff (PAS), and Gomori's silver impregnation technique. For immunohistologic labeling, deparaffinized sections were incubated with the primary monoclonal antibodies listed in Table 1. Visualization of the antigenic sites was achieved with employment of the alkaline phosphatase and monoclonal anti-alkaline phosphatase (APAAP) method of Cordell et al.¹⁷

Results

The diagnosis of paragranuloma was primarily based on morphologic criteria (low number of classic HSR cells, occurrence of typical L&H variants of Hodgkin cells, high number of small lymphocytes, no relevant numbers of intermingled eosinophils or plasma cells)^{1,10} and confirmed by additional immunostaining with the MAbs L26, CD30,²⁷ and CD15.

Nodular/Diffuse Paragranuloma

In 10 cases, the lymph node biopsies showed a partially nodular, partially diffuse pattern. In these cases, approximately half of the lymph node sections were composed of nodules dominated by small lymphocytes, whereas the other half showed a diffuse growth pattern, as is best seen in the silver staining (Figure 1a). In the nodular areas, one could see a few epithelioid cell clusters, remnants of germinal centers, and occasionally L&H and HSR cells. Between the nodules there were areas rich in epithelioid venules composed mainly of lymphocytes. Small lymphocytes dominated in the diffuse areas as well, surrounding epithelioid cell groups, histiocytes, L&H, and HSR cells.

Immunohistologically, the MAb 2G7 detected FDCs in the nodular as well as the diffuse areas. The appearance and distribution of FDCs in these areas was, however,

Table 1.	Primary	Monoclonal	Antibodies	(MAb)
----------	---------	------------	------------	-------

•		
MAb	Specificity	Source/reference
Ki-B3	Subtype of leukocyte common antigen predominantly expressed on B cells	Pathol. Inst., Kiel Hansmann et al ⁷ Feller et al ²⁶
L26	pan B cell	Dakopatts
MT1 (CD43)	pan T cell, some B-	Laboserv
	cell lymphomas, granulocytes, macrophages	Diagnostika, FRG
UCHL1 (CD45RO)	T cells, some B-cell lymphomas, granulocytes, and macro- phages	Dakopatts
Ber-H2 (CD30)	Formalin-resistant epitope of CD30- antigen, Hodgkin cells	Dakopatts Schwarting et al ²⁷
2G7 (CD21)	Follicular dendritic cells	Petzer et al ¹²
1F8 (CD21)	Follicular dendritic cells	Petzer et al ¹²
Leu-M1 (CD15)	Myeloid cells, many Hodgkin cells	Becton Dickinsen

quite different. In the nodular areas, medium-sized to large meshworks of FDCs could be seen (Figure 1b; Table 2). The nodules were more or less demarcated from the interfollicular areas. The FDCs appeared to surround single cells or small clusters of lymphoid cells.

Occasionally L&H or HSR cells were in direct contact with the FDC processes (Figure 1b, inset). The appearance of medium-sized to large nodular FDC meshworks showed a direct correlation to that of the nodules demarcated by reticulin fibers visualized in the silver staining.

Compared with these nodular areas of the lymph nodes, the diffuse areas showed a quite different FDC distribution. In the diffuse areas, FDCs formed only small and mostly ill-defined meshworks. In these areas, the FDC processes seemed thinner and were not situated so closely together as in the nodular areas. The meshworks occasionally showed large holes containing lymphoid cells that apparently had no contact to the FDC processes.

B cells were stained with the pan-B MAbs Ki-B3^{7,26} and L26. B cells could be found in large clusters in the FDCrich nodules (Figure 2; Table 2). A few UCHL-1⁺ and MT1⁺ T cells could also be seen in these nodular areas (Table 2). In contrast, the diffuse areas contained only low or occasionally moderate amounts of Ki-B3⁺ and L26⁺ lymphocytes (Figure 3a; Table 2). Clusters of B cells could be detected in those areas containing remnants of FDC meshworks. Around these small foci of FDC and B cells, UCHL-1⁺ (Figure 3b) and MT1⁺ T cells were seen (Table 2).



Figure 1. a: Lympb node section of partly nodular, partly diffuse paragranuloma. On the right side nodular, on the left side diffuse areas (Silver impregnation, ×56). b: Immunobistochemical demonstration of follicular dendritic cells in partly nodular, partly diffuse paragranuloma. On the right side large nodules, consisting of follicular dendritic cells (FDC). On the left side in the diffuse area small clusters of FDC. Paraffin section, APAAP metbod, MAb 2G7, ×56. Inset: LGH cell in direct contact with follicular dendritic cell (APAAP metbod, MAb 2G7, paraffin section, ×350).

Diffuse Paragranuloma

In contrast to nodular/diffuse paragranuloma, silver stainings of diffuse paragranuloma sections (Figure 4a) showed no nodules surrounded by reticulin fibers. The 10 cases of diffuse paragranuloma showed a picture very similar to the diffuse areas of nodular/diffuse paragranuloma with regard to cell types and their distribution. Small lymphocytes also dominated in these cases. Occasionally, one could see some germinal center cells, as well as L&H and HSR cells. Many macrophages and small clusters of epithelioid cells could also be seen. The immunohistologic findings in the cases of diffuse paragranuloma were quite similar to those in diffuse areas in the cases of nodular/ diffuse paragranuloma described above. Follicular dendritic cells formed small meshworks with loosely arranged, relatively thin processes (Figure 4b). In the FDC foci, a small to moderate number of B cells could be demonstrated with the MAbs Ki-B3 and L26, whereas T cells (UCHL-1⁺, MT1⁺) dominated in diffuse areas.

Immunophenotype of L&H and HSR Cells

The immunophenotypes of L&H and HSR cells were identical in nodular and diffuse areas in cases of nodular/ diffuse paragranuloma. In nodular/diffuse paragranuloma, L&H and HSR cells reacted with the B-cell MAb Ki-B3 in one case and with L26 in 6 of 10 cases (Table 3), whereas they were negative for CD15 (Leu-M1). In sections stained with the T-cell MAbs UCHL-1 and MT1, the tumor cells were always negative, but were often surrounded by T lymphocytes. In 4 of 10 cases, L&H and HSR cells showed a positive reaction with the CD30 MAb Ber-H2. The reaction product of all antibodies applied was located mainly on the cell surface. The Ber-H2 (CD30) MAb occasionally

Nodular and diffuse paragranuloma $(n = 10)$	Nodular area Diffuse area		Diffuse paragranuloma (n = 10)	
FDC				
Small meshworks without sharp border	_	++	++	
Medium-sized to large meshworks	++	_	-	
B cells				
Ki-B3+	+++	+/++	+/++	
L26+	++	+/++	+/++	
T cells				
$UCHL1 + (CD45RO^{+})$	+	++/+++	++/+++	
MT1+ (CD43 ⁺)	+	++/+++	++/+++	

Table 2. Distribution of Follicular Dendritic Cells (FDC) Immunostained with MAb 2G7 and 1F8 and Number of Band T Cells in Nodular and Diffuse Paragranuloma and in Diffuse Paragranuloma

showed an intracytoplasmic reaction in the Golgi region of L&H and HSR cells.

In diffuse paragranuloma cases, ie, with completely diffuse growth pattern, the reaction of L&H and HSR cells was similar to that described above (Table 3). A positive staining with MAb Ki-B3 occurred in three cases (Figure 5), and with L26 in 8 of 10 cases (Figure 6). L&H and HSR cells were always negative with MAbs directed against T cells. A positive reaction with the MAb Ber-H2 (CD30) was seen in 2 of 10 cases. In 1 of 10 cases, a small portion of the HSR cells showed a weak paranuclear positivity with MAb Leu-M1 (CD15).

Discussion

The present study shows that B-cell antigen expression (especially L26, and less often Ki-B3) is usually found on Hodgkin cells in the different subtypes of Hodgkin's disease such as nodular/diffuse and purely diffuse paragranuloma. Although B-cell properties of Hodgkin cells are usually confined to the paragranuloma subtypes and are not expressed in nodular sclerosis and the mixed cellularity type, there are exceptions. First, there are cases of nodular sclerosis and mixed cellularity type in which Hodakin cells show positive immunoreactions with B-cell markers.^{18,19} Second, in 40% of typical cases of nodular and diffuse paragranuloma and in 20% of the cases of diffuse paragranuloma in this study, the B-cell lineage of the Hodgkin cells could not be confirmed immunohistochemically. Absence of L26 positivity does not necessarily speak against a B-cell nature, however, because it is well known that B-cell lymphomas can lack a typical B-cell antigen on their cell membranes during tumor cell differentiation. The L26-negative cases were included in this study because the classical morphologic criteria of paragranuloma were fulfilled. These cases did not show the morphologic features of the lymphocyte-rich variant of mixed cellularity type, which may be difficult to distinguish from diffuse paragranuloma in the differential diagnosis. The morphologic features of the lymphocyte-rich variant of mixed cellularity type are: a larger number of classic HSR cells, the lack of typical L&H cells, and a larger number of intermingled eosinophils and plasma cells.

Hodgkin cells in lymph nodes with nodular/diffuse and completely diffuse paragranuloma were nearly identical in CD15 expression. CD15 (Leu-M1) is detectable in Hodgkin's cells in most cases of the mixed and nodular sclerosing types of Hodgkin's disease but usually absent in paragranuloma. There are, however, exceptions that account for approximately 15% of the cases of Hodgkin's disease of nodular paragranuloma type.¹¹ In the present study, we found one exception of CD15-positive Hodgkin cells in a case of diffuse paragranuloma. Nonetheless, CD15 proved to be of considerable aid in distinguishing between cases of paragranuloma and lymphocyte-rich mixed type of Hodgkin's disease (which shows CD15⁺ Hodgkin cells), the most important differential diagnosis in paragranuloma¹¹ (for a review of the literature, see Hall and D'Ardenne²⁰).

The above findings suggest that the tumor cells in nodular, nodular/diffuse paragranuloma and diffuse paragranuloma are B cell derived and closely related. They furthermore confirm the justification to group these Hodgkin's disease subtypes into the categories paragranuloma or lymphocyte predominance, separating them from the other types of HD. The close relationship of the tumor cells in LP subtypes raises the question of the difference between these subtypes. According to Regula et al,²¹ prognosis differs between nodular paragranuloma and diffuse paragranuloma, ie, the patients with diffuse paragranuloma showed significantly fewer relapses and a shorter overall survival time than those with nodular paragranuloma. In our clinical study on LPHD cases, however, we found a similarly favorable prognosis in cases of both nodular paragranuloma and diffuse paragranuloma.22,23 This finding further supports the assumption that, in principle, diffuse paragranuloma and nodular paragranuloma are variants of the same disease entity. Because patients

Figure 2. Nodular areas in paragranuloma showing large numbers of B cells (Ki-B3+) (APAAP method, paraffin section, ×56).



Figure 3. a: Small clusters and solitary B cells (Ki-B3+) in diffuse parts of paragranuloma (APAAP metbod, paraffin section, \times 56). b: Diffuse parts of paragranuloma. The infiltrate contains many T lymphocytes positively immunostained with the monoclonal antibody UCHL1 (APAAP metbod, paraffin section, \times 150).



Figure 4. a: Fiber network of diffuse paragranuloma (Silver impregnation, paraffin section, \times 56). b: Small clusters of follicular dendritic cells in diffuse paragranuloma demonstrated with the monoclonal antibody 2G7 (APAAP method, paraffin section, \times 56).

with diffuse paragranuloma dominated in the study of Regula et al,²¹ whereas in our series of LPHD cases, patients with diffuse paragranuloma were very rare, it is conceivable that Regula et al included lymphocyte-rich cases of MCHD in their series, whereas we did not. This might explain the different prognoses reported in the two studies. At present, however, this conclusion must remain an assumption, as Regula et al did not perform any immunohistologic investigations and based the diagnosis of LPHD on morphologic criteria only.

In conventional stains, the only difference between diffuse paragranuloma and nodular paragranuloma is the presence or absence of nodularity or a mixture of both. Immunostaining of FDCs demonstrated a close correlation

Table 3.	Phenotype of L&H, Hodgkin-,	and Sternberg-Reed Cells,
Defined	by Monoclonal Antibodies in	Paraffin Sections

	Ki-B3	L26	UCHL1 CD45RO	MT1 CD43	Ber-H2 CD30	Leu-M1 CD15
Nodular and diffuse paragranuloma (n = 10)	1/10	6/10	0/10	0/10	4/10	0/10
Diffuse paragranuloma (n = 10)	3/10	8/10	0/10	0/10	2/10	1/10



Figure 5. Diffuse paragranuloma. L&H cell positively stained with the monoclonal antibody Ki-B3, also small lympbocytes showing a positive reaction. Small lympbocytes intimately surrounding L&H cells are obviously T cells (Ki-B3–) (APAAP metbod, paraffin section, $\times 860$).

between the degree of nodularity, or its absence, and the FDC meshwork pattern; ie, a relatively sharply defined and large spherical meshwork was present in nodular paragranuloma (perhaps indicating a relationship to preexisting progressively transformed germinal centers), whereas either no FDCs or only a diffuse, ill-defined meshwork was visible in some areas of nodular/diffuse and in diffuse paragranuloma.

The FDC meshwork correlated roughly with the number of B cells in the tumor: the denser and more nodular the FDC meshworks were, the higher was the proportion of B cells. In other words, the diffuse cases contained considerably fewer B cells and relatively more T lymphocytes. In contrast, an even smaller number of B cells and a larger number of T cells are found in MCHD with a large content of lymphocytes (23% of B-cell areas in tumors of diffuse paragranuloma type versus 15% of B-cell areas in lymphocyte-rich variant of mixed cellularity type in individual cases).

The FDC network pattern in HD of other types than paragranuloma is known to vary greatly, ranging from large FDC networks to small foci to complete absence of these cells.¹⁶ Even large FDC networks typical for nodular paragranuloma are not specific but can also be seen in cases of the nodular sclerosing type.²⁴

In summary, nodular paragranuloma, nodular/diffuse paragranuloma, and diffuse paragranuloma have identical tumor cells in common but differ in the pattern of FDC networks. A convincing explanation for this is the hypothesis that the tumor cells themselves, by secreting cytokines, determine the number and types of intermingled nonmalignant cells. This also might apply to the expanded

Figure 6. L&H cells showing a positive reaction with the monoclonal antibody L26. The reaction product is mainly located on the cell surface (APAAP method, paraffin section, $\times 860$).



FDC meshworks present in angioimmunoblastic type of peripheral T-cell lymphoma.²⁵ If true, this would mean that the tumor cells found in the cases of various LP types differ mainly in the number or types or mixtures of cytokines they secrete. This concept postulates the existence of cytokines that can induce the presence of FDC meshwork as well as the secretion of large quantities of FDCinducing cytokines by tumor cells in cases of nodular paragranuloma and not in cases of diffuse paragranuloma without FDCs.

Acknowledgment

This work is dedicated to Professor Karl Lennert, who has entered retirement after more than 27 years of active lymphoma research in the Department of Pathology at the University of Kiel, West Germany.

References

- Lukes RJ, Butler JJ, Hicks EB: Natural history of Hodgkin's disease as related to its pathologic picture. Cancer 1966b, 19:317–344
- Jackson H Jr, Parker F Jr: Hodgkin's Disease and Allied Disorders. New York, Oxford University Press, 1947
- Lukes RJ, Craver LF, Hall TC, Rappaport H, Ruben P: Report of the nomenclature committee. Cancer Res 1966, 26:1311
- Poppema S, Kaiserling E, Lennert K: Hodgkin's disease with lymphocytic predominance, nodular type (nodular paragranuloma) and progressively transformed germinal centers—A cytohistological study. Histopathology 1979, 3:295–308
- Poppera S: The diversity of the immunohistological staining pattern of Sternberg-Reed cells. J Histochem Cytochem 1980, 28:788–791
- Pinkus GS, Said JW: Hodgkin's disease, lymphocyte predominance type, nodular: A distinct entity? Am J Pathol 1985, 118:1–6
- Hansmann ML, Wacker HH, Radzun HJ: Paragranuloma is a variant of Hodgkin's disease with predominance of B cells. Virchows Arch [A] 1986, 409:171–181
- Stein H, Hansmann ML, Lennert K, Brandtzaeg P, Gatter KC, Mason DY: Reed-Sternberg and Hodgkin cells in lymphocyte-predominant Hodgkin's disease of nodular subtype contain J chain. Am J Clin Pathol 1986, 86:292–297
- Timens W, Visser L, Poppema S: Nodular lymphocyte predominance type of Hodgkin's disease is a germinal center lymphoma. Lab Invest 1986, 54:457–461
- Lennert K, Mohri N: Histologische Klassifizierung und Vorkommen des M. Hodgkin. Internist 1974, 15:57–65
- Hansmann ML, Fellbaum Ch, Hui PK, Zwingers T: Correlation of content of B cells and Leu7-positive cells with subtype and stage in Hodgkin's disease of lymphocyte predominance type. J Cancer Res Clin Oncol 1988, 114:405–410
- Petzer AJ, Schulz TF, Stauder R, Eigentler A, Myones BL, Dierich MP: Structural and functional analysis of CR2/EBV receptor by means of monoclonal antibodies and limited tryptic digestion. J Immunol 1988, 63:47–53
- 13. Stein H, Dallenbach F, Schulz TF, Dienemann D, Meyer-

Hauser U, Pallesen G: Demonstration of follicular dendritic cells in routinely fixed paraffin sections from reactive and neoplastic lymphoid tissue with two monoclonal antibodies (2G7 and Ber-Mac DRC). (Manuscript in preparation)

- Ishii Y, Takami T, Yuasa H, Takei T, Kokai Y, Kikuchi K: Six distant antigen systems of human B cells as defined by monoclonal antibodies, Leukocyte Typing II. Vol 2, Human B Lymphocytes. Edited by EL Reinherz. BF Haynes, LM Nadler, ID Bernstein. Berlin, Springer-Verlag, 1986, pp 109– 119
- Cartun RW, Coles FB, Pastuszak WT: Utilization of monoclonal antibody L26 in the identification and confirmation of B-cell lymphomas. Am J Pathol 1987, 129:415–421
- Abdulaziz Z, Mason DY, Stein Y, Gatter KC, Nash JRG: An immunohistological study of the cellular constituents of Hodgkin's disease using a monoclonal antibody panel. Histopathology 1984, 8:1–25
- Cordell JL, Falini B, Erber WN, Gosh AK, Abdulaziz Z, MacDonald S, Pulford K, Stein H, Mason DY: Immunoenzymatic labeling of monoclonal antibodies using immune complexes of alkaline phosphatase and monoclonal antialkaline phosphatase (APAAP-complexes). J Histochem Cytochem 1984, 32:219–229
- Pinkus GS, Said JW: Hodgkin's disease, lymphocyte predominance type, nodular—Further evidence for a B cell derivation. Am J Pathol 1988, 133;211–217
- Hall PA, D'Ardenne AJ, Stansfeld AG: Paraffin section immunohistochemistry. II. Hodgkin's disease and large cell anaplastic (Kil) lymphoma. Histopathology 1988, 13:161–169
- Hall PA, D'Ardenne AJ: Value of CD15 immunostaining in diagnosing Hodgkin's disease: A review of published literature. J Clin Pathol 1987, 40:1298–1304
- Regula DP, Hoppe RT, Weiss LM: Nodular and diffuse types of lymphocyte predominance Hodgkin's disease. N Engl J Med 1988, 318:214–219
- Hansmann ML, Zwingers T, Böske A, Löffler H, Lennert K: Clinical features of nodular paragranuloma (Hodgkin's disease, lymphocyte predominance type, nodular). J Cancer Res Clin Oncol 1984, 108:321–330
- Hansmann ML, Lennert K: Der lymphozytenreiche M. Hodgkin. Verh Dtsch Ges Pathol 1985, 69:648
- Alavaikko MJ, Hansmann ML, Parwaresch MR, Nebendahl C, Lennert K: Follicular dendritic cells in Hodgkin's disease. Am J Clin Pathol (In press)
- Suchi T, Lennert K, Tu LY, Kikuchi M, Sato E, Stansfeld AG, Feller AC: Histopathology and immunohistochemistry of peripheral T cell lymphomas: A proposal for their classification. J Clin Pathol 1987, 40:995–1015
- Feller AC, Wacker HH, Moldenhauer G, Radzun HJ, Parwaresch MR: Monoclonal antibody Ki-B3 detects a formalin resistant antigen on normal and neoplastic B cells. Blood 1987, 70:629–636
- Schwarting R, Gerdes J, Stein H: Ber-H2—A new monoclonal antibody of the Ki-1 family for the detection of Hodgkin's disease in formaldehyde fixed tissue, Leukocyte Typing III. Edited by McMichael AJ, Beverly PCL, Cobbold S, Crumpton MJ, Gilks W, Gotsch FM, Hogg N, Horton M, Ling N, MacLennan JCM, Mason DY, Milstein C, Spiegelhalter D, Waldmann H. Oxford, Oxford University Press, 1987, pp 574– 575