CD10 down expression in follicular lymphoma correlates with gastrointestinal lesion involving the stomach and large intestine

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Follicular lymphoma (FL) shows co-expression of B-cell lymphoma 2 (BCL2) and CD10, whereas downexpression of CD10 is occasionally experienced in gastrointestinal (GI) FL with unknown significance. Gastrointestinal FL is a rare variant of FL, and its similarity with mucosa-associated lymphoid tissue lymphoma was reported. We investigated the clinicopathological and genetic features of CD10 downexpressed (CD10<sup>down</sup>) GI-FL. The diagnosis of CD10<sup>down</sup> FL was carried out with a combination of pathological and molecular analyses. The incidence of CD10<sup>down</sup> GI-FL was shown in 35/172 (20.3%) cases, which was more frequent than nodal FL (3.5%, P < 0.001). The difference was additionally significant between GI-FL and nodal FL when the analysis was confined to primary GI-FL (55.2% vs 3.5%, P < 0.001). Compared to CD10<sup>+</sup> GI-FL, CD10<sup>down</sup> GI-FL significantly involved the stomach or large intestine (P = 0.015), and additionally showed the downexpression of BCL6 (P < 0.001). The follicular dendritic cell meshwork often showed a duodenal pattern in the CD10<sup>down</sup> group (P = 0.12). Furthermore, a lymphoepithelial lesion was observed in 5/12 (40%) gastric FL cases, which indicated caution in the differentiation of mucosa-associated lymphoid tissue lymphoma. Molecular analyses were undertaken in seven cases of CD10<sup>down</sup> GI-FL, and an identical clone was found between CD10<sup>down</sup> follicles and CD10<sup>+</sup>BCL2<sup>+</sup> neoplastic follicles. In the diagnosis of cases with CD10<sup>down</sup> BCL2<sup>+</sup> follicles, careful examination with molecular studies should be carried out.

Approximately 15% of FL occurs in extranodal sites<sup>(6)</sup> and the GI tract is the most commonly affected site.<sup>(7,8)</sup> With the recognition of this FL variant and the development of endoscopic technology, the characteristics of GI-FL have been gradually revealed. Gastrointestinal FL is predominantly found in the second part of the duodenum, and certain GI-FL spread over the small intestine.<sup>(4,5,9)</sup> Although a case that showed a transformation from duodenal FL to diffuse large B-cell lymphoma (DLBCL) was reported,<sup>(10)</sup> GI-FL is generally an indolent disease, and certain cases showed spontaneous regression.<sup>(11)</sup> Duodenal FL shares some characteristics with MALT lymphoma, such as a lack of a follicular dendritic cell (FDC) meshwork, the deviation of VH usage, a lack of activation-induced cytidine deaminase, and differentiation to memory cells, which are different from nodal FL.<sup>(12)</sup> Furthermore, a genetic similarity between duodenal FL and MALT lymphoma was identified by comprehensive gene expression analysis.<sup>(13)</sup>

Considering these facts, downexpression of CD10 in GI-FL may have a different level of significance from that in nodal FL.

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Therefore, in the present study, we investigated the clinical, morphologic, and immunophenotypical features of CD10<sup>down</sup> GI-FL and compared them with those of CD10<sup>+</sup> GI-FL.

Materials and Methods

**Patient selection.** The cases retrieved from the consultation files of the Department of Pathology, Okayama University Graduate School of Medicine, Dentistry, and Pharmaceutical Sciences (Okayama, Japan) included 172 cases of GI-FL (1993–2012), 144 cases of nodal FL (2012–2013), and 1024 cases of MALT lymphoma in the GI tract (1989–2013). Cases of FL in situ, grade 3 FL, and FL with a diffuse area or DLBCL in other sites were excluded from the present study.

CD10<sup>down</sup> FL was defined by one of the following findings (Fig. 1): (i) the presence of the co-expression of CD10/BCL6 (1, orange dot) and BCL2 (2, green dot) in parts of the typical neoplastic follicles (blue circle) using immunohistochemistry. (b) Translocation of IGH/BCL2 (yellow dot) in CD10<sup>down</sup> tumor follicles (white circle) using FISH. (c) Identical clone between CD10<sup>down</sup> follicles (1) and typical neoplastic follicles with the coexpression of CD10 and BCL2 (2) using PCR. (d) Presence of typical neoplastic follicles with coexpression of CD10 and BCL2 (1) and CD10<sup>down</sup> follicle (2) in different samples taken from the same lesion.

![Fig. 1. Schema of criteria for CD10 downexpressed (CD10<sup>down</sup>) follicular lymphoma.](image)

**Table 1. Antibodies used in this study**

| Antibody | Source | Clone | Dilution |
|----------|--------|-------|----------|
| CD20     | Novocastra, Newcastle Upon Tyne, UK | L26    | 1:200    |
| CD3      | Novocastra, Newcastle Upon Tyne, UK | LN10   | 1:50     |
| CD10     | Novocastra, Newcastle Upon Tyne, UK | 56C6   | 1:50     |
| BCL2     | Novocastra, Newcastle Upon Tyne, UK | 3.1    | 1:200    |
| BCL6     | Santa Cruz Biotechnology, Santa Cruz, CA, USA | D-8 | 1:100 |
| CD21     | Dako, Glostrup, Denmark | 1F8    | 1:20     |
| Cyclin D1| Nichirei, Tokyo, Japan | SP4    | Ready to use |
| CAM5.2   | Becton Dickinson, Franklin Lakes, IL, USA | CAM5.2 | Ready to use |

Complete clinical information was obtained from 58 of 172 cases of GI-FL. The International Workshop classification (Lugano classification)<sup>14</sup> was used for the clinical staging of GI-FL. Twenty-nine of 58 cases with stage I and II<sub>1</sub> were recognized as a primary GI-FL.<sup>5</sup> The site of involvement was based on biopsy or operation specimens. The Follicular Lymphoma International Prognostic Index was used for the evaluation of patient status.<sup>15</sup> The study protocol was approved by the Institutional Review Board of Okayama University (Okayama, Japan). All study procedures were

**Table 2. Comparison of CD10 expression between nodal and gastrointestinal (GI) follicular lymphoma**

|          | CD10<sup>+</sup> | CD10 downexpressed | P-value |
|----------|-----------------|--------------------|---------|
| Nodal lesion (primary nodal) (n=144) | 139 | 5 | <0.001 |
| GI lesion (n=172) | 137 | 35 | <0.001 |
| Primary nodal (n=144) | 139 | 5 | <0.001 |
| Primary GI (n=29) | 13 | 16 | <0.001 |

Bold values indicate significance. Downexpressed, ≤50% positive cells in neoplastic follicles; positive, >50% positive cells in neoplastic follicles.
carried out in accordance with guidelines of the Declaration of Helsinki.

**Histology and immunohistochemistry.** Histological and immunophenotypical features were studied on 10% formalin-fixed paraffin-embedded tissue sections (FFPET). Immunohistochemistry was carried out using an automated Bond-Max stainer (Leica Biosystems, Nussloch, Germany) according to the manufacturer’s instructions. The primary antibodies used in the present study are summarized in Table 1. The expression of CD10 and BCL6 were scored as positive (>50% positive cells in neoplastic follicles) or downexpressed (≤50% positive cells in neoplastic follicles).

In the present study, samples that included no obvious follicles in sections were categorized as positive for CD10 and BCL6. The FDC pattern was classified as nodal (>30% positive FDC cells), intermediate (5–30% positive FDC cells), and duodenal (<5% positive FDC cells and FDC located at the periphery tumor follicles), as previously

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**Fig. 2.** Pathological features of CD10 downexpressed gastrointestinal follicular lymphoma (FL). (a) Neoplastic follicles are present in the lamina propria mucosa (HE, ×200). (b) Tumor cells were composed of a monotonous population of small- to medium-sized and a few large-sized cells (HE, ×400). (c) CD20 was positive, and (d) CD3 was negative in the neoplastic follicle. (e) CD10 was downexpressed in the neoplastic follicle (×400). (f) BCL2 was positive (×400). (g) BCL6 was downexpressed (×400). (h) A few Ki-67+ cells were seen. (i) CD21+ follicular dendritic cells present at the periphery of the neoplastic follicle (duodenal pattern).
Table 3. Comparison between CD10-positive and CD10 down-expressed FL

| Site of involvement of GI | CD10 positive | CD10 downexpressed | P value |
|--------------------------|----------------|--------------------|---------|
| All cases, n=172         |                |                    |         |
| Small intestine only     | 128            | 28                 |         |
| Stomach or large intestine with/without small intestine | 9          | 7                  | 0.015   |
| Primary GI-FL cases, n=29 |                |                    |         |
| Small intestine only     | 13             | 13                 |         |
| Stomach or large intestine with/without small intestine | 0          | 3                  | 0.099   |
| Sex                      |                |                    |         |
| Male                     | 16             | 15                 | 0.76    |
| Female                   | 15             | 12                 |         |
| Age: median(range)       | 59 (40–85)     | 63 (38–78)         | 0.75    |
| FLIPI                    |                |                    |         |
| Low                      | 1,2            | 18                 | 0.53    |
| Intermediate             | 3              | 9                  |         |
| High                     | 1,2            | 18                 | 0.53    |
| Anemia*                  | 1              | 1                  | 1.00    |
| Absent                   | 29             | 24                 | 0.90    |
| LDH                      |                |                    |         |
| Normal                   | 22             | 20                 |         |
| Elevated                 | 8              | 5                  | 0.56    |
| sIL-2R                   |                |                    |         |
| Normal                   | 20             | 12                 |         |
| Elevated                 | 8              | 6                  | 0.73    |
| WBC (×1000)              |                |                    |         |
| <9000                    | 30             | 25                 | 0.28    |
| ≥9000                    | 0              | 1                  |         |
| Thrombocytopenia**       | 7              | 4                  | 0.50    |
| Absent                   | 23             | 21                 |         |
| Hypoalbuminemia***       | 2              | 2                  | 0.71    |
| Absent                   | 25             | 17                 |         |
| Hypocalcemia****         | 4              | 2                  | 0.22    |
| Absent                   | 14             | 21                 |         |
| Primary therapy          |                |                    |         |
| Watchful wait            | 17             | 17                 |         |
| R                        | 3              | 2                  |         |
| R-CHOP                   | 4              | 2                  |         |
| CHOP and CHOP-like       | 4              | 2                  |         |
| operation or endoscopic  | 2              | 2                  |         |
| resection                | 2              | 2                  |         |
| Other                    | 1              | 1                  |         |
| Unknown                  | 1              |                    |         |
| Follow-up time: median   | 68 (7–157)     | 70 (1–201)         | 0.42    |
| (range) (month)          |                |                    |         |

Table 3 (Continued)

| BCL6        | CD10 positive | CD10 downexpressed | P value |
|-------------|----------------|--------------------|---------|
| Positive    | 12             | 4                  |         |
| Negative    | 5              | 22                 | <0.001  |
| FLIPI       |                |                    |         |
| Duodenal    | 9              | 19                 |         |
| Nodal       | 6              | 4                  | 0.12    |

*Anemia: serum hemoglobin level <12 g/dL (male), <10 g/dL (female)
**Hypocalcemia, serum calcium level <8.6 mg/dL
***Hypoalbuminemia, serum albumin level <3.9 g/dL
****Hypocalcemia, serum calcium level <8.6 mg/dL

Results

Clinical features. The morphology and immunohistochemistry of CD10<sup>down</sup> GI-FL are shown in Fig. 2. The frequency and clinicopathological features of CD10<sup>down</sup> GI-FL and nodal FL are summarized in Tables 2 and 3. A total of 172 cases of FL in the GI tract included 82 male and 90 female patients with a median age of 60.5 years (range, 37–85 years), and 144 cases of FL in the lymph node included 60 male and 84 female patients with a median age of 63.5 years (range, 32–84 years). Among each of the FL cases, 35 cases in the GI tract (20.3%, 18 men and 17 women) and five cases (3.5%, 5 women) in the lymph node were classified as within the CD10<sup>down</sup> group. CD10 downexpression was consequently significantly more frequent in GI-FL than in nodal FL (3.5%, P < 0.001; Table 2). In addition, when we confined the analysis to primary GI-FL, the difference was additionally significant between GI-FL and nodal FL (55.2% vs 3.5%, P < 0.001; Table 2).
The clinical information of GI-FL was obtained in 58 cases (31 CD10⁺ GI-FL and 27 CD10⁻⁻ GI-FL). The median follow-up time of the CD10⁺ GI-FL group was 68 months, and that of the CD10⁻⁻ GI-FL group was 70 months. More than 50% of cases were followed up without any treatment (watch and wait), and no patient died of the primary disease. CD10⁻⁻ GI-FL significantly involved the stomach and/or large intestine (P = 0.015), and all cases involved the small intestine. When confined to primary GI-FL, CD10⁻⁻ GI-FL tended to involve the stomach and/or the large intestine although it was not significant (P = 0.099; Table 3). There was no significant difference in other clinical characteristics.

In the present study, the entire gastrointestinal tract was examined using double balloon endoscopy and/or capsule endoscopy in 13 cases, and all involved the duodenum. Two cases (one CD10⁺ case, one CD10⁻⁻ case) were localized in the duodenum, and 11 cases (five CD10⁺ cases, six CD10⁻⁻ cases) involved the duodenum and other parts of the small intestine. There was no significant difference between these two groups in CD10 expression (P = 0.91) and other clinicopathological characteristics.

**Pathological features.** There was no difference in the morphology of CD10⁻⁻ GI-FL and CD10⁺ GI-FL, and both showed neoplastic follicles composed of monotonous tumor cells of a small to medium size and a few large-sized cells without tingible body macrophages.

It was found that BCL6 was significantly downexpressed in CD10⁻⁻ GI-FL (P < 0.001). Duodenal pattern of FDC was often observed in CD10⁻⁻ GI-FL, although there was no significant difference (P = 0.12; Table 3). The pathological features of the 35 cases of CD10⁻⁻ GI-FL are shown in Table 4. The average proportion of CD10⁺ and BCL6⁺ tumor cells in the follicle were 12.6% (range, 0–50%) and 28.5% (range, 0–100%), respectively.

Lymphoepithelial lesions (LEL) in gastric lesions were observed in 5/12 (41.6%) cases (Fig. 3). The macroscopic

**Table 4. Immunohistochemical and immunogenotypical results in 35 cases of CD10 downexpressed follicular lymphoma**

| Patient no. | Age, years | Sex | Site of involvement† | Proportion of CD10⁺ cells, ‡ | Proportion of BCL6⁺ cells, ‡ | PCR* | FISH** | CD10⁺ lesion*** | CD21 |
|-------------|------------|-----|----------------------|-----------------------------|-----------------------------|------|--------|----------------|------|
| 1           | 73         | M   | SI                   | 0                           | ND                          | 1    | ND     | 1              | Duodenal |
| 2           | 67         | M   | SI                   | 10                          | 100                         | ND   | 1      | 2              | Nodal |
| 3           | 66         | F   | SI                   | 20                          | 20                          | 1    | ND     | 1              | Mismatch |
| 4           | 54         | M   | SI, St, LI           | 50                          | <10                         | 1    | ND     | 1              | Duodenal |
| 5           | 61         | M   | SI                   | 0                           | 0                           | ND   | 1      | 1              | Duodenal |
| 6           | 51         | M   | SI                   | 0                           | 20                          | 1    | ND     | 1              | Duodenal |
| 7           | 54         | M   | St, SI               | <10                         | 30                          | 2    | +      | 1              | Mismatch |
| 8           | 66         | F   | SI                   | 20                          | 20                          | 2    | +      | 1              | Duodenal |
| 9           | 37         | F   | SI                   | <10                         | 0                           | ND   | +      | 1              | Duodenal |
| 10          | 55         | M   | SI                   | 0                           | 100                         | ND   | 2      | 1              | Duodenal |
| 11          | 69         | F   | SI                   | 50                          | <10                         | 2    | ND     | 1              | Duodenal |
| 12          | 63         | M   | SI                   | 0                           | 0                           | 2    | +      | 2              | Duodenal |
| 13          | 52         | M   | SI                   | 0                           | 100                         | ND   | 2      | 1              | Duodenal |
| 14          | 54         | M   | SI                   | 0                           | 15                          | 2    | ND     | 1              | Nodal |
| 15          | 69         | F   | SI                   | 30                          | 30                          | ND   | 1      | 1              | Nodal |
| 16          | 61         | F   | SI                   | 0                           | 100                         | ND   | 1      | 1              | Duodenal |
| 17          | 73         | M   | SI                   | 40                          | 40                          | ND   | 1      | 1              | Duodenal |
| 18          | 56         | M   | SI                   | 0                           | 30                          | ND   | 1      | 1              | Duodenal |
| 19          | 76         | F   | SI                   | 30                          | 30                          | ND   | 1      | 1              | Nodal |
| 20          | 68         | M   | SI                   | 20                          | ND                          | ND   | 1      | 1              | Nodal |
| 21          | 55         | F   | SI                   | 30                          | ND                          | ND   | 1      | 1              | Duodenal |
| 22          | 75         | F   | SI                   | 20                          | ND                          | ND   | 1      | 1              | Nodal |
| 23          | 48         | M   | St, SI               | 0                           | 15                          | ND   | 1      | 1              | Nodal |
| 24          | 65         | M   | SI                   | 0                           | ND                          | ND   | 1      | 1              | Duodenal |
| 25          | 57         | F   | SI                   | 10                          | ND                          | ND   | 1      | 1              | Nodal |
| 26          | 64         | F   | SI                   | 0                           | 20                          | ND   | 1      | 1              | Duodenal |
| 27          | 78         | F   | SI                   | 30                          | ND                          | ND   | 1      | 1              | Duodenal |
| 28          | 58         | M   | St, SI               | 0                           | 20                          | ND   | 1      | 1              | Nodal |
| 29          | 38         | M   | St, SI               | 0                           | 30                          | ND   | +      | 1              | Duodenal |
| 30          | 46         | M   | SI                   | 0                           | 10                          | ND   | 1      | 1              | Duodenal |
| 31          | 45         | M   | St, LI               | 20                          | ND                          | ND   | 1      | 1              | Nodal |
| 32          | 70         | F   | SI                   | 20                          | 0                           | ND   | 1      | 1              | Duodenal |
| 33          | 62         | M   | St, SI               | 0                           | 50                          | ND   | 2      | 1              | Duodenal |
| 34          | 49         | M   | SI                   | 10                          | ND                          | ND   | 1      | 1              | Duodenal |

LI, large intestine; ND, not done; SI, small intestine; St, stomach. †Italic text indicates sites where CD10 downexpressed follicles were seen. ¤:10% indicates <10% CD10⁺ or BCL6⁺ tumor cells. *1, identical clone between CD10 downexpressed follicles and typical CD10 and BCL2 positive neoplastic follicles; 2, negative in both CD10 downexpressed follicles and typical CD10 and BCL2 positive neoplastic follicles. **+, positive for a IgH/ BCL2 translocation (a fusion signal was observed in more than 7% of nuclei). ***0, the case without CD10 positive neoplastic follicles in the gastrointestinal (GI) tract; 1, the case with CD10 positive neoplastic follicles in same lesion; 2, the case with CD10 positive neoplastic follicles in another GI lesion.
findings of these five cases were as follows: two cases presented with a submucosal tumor-like lesion, one with multiple nodules, one with multiple nodules on a flat elevated lesion, and one was unknown. Three cases were in the CD10+ group, and the remaining two cases were in the CD10down group.

Molecular features. The results of PCR and FISH in 35 cases of CD10down GI-FL are shown in Table 4. Polymerase chain reaction analysis was undertaken for 14 cases. Seven cases were successfully amplified, and in all cases, an identical clone was found between CD10down follicles and CD10+BCL2+ neoplastic follicles (Fig. 4a,b). Five cases were examined for further FISH analysis (three duodenal lesions and two ileal lesions), and all five cases of CD10down GI-FL showed IGH/BCL2 translocation (Fig. 4c). The diagnostic algorithm in CD10down GI-FL is shown in Fig. 5.

Discussion

In the present study, we found that CD10 downexpression was frequently observed along with an additional distinct feature of GI-FL. CD10down GI-FL frequently involved the stomach or large intestine, and showed the simultaneous downexpression of BCL6. Furthermore, gastric FL occasionally contained LEL in parts of the lesions.

For the diagnosis of CD10down FL, a careful differentiation of the follicular colonization of MALT lymphoma and normal primary follicles is always required because both have identical immunohistochemical features (CD10−/BCL6+ and BCL2+). Follicular colonization is the phenomenon in which MALT lymphoma invades to reactive GC and closely resembles FL. In the present study, we carefully excluded MALT lymphoma showing this phenomenon, and diagnosed CD10down FL by one of the following findings: (i) the presence of the co-expression of CD10/BCL6 and BCL2 in parts of the typical neoplastic follicles that are composed of small- to medium-sized and a few large-sized cells (grade 1–2); (ii) the translocation of IGH/BCL2 in CD10down tumor follicles by FISH; (iii) an identical clone between CD10down follicles and CD10*BCL2+ neoplastic follicles using PCR; or (iv) the presence of CD10*BCL2+ neoplastic follicles in different samples taken from the same lesion. In the diagnosis of these cases, as shown in the algorithm for the diagnosis of CD10down GI-FL, it is important to carefully search for the evidence of FL. Following the above criteria, the addition of BCL6 staining, the re-biopsy of several areas, and the examination of the translocation of IGH/BCL2 using FISH, and an identical clone verified between CD10down follicles and typical CD10*BCL2+ neoplastic follicles using PCR is required.

Similarity between GI-FL and MALT lymphoma was described in several previous studies. Both were frequently present within localized diseases, resulted in indolent clinical behavior, and shared gene expression profiles.
Interestingly, it has been reported that, similar to MALT lymphoma, certain GI-FL showed partial regression after antibiotic treatment. (9,24,25) The frequent downexpression of GC markers (CD10 and BCL6) in GI-FL of the present study was consistent with these previous data.

In the present study, LEL was shown in 40% of FL with gastric lesion. It is considered that LEL is a characteristic finding of MALT lymphoma in which lymphoma cells have invaded and destroyed the epithelium. (8) It was of interest that a few cases of GI-FL additionally showed LEL. It should be kept in mind that LEL itself was not a MALT-specific phenomenon.

Follicular lymphoma with marginal zone differentiation is known to show morphological features, such as marginal zone lymphoma (MZL) in parts of FL, and have both CD10"BCL2" neoplastic follicles of FL and the morphology of MZL, with monocytoid or plasmacytoid B cells in the interfollicular area.

Fig. 4. (a, b) Polymerase chain reaction for immunoglobulin heavy chain rearrangements in with gastrointestinal follicular lymphoma. Identical clone (133 nt) was detected between CD10 downexpressed (a) and CD10"BCL2" follicles (b) in the same patient. (c) FISH for IGH/BCL2 translocation in CD10 downexpressed tumor follicle. Fusion signal for IGH/BCL2 (yellow signal; arrow) was seen.

Fig. 5. Algorithm of diagnosis in CD10 downexpressed gastrointestinal follicular lymphoma (GI-FL). IHC, immunohistochemistry.
It is considered that this is not composite lymphoma, but that the two components are clonally related. Follicular lymphoma with LEL could be considered as FL with marginal zone differentiation because parts of them have a similar morphology to MZL. These cases might be misdiagnosed as MALT lymphoma with LEL could be considered as FL with marginal differentiation because parts of them have a similar morphology. FL with LEL could be diagnosed as MALT lymphoma in the ileum and FL in the jejunum. Therefore, FL with LEL could be misdiagnosed as MALT lymphoma if a CD10+ area is not obtained in the small intestine to MZL. These cases might be misdiagnosed as MALT lymphoma because parts of them have a similar morphology. It is suggested that there is currently no consensus on the cut-off value of CD10 in GI lymphomas. We reclassified FL by setting the cut-off value of CD10 downexpressed at 30% and repeated the comparison between the clinicopathological characteristics of CD10+ and CD10down FL. As a result, a similar tendency was observed: CD10 downexpression was significantly more frequent in GI-FL than in nodal FL ($P < 0.001$). Even if confined to primary GI-FL, the difference was also significant between GI-FL and nodal FL ($P < 0.001$). CD10down GI-FL significantly involved the stomach and/or large intestine ($P = 0.007$), and BCL6 was significantly downexpressed in CD10down GI-FL ($P = 0.004$). We believe that this occurred because the proportion of CD10+ cells was <30% in most CD10down cases, as shown in Table 4. In addition, unlike biopsy specimens of lymph nodes, biopsy specimens of GI lymphomas are very small and easily crushed. Based on these facts, we set the cut-off value of CD10 downexpressed to 50% to prevent a complicated diagnosis and to improve reproducibility.

In conclusion, CD10 downexpression was more frequent in GI-FL than in nodal FL and significantly involved the stomach or large intestine. Furthermore, gastric FL occasionally had LEL in part of the lesion. In the diagnosis of cases with CD10down FL, BCL6, molecular analysis should be undertaken. Further prospective studies are warranted to clarify the pathophysiology of GI-FL.

**Disclosure Statement**

The authors have no conflict of interest.

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### Table 5. Tumor distribution among cases of CD10+ follicular lymphoma (FL), CD10 downexpressed FL, and MALT lymphoma

|          | Esophagus | Stomach | Small intestine | Large intestine |
|----------|-----------|---------|----------------|----------------|
| FL       |           |         |                |                |
| CD10+    | 0         | 5       | 133            | 4              |
| (n = 137)|           |         |                |                |
| CD10 down | 0         | 7       | 35             | 3              |
| (n = 35) |           |         |                |                |
| MALT lymphoma | 2     | 815     | 32             | 176            |
| (n = 1024)|           |         |                |                |

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