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MALT GASTRIC LYMPHOMA: AN UPDATE OF PATHOGENETIC FEATURES

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Abstract – *Extranodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma) is a low-grade lymphoma comprising 7-8% of all B-cell non-Hodgkin lymphomas. Common sites of involvement include lung, head and neck, ocular adnexa, skin, thyroid and breast, but the gastrointestinal tract is by far the most common site and the stomach is involved in almost two-thirds of all cases. Infection and autoimmune diseases are commonly considered as etiopathogenetic factors, being related to chronic stimulation of B-cell proliferation. The association between Helicobacter pylori infection and gastric MALT lymphoma provides the best evidence of an etiopathogenetic link between lymphoma and infection. Indeed, successful eradication of this microorganism can be followed by lymphoma regression in most cases. In recent years the role of other pathogenetic factors including genetic predisposition, somatic genetic mutations and chemokines activity, has become more evident. Particularly specific genetic abnormalities have been observed in MALT lymphomas, with different distribution accordingly to the site of development.*

This review, therefore, addresses the major findings obtained in the last few years about MALT lymphoma and summarizes recent advances in its molecular pathogenesis.

KEYWORDS: *MALT, MALT lymphoma, Gastric lymphoma, Pathogenesis, H. pylori.*

INTRODUCTION

Extra-nodal marginal zone B-cell lymphoma of mucosa-associated lymphoid tissue represents approximately 8% of all non-Hodgkin lymphomas[1,2]. Extranodal low-grade lymphomas were described at different sites including the gastrointestinal tract, salivary glands, lung and thyroid, showed similar clinical and histological features and are grouped into the MALT (Mucosa Associated Lymphoid Tissue) lymphoma[3-6]. The most common sites of involvement of MALT lymphomas include the stomach (70%), lung (14%), ocular adnexa (12%), thyroid (4%), and small intestine (including immunoproliferative small intestinal disease; 1%)[7]. Thus, the stomach is involved in almost two-thirds of all cases[8]. In some geographic areas, such as north-eastern Italy, the frequency of MALT gastric lymphoma is particularly high, with an incidence of 13.2 cases per 100,000 per year, significantly higher than in other European countries[9]. Gastric MALT lymphoma is an indolent disease, remaining confined to the stomach for long periods, with ten-year survival rate approximately of 90%[10,11]. However, in some cases a diffuse large B-cell lymphoma (DLBCL) could develop in MALT lymphoma, reducing the ten-year survival rate drops to approximately 42%[10].

HISTOPATHOLOGY AND IMMUNOHISTOCHEMISTRY

All tissues with native or acquired mucosa-associated lymphoid tissue can be involved by MALT lymphoma. Histologically MALT lymphoma is

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characterized by marginal zone neoplastic cells diffusely infiltrating surrounding tissues, including reactive lymphoid tissue, a process known as follicular colonization[12]. In addition, in epithelized tissue, the neoplastic lymphoid cells often infiltrate the epithelial structures resulting in the formation of lymphoepithelial lesions (LELs). Neoplastic cells are constituted by centrocyte-like, monocytoid or plasmacytoid cells, with an admixture of scattered large cells. Finally, immunophenotypical profile (CD20+, CD21+, CD35+, IgM+, and IgD−) is superimposable to normal marginal zone cells. DLBCL may be observed in MALT lymphoma, suggesting a derivation from MALT lymphoma. The demonstration of identically rearranged immunoglobulin (Ig) genes between the low- and high-grade components of the same cases seems to confirm this hypothesis[13]. Transformed MALT lymphomas are CD10− and BCL2− but, in contrast to MALT lymphoma, they usually express BCL6[14]. Rarely, DLBCL develops in extra-lymphoid tissues in the absence of a previous MALT lymphoma (de novo DLBCL), with no clinical difference with respect to ex MALT DLBCL[10] (Figure 1).

PATHOGENESIS

The development of MALT gastric lymphoma has been related to certain *Helicobacter pylori* (*Hp*) strains affecting genetically predisposed patients, suggesting the need of a strain-host-organ specific process for the definitive neoplastic transformation of acquired MALT in gastric mucosa[15-18] (Figure 2).

H. pylori strains

H. pylori is the prerequisite for gastric MALT lymphoma development. Indeed chronic antigenic stimulation causes genetic instability and clonal growth of MALT lymphoma. Additional mutations of tumor suppressor genes such as p53 and p16, could induce progression to DLBCL[15-18].

The role of antigen-driven clonal expansion of MALT lymphoma has been demonstrated by ongoing somatic hypermutation in the Ig *V* genes[19]. Also, the Ig V gene selection in MALT lymphoma development could suggest selective pressure of an antigen to increase the affinity of the immunoglobulin for antigens[20]. Thus, the early stages of gastric MALT lymphoma growth may be induced by antigen-driven T cells specific for the *H. pylori* and the cure rate after bacterial eradication is higher than 75%[21,22]. However, the role of host immune response has been not well studied, but it could play a relevant function, being only a minority of infected patients affected by gastric MALT lymphoma[23]. Thus each *H. pylori*-related gastritis patients could develop gastric MALT lymphoma, but considering the very high prevalence of *H. pylori* infection in the general population and the low incidence of gastric lymphoma, it is arguable that some particular conditions

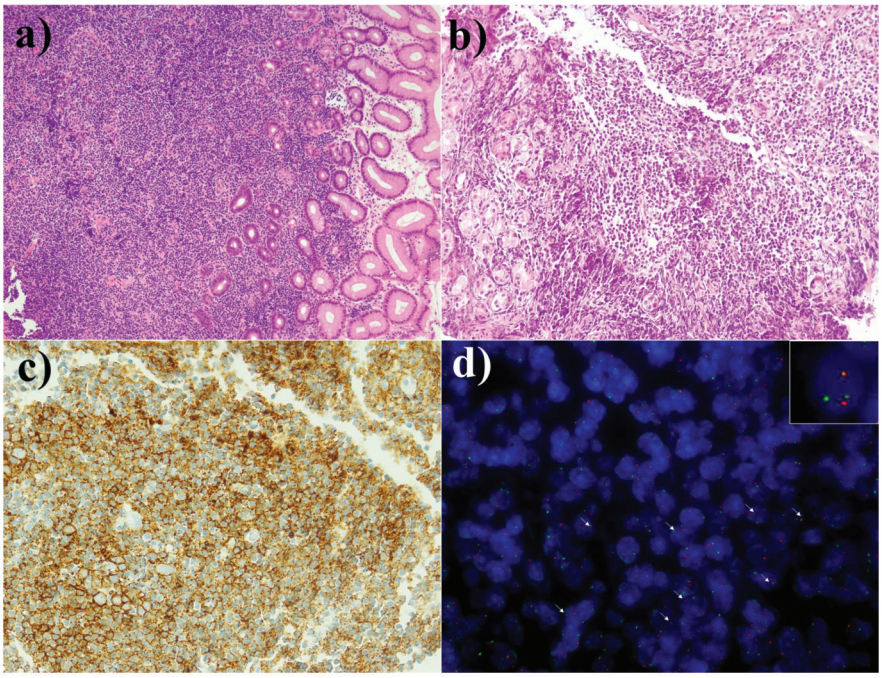

Figure 1. Histology, Immunohistochemistry and FISH for t (11;18). *A-B*, Haematoxylin and eosin-stained section of a stomach biopsy with a dense infiltrate of small lymphocytes (objective 20x and 40x). *C*, Immunohistochemical stain for the B-cell antigen CD20, demonstrating a dominance of the B-lymphocytic population (objective 40x). *D*, FISH positive analysis of chromosomal translocations t(11;18) (q21;q21), the most common structural chromosomal abnormality in gastric MALT lymphomas (objective 60x).

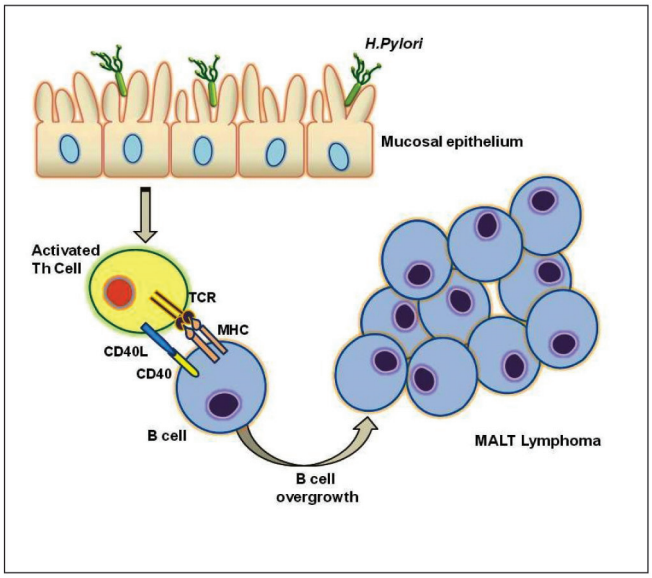

Figure 2. ***H. pylori*-related gastric autoimmunity and MALT gastric lymphoma.** H. pylori infection induces a strong gastric autoimmune response of Th-cells leading to B-cells proliferation through CD40-mediated signaling, as well as by Th2 cytokines. In a minority of infected patients *H. pylori-specific* Th-cells could have a deficient cytotoxic control resulting in impaired regulation of B-cell growth. The chronic proliferative state and the neoplastic trasformation of these B-cells could induce the onset of gastric low-grade MALT lymphoma.

are needed for neoplasia development. Indeed, by co-culturing neoplastic lymphoid cells from gastric MALT-lymphoma patients and different inactivated *H. pylori* strains, a proliferation of B-cell expressing IL-2 receptors was observed, and IL-2 production by T cells in the supernatant was also detected[21]. Only 1 of the 13 different *H. pylori* strains tested could induce B-cell proliferation. The virulent factor of *H. pylori* does not impact on the development of MALT lymphomas as in gastric cancer and peptic ulcer disease[24]. However, CagA positive strains have been found significantly more present in DLBCL than in low-grade MALT lymphoma[25]. In addition, *H. pylori* may localize CagA protein into B-cells where it stimulates Bcl-2 expression, with consequent apoptosis inhibition[26].

Host organ features

Genetic predisposition

Genetic predisposition or development of MALT gastric lymphoma has been postulated, being the prevalence of *HLADQA1*0103* and *HLA-DQB1*0601* alleles and of *DQA1*0103-DQB1*0601* haplotypes higher in MALT-lymphoma patients as compared to controls[27]. The allele frequencies of HLA-DQA1*0103 and HLADQB1*0601 in patients with gastric MALT lymphoma are about 41.6% and 36.1% respectively, resulting in the formation of the haplotype DQA1*0103-DQB1*0601 in approximately 55,5% of the patients[27]. Also, the presence of *TNF-857 T* allele and the rare allele G of Toll-like receptor 4 (TLR4 Asp299Gly) were found approximately in 10% of MALT-lymphoma patients, suggesting their possible role in the genetic susceptibility to gastric lymphoma[28,29]. Finally, homozygous haplotypes for the rare allele G of *SNP3* (*rs12969413*) of the *MALT1* gene was identified approximately in 30% of patients and seems to protect patients from high- but not from low-grade gastric lymphoma[30].

Chemokines role

Lymphoepithelial lesions (LELs) are thought to be the origin of MALT lymphomas[31]. Indeed the close interaction among epithelial cells, T-cells, and B-cells induce survival in LELs with a reduced rate of apoptosis[32]. Gastric epithelial cells express high levels of HLA-DR during chronic *H. pylori* infection, with the recruitment of T-cells expressing CD40 ligand molecules. CD40 ligand interacts with CD40 molecule expressed on B-cells. Thus, B-cell stimulation is favored by CD40L-CD40 interaction associated to the action of various cytokines and chemokines**.** The transition from polyclonal to a monoclonal lesion is facilitated by chronic stimulation, causing B-cell proliferation with higher possibilities of acquiring genetic abnormalities[33-35]. Moreover, B-cell proliferation is sustained by cytokine APRIL, synthetized by macrophages, induced by *H. pylori* and *H. pylori*-specific T cells[36].

Chemokine Receptors in MALT Lymphomas

The large superfamily of chemokines includes peptides playing several biological functions. Indeed,

interaction between chemokines and chemokine receptors induces chemotaxis during inflammation[37-39]. CCR6, CCR7, CXCR3, CXCR4, and CXCR5 play the main role in B-cell homing process[40-42]. Integrated analysis of chemokine receptors in extra-gastric MALT lymphomas respect to gastric MALT lymphomas demonstrated the up-regulation of CXCR1 and CXCR2 with down-regulation of CCR8 and CX3CR1 and loss of XCR1 expression[43]. Also, CXCL12-receptor CXCR4 loss was documented in gastric MALT lymphomas when comparing to gastric extranodal DLBCL, nodal MZL, and nodal DLBCL[44] suggesting that CXCR4 expression is related to nodal lymphomas. Finally, another CXCL12 receptor, CXCR7, is overexpressed during the transformation of gastric MALT lymphomas into gastric DLBCL[44].

Somatic Hypermutation and genetic abnormalities

H. pylori infection increases activation-induced cytidine deaminase (AID) expression via NF-κB in gastric cells both *in vitro* and *in vivo,* with subsequent accumulation of p53 mutation *in vitro*[45]. AID is a key enzyme somatic hypermutation (SHM) and class switch recombination (CSR), immunological events acting to generate antibody diversity and maturity. Thus AID activity seems to play a role in lymphomagenesis through aberrant SHM (ASHM) of the 5 sequences of several protooncogenes, including PIM1, PAX5, RhoH/TTF, and cMYC and/or distinct genetic lesions, including chromosomal translocations[46-50]. ASHM has widely described in DLBCL, but it has also been found in 13 (76.5%) of 17 cases of MALT lymphomas and all 17 (100%) cases of extranodal DLBCL – still exhibiting a low-grade MALT lymphoma component (the so-called transformed MALT lymphoma) – were targeted by ASHM[50].

The main chromosomal and genetic abnormalities are reported in Table I.

Specific genetic abnormalities have been observed in MALT lymphomas, with different distribution accordingly to the site of MALT lymphomas development. Chromosome 3 and chromosome 18 trisomy have been described in up to 68% and 57% of patients, respectively[51-55].

Particularly, trisomy of chromosome 3 has been mainly shown in orbital, than in lacrimal gland and conjunctival OAML[53]. Trisomy of chromosome 18, instead, is more frequent in the conjunctival OAML and predominantly affects young women[55]. A comparative genomic hybridization (CGH) carried out in 10 OAML cases showed recurrent chromosomal gains at 6p21 and 9q33-qter, in addition to trisomy 3, 12 and 18[56].

The mechanism through which these numerical aberrations are implicated in MALT lymphomagenesis has not been well studied, but some critical genes on chromosome 3 particularly have been proposed as related to lymphoma development, such as bcl6, FOXP1 and CCR4[57,58].

t(11;18) (q21;q21) is the most common chromosomal aberration observed in MALT lymphomas, mainly of gastric and pulmonary districts. Particularly it occurs in 10-50% of gastric MALT lymphomas[51]. The effect of translocation is the fusion of the N-terminal region of the BIRC2 (API2-apoptosis inhibitor 2) gene (located on chromosome 11) and the C-terminal region of the MALT1 gene (located on chromosome 18), with the formation of the API2-MALT1 chimeric fusion protein, able to activate the NF-kB pathway[59-64]. Of note, it has been found that the prevalence of CagA-positive *H. pylori* strains was significantly higher in gastric MALT-lymphoma patients with the t(11;18) (q21;q21) compared to those without such a translocation[65] (Figure 3).

Mutation	Affected genes	Genetic alteration	Frequence	Main MALT lymphoma localization
Trisomy 3	FOXP1, BCL6, CCR4	Trisomy	68%	Gastrointestinal
Trisomy 12	Unkown	Trisomy	57%	Gastrointestinal
Trisomy 18	Unknown	Trisomy	20%	Gastrointestinal; mainly high grade
t(11;18)(q21;q21)	BIRC2(API2), MALT1	Translocation	10-50%	Stomach and lung
t(14;18)(q32;q21)	MALT1	Translocation	10-20%	Ocular adnexa, orbit, skin, and salivary glands
t(1;14)(p22;q32)	BCL10	Translocation	1-2%	Stomach, lung, skin; mainly high grade
t(3;14)(p14;q32)	FOXP1, IGH	Translocation	10%	Orbit, thyroid, skin
17p-	P53	Deletion	10-30%	Mainly high grade
6q23-	TNFAIP3	Deletion	Unknown	Ocular adnexal, salivary gland, thyroid,
cMYC	cMYC	Mutation	10-15%	Gastrointestinal, lung, ocular adnexa
P16	P16/INK4A	Hypermethylation	40-60%	Lung; mainly high grade
P57	P57(KIP2)	Hypermethylation	20-30%	Stomach; mainly high grade

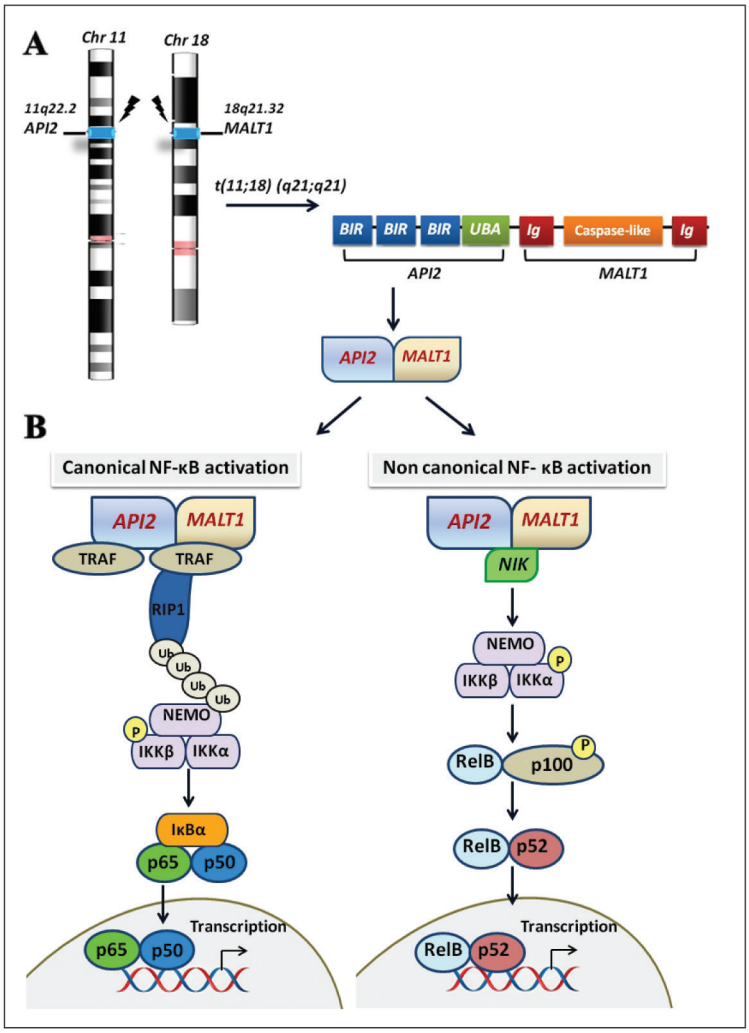

Figure 3. API2-MALT1 chimeric fusion protein and Nuclear Factor-kappa B (NF-κB) pathway activation in gastric MALT lymphomas. *A,* The translocation t(11;18)(q21;q21) leads to the formation of API2-MALT1 fusion protein that contains regardless of different breakpoints the N-terminal of API2 and the C-terminal of MALT1 including the following domains: BIR: Baculovirus inhibitor of apoptosis repeat, UBA: Ubiquitin-associated domain, Ig: Immunoglobulin-like, Caspase-like domain. *B,* API2-MALT1 fusion protein induces NF-κB activation through canonical and non-canonical pathway. In the canonical signaling, API2-MALT1 binding of TNF receptor associated factor 2 (TRAF2) induces RIP1 ubiquitination, promoting activation of the IKK complex, which consists of catalytic kinase subunits IKKα and IKKβ and a regulatory scaffold protein called NF-κB essential modulator (NEMO; also called IKKγ). IKK complex stimulates directly NF-κB, subsequently p65 and p50 translocate to the nucleus leading to the transcription of several genes. In the case of non-canonical signaling, API2-MALT1 fusion protein induces the proteolytic cleavage of NF-kB-inducing kinase (NIK), resulting in non-canonical NF-κB activation with the simulation of RelB and p52.

t(14;18) (q32;q21) occurs in 15-20% of MALT lymphomas, mainly in non-gastrointestinal districts. This aberration leads MALT1 gene under the control of the IGH enhancer.

In t(1;14) (p22;q32) the entire coding region of the BCL10 gene on chromosome 1 is under the control of the enhancer region of IGH gene on chromosome 14, leading to uncontrolled expression of the BCL10 gene[66]. It is rarely observed, being described in 1-2% of MALT lymphomas, mainly stomach, lung, and skin[67]. BCL10 is an intracellular protein that is essential for both the development and function of mature B-cells and T-cells. Recent studies show that BCL10 specifically links antigen receptor signaling in B and T cells to NF-kB activation[68,69]. In MALT lymphomas with t(11;18) (q21;q21), t(14;18) (q32;q21) or t(1;14) (p22;q32) MALT1, with or without BCL10 cooperation, activates the phosphorylation cascade leading to IkB-α phosphorylation. IkB-α links NF-kB in the cytoplasm. IkB-α phosphorylation enables the release NF-kB, which shuttles into the nucleus, playing its transcriptional role with up-regulation of the cell cycle regulators expression anti-apoptotic proteins, growth factors, negative regulators of the NF-kB pathway and immunoregulatory cytokines[70-75].

The translocations could be demonstrated through Fluorescent In Situ Hybridization (FISH) on neoplastic cells. Alternatively, BCL10 immunohistochemical expression could be used as a good surrogate marker of translocations in MALT lymphomas. Thus, the nuclear BCL10 expression suggests NF-kB activation after t(11;18)(q21;q21) or t(1;14)(p22;q32), while strong cytoplasmic perinuclear expression is related to t(14;18)(q32;q21) [70, 76-79]. However, it has been noticed that MALT lymphomas lacking both t(11;18) or t(1;14) showed a moderate nuclear BCL10 expression, related to a poor prognosis[80,81]. Moreover, an association between weak cytoplasmic BCL10 expression and translocation (14;18) has been found in only 3 cases[80].

Recently, FOXP1 (located at 3p14) was identified as a new translocation partner of IGH (q32) at low frequency in MALT lymphomas and DLBCL[82,83].

Overexpression of FOX1P in lymphoma cells demonstrates that FOX1P is a powerful transcriptional repressor of multiple pro-apoptotic genes[84].

The neoplastic growth-dependence from *H. pylori* has been associated to specific genetic status. Thus, *H. pylori*-dependent MALT lymphoma carrying trisomies 3, 12, or 18 could become *H. pylori*-independent and the transformation into high-grade tumors occurs through *P53* inactivation, *P16* gene deletion or chromosomal translocation of cMYC and BCL6[15,85-88]. On the other hand MALT lymphomas with t(11;18)(q21;q21) are definitively *H. pylori*-independent but it rarely has the ability to transform into aggressive lymphomas[7].

Recently, another possible mechanism for uncontrolled NF-kB activation in MALT lymphoma, but not observed in gastric MALT lymphomas, is generated by homozygous deletion of the chromosomal band 6q23 with subsequent loss of the tumor necrosis factor alpha-induced protein 3 (TNFAIP3, A20)[89], an essential global NF-kB inhibitor. In OAML, A20 inactivation is associated with poor lymphoma-free survival[89-92] and with a range of chronic inflammatory disorders[93-97]. A20 is also inactivated frequently by somatic mutations[90,98,99].

CONCLUSIONS

MALT lymphomas include a heterogeneous group of B-cell lymphomas, with different localizations and different genetic anomalies[100-104]. Infection and autoimmune disease are commonly considered as etiopathogenetic factors, being related to chronic stimulation of B-cell proliferation[80,105-107]. Thus eradication of bacterial pathogens, in the early stage of disease, could be the cause of MALT lymphoma regression, particularly in gastric and ocular adnexa B-cell lymphomas [108,109]. In more advanced stages some genetic alterations could occur in neoplastic B-cells. All the described genetic abnormalities concur to deregulate NF-kB signal pathway[61,63,110-112]. In this view, a complete remission in a large portion of MALT lymphoma patients has been obtained by the use of bortezomib[113,114] – a proteasome inhibitor inhibiting the NF- kB signal pathway [115]. Also, the deregulation of NF-kB has also been found in MALT lymphoma patients without known genetic abnormalities.

In this view, the therapy targeting NF-kB may open new prospective in the treatment of this neoplasia.

Conflict of Interests:
The Authors declare that they have no conflict of interests.

REFERENCES

1. Isaacson P, Wright PH. Malignant lymphoma of mucosa-associated lymphoid tissue. A distinctive type of B-cell lymphoma. Cancer 1983; 52: 1410-1416.
2. The Non-Hodgkin's Lymphoma Classification Project. A clinical evaluation of the International Lymphoma Study Group classification of non-Hodgkin's lymphoma. Blood 1997; 89: 3909-3918.
3. Addis BJ, Hyjek E, Isaacson PG. Primary pulmonary lymphoma: a re-appraisal of its histogenesis and its relationship to pseudolymphoma and lymphoid interstitial pneumonia. Histopathology 1988; 13: 1-17.
4. Hyjek E, Isaacson PG. Primary B-cell lymphoma of the thyroid and its relationship to Hashimoto's Thyroiditis. Hum Pathol 1988; 19: 1315-1326.
5. Hyjek E, Smith WJ, Isaacson PG. Primary B-cell lymphoma of salivary glands and its relationship to myoepithelial sialadenitis. Hum Pathol 1988; 19: 766-776.
6. Isaacson P, Wright DH. Extranodal malignant lymphoma arising from mucosa-associated lymphoid tissue. Cancer 1984; 53: 2515-2524.
7. Isaacson PG, Du MQ. MALT lymphoma: from morphology to molecules. Nat Rev Cancer 2004; 4: 644-653.
8. Zucca E, Roggero E, Bertoni F, Cavalli F. Primary extranodal non-Hodgkin's lymphomas. Part 1: Gastrointestinal, cutaneous and genitourinary lymphomas. Ann Oncol 1997; 8: 727-737.
9. Doglioni C, Wotherspoon AC, Moschini A, de Boni M, Isaacson PG. High incidence of primary gastric lymphoma in northeastern Italy. Lancet 1992; 339: 834-835.
10. Cogliatti SB, Schmid U, Schumacher U, Eckert F, Hansmann ML, Hedderich J, Takahashi H, Lennert K. Primary B-cell gastric lymphoma: a clinicopathological study of 145 patients. Gastroenterol 1991; 101: 1159-1170, 1991.
11. Thieblemont C, Berger F, Dumontet C Moullet I, Bouafia F, Felman P, Salles G, Coiffier B. Mucosa-associated lymphoid tissue lymphoma is a disseminated disease in one third of 158 patients analyzed. Blood 2000; 95: 802-806.
12. Isaacson PG, Wotherspoon AC, Diss T, Pan LX. Follicular colonization in B-cell lymphoma of mucosa-associated lymphoid tissue. Am J Surg Pathol 1991; 15: 819-828.
13. Chan JKC, Ng CS, Isaacson PG. Relationship between high-grade lymphoma and low-grade B-cell mucosa-associated lymphoid tissue lymphoma (MALToma) of the stomach. Am J Pathol 1990; 136: 1153-1164.
14. Villuendas R, Piris MA, Orradre JL, Mollejo M, Rodriguez R, Morente M. Different bcl-2 protein expression in high-grade B-cell lymphomas derived from lymph node or mucosa-associated lymphoid tissue. Am J Pathol 1991; 139: 989-993.
15. Neumeister P, Hoefler G, Beham-Schmid C, Schmidt H, Apfelbeck U, Schaider H, Linkesch W, Sill H. Deletion analysis of the p16 tumor suppressor gene in gastrointestinal mucosa-associated lymphoid tissue lymphomas. Gastroenterol 1997; 112: 1871-1875.
16. Kaune KM, Neumann C, Hallermann C, Haller F, Schön MP, Middel P. Simultaneous aberrations of single CDKN2A network components and a high Rb phosphorylation status can differentiate subgroups of primary cutaneous B-cell lymphomas. Exp Dermatol 2011; 20: 331-335.
17. Camacho FI, Mollejo M, Mateo MS, Algara P, Navas C, Hernández JM, Santoja C, Solé F, Sánchez-Beato M, Piris MA. Progression to large B-cell lymphoma in splenic marginal zone lymphoma: a description of a series of 12 cases. Am J Surg Pathol 2001; 25: 1268-1276.

18. Dierlamm J, Stefanova M, Wlodarska I, Hinz K, Maes B, Michaux L, Stul M, Verhoef G, Thomas J, De Wolf-Peeters C, Van den Berghe H, Hossfeld DK, Hagemeijer A. Analysis of the P53, RB/D13S25, and P16 tumor suppressor genes in marginal zone B-cell lymphoma: an interphase fluorescence in situ hybridization study. Cancer Genet Cytogenet 2000; 120: 1-5.
19. Du MQ, Xu CF, Diss TC Peng HZ, Wotherspoon AC, Isaacson PG, Pan LX. Intestinal dissemination of gastric mucosa-associated lymphoid tissue lymphoma. Blood 1996; 88: 4445-4451.
20. Du M, Diss TC, Xu C, Peng H, Isaacson PG, Pan L. Ongoing mutation in MALT lymphoma immunoglobulin gene suggests that antigen stimulation plays a role in the clonal expansion. Leukemia 1996; 10: 1190-1197.
21. Hussell T, Isaacson PG, Crabtree JE, Spencer J. The response of cells from low-grade B-cell gastric lymphomas of mucosa-associated lymphoid tissue to Helicobacter pylori. The Lancet 1993; 342: 571-574.
22. Wotherspoon AC, Doglioni C, Diss TC Pan L, Moschini A, de Boni M, Isaacson PG. Regression of primary low-grade-B-cell gastric lymphoma of mucosa-associated lymphoid tissue type after eradication of Helicobacter pylori. Lancet 1993; 342: 575-577.
23. Suerbaum S, Michetti P. Helicobacter pylori infection. N Engl J Med 2002; 347: 1175-1186.
24. Miehlke S, Meining A, Morgner A, Bayerdörffer E, Lehn N, Stolte M, Graham DY, Go MF. Frequency of vacA genotypes and cytotoxin activity in Helicobacter pylori associated with low-grade gastric mucosa-associated lymphoid tissue lymphoma. J Clin Microbiol 1998; 36: 2369-2370.
25. Peng H, Ranaldi R, Diss TC, Isaacson PG, Bearzi I, Pan L. High frequency of cagA+ Helicobacter pylori infection in high-grade gastric MALT B-cell lymphomas. J Pathol 1998; 185: 409-412.
26. Lin WC, Tsai HF, Kuo SH, Wu MS, Lin CW, Hsu PI, Cheng AL, Hsu PN. Translocation of Helicobacter pylori CagA into human B lymphocytes, the origin of mucosa-associated lymphoid tissue lymphoma. Cancer Res 2010; 70: 5740-5748.
27. Kawahara Y, Mizuno M, Yoshino T, Yokota K, Oguma K, Okada H, Fujiki S, Shiratori Y. HLA-DQA1*0103-DQB1*0601 haplotype and Helicobacter pylori-positive gastric mucosa-associated lymphoid tissue lymphoma. Clin Gastroenterol Hepatol 2005; 3: 865-868.
28. Hellmig S, Fischbach W, Goebeler-Kolve ME, Fölsch UR, Hampe J, Schreiber S. A functional promotor polymorphism of TNF-alpha is associated with primary gastric B-Cell lymphoma. Am J Gastroenterol 2005; 100: 2644-2649.
29. Hellmig S, Fischbach W, Goebeler-Kolve ME, Fölsch UR, Hampe J, Schreiber S. Association study of a functional Toll-like receptor 4 polymorphism with susceptibility to gastric mucosa-associated lymphoid tissue lymphoma. Leuk Lymphoma 2005; 46: 869-872.
30. Hellmig S, Bartscht T, Fischbach W, Ott SJ, Rosenstiel P, Klapper W, Fölsch UR, Schreiber S. Germline variations of the MALT1 gene as risk factors in the development of primary gastric B-cell lymphoma. Eur J Cancer 2009; 450: 1865-1870.
31. Schmid U, Helbron D, Lennert K. Development of malignant lymphoma in myoepithelial sialadenitis (Sjögren's syndrome). Virchows Arch A Pathol Anat Histol 1982; 395: 11-43.
32. Ogawa N, Ping L, Zhenjun L, Takada Y, Sugai S. Involvement of the interferon-γ-induced T cell-attracting chemokines, interferon-γ-inducible 10-kd protein (CXCL10) and monokine induced by interferon-γ (CXCL9), in the salivary gland lesions of patients with Sjögren's syndrome. Arthritis Rheum 2002; 46: 2730-2741.
33. Berard CW, Greene MH, Jaffe ES. A multidisciplinary approach to non-Hodgkin's lymphomas. Ann Intern Med 1981; 94: 218-235.
34. Kipps TJ, Tomhave E, Chen PP, Fox RI. Molecular characterization of a major autoantibody-associated cross-reactive idiotype in Sjogren's syndrome. J Immunol 1989; 142: 4261-4268.
35. Bahler DW, Miklos JA, Swerdlow SH. Ongoing Ig gene hypermutation in salivary gland mucosa-associated lymphoid tissue-type lymphomas. Blood 1997; 89: 3335-3344.
36. Munari F, Lonardi S, Cassatella MA, Doglioni C, Cangi MG, Amedei A, Facchetti F, Eishi Y, Rugge M, Fassan M, de Bernard M, D'Elios MM, Vermi W. Tumor-associated macrophages as major source of APRIL in gastric MALT lymphoma. Blood 2011; 117: 6612-6616.
37. Campbell DJ, Kim CH, Butcher EC. Chemokines in the systemic organization of immunity. Immunol Rev 2003; 195: 58-71.
38. Laurence ADJ. Location, movement and survival: the role of chemokines in haematopoiesis and malignancy. Br J Haematol 2006; 132: 255-267.
39. Balkwill F. Cancer and the chemokine network. Nat Rev Cancer 2004; 4: 540-550.
40. Bowman EP, Campbell JJ, Soler D, Dong Z, Manlongat N, Picarella D, Hardy RR, Butcher EC. Developmental switches in chemokine response profiles during B-cell differentiation and maturation. J Exp Med 2000; 191: 1303-1318.
41. Cyster JG. Chemokines, sphingosine-1-phosphate, and cell migration in secondary lymphoid organs. Annu Rev Immunol 2005; 23: 127-159.
42. Muller G, Hopken UE, Lipp M. The impact of CCR7 and CXCR5 on lymphoid organ development and systemic immunity. Immunol Rev 2003; 195: 117-135.
43. Deutsch AJA, Aigelsreiter A, Steinbauer E, Neumeister P. Distinct signatures of B-cell homeostatic and activation-dependent chemokine receptors in the development and progression of extragastric MALT lymphomas. J Pathol 2008; 215: 431-444.
44. Dieguez-Gonzalez R, Calaza M, Perez-Pampin E, Balsa A, Blanco FJ, Cañete JD, Caliz R, Carreño L, de la Serna AR, Fernandez-Gutierrez B, Ortiz AM, Herrero-Beaumont G, Pablos JL, Narvaez J, Navarro F, Marenco JL, Gomez-Reino JJ, Gonzalez A. Analysis of TNFAIP3, a feedback inhibitor of nuclear factor-kappaB and the neighbor intergenic 6q23 region in rheumatoid arthritis susceptibility. Arthritis Res Ther 2009; 11: 42-10.
45. Matsumoto Y, Marusawa H, Kinoshita K, Endo Y, Kou T, Morisawa T, Azuma T, Okazaki IM, Honjo T, Chiba T. Helicobacter pylori infection triggers aberrant expression of activation-induced cytidine deaminase in gastric epithelium. Nat Med 2007; 13: 470-476.
46. Bödör C, Bognár A, Reiniger L, Szepesi A, Tóth E, Kopper L, Matolcsy A. Aberrant somatic hypermutation and expression of activation-induced cytidine deaminase mRNA in mediastinal large B-cell lymphoma. Br J Haematol 2005; 129: 373-376.
47. Dijkman R, Tensen CP, Buettner M, Niedobitek G, Willemze R, Vermeer MH. Primary cutaneous follicle center lymphoma and primary cutaneous large B-cell lymphoma, leg type, are both targeted by aberrant somatic hypermutation but demonstrate differential expression of AID. Blood 2006; 107: 4926-4929, 2006.

48. Gaidano G, Pasqualucci L, Capello D, Berra E, Deambrogi C, Rossi D, Maria Larocca L, Gloghini A, Carbone A, Dalla-Favera R. Aberrant somatic hypermutation in multiple subtypes of AIDS-associated non-Hodgkin lymphoma. Blood 2003; 102: 1833-1841.
49. Halldórsdóttir AM, Frühwirth M, Deutsch A, Aigelsreiter A, Beham-Schmid C, Agnarsson BA, Neumeister P, Richard Burack W. Quantifying the role of aberrant somatic hypermutation in transformation of follicular lymphoma. Leuk Res 2008; 32: 1015-1021.
50. Deutsch AJA, Aigelsreiter A, Staber PB, Beham A, Linkesch W, Guelly C, Brezinschek RI, Fruhwirth M, Emberger W, Buettner M, Beham-Schmid C, Neumeister P. MALT lymphoma and extranodal diffuse large B-cell lymphoma are targeted by aberrant somatic hypermutation. Blood 2007; 109: 3500-3504.
51. Streubel B, Simonitsch-Klupp I, Muellauer L, Lamprecht A, Huber D, Siebert R, Stolte M, Trautinger F, Lukas J, Püspök A, Formanek M, Assanasen T, Müller-Hermelink HK, Cerroni L, Raderer M, Chott A. Variable frequencies of MALT lymphoma-associated genetic aberrations in MALT lymphomas of different sites. Leukemia 2004; 18: 1722-1726.
52. Lee SB, Yang JW, Kim CS. The association between conjunctival MALT lymphoma and Helicobacter pylori. Br J Ophtalmol 2008; 92: 534-536.
53. Ruiz A, Reischl U, Swerdlow SH, Hartke M, Streubel B, Procop G, Tubbs RR, Cook JR. Extranodal marginal zone lymphomas of the ocular adnexa. Multiparameter analysis of 34 cases including interphase molecular cytogenetics and PCR for Chlamydia psittaci. Am J Surg Pathol 2007; 31: 792-802.
54. Gruenberger B, Woehrer S, Troch M, Hauff W, Lukas J, Streubel B, Muellauer L, Chott A, Raderer M. Assessment of the role of hepatitis C, Helicobacter phylori and autoimmunity in MALT lymphoma of the ocular adnexa in 45 Austrian patients. Acta Oncol 2008; 47: 355-359.
55. Tanimoto K, Sekiguchi N, Yokota Y, Kaneko A, Watanabe T, Maeshima AM, Matsuno Y, Harada M, Tobinai K, Kobayashi Y. Fluorescence in situ hybridization (FISH) analysis of primary ocular adnexal MALT lymphoma. BMC Cancer 2006, 6: 249-258.
56. Matteucci C, Galieni P, Leoncini L, Lazzi S, Lauria F, Polito E, Martelli MF, Mecucci C. Typical genomic imbalance in primary MALT lymphoma of the orbit. J Pathol 2003; 200: 656-660.
57. Dierlamm J, Wlodarska I, Michaux L. Genetic abnormalities in marginal zone B-cell lymphoma. Hematol Oncol 2000; 18. 1-13.
58. Deutsch AJA, Aigelsreiter A, Steinbauer E, Neumeister P. Distinct signatures of B-cell homeostatic and activation-dependent chemokine receptors in the development and progression of extragastric MALT lymphomas. J Pathol 2008; 215: 431-444.
59. Dierlamm J, Baens M, Wlodarska I, Stefanova-Ouzounova M, Hernandez JM, Hossfeld DK, De Wolf-Peeters C, Hagemeijer A, Van den Berghe H, Marynen P. The apoptosis inhibitor gene API2 and a novel 18q gene, MLT, are recurrently rearranged in the t(11;18) (q21;q21) associated with mucosa-associated lymphoid tissue lymphomas. Blood 1999; 93: 3601-3609.
60. Akagi T, Motegi M, Tamura A, Suzuki R, Hosokawa Y, Suzuki H, Ota H, Nakamura S, Morishima Y, Taniwaki M, Seto M: A novel gene, MALT1 at 18q21, is involved in t(11;18) (q21;q21) found in low-grade B-cell lymphoma of mucosa-associated lymphoid tissue. Oncogene 1999; 18: 5785-5794.
61. Morgan JA, Yin Y, Borowsky AD, Kuo F, Nourmand N, Koontz JI, Reynolds C, Soreng L, Griffin CA, Graeme-Cook F, Harris NL, Weisenburger D, Pinkus GS, Fletcher JA, Sklar J. Breakpoints of the t(11;18)(q21;q21) in mucosa-associated lymphoid tissue (MALT) lymphoma lie within or near the previously undescribed gene MALT1 in chromosome 18. Cancer Res 1999; 59: 6205-6213.
62. Du MQ. MALT lymphoma: many roads lead to nuclear factor-kb activation. Histopathology 2011; 58: 26-38.
63. Lucas PC, Yonezumi M, Inohara N, McAllister-Lucas LM, Abazeed ME, Chen FF, Yamaoka S, Seto M, Nunez G. Bcl10 and MALT1, independent targets of chromosomal translocation in malt lymphoma, cooperate in a novel NF-kappa B signaling pathway. J Biol Chem 2001; 276: 19012-19019.
64. Uren AG, O'Rourke K, Aravind LA, Pisabarro MT, Seshagiri S, Koonin EV, Dixit VM. Identification of paracaspases and metacaspases: two ancient families of caspase-like proteins, one of which plays a key role in MALT lymphoma. Mol Cell 2000; 6: 961-967.
65. Ye H, Liu H, Attygalle A, Wotherspoon AC, Nicholson AG, Charlotte F, Leblond V, Speight P, Goodlad J, Lavergne-Slove A, Martin-Subero JI, Siebert R, Dogan A, Isaacson PG, Du MQ. Variable frequencies of t(11;18) (q21;q21) in MALT lymphomas of different sites: significant association with CagA strains of H. pylori in gastric MALT lymphoma. Blood 2003; 102: 1012-1018.
66. Ruland J, Duncan GS, Elia A, Del Barco Barrantes I, Nguyen L, Plyte S, Millar DG, Bouchard D, Wakeham A, Ohashi PS, Mak TW. Bcl10 is a positive regulator of antigen receptor-induced activation of NF-kappaB and neural tube closure. Cell 2001; 104: 33-42.
67. Streubel B, Simonitsch-Klupp I, Müllauer L, Lamprecht A, Huber D, Siebert R, Stolte M, Trautinger F, Lukas J, Püspök A, Formanek M, Assanasen T, Müller-Hermelink HK, Cerroni L, Raderer M, Chott A. Variable frequencies of MALT lymphoma-associated genetic aberrations in MALT lymphomas of different sites. Leukemia 2004; 18: 1722-1726.
68. Xue L, Morris SW, Orihuela C, Tuomanen E, Cui X, Wen R, Wang D. Defective development and function of Bcl10-deficient follicular, marginal zone and B1 B-cells. Nat Immunol 2003; 4: 857-865.
69. Thome M. CARMA1, BCL-10 and MALT1 in lymphocyte development and activation. Nat Rev Immunol 2004; 4: 348-359.
70. Sanchez-Beato M, Sanchez-Aguilera A, Piris MA. Cell cycle deregulation in B-cell lymphomas. Blood 2003; 101: 1220-1235.
71. Liu Y, Dong W, Chen L, Zhang P, Qi Y. Characterization of bcl10 as a potential transcriptional activator that interacts with general transcription factor TFIIB. Biochem Biophys Res Commun 2004; 320: 1-6.
72. Ghosh S, May MJ, Kopp EB. NF-kB and Rel proteins: evolutionarily conserved mediators of immune responses. Annu Rev Immunol 1998; 16: 225-260.
73. Johnson C, Van Antwerp D, Hope TJ. An N-terminal nuclear export signal is required for the nucleocytoplasmic shuttling of IkBalpha. EMBO J 1999; 18: 6682-6693.
74. Karin M, Ben-Neriah Y. Phosphorylation meets ubiquitination: the control of NF-kB activity. Annu Rev Immunol 2000; 18: 621-663.
75. Holzmann K, Kohlhammer H, Schwaenen C, Wessendorf S, Kestler HA, Schwoerer A, Rau B, Radlwimmer B, Döhner H, Lichter P, Gress T, Bentz M. Genomic DNA-chip hybridization reveals a higher incidence of genomic amplifications in pancreatic cancer than con-

ventional comparative genomic hybridization and leads to the identification of novel candidate genes. Cancer Res 2004; 64: 4428-4433.
76. Streubel B, Lamprecht A, Dierlamm J, Cerroni L, Stolte M, Ott G, Raderer M, Chott A. T(14;18)(q32;q21) involving IGH and MALT1 is a frequent chromosomal aberration in MALT lymphoma. Blood 2003; 101: 2335-2339.
77. Ye H, Gong L, Liu H, Hamoudi RA, Shirali S, Ho L, Chott A, Streubel B, Siebert R, Gesk S, Martin-Subero JI, Radford JA, Banerjee S, Nicholson AG, Ranaldi R, Remstein ED, Gao Z, Zheng J, Isaacson PG, Dogan A, Du MQ. MALT lymphoma with t(14;18) (q32;q21)/IGH-MALT1 is characterized by strong cytoplasmatic MALT1 and bcl10 expression. J Pathol 2005; 205: 293-301.
78. Capello D, Gaidano G. Molecular pathophysiology of indolent lymphoma. Haematologica 2000; 85: 195-201.
79. Kuo SH, Chen LT, Yeh KH, Wu MS, Hsu HC, Yeh PY, MAO TL, Chen CL, Doong SL, Lin JT, Cheng AL. Nuclear expression of bcl10 or nuclear factor kappa B predicts Helicobacter pylori-independent status of early-stage, highgrade gastric mucosa-associated lymphoid tissue lymphomas. J Clin Oncol 2004; 22: 3491-3497.
80. Franco R, Camacho FI, Caleo A, Staibano S, Bifano D, De Renzo A, Tranfa F, De Chiara A, Botti G, Merola R, Diez A, Bonavolontà G, De Rosa G, Piris MA. Nuclear bcl10 expression characterizes a group of ocular adnexa MALT lymphomas with shorter failure-free survival. Mod Pathol 2006; 19: 1055-1067.
81. Cerroni L, Zochling N, Putz B, Kerl K. Infection by Borrelia burgdorferi and cutaneous B-cell lymphoma. J Cutan Pathol 1997; 24: 457-461.
82. Streubel B, Vinatzer U, Lamprecht A, Raderer M, Chott A. T(3;14) (p14.1;q32) involving IGH and FOXP1 is a novel recurrent chromosomal aberration in MALT lymphoma. Leukemia 2005; 19: 652-658.
83. Haralambieva E, Adam P, Ventura R, Katzenberger T, Kalla J, Höller S, Hartmann M, Rosenwald A, Greiner A, Muller-Hermelink HK, Banham AH, Ott G. Genetic rearrangement of FOXP1 is predominantly detected in a subset of diffuse large B-cell lymphomas with extranodal presentation. Leukemia 2006; 20: 1300-1303.
84. van Keimpema M, Grueneberg LJ, Mokry M, et al. FOXP1 directly represses transcription of pro-apoptotic genes and cooperates with NF-kappaB to promote survival of human B-cells. Blood 2014; 124: 3431-3440.
85. Du M, Peng H, Singh N, Isaacson PG, Pan L. The accumulation of p53 abnormalities is associated with progression of mucosa-associated lymphoid tissue lymphoma. Blood 1995; 86: 4587-4593.
86. Pan LX, Ramani P, Diss TC, Liang LN, Isaacson PG. Epstein-Barr virus associated lymphoproliferative disorder with fatal involvement of the gastrointestinal tract in an infant. J Clin Pathol 1995; 48: 390-392.
87. Chen YW, Liang ACT, Au WY et al. Multiple BCL6 translocation partners in individual cases of gastric lymphoma. Blood 2003; 102: 1931-1932.
88. Liang R, Chan WP, Kwong YL, Xu WS, Srivastava G, Ho FCS. High incidence of BCL-6 gene rearrangement in diffuse large B-cell lymphoma of primary gastric origin. Cancer Genet Cytogenet 1997; 97: 114-118.
89. Honma K, Tsuzuki S, Nakagawa M, Karnan S, Aizawa Y, Kim WS, Kim YD, Ko YH, Seto M. TNFAIP3 is the target gene of chromosome band 6q23.3-q24.1 loss in ocular adnexal marginal zone B-cell lymphoma. Genes Chromosomes Cancer 2008; 47: 1-7.
90. Chanudet E, Huang Y, Ichimura K, Dong G, Hamoudi RA, Radford J, Wotherspoon AC, Isaacson PG, Ferry J, Du MQ. A20 is targeted by promoter methylation, deletion and inactivating mutation in MALT lymphoma. Leukemia 2010; 24: 483-487.
91. Chanudet E, Ye H, Ferry J, Bacon CM, Adam P, Müller-Hermelink HK, Radford J, Pileri SA, Ichimura K, Collins VP, Hamoudi RA, Nicholson AG, Wotherspoon AC, Isaacson PG, Du MQ. A20 deletion is associated with copy number gain at the TNFA/B/C locus and occurs preferentially in translocation-negative MALT lymphoma of the ocular adnexa and salivary glands. J Pathol 2009; 217: 420-430.
92. Kim WS, Honma K, Karnan S, Tagawa H, Kim YD, Oh YL, Seto M, Ko YH. Genome-wide array-based comparative genomic hybridization of ocular marginal zone B-cell lymphoma: comparison with pulmonary and nodal marginal zone B-cell lymphoma. Genes Chromosomes Cancer 2007; 46: 776-783.
93. Vereecke L, Beyaert R, van Loo G. The ubiquitin-editing enzyme A20 (TNFAIP3) is a central regulator of immunopathology. Trends Immunol 2009; 30: 383-391.
94. Graham RR, Cotsapas C, Davies L, Hackett R, Lessard CJ, Leon JM, Burtt NP, Guiducci C, Parkin M, Gates C, Plenge RM, Behrens TW, Wither JE, Rioux JD, Fortin PR, Graham DC, Wong AK, Vyse TJ, Daly MJ, Altshuler D, Moser KL, Gaffney PM. Genetic variants near TNFAIP3 on 6q23 are associated with systemic lupus erythematosus. Nat Genet 2008; 40: 1059-1061.
95. Dieguez-Gonzalez R, Calaza M, Perez-Pampin E, Balsa A, Blanco FJ, Cañete JD, Caliz R, Carreño L, de la Serna AR, Fernandez-Gutierrez B, Ortiz AM, Herrero-Beaumont G, Pablos JL, Narvaez J, Navarro F, Marenco JL, Gomez-Reino JJ, Gonzalez A. Analysis of TNFAIP3, a feedback inhibitor of nuclear factor-kappaB and the neighbor intergenic 6q23 region in rheumatoid arthritis susceptibility. Arthritis Res Ther 2009; 11: 42-10.
96. Plenge RM, Cotsapas C, Davies L, Price AL, de Bakker PI, Maller J, Pe'er I, Burtt NP, Blumenstiel B, DeFelice M, Parkin M, Barry R, Winslow W, Healy C, Graham RR, Neale BM, Izmailova E, Roubenoff R, Parker AN, Glass R, Karlson EW, Maher N, Hafler DA, Lee DM, Seldin MF, Remmers EF, Lee AT, Padyukov L, Alfredsson L, Coblyn J, et al. Two independent alleles at 6q23 associated with risk of rheumatoid arthritis. Nat Genet 2007; 39: 1477-1482.
97. Musone SL, Taylor KE, Lu TT, Nititham J, Ferreira RC, Ortmann W, Shifrin N, Petri MA, Kamboh MI, Manzi S, Seldin MF, Gregersen PK, Behrens TW, Ma A, Kwok PY, Criswell LA. Multiple polymorphisms in the TNFAIP3 region are independently associated with systemic lupus erythematosus. Nat Genet 2008; 40: 1062-1064.
98. Novak U, Rinaldi A, Kwee I, Nandula SV, Rancoita PM, Compagno M, Cerri M, Rossi D, Murty VV, Zucca E, Gaidano G, Dalla-Favera R, Pasqualucci L, Bhagat G, Bertoni F. The NF-{kappa}B negative regulator TNFAIP3 (A20) is inactivated by somatic mutations and genomic deletions in marginal zone lymphomas. Blood 2009; 113: 4918-4921.
99. Kato M, Sanada M, Kato I, Sato Y, Takita J, Takeuchi K, Niwa A, Chen Y, Nakazaki K, Nomoto J, Asakura Y, Muto S, Tamura A, Iio M, Akatsuka Y, Hayashi Y, Mori H, Igarashi T, Kurokawa M, Chiba S, Mori S, Ishikawa Y, Okamoto K, Tobinai K, Nakagama H, Nakahata T, Yoshino T, Kobayashi Y, Ogawa S. Frequent inactivation of A20 in B-cell lymphomas. Nature 2009; 459: 712-716.
100. Willis TG, Jadayel DM, Du MQ, Peng H, Perry AR, Abdul-Rauf M, Price H, Karran L, Majekodunmi O, Wlodarska I, Pan L, Crook T, Hamoudi R, Isaacson PG, Dyer MJ. Bcl10 is involved in t(1;14)(p22;q32) of MALT B-cell lymphoma and mutated in multiple tumor types. Cell 1999; 96: 35-45.

101. Dierlamm J, Baens M, Wlodarska I, Stefanova-Ouzounova M, Hernandez JM, Hossfeld DK, De Wolf-Peeters C, Hagemeijer A, Van den Berghe H, Marynen P. The apoptosis inhibitor gene API2 and a novel 18q gene, MLT, are recurrently rearranged in the t(11;18)(q21;q21) associated with mucosa-associated lymphoid tissue lymphomas. Blood 1999; 11: 3601-3609.
102. Streubel B, Lamprecht A, Dierlamm J, Cerroni L, Stolte M, Ott G, Raderer M, Chott A. T(14;18)(q32;q21) involving IGH and MALT1 is a frequent chromosomal aberration in MALT lymphoma. Blood 2003; 101: 2335-2339.
103. Streubel B, Vinatzer U, Lamprecht A, Raderer M, Chott A. T(3;14)(p14.1;q32) involving IGH and FOXP1 is a novel recurrent chromosomal aberration in MALT lymphoma. Leukemia 2005; 19: 652-658.
104. Streubel B, Simonitsch-Klupp I, Müllauer L, Lamprecht A, Huber D, Siebert R, Stolte M, Trautinger F, Lukas J, Püspök A, Formanek M, Assanasen T, Müller-Hermelink HK, Cerroni L, Raderer M, Chott A. Variable frequencies of MALT lymphoma-associated genetic aberrations in MALT lymphomas of different sites. Leukemia 2004; 18: 1722-1726.
105. Isaacson PG, Spencer J. The biology of low grade MALT lymphoma. J Clin Pathol 1995; 48: 395-397.
106. de Cremoux P, Subtil A, Ferreri AJ, Vincent-Salomon A, Ponzoni M, Chaoui D, Arnaud P, Lumbroso-Le Rouic L, Sacchetti F, Dendale R, Thioux M, Escande MC, Stern MH, Dolcetti R, Decaudin D. Evidence for an association between Chlamydia psittaci and ocular adnexal lymphomas. J Natl Cancer Inst 2004; 96: 586-594.
107. Chanudet E, Zhou Y, Bacon CM, Wotherspoon AC, Müller-Hermelink HK, Adam P, Dong HY, de Jong D, Li Y, Wei R, Gong X, Wu Q, Ranaldi R, Goteri G, Pileri SA, Ye H, Hamoudi RA, Liu H, Radford J, Du MQ. Chlamydia psittaci is variably associated with ocular adnexal MALT lymphoma in different geographical regions. J Pathol 2006; 209: 344-351.
108. Ferreri AJ, Govi S, Pasini E, Mappa S, Bertoni F, Zaja F, Montalbán C, Stelitano C, Cabrera ME, Giordano Resti A, Politi LS, Doglioni C, Cavalli F, Zucca E, Ponzoni M, Dolcetti R. Chlamydophila Psittaci eradication with doxycycline as first-line targeted therapy for ocular adnexae lymphoma: final results of an international phase II trial. J Clinic Oncol 2012; 30: 2988-2994.
109. Wotherspoon AC, Doglioni C, Diss TC, Pan L, Moschini A, de Boni M, Isaacson PG. Regression of primary low-grade-B-cell gastric lymphoma of mucosa-associated lymphoid tissue type after eradication of Helicobacter pylori. Lancet 1993; 342: 575-577.
110. Sanchez-Izquierdo D, Buchonnet G, Siebert R, Gascoyne RD, Climent J, Karran L, Marin M, Blesa D, Horsman D, Rosenwald A, Staudt LM, Albertson DG, Du MQ, Ye H, Marynen P, Garcia-Conde J, Pinkel D, Dyer MJ, Martinez-Climent JA. MALT1 is deregulated by both chromosomal translocation and amplification in B-cell non-Hodgkin lymphoma. Blood 2003; 101: 4539-4546.
111. Hozak RR, Manji GA, Friesen PD. The BIR motifs mediate dominant interference and oligomerization of inhibitor of apoptosis Op-IAP. Mol Cell Biol 2000; 20: 1877-1885.
112. McAllister-Lucas LM, Inohara N, Lucas PC, Ruland J, Benito A, Li Q, Chen S, Chen FF, Yamaoka S, Verma IM, Mak TW, Núñez G. Bimp1, a MAGUK family member linking protein kinase C activation to Bcl10-mediated NF-κB induction. J Biol Chem 2001; 276 30589-30597.
113. Conconi A, Martinelli G, Lopez-Guillermo A, Zinzani PL, Ferreri AJ, Rigacci L, Devizzi L, Vitolo U, Luminari S, Cavalli F, Zucca E; International Extranodal Lymphoma Study Group (IELSG). Clinical activity of bortezomib in relapsed/refractory MALT lymphomas: results of a phase II study of the International Extranodal Lymphoma Study Group (IELSG). Ann Oncol 2011; 22: 689-695.
114. Troch M, Jonak C, Müllauer L, Püspök A, Formanek M, Hauff W, Zielinski CC, Chott A, Raderer M. A phase II study of bortezomib in patients with MALT lymphoma. Haematologica 2009; 5: 738-742.
115. Panwalkar A, Verstovsek S, Giles F. Nuclear factor-kappaB modulation as a therapeutic approach in hematologic malignancies. Cancer 2004; 100: 1578-1589.