HIGHLIGHTS IN EMATOLOGIA

TREVISO
7-8 NOVEMBRE 2025

Biology of MALT lymphomas

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Disclosures of Stefano Pileri

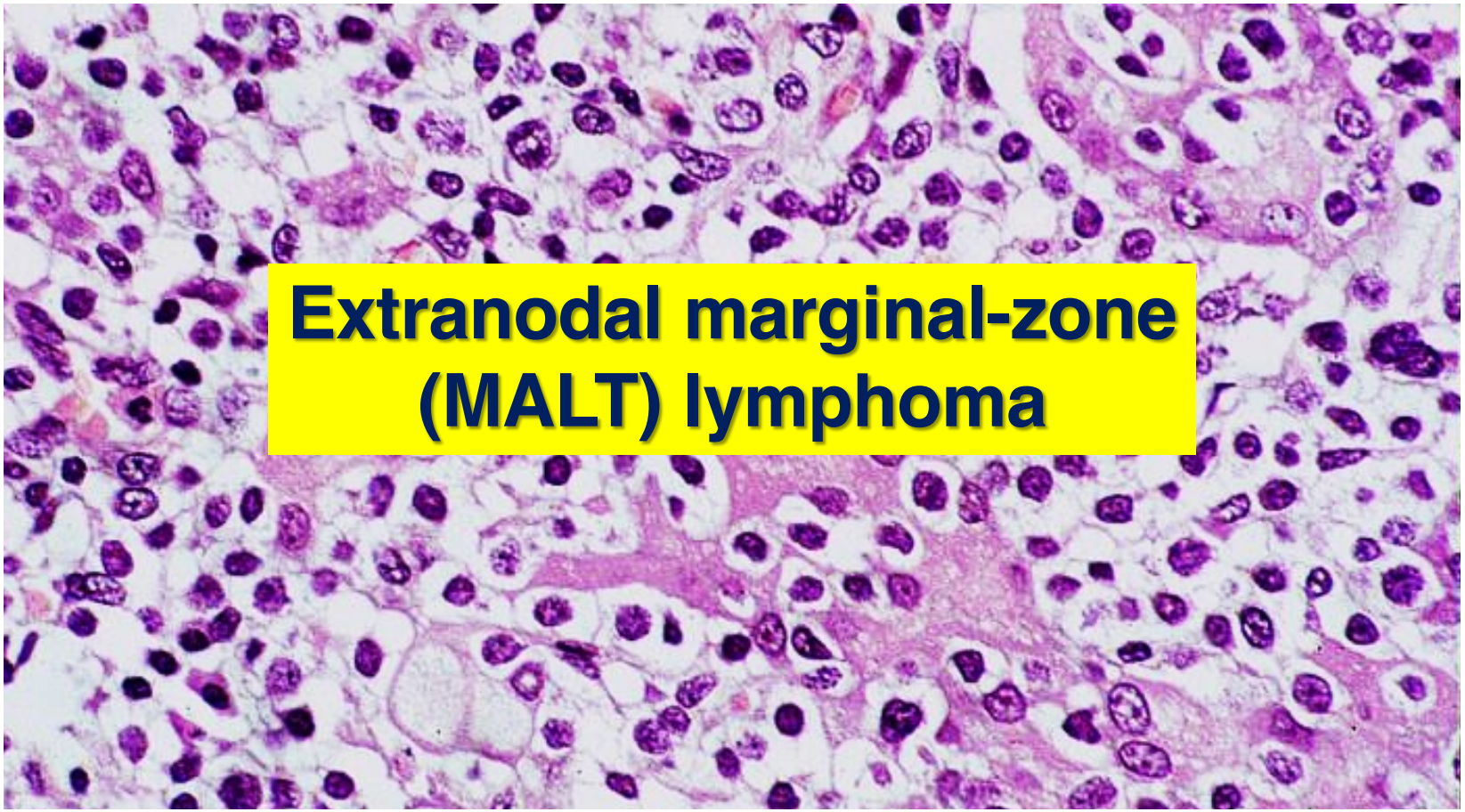
Company name	Research support	Employee	Consultant	Stockholder	Speaker bureau	Advisory board	Other
Eli Lilly					+		
BeiGene					+		
Stemline					+		
Roche					+		
Takeda					+		
Diatech					+	+	

MBL-MZ

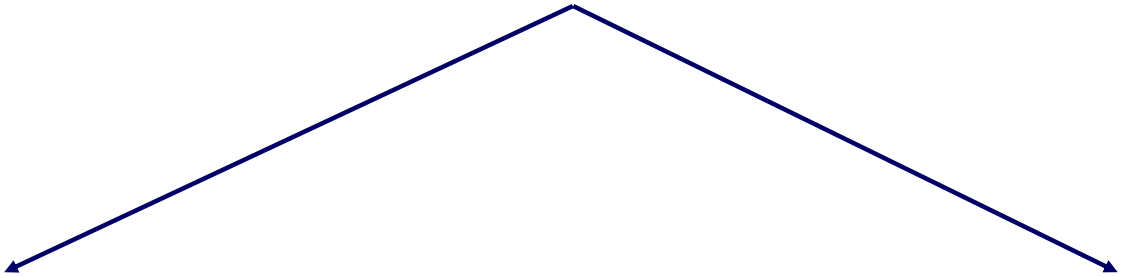
MZL in 15% of cases

Meaning???

Next Classification


Extranodal marginal-zone
(MALT) lymphoma

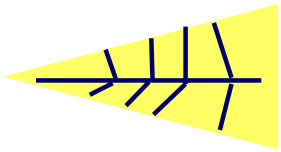
MALT = Mucosa-Associated Lymphoid Tissue



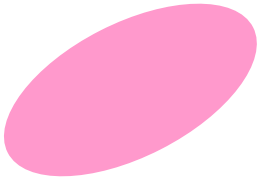
Congenital MALT

Acquired MALT

Acquired MALT

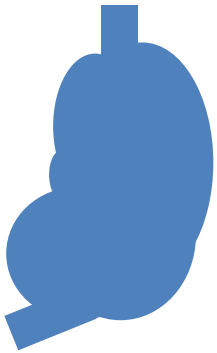


Salivary glands: Sjogren S.



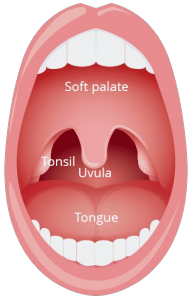
Skin

Thyroid: Hashimoto

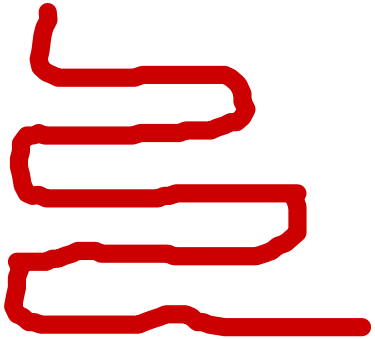


Stomach

Lung: LIP



Congenital MALT

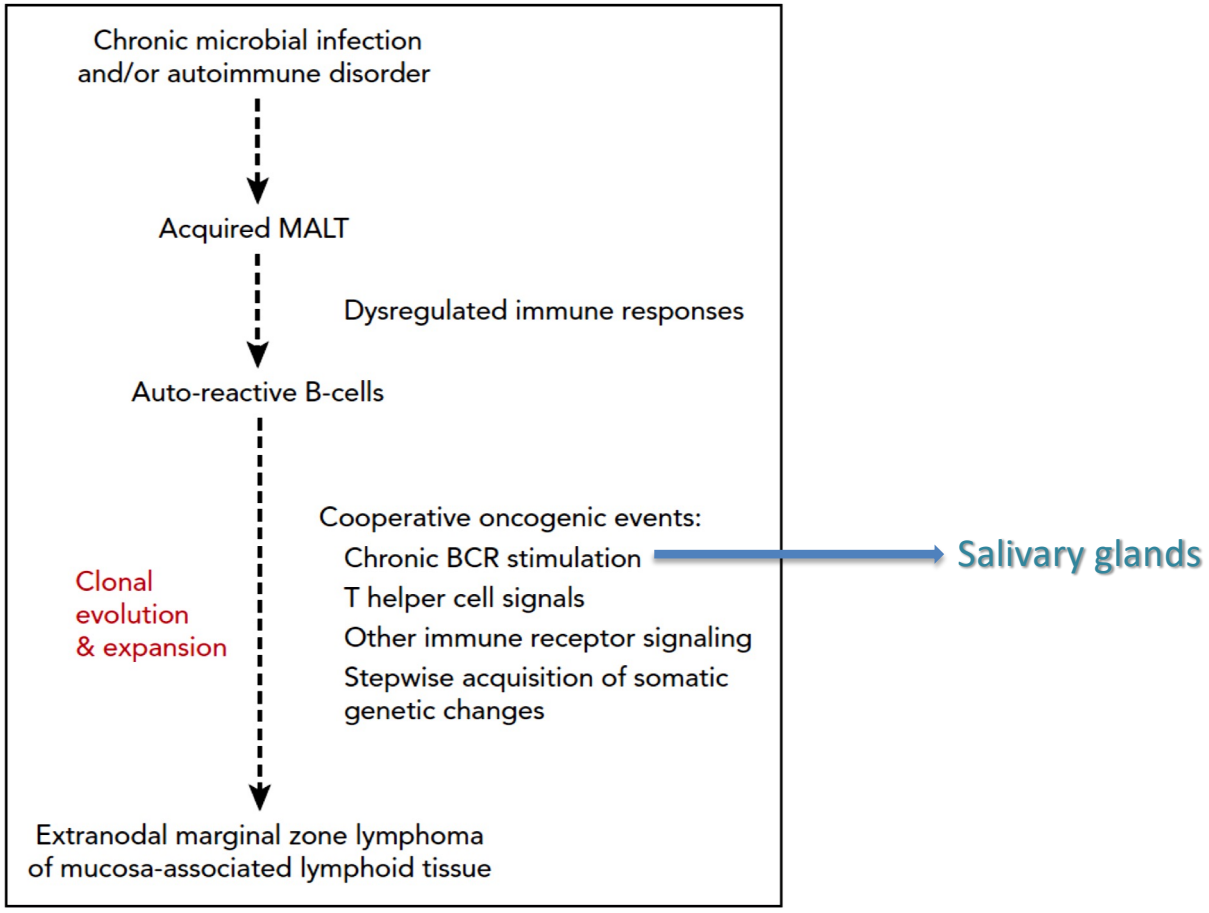


Peyer Patches
Tonsil

EMZL at various sites: learning from each other

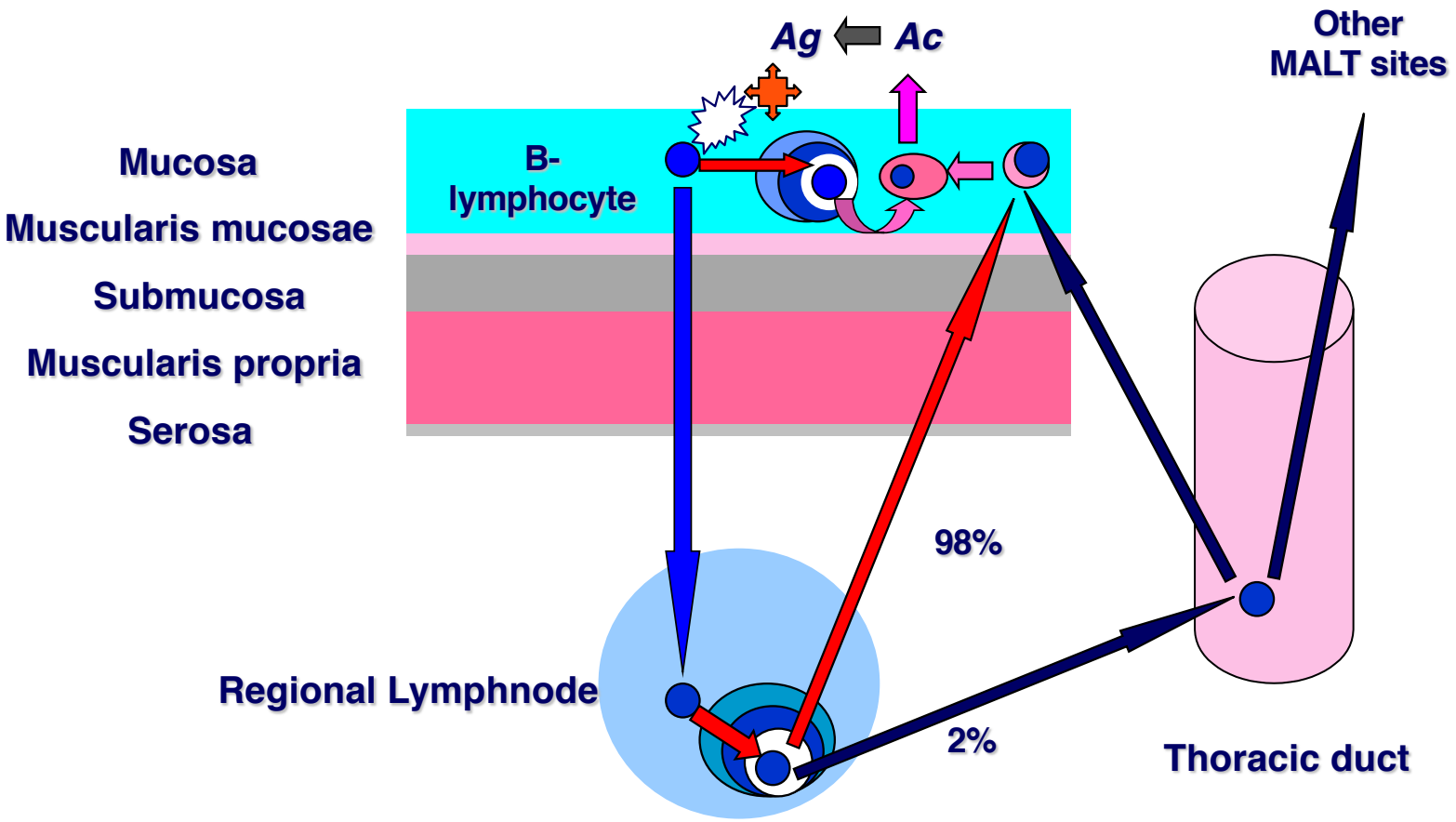
Ming-Qing Du

blood® 8 MAY 2025 | VOLUME 145, NUMBER 19 2117

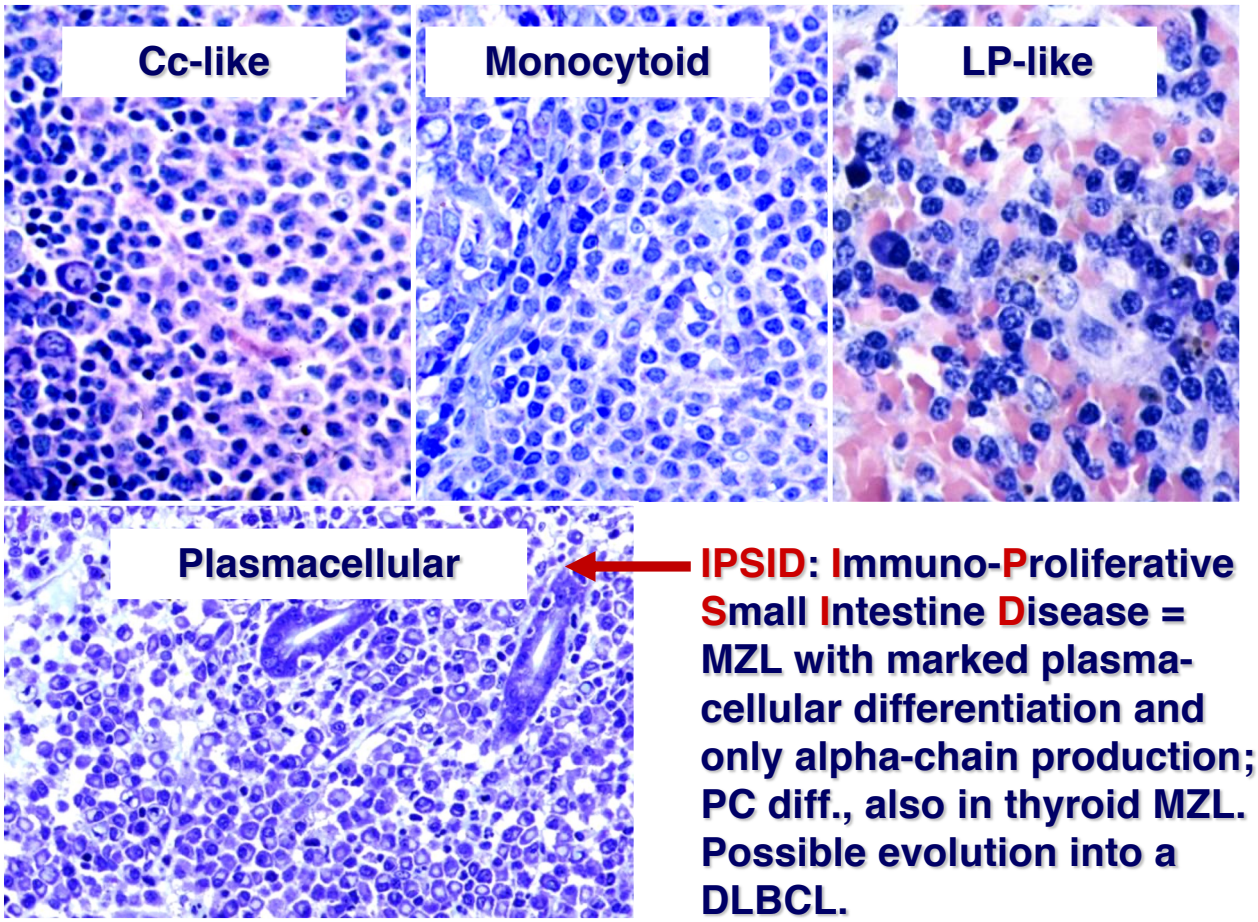


Extranodal Marginal Zone Lymphoma

- Commonest MZL form (70%), representing 5-8% of all NHLs.
- Mostly in patients in the 7th decade (M/F=1/1).
- Most cases present as localized disease (Staged IE or IIE).
- BM involvement in 10% of cases.
- Widespread dissemination very rare.
- Possible regression.



Local recirculation based on the relationships between the homing receptor $\alpha 4\beta 7$ and the adhesion molecule MAdCAM-1



IPSID: Immuno-Proliferative Small Intestine Disease = MZL with marked plasma-cellular differentiation and only alpha-chain production; PC diff., also in thyroid MZL. Possible evolution into a DLBCL.

Phenotype

CD20^{+}, CD79a^{+}, IgM^{+}/IgD^{-}, Ig light chain restriction^{+*}, IRF4^{+*}

IRTA1^{+} (LEL)

CD5^{-} (+20%), CD23^{-}, CD43^{-} (+30%)

Cyclin D1^{-}

CD10^{-}, BCL6^{-},

BCL-2$^{+/-}$ weak

***plasma cell differentiation**

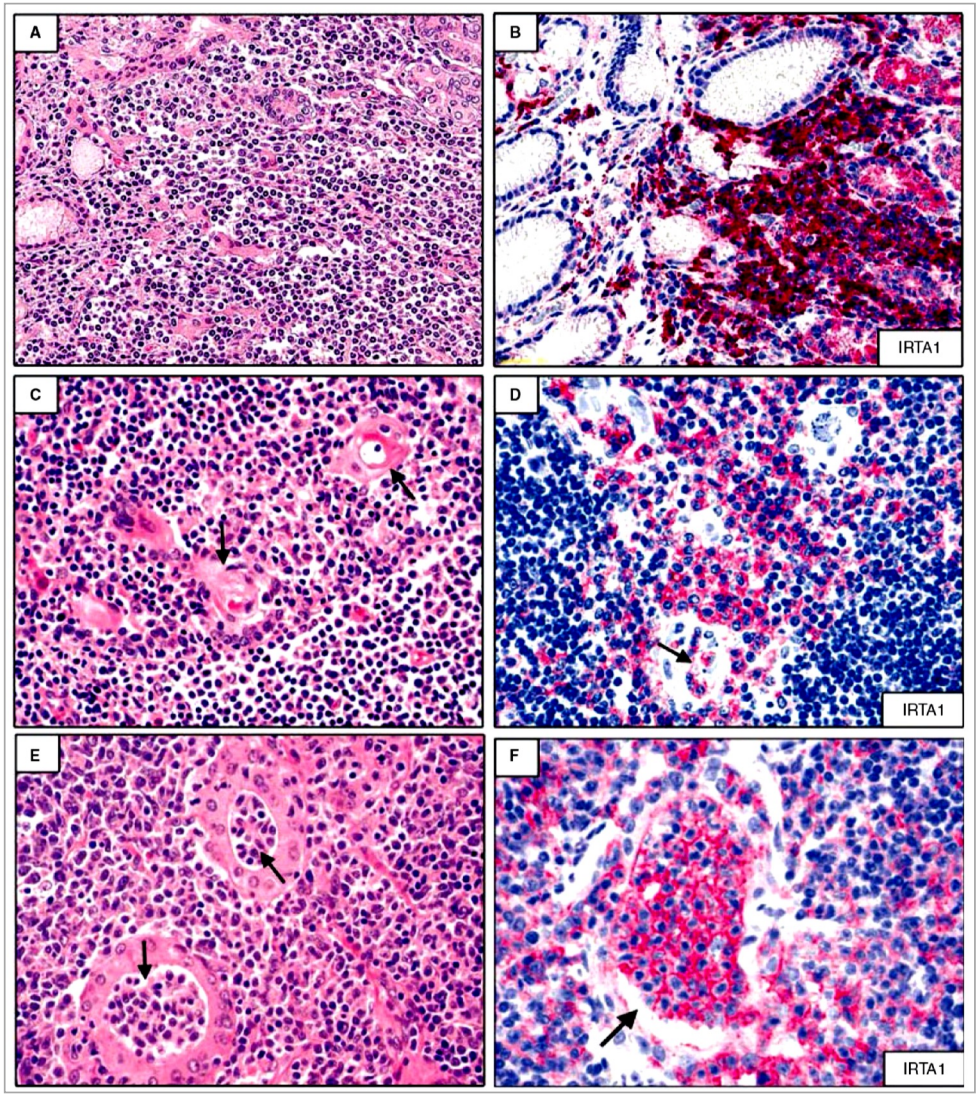
Histopathology

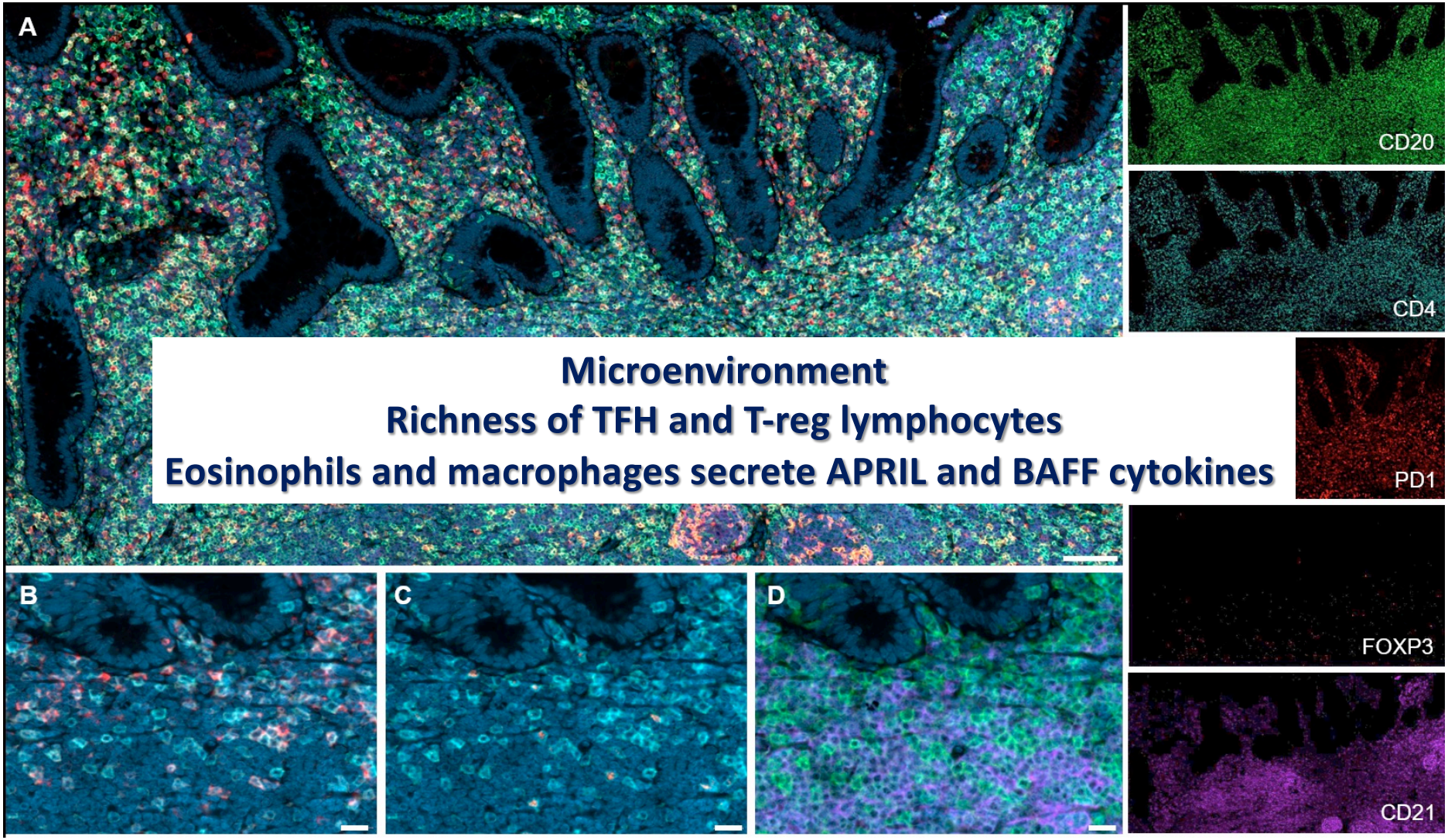
Histopathology 2012 DOI: 10.1111/j.1365-2559.2012.04289.x

IRTA1 is selectively expressed in nodal and extranodal marginal zone lymphomas

Brunangelo Falini, Claudio Agostinelli,[1] Barbara Bigerna, Alessandra Pucciarini, Roberta Pacini, Alessia Tabarrini, Flavio Falcinelli, Milena Piccioli,[1] Marco Paulli,[2] Marcello Gambacorta,[3] Maurilio Ponzoni,[4] Enrico Tiacci, Stefano Ascani,[5] Maria Paola Martelli, Riccardo Dalla Favera,[6] Harald Stein[7] & Stefano A Pileri[1]

B-cell marginal zone lymphoma			
Splenic	21	0*	0
Nodal	210	154	73
Extranodal	329	307	93
NOS	30	22	73


A
B
IRTA1
C
D
IRTA1
E
F
IRTA1



Microenvironment
Richness of TFH and T-reg lymphocytes
Eosinophils and macrophages secrete APRIL and BAFF cytokines

Abnormalities of *TNFAIP3* on chromosome 6q23, which may include deletions, mutations, and promoter methylation, occur in 15–30% of cases, most frequently cases lacking specific translocations {657,1045,2898}. However, *TNFAIP3* abnormalities are not specific for MALT lymphoma, and can be found in many types of non-Hodgkin lymphoma {1681}. *MYD88* L265P mutation has been reported in 6–9% of MALT lymphomas {1267, 2315,2860}.

Features	EMZL
NF-kB pathway activation	Frequent (via translocation or *TNFAIP3* mutation)
Chromosomes abnormalities	Trisomies 3 and 18, del 6q (*TNFAIP3*)
Recurrent translocations	t(11;18), t(14;18), t(3;14), t(1;14)
Key gene mutations	*TNFAIP3, GPR34, KMT2D/2C, CREBBP, TET2, TBL1XR1.*
IGHV usage	No characteristic association.

Blood (2025) E-pub ahead of print

Site	Translocations/trisomies	Mutations
Stomach	*BIRC3::MALT1* (6–23%) *IGH::MALT1* (1–5%) +3 (11%) +18 (6%)	*NOTCH1* (17%) *NF1* (16%) *TNFAIP3* (15%) *ATM* (13%) *TRAF3* (13%)
Occular adnexa/orbit	*IGH::MALT1* (0–25%) *FOXP1::IGH* (0–20%) *BIRC3::MALT1* (0–10%) +3 (38%) +18 (13%)	*TNFAIP3* (39%) *KMT2D* (15%) *CREBBP* (10%) *LRP1B* (10%) *MYD88* (10%)
Salivary gland	*IGH::MALT1* (0–16%) *BIRC3::MALT1* (0–5%) *BCL10::IGH* (0–2%) +3 (55%) +18 (19%)	*TBL1XR1* (24%) *GRP34* (16%) *NOTCH2* (11%) *SPEN* (11%) *KMT2C* (11%)
Lung	*BIRC3::MALT1* (31–53%) *IGH::MALT1* (6–10%) *BCL10::IGH* (2–7%) +3 (20%) +18 (4%)	*KMT2D* (25%) *TNFAIP3* (18%) *PRDM1* (12%) *NOTCH1* (12%) *EP300* (11%)
Thyroid	*FOXP1::IGH* (0–50%) *BIRC3::MALT1* (0–17%) +3 (17%)	*TET2* (61%) *TNFRSF14* (44%) *PIK3CD* (23%) *SPEN* (17%) *CREBBP* (8%)

Virchows Archiv (2023) 482:149–162

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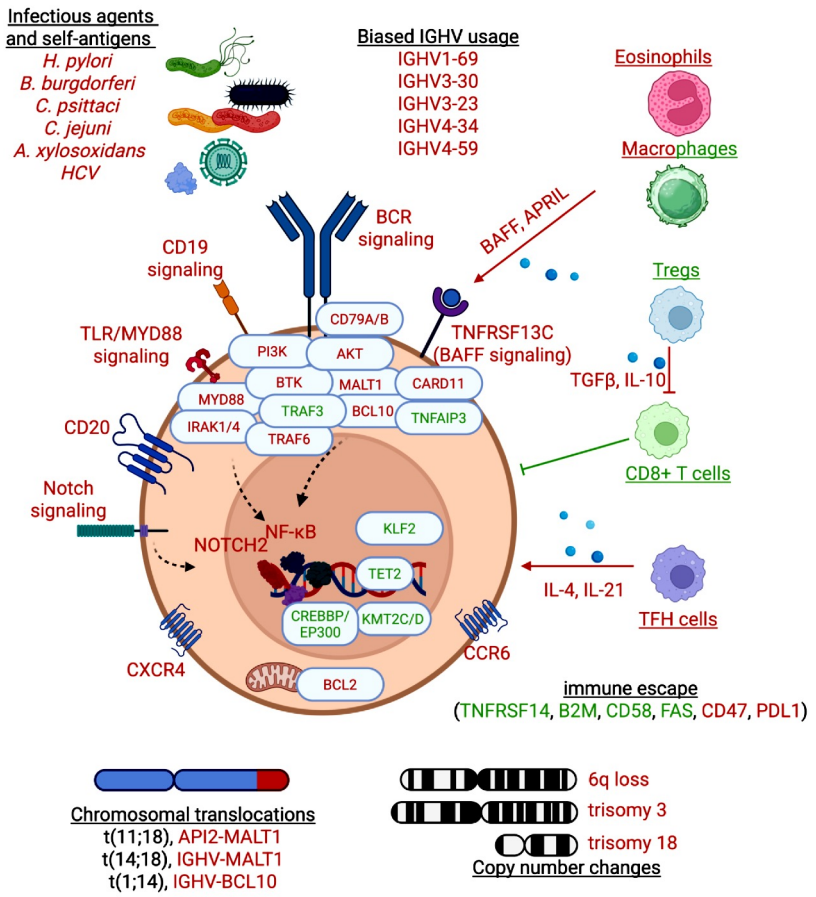
Extranodal marginal zone lymphoma



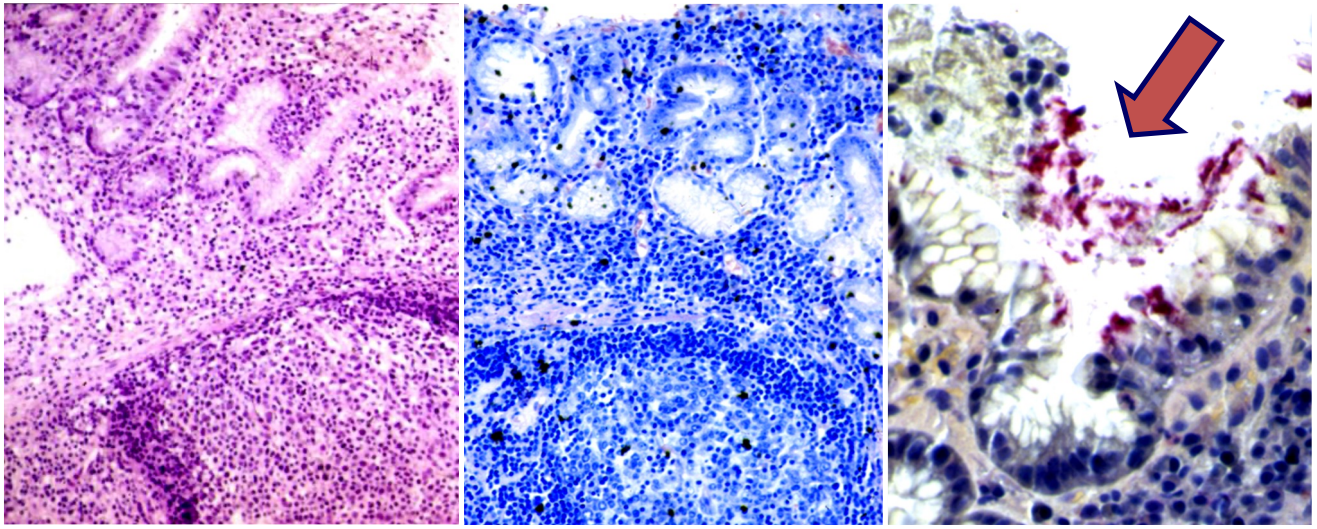
The most extensively studied form of MALT lymphoma corresponds to the gastric one, which in most if not all instances shows a pathobiological correlation with *Helicobacter Pylori* infection.

It represents a model, as other infectious agents involved such as *Borrelia Burgdorferis* in the skin, *Chlamydia psittaci* at the eye level, *Chlamydia pneumoniae* and *Chlamydia trachomatis* in the lung, and *Campylobacter jejune* in the intestine.

Gastric MZL and HP infection

- HP infection occurs in more than 95% of gastric MALTomas.
- The infection causes the development of the acquired gastric MALT, which is responsible for the onset of autoimmune phenomena.
- More often, it is sustained by the $CagA^+$ strain, which causes IL8 release by the epithelial component, neutrophilic activation and genomic damage.

Acquired gastric MALT and HP infection



Gastric MZL: Clinics

- Localised to the stomach for a long time.
- Late dissemination to:
  - loco-regional lymph nodes
  - Malpighi's corpuscles
  - bone-marrow (5-10%)
- In 50% of patients, regression with antibiotic therapy (HP eradication) even if transformed.

Gastric Marginal Zone Lymphoma

- **Architecture:**

  growth: peri-follicular,

  diffuse,

  follicle colonization,

  multi-focal,

  lympho-epithelial lesions (thyroid).

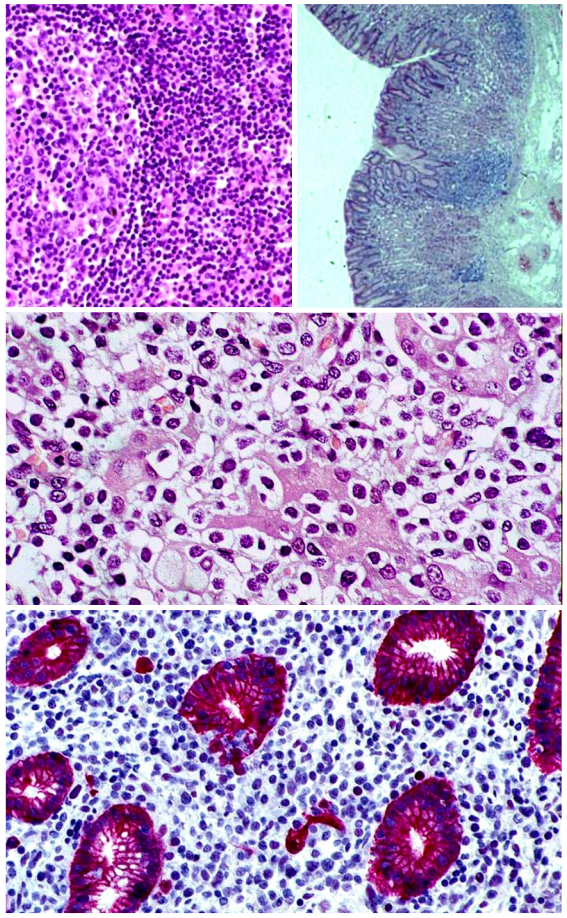
  Blastic transformation (3-15%)

- **Depth of the infiltrate:**

  mucosa/sub-mucosa = regr.$^{+}$

  muscularis propria = regr.$^{-}$

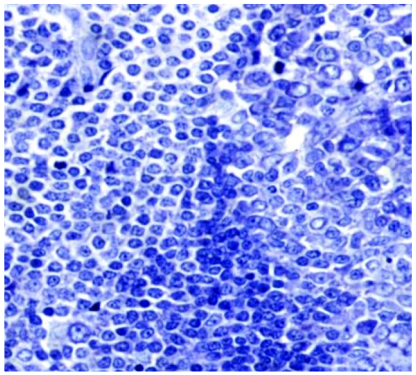
  echo-endoscopy.

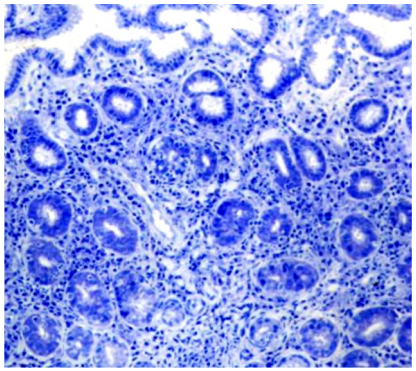


Gela histological scoring system for post-treatment biopsies of patients with gastric MALT lymphoma is feasible and reliable in routine practice

British Journal of Haematology, 2012, **160**, 47–52

Christiane Copie-Bergman,[1,2,3] Andrew C. Wotherspoon,[4] Carlo Capella,[5] Teresio Motta,[6] Ennio Pedrinis,[7] Stefano A. Pileri,[8] Francesco Bertoni,[9] Annarita Conconi,[10] Emanuele Zucca,[9] Maurilio Ponzoni[11]* and Andrés J. M. Ferreri[12]*





- **Evaluation of regression:**

  Histology (more reliable than PCR);

  time required: 2-14 months.

Table I. GELA histological grading system for post-treatment evaluation of gastric MALT lymphoma.

Score	Lymphoid infiltrate	LEL	Stromal changes
Complete Histological remission (CR)	Absent or scattered plasma cells and small lymphoid cells in the LP	Absent	Normal or empty LP and/or fibrosis
Probable minimal residual disease (pMRD)	Aggregates of lymphoid cells or lymphoid nodules in the LP/MM and/or SM	Absent	Empty LP and/or fibrosis
Responding residual disease (rRD)	Dense, diffuse or nodular, extending around glands in the LP	Focal LEL or absent	Focal empty LP and/or fibrosis
No change (NC)	Dense diffuse or nodular	Present 'may be absent'	No changes

MM, muscularis mucosa; LP, lamina propria; SM, submucosa; LEL, lymphoepithelial lesions.

EGILS consensus report.

Recommendations

- Demonstration of monoclonality by PCR analysis of the rearranged immunoglobulin genes using the BIOMED-2 protocols is not a prerequisite for the diagnosis of gastric MALT lymphoma.
- Testing for translocation t(11;18) should be considered at diagnosis. During post-treatment follow-up routine clonality analysis is not recommended.

REVIEW

Mucosa-associated lymphoid tissue (MALT) lymphoma: a practical guide for pathologists

Chris M Bacon, Ming-Qing Du, Ahmet Dogan

J Clin Pathol 2007;**60**:361–372. doi: 10.1136/jcp.2005.031146

Resistance to antibiotic therapy!

Primary Cutaneous MZLPD

- PCMZLPD is a clonal disorder with excellent long-term survival (99% at 5 years) despite the risk of recurrence.

Virchows Archiv (2023) 482:281–298
https://doi.org/10.1007/s00428-022-03421-5

REVIEW

Check for updates

Recent advances in cutaneous lymphoma—implications for current and future classifications

JR Goodlad[1] · L Cerroni[2] · SH Swerdlow[3]


thank you
danke
謝謝
ngiyabonga
teşekkür ederim
gracias
merci
obrigado
bedankt
dziękuję
go raibh maith agat
mochchakkeram
sukriya
kop khun krap
terima kasih
grazie
arigatô
dakujem
спасибо
мерси
감사합니다
ありがとう
ευχαριστώ
dank je
tapadh leat
hvala
mauruuru
sagolun
taiku
takk
рахмат
Баярлалаа
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mersi
barka
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vinaka
blagodaram
misaotra
matondo
paldies
grazzi
mahalo
asante
manana
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mamnun
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bayarlalaa
gracie
koszonom
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sobodi
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mesi
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xièxie
kam sah hamnida
rahmat
didi madloba
спасибі