analysed using Excel spreadsheets designed by the National Genetics Reference Laboratory. The 10 most frequently hypermethylated TSGs were the same for EMZL, DLBL and MCL, suggesting a similar epigenetic aetiology. These genes were CDH13, DAPK1, ESR1, GATA5, IGSF4, PAX6, RAR-β, THBS1, TIMP3, and WT1. Patient prognosis is poorer when the OAL develops in the orbit. We hypothesized that more aggressive lymphomas would show greater epigenetic deregulation. For non-EMZL OAL, a greater number of genes showed hypermethylation when the tumour was diagnosed in the orbit. However, it is interesting to note that the opposite was observed for EMZL. Hypermethylation of common TSGs suggests epigenetic deregulation may play a role in the development of OAL. Correlation of hypermethylation data with clinical presentation and follow-up could reveal epigenetic markers of prognostic value in these tumours.

Leukaemias

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BCR-signaling profiles associated with prognosis and progression in B-CLL

M.T. Scupoli[1]*, O. Perbellini[2], F. Cioffi[2], R. Chignola[3], E. Evensen[5], R. Zanotti[2], I. Nichele[1], O. Lovato[4], G. Pizzolo[2]. [1]*University of Verona, Department of Clinical and Experimental Medicine / Interdepartmental Center for Medical Research (LURM), Verona, Italy,* [2]*University of Verona, Department of Clinical and Experimental Medicine, Verona, Italy,* [3]*University of Verona, Department of Biotechnology, Verona, Italy,* [4]*University of Verona, Interdepartmental Center for Medical Research (LURM), Verona, Italy,* [5]*Nodality Inc., South San Francisco, USA*

Several biological parameters have been shown to be associated with clinical outcome in CLL. Among them, the most reliable markers are represented by the absence of somatic mutations within the immunoglobulin variable heavy chain genes (IGHV), the expression of CD38 antigen, the presence of the ZAP-70 tyrosine kinase. These parameters of poor clinical outcome are structurally and/or functionally linked to B-cell Receptor (BCR) expressed by CLL cells, thereby strengthening the hypothesis that antigenic stimulation mediated by the BCR represents a driving event in the onset and progression of the malignant B cells. To investigate whether different BCR signaling networks may distinguish clinical-biological groups of CLL patients, we applied a "network level" analysis of BCR signaling by measuring single-cell profiles of phosphoprotein networks by flow cytometry. We evaluated the response to BCR engagement in primary cells isolated from 27 CLL patients by analyzing the phosphorylation states of 5 phosphoproteins on the route of BCR signaling, including p-Syk, p-NF-kappaB, p-Erk1/2, p-p38 and p-JNK. BCR was cross-linked by incubating cells with anti-IgM antibodies. The unsupervised clustering analysis distinguished BCR response profiles of phospho-proteins that differentiated cases of CLL with mutated IGHV from those with unmutated IGHV ($P = 0.0003$), cases with low levels of CD38 expression from those with high levels ($P = 0.0004$) and cases with ZAP-70-negative leukemic cells from cases that were ZAP-70-positive ($P = 0.001$). Furthermore, the same BCR response profiles were also associated with time to progression ($P = 0.0014$) and with overall survival ($P = 0.049$), as assessed by Kaplan–Meier curves and the log-rank test. Independent survival analysis of time to progression via fitting Cox proportional hazards models comprising clinical covariates and/or BCR network response to modulation demonstrated that measuring modulated BCR network signaling can yield improved prognostic information compared to CD38 status alone (likelihood ratio test 5.8 for CD38 versus 10.6 for signaling) and enhance prognostic assessment using IGHV status (likelihood ratio test for IGHV = 14.8 versus for IGHV + signaling = 17.9).
This study shows that single-cell profiles of BCR phosphoprotein networks are associated with prognostic parameters, disease progression and overall survival in CLL.

Lymphomas and myeloma

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Cytomegalovirus (CMV) retinitis post rituximab therapy: A case report

E.L.M. Nga[1]*, S. Sadullah[1], C.A. Gomez[1], B.J.L. Burton[2]. [1]*James Paget University Hospital NHS Foundation Trust, Department of Haematology, Gorleston, Great Yarmouth, United Kingdom,* [2]*James Paget University Hospital NHS Foundation Trust, Department of Opthalmology, Gorleston, Great Yarmouth, United Kingdom*

Rituximab, a chimeric monoclonal antibody against CD20 antigen is used in combination with chemotherapy to treat most B-cell non-Hodgkin's lymphoma. Several serious viral infections have been reported in association with rituximab use. We report a case of acute retinal necrosis secondary to cytomegalovirus (CMV) reactivation in a 59 year old male patient nine weeks following completion of six courses of cyclophosphamide, doxorubicin, vincristine and prednisolone (CHOP) and rituximab regimen for stage 3b diffuse large B-cell lymphoma. Diagnosis of CMV retinitis was confirmed on polymerase chain reaction (PCR) performed on vitreous fluid sample. Peripheral blood was negative for PCR amplified CMV deoxyribonucleic acid (DNA) in serum. While several infections have been reported in the literature, this is the first case report of CMV retinitis following rituximab therapy. In patients undergoing treatment with rituximab, the clinician should be vigilant of this rare but treatable cause of blindness. The case report and review of the literature are presented.

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Diffuse skin hyperpigmentation in CD30+ lymphoproliferation: A case report

Z. Prka[1]*, C. Tomasovic-Loncaric[2], V. Pejsa[1], B. Nevajda[3], R. Kusec[1]. [1]*University Hospital Dubrava, Department of Internal Medicine, Division of Hematology, Zagreb, Croatia,* [2]*University Hospital Dubrava, Department of Pathology, Zagreb, Croatia,* [3]*University Hospital Dubrava, Department of Neurology, Zagreb, Croatia*

Introduction: CD 30+ T-cell lymphoproliferative disorders (LD) comprise two main groups of diseases: CD30+ LD of the skin and systemic anaplastic large cell lymphoma. The main feature of these disorders is the expression of CD30. We report on a patient with an unusual clinical presentation of CD30+ lymphoproliferative disease.
Case report: A 54-year old Caucasian male was transferred to our hospital with generalized lymphadenopathy and pronounced skin hyperpigmentation. At admission patient was anemic, with hepatosplenomegaly, generalized lymphadenopathy and with low performance status (ECOG 3). The most prominent feature was his skin color. Whole skin was purple-brownish, except his palms and soles, dry and atrophic with desquamation. He stated that his skin started to get brownish 18 months ago. In the lymph nodes and skin CD30+ lymphoproliferation – anaplastic large cell lymphoma – was diagnosed. Prussian blue staining identified that pigment, responsible for skin color, was hemosiderin. Chemotherapy was started but patient's condition was progressively worsening and he died a week after the first cycle.