only expressed intracellularly. Co-staining of IgA with pPTKs showed that IgA^+ PC in both subsets are responsible for enhanced PTK phosphorylation independently of CD19 expression.
Conclusions: $CD19^+$ and $CD19^-$ BM PC express kinases involved in BCR signalling and respond by enhanced phosphorylation of PTKs upon BCR stimulation with IgA-expressing cells being exclusively responsible for this increase. Further functional consequences of IgA expression in BM PC and autoimmunity remain to be delineated.

REFERENCES:
[1] Manz RA, et al. Lifetime of plasma cells in the bone marrow. Nature 1997;388(6638):133–134.
[2] Tokoyoda K, et al. Organization and maintenance of immunological memory by stroma niches. Eur J Immunol 2009;39(8):2095–2099.
[3] Mei HE, et al. A unique population of IgG-expressing plasma cells lacking CD19 is enriched in human bone marrow. Blood 2015;125(11):1739–1748.
[4] Hoyer BF, et al. Short-lived plasmablasts and long-lived plasma cells contribute to chronic humoral autoimmunity in NZB/W mice. J Exp Med 2004;199(11):1577–1584.
[5] Pinto D, et al. A functional BCR in human IgA and IgM plasma cells. Blood 2013;121(20):4110–4114.

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AB0025 MTOR PATHWAY ACTIVATION IN LARGE VESSEL VASCULITIS

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Background: Mammalian target of rapamycin complex 1 (mTORC 1) drives the proinflammatory expansion of T helper (TH) type 1, TH17 cells and controls fibroblast proliferation, typical features of large vessel vasculitis (LVV) pathogenesis. Molecular pathways involved in arterial lesions of LVV are unknown.
Objectives: To analyse mTOR pathway activation in LVV (giant cell arteritis and Takayasu arteritis).
Methods: We evaluate pathway activation in the mTORC and the nature of cell proliferation in blood and vessels of patients with LVV compared non-inflammatory aorta by using double immunostaining, western blot and flow cytometry. Finally, using flow cytometry, we study the effect of rapamycin on T cells homeostasis in LVV compared to HD.
Results: Proliferation of both endothelial cells and vascular smooth-muscle cells was shown in vascular lesions in LVV. The vascular endothelium of proliferating aorta vessels from patients with LVV showed indications of activation of the mTORC1 pathway en endothelial cells (S6RP phosphorylation) compared to non-inflammatory aorta ($45\%^{24;48}$ versus 10.4% [9.7;14.9] positive S6RP endothelial cells, p=0.03). In cultured vascular endothelial cells, sera from patients with LVV stimulated mTORC1 through the phosphorylation of S6RP. Activation of mTORC1 was also found in Th1 and Th17 cells both systemically and in the blood vessels. Patients with LVV exhibited a diminished S6RP phosphorylation in Tregs. Inhibition of mTORC1 pathway with rapamycin, increase Tregs and decrease effector $CD4^+IFN\gamma^+$, $CD4^+IL17^+$ and $CD4^+IL21^+$ T cells in patients with LVV.
Conclusions: Our results suggest that the mTORC1 pathway is involved in the vascular lesions of LVV. Targeting mTORC pathway may represent a new therapeutic option in patients with LVV.
Disclosure of Interest: None declared
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AB0026 TLR9 STIMULATION OF ANERGIC HCV-ASSOCIATED ATYPICAL MEMORY B CELLS TRIGGERS RHEUMATOID FACTOR AUTOIMMUNITY BY THE TNF-A PATHWAY

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Background: Hepatitis C virus (HCV) infection contributes to the development of autoimmune disorders, but the mechanisms responsible for HCV-associated autoimmunity are not well understood.
Results: Here we show that TLR9 stimulation of atypical memory (AtM) B cells from patients with HCV-associated cryoglobulinemia vasculitis induce the secretion of IFNγ, TNFα but not IL17A by $CD4^+CD25^-$ effector T cells and stimulate their proliferation. Conversely, they reduce the proliferative capacity of $CD4^+CD25^{hi}CD127^{-/low}FoxP3^+$ regulatory T cells. TLR9-stimulated AtM secrete TNFα and IgMs with rheumatoid factor activity. We identify a transcriptional signature specific of TLR9-stimulated AtM, centred on TNFα overexpression. AtM B-cell expansions display intraclonal diversity of mutated IgM with features of antigen-driven maturation. AtM-derived antibodies possess rheumatoid factor activity, with each antibody clone targeting a unique epitope on the human IgG Fc region. AtM antibodies are neither polyreactive nor reactive to ubiquitous autoantigens and importantly, not cross-reactive against HCV antigens including NS3 and E2 proteins.
Conclusions: These data strongly suggest a central role for AtM in defective tolerance of HCV-CV patients through TLR9 reactivation of anergic AtM and production of IgM antibodies with rheumatoid factor activity.
Disclosure of Interest: None declared
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AB0027 SCREENING FOR ANTIBODY REACTIVITY IN EARLY AXIAL SPONDYLOARTHRITIS IDENTIFIES NOVEL ANTIGENIC TARGETS

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Background: Diagnosis of axial spondyloarthritis (axSpA) is challenging since clinical manifestations, such as inflammatory back pain, peripheral arthritis, enthesitis and inflammatory bowel disease, often overlap with other disorders. Despite the use of the genetic marker Human Leukocyte Antigen (HLA)-B27 in axSpA patients, an appropriate serological test is still lacking. Although antibodies are not considered to be a hallmark of axSpA, emerging evidence suggests plasma cells and antibodies to be involved in the disease course[1].
Objectives: Our aim is to screen for antibodies reactive against antigenic targets in plasma of early axSpA patients which may potentially result in novel antibody biomarkers to improve axSpA diagnosis and can enhance the assessment of disease activity, prognosis and therapy response.
Methods: We applied Serological Antigen Selection (SAS), un unbiased and high-throughput antibody profiling procedure based on cDNA phage display. First, a cDNA phage display library was constructed from synovial hip tissue from 3 axSpA patients and screened for antibody reactivity in pooled plasma of early axSpA patients (n=*10*). By performing SAS, we identified antibodies in the axSpA plasma pool that were reactive against 104 different antigenic targets. These targets correspond to both known proteins and novel lineair peptides. In a first validation, antibody reactivity against each of these 104 SAS-identified targets was determined in pooled plasma of additional early axSpA patients (n=*50*) and healthy controls (HC, n=*30*). Antigenic targets that showed highest reactivity in axSpA plasma pools were further validated in individual plasma samples of early axSpA patients (n=*71*) and HC (n=*73*) using phage enzyme-linked immunosorbent assay (ELISA).
Results: Increased antibody reactivity against 7 targets was found in pooled plasma of additional early axSpA patients. Further validation of these 7 antigenic targets in individual plasma samples revealed antibody reactivity in 39% of the early axSpA patients (28/71) compared with 21% of the HC (15/73). By forming a biomarker panel with 4 of these targets, specificity could be improved to 88% (9/73 HC) with only a slightly decrease in sensitivity (34%, 24/71).
Conclusions: We identified autoantibody reactivity to novel antigenic targets in early AS patients. In order to establish the true biomarker potential, antibody reactivity against our identified novel antigenic targets will be further validated in an independent cohort of axSpA patients, rheumatic controls and low back pain controls. Identification of antibody reactivity against novel antibody targets in early axSpA patients can contribute to novel biomarkers for an enhanced diagnosis and might provide more insight into the underlying disease pathology, resulting in novel treatment strategies and eventually improve disease outcome in axSpA patients.

REFERENCE:
[1] Quaden D, et al. Autoimmun Rev. 2016 Aug;15(8):820–32.

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