Methods Patients with symptomatic gout and elevated sUA (≥6 mg/dL) were treated with fixed doses of pegsiticase (0.2 mg/kg or 0.4 mg/kg) alone or co-administered with SVP-R (0.05, 0.08, or 0.1 mg/kg). SEL-212 was infused in 28 day cycles x3 doses followed by challenge with pegsiticase alone on 28 day cycles x2 doses. Safety, tolerability, sUA, and ADAs were monitored

Results In the SEL-212 Phase 1b study, 70% of patients administered 0.4 mg/kg pegsiticase with a mid-dose of 0.1 mg/kg SVP-R showed low or no ADA formation correlating with sustained low sUA levels for at least 30 days after a single dose, compared to 20% for patients treated with pegsiticase alone. In the ongoing Phase 2 study, the majority of patients receiving 0.1 mg/kg SVP-R administered with either 0.2 or 0.4 mg/kg pegsiticase also showed low or no ADAs and maintained low sUA levels after 3 monthly doses of SEL-212, indicating sustained activity with repeated doses of SEL-212. However after 2 subsequent doses of pegsiticase alone, a drop in activity was noted. These data suggest that either a higher dose of SVP-R or the addition of SVP-R at the 4th and 5th dose may be required to sustain activity through 5 months. Currently patients are being dosed with 0.15 mg/kg SVP-R, a dose level which enabled sustained control of sUA levels in all patients in Phase 1b. SEL-212 was generally well tolerated and associated with a low rate of gout flare rates compared to those treated with pegsiticase alone.

Conclusions SVP-R showed a dose-dependent reduction in ADAs and enabled sustained control of sUA with repeated dosing of SEL-212. SVP-R is a promising approach to prevent the formation of ADAs against immunogenic biologic therapies.

REFERENCE

1. Kishimoto TK, *et al*. *Nature Nanotechnol* 2016;**11**:890–899.

Acknowledgements We thank the patients that participated in these studies, the clinical study site investigators, and the entire SEL-212 project team.

Disclosure of interest E. Sands Employee of: Selecta Biosciences, A. Kivitz: None declared, W. DeHaan Employee of: Selecta Biosciences, L. Johnston Employee of: Selecta Biosciences, T. Kishimoto Employee of: Selecta Biosciences

P110 TOFACITINIB IS ASSOCIATED WITH AN IMPAIRED FUNCTION OF NK CELLS AND A DEFECTIVE IMMUNOSURVEILLANCE AGAINST B-CELL LYMPHOMAS

[1]G Nocturne*, [2]J Pascaud, [2]B Ly, [2]F Tahmasebi, [2]S Boudaoud, [1]R Seror, [3]L Stimmer, [1]X Mariette. *[1]Université Paris Sud; [2]INSERM, Le Kremlin Bicetre; [3]CEA, Fontenay aux Roes, France*

10.1136/annrheumdis-2018-EWRR2018.125

Introduction Patients with rheumatoid arthritis (RA) are exposed to an increased risk of lymphoma and the impact of treatments is difficult to assess. Tofacitinib, an oral Janus Kinase (Jak) 3 and 1 inhibitor that has shown positive results in RA patients, may impair NK-cell function due to its inhibitory action on IL2 and IL15 signalling.

Objectives Given the fact that NK cells have been recently shown to participate to anti–lymphoma immunosurveillance, we aimed to assess if tofacitinib might impact NK-cell function and anti-lymphoma activity *in vitro* and *in vivo* in BAFF transgenic mice (a model of B cell autoimmunity associated with an increased risk of lymphoma).

Methods We have studied the consequences of *in vitro* exposure of NK to tofacitinib (10, 50 and 100 nM) or to DMSO (vehicle) during 6 days in presence of IL-2 (200 UI/ml): phenotype has been studied and then cytotoxicity against 2 non-Hodgkin B-cell lymphoma cell lines [Farage (EBV+) and SU-DHL4 (EBV-)] was assessed. In addition, BAFF transgenic mice were treated for 6 months with tofacitinib (2.25 mg/kg/d n=11; 4.5 mg/kg/d n=10) or vehicle (PEG: DMSO, n=6). Incidence of lymphoma was assessed by histologic examination using a composite score.

Results Firstly, we did not observe difference concerning the survival of NK cells in presence of tofacitinib or vehicle after 6 day culture. Secondly, we observed that culture in presence of tofacitinib was associated with a decreased level of activation with a dose effect. In addition, we observed a decreased expression of activating receptors such as NKp30, NKp44 and NKG2D. Last, we found that tofacitinib blocked NK cell maturation as observed with the significant decreased expression of CD57 on NK cells exposed to tofacitinib at 50 and 100 nM. These phenotypic abnormalities were associated with an impaired function of NK as assessed by co-culture: degranulation and cytotoxicity were significantly decreased after exposure to tofacitinib. In BAFF transgenic mice, the crude mortality and incidence of lymphoma did not differ between the 3 groups of treatment.

Conclusions This study demonstrates that tofacitinib treatment negatively impact the state of activation, maturation and functions of NK cells. These defects were not associated with a higher incidence of lymphoma in BAFF Tg mice after 6 months of exposure. However, this negative impact of tofacitinib on NK cells might participate to the increased risk of herpes zoster infection in patients treated with tofacitinib and suggest to remains cautious about a possible increased risk of lymphoma.

Disclosure of interest None declared

P111 MESENCHYMAL STEM CELL ENCAPSULATION IN ALGINATE MICRO-PARTICLES FOR INTRA-ARTICULAR INJECTION IN OSTEOARTHRITIS

[1]A Smith, [2]A Des Rieux, [3]M Marquis, [3]D Renard, [1]C Vinatier, [1,4]J Guicheux*, [1]C Le Visage. *[1]INSERM UMR 1229 – RMeS, Regenerative Medicine and Skeleton, STEP Team, University of Nantes, UFR Odontology, Nantes, France; [2]Louvain Drug Research Institute, Advanced Drug Delivery and Biomaterials, Université Catholique de Louvain, Louvain, Belgium; [3]UR1268 BIA (Biopolymères Interactions Assemblages), INRA; [4]PHU 4 OTONN, CHU Nantes, Nantes, France*

10.1136/annrheumdis-2018-EWRR2018.126

Introduction Owing to their ability to secrete anti-inflammatory and immuno-modulatory factors Mesenchymal Stromal Cells (MSCs) are an attractive tool for the treatment of osteoarthritis. Considering cell death and the risk of cell leakage upon intra-articular injection, MSCs encapsulation therefore could protect cell from death, avoid cell effusion outside the articular space, and supply a suitable 3D microenvironment supporting the biological activity of MSCs.

Objectives Our objective was to develop a method of MSC encapsulation compatible with their intra-articular injection through a 26G needle.

Methods Human adipose-derived stem cells (hASCs) were encapsulated via a micromolding method. We first manufactured polydimethylsiloxane chips containing 1600 micromolds with a circular shape, 150 µm in diameter and 100 µm in depth. For cell encapsulation, a solution of 2% alginate (w/v) containing 3 million of hASCs per mL polymer was deposited onto the chips, loaded in the moulds either by sedimentation or centrifugation and crosslinked using an agarose gel charged with CaCl2. The number of encapsulated cells was evaluated by a CyQUANT assay immediately and 24 hour after encapsulation. The impact of encapsulation on metabolic activity was determined by a presto blue assay 24 hours after encapsulation and 24 hour after their injection through a 26G needle.
Results We successfully obtained cylindrical alginate microparticles presenting a diameter of 103±0.7 µm. Using cell quantification, we determined that the centrifugation method allowed the encapsulation of 30 333 (±5552) cells within one chip versus 6056 (±2862) by sedimentation. Cell number and metabolic activity remained stable for 24 hours after encapsulation. We also demonstrated that injection through a 26G needle had no impact on the viability of encapsulated cells.
Conclusions Our results show that micromolding allows hASCs encapsulation into alginate particles injectable through a 26 G needle without impacting cell viability. Future work will focus on evaluating *in vitro* long-term encapsulated cell survival and functionality. In case of success, we will then consider intra-articular injection in an animal model of osteoarthritis.
Disclosure of interest None declared

P112 TARGETING T-CELL TRAFFICKING IN A MURINE MODEL OF SJÖGREN'S SYNDROME

[1]J Campos*, [1]S Nayar, [2]M Chimen, [1]V Iannizzotto, [1]HM McGettrick, [1]BA Fisher, [1]SJ Bowman, [1]CD Buckley, [2]GE Rainger, [1]F Barone. [1]*Institute of Inflammation and Ageing*; [2]*Institute of Cardiovascular Sciences, University of Birmingham, Birmingham, UK*

10.1136/annrheumdis-2018-EWRR2018.127

Introduction Salivary glands of primary Sjögren's syndrome (pSS) are characterised by complex leukocyte infiltration organised into tertiary lymphoid structures (TLS). The mechanisms regulating leukocyte trafficking into inflamed salivary glands are poorly described, but dysregulated T-cell recruitment during inflammation is believed to contribute to disease onset and chronicity. We recently described a homeostatic pathway in which a B cell-derived peptide (PEPITEM), secreted in response to adiponectin, regulates T-cell trafficking during inflammation via sphingosyne 1 phospate activity on endothelial cells.[1] Loss of this pathway by downregulation of adiponectin receptor on circulating B cells has been demonstrated in type 1 diabetes and rheumatoid arthritis, suggesting a potential role for PEPITEM in the pathogenesis of autoimmune diseases and indicating a role for adiponectin receptor as biomarker in autoimmune diseases.[1]
Objectives We aimed to investigate the efficacy of PEPITEM as an inhibitor of T-cell trafficking in an inducible animal model of salivary gland inflammation that mimics the histological features of pSS and to investigate the potential translatability of this pathway in patients with pSS.
Methods Submandibular salivary glands of C57BL/6 mice were intra-ductally cannulated with luciferase-encoding replication-deficient adenovirus to induce TLS formation as previously described.[2] Mice were administered daily either with PBS or PEPITEM by intraperitoneal injection from day 0, and their salivary glands dissected at day 5 post cannulation. T-cell infiltration into salivary glands was assessed using a combination of flow cytometry, immunofluorescence and qRT-PCR.
Results B cells in sera from cannulated animals express lower levels of both adiponectin receptors 1 and 2 in comparison with non-inflamed control mice. In cannulated animals treated with PEPITEM, histological analysis of salivary glands revealed fewer, as well as less aggregated, infiltrating T cells. Both CD4 +and CD8+numbers were significantly lower in the salivary glands of PEPITEM-treated animals. Furthermore, administration of PEPITEM also decreased mRNA transcripts for lymphotoxin beta, IL-7, lymphoid chemokines (CCL19 and CXCL13) and T cell chemokine receptor CCR7, cytokines and chemokines known to regulate ectopic lymphoneogenesis in pSS. Human samples of pSS are currently being assessed to validate the relevance of this pathway in pSS.
Conclusions These results demonstrate that administration of exogenous PEPITEM can reduce T-cell influx into salivary glands. This may represent a rescue of the homeostatic regulation of leukocyte trafficking, which is disrupted in inflammation. Our work suggests that PEPITEM should be considered to address the therapeutic needs in chronic inflammatory conditions and that the detection of decreased levels of adiponectin receptor could be used as biomarkers in pSS.

REFERENCES

1. Chimen McGettrick, *et al*. *Nat Med* 2015.
2. Bombardieri Barone, *et al*. *JI* 2012.

Disclosure of interest None declared

P113 ARGINASE I AND THE METABOLIC CONTROL OF OSTEOCLASTOGENESIS

[1]JS Brunner*, [1]M Hofmann, [2]V Saferding, [1]A Vogel, [3]A Lercher, [4]P Cheng, [1]G Schabbauer, [2]S Blüml. [1]*Institute for Vascular Biology*; [2]*Dpt. of Rheumatology, Medical University Vienna*; [3]*CeMM, Vienna, Austria*; [4]*Bio Cancer Treatment International Ltd, Hong Kong, China*

10.1136/annrheumdis-2018-EWRR2018.128

Introduction Osteoclasts are giant, multi-nucleated cells that derive from the monocyte-macrophage linage and are regulators of bone turnover. Availability and catabolism of L-Arginine have been implicated with immune cell biology, skewing inflammatory responses within myeloid cells in a pro- or anti-inflammatory manner.
Objectives While the role of L-Arginine within certain myeloid lineages such as macrophages is well appreciated, its role within osteoclasts is relatively unknown. We therefore aim to investigate L-Arginine metabolism in the context of osteoclastogenesis.
Methods We analysed osteoclastogenesis of C57BL/6J wildtype bone marrow cells *in vitro* in the presence and absence of recombinant Arginase 1 (recArg1). This approach was complemented via qPCR analysis of relevant osteoclast marker genes and an extracellular flux assay. We further investigated the