

Background and aims Allergy is a common condition that is caused by an overreaction of the immune system to foreign substances. Severe allergic reactions can result in a systemic life-threatening state referred to as an anaphylactic shock. The progression of the anaphylactic reaction is hard to control after onset, and there is no effective prophylactic treatment available. Recently, mice deficient of the group III metabotropic glutamate receptor mGluR7 were shown to display an anaphylactic-like behaviour when exposed to peripheral histamine, suggesting that mGluR7 works as a neuronal brake on peripheral neurons involved in allergy and anaphylaxis. However, the role of mGluR7 in allergen-induced anaphylaxis is still unknown.

Methods In the PCA model, on the first day, BALB/C mice were lightly anaesthetised with isoflurane and their left ears were intradermally (i.d.) injected with a monoclonal antibody (IgE directed against OVA- trinitrophenol (TNP), 1 µg in 10 µl PBS), whereas the right ears were used as controls (receives an i.d. injection of 10 µl PBS as vehicle). The PCA reaction was induced 24 hours later by an intravenous injection of 50 µg OVA-TNP in 200 µl of 2% Evans blue in PBS.

Results Here, we show that central activation of mGluR7 dampens the development of allergen-induced anaphylaxis as intrathecal, but not intraperitoneal, prophylactic administration of the mGluR7 allosteric agonist N, N'-dibenzhydriethane-1, 2-diamine dihydrochloride [ML1] AMN082 attenuated the development of passive cutaneous anaphylaxis in mice.

Conclusions Activating the mGluR7 system thus represents a potential preventive treatment for anaphylaxis.

72 IMPLICATIONS OF AUTOPHAGY FOR FUNCTIONAL CHANGES OF RHEUMATOID ARTHRITIS FIBROBLAST-LIKE SYNOVIOCYTES

¹JM Kim*, ²J Bang, ³YG Jeong, ⁴CH Lee, ¹CN Son, ¹SH Kim. ¹Keimyung University Dongsan Medical Centre, Division of Rheumatology- Department of Internal Medicine, Daegu, Republic of Korea; ²Keimyung University Graduate School, Medicine, Daegu, Republic of Korea; ³Changwon Fatima Hospital, Division of Rheumatology- Department of Internal Medicine, Changwon, Republic of Korea; ⁴School of Medicine- Wonkwang University, Division of Rheumatology- Department of Internal Medicine, Iksan, Republic of Korea

10.1136/lupus-2017-000215.72

Background and aims Rheumatoid arthritis (RA) is characterised by exaggerated synovial proliferation in which interleukin-17A (IL-17A) plays a key role. Recently several evidences support the implication of autophagy in the pathogenesis of RA. The aims of this study are (1) to evaluate whether IL-17A influences on autophagic flux in RA synovium and (2) to investigate whether the modulation of autophagy can regulate migration and proliferation of fibroblast-like synoviocytes (FLS) from the patients with RA (RA-FLS) under inflammatory milieu.

Methods FLS from the patients with RA or osteoarthritis (OA) were cultured with IL-17A and/or autophagy regulators. The expression of marker proteins for autophagic flux or the formation of autophagolysosome was analysed by western blot or immunofluorescence study. A migration scratch assay was used to assess FLS migration. Proliferation of FLS was determined by the viable cell count using trypan blue.

Results LC3 conversion from LC3-I to LC3-II was increased in RA-FLS than in OA-FLS. IL-17A upregulated the expression of LC3B, Atg5, Beclin1, LAMP1 in RA-FLS. The accumulation of p62 was also prominent in RA-FLS. Migration and

proliferation of FLS stimulated by IL-17A was suppressed by Bafilomycin A1 which prevented the formation of autophagolysosomes. P62-silencing enhanced IL-17A-induced autophagy activation in RA-FLS.

Conclusions This study reveals that IL-17A stimulates autophagy and that intervention of autophagy can control IL-17A-induced migration and proliferation of FLS. Our results also provide additional evidence for a significant role of autophagy in the pathogenesis of RA. Thus, we suggest that autophagy might be a potential therapeutic target for the management of RA.

73 ANTIARTHRITIC EFFECT OF CROCETIN AGAINST ADJUVANT INDUCED AUTOINFLAMMATORY DISEASE VIA SUPPRESSION THE NF-KB EXPRESSION AND ACTIVATING OF HEM OXYGENASE (HO)-1/NUCLEAR FACTOR-E2-RELATED FACTOR SIGNALLING PATHWAY

¹V Kumar*, ²P Bhatt. ¹Sam Higginbottom Institute of Agriculture – Technology and Sciences, Pharmaceutical Sciences, Allahabad, India; ²Jamia Hamdard, Pharmacy, New Delhi, India

10.1136/lupus-2017-000215.73

Background and aims Rheumatoid arthritis (RA) is chronic autoimmune diseases, which inducing the cartilage obliteration, synovial joints destruction and typically producing the symmetrical inflammation, which further leads to disability, demolition and deformity into the joint. The aim of the current study was to scrutinise the anti-arthritis potential of crocetin in formaldehyde induced inflammation and complete Freund's adjuvant (CFA) induced arthritis.

Methods Formaldehyde used for the induction of acute inflammation and CFA used for induction the arthritis. Both method, the rats were divided into different groups and each group contains the 6 rats. The different doses of crocetin (10, 20 and 40 mg/kg) was used in this model. The body weight, arthritic index were scrutinised at regular interval. Hepatic and antioxidant parameter were determined, respectively.

Results Crocetin dose dependently reduced joint inflammation as support via reduce the joint diameter and decreased inflammatory cell infiltration. Crocetin showed the improvement the synovium redox status (down-regulation in MDA and GSH and boost the CAT and SOD level). Crocetin significantly reduced the expression of inflammatory marker viz., TNF-α. Crocetin enhanced The HO-1/Nrf-2 and reduced the NF-κB mRNA expression in adjuvant joint. Additionally, crocetin treatment decreased the expression of degrading enzymes such AS MMP-3 and MMP-9 in adjuvant induced arthritic rats.

Conclusions Collectively, we can conclude that crocetin showed the anti-arthritis effect via down-regulating the NF-κB and Nrf-2/HO-1 pathway.

74 INFLAMMATORY Vδ2 T CELLS CHEMOTAXIS TO THE JOINTS AND CONTRIBUTE TO THE PATHOGENESIS OF RHEUMATOID ARTHRITIS

W Mo*, S Yin, H Chen, X Zhang. Beijing peking union medical college hospital, rheumatology, Beijing, China

10.1136/lupus-2017-000215.74

Background and aims $\gamma\delta$ T cells are important in combating infectious agents and tumour cells. Their role in the pathogenesis of rheumatoid arthritis (RA) remains unknown.

Methods 68 patients with rheumatoid arthritis, 21 patients with osteoarthritis and 21 healthy controls were enrolled in the study. Peripheral V δ 2T population, apoptosis, proliferation, chemokine receptor expression and pro-inflammatory cytokine secretion were quantified by flow cytometry. The infiltration of V δ 2 T cells within synovium was examined by immunohistochemistry and flow cytometry. The effect of TNF- α and IL-6 on V δ 2 T migration was determined by flow cytometry and trans-well migration assay.

Results The percentage of peripheral V δ 2T cells of active RA were significantly decreased compared with healthy controls, which were negatively correlated with the disease activity indexes including DAS28, CRP and ESR. However, the V δ 2T cells infiltrated in the synovium of RA were increased compared with OA ($p < 0.05$). Comparing with OA V δ 2T cells, both peripheral and synovium V δ 2T cells of RA produced higher level of IFN- γ and IL-17 ($p < 0.05$). The chemokine receptor CCR5 and CXCR3 expressed on V δ 2T cells in RA were significantly higher than HC and OA patients ($p < 0.05$), which were induced by TNF- α and IL-6. TNF- α antagonist therapy restored the peripheral V δ 2 T cell in RA.

Conclusions Elevated TNF- α in RA patients induced high expression of CCR5 and CXCR3 on V δ 2T cells, which subsequently promote V δ 2 T cells infiltrate into synovium and play an important role in the pathogenesis of RA. V δ 2 T cell is a promising potential biomarker and therapeutic target of RA.

75 MORINGA OLEIFERA LAM AMELIORATES ADJUVANT INDUCED ARTHRITIS VIA INHIBITION OF INFLAMMATORY MEDIATORS AND DOWN-REGULATION OF MMP3 AND MMP-9 PROTEINS

¹P Pandey*, ²PC Bhatt, ¹V Kumar. ¹Sam Higginbottom Institute of Agriculture – Technology and Sciences, Department of Pharmaceutical Sciences, Allahabad, India; ²JAMIA HAMDARD, pharmacognosy and phytochemistry, Delhi, India

10.1136/lupus-2017-000215.75

Background and aims Rheumatoid arthritis (RA) is an autoimmune disease, which induces systematic and typical inflammation and affects 1% younger population Worldwide. Natural products are being preferred over the available treatment regimes for arthritis. *Moringa oleifera* has been very popular ethanomedicine for the treatment of inflammatory disorders in North-eastern part of India. With this background, the current investigation was carried out to scrutinise the anti-arthritis potential of *Moringa oleifera* in complete Freund's adjuvant (CFA) induced arthritis animal model.

Methods In the present investigation, we used the CFA, turpentine and formaldehyde into the sub-plantar region of hind paw of rats for induction of arthritis. After induction, joint diameter, arthritis score and body weight were estimated at regular interval. We studied the effect of plant extract on pro-inflammatory cytokines and inflammatory mediator, respectively. Histological architecture and other changes were also studied.

Results Oral treatment of MO at doses of 25, 50 and 100 mg/kg significantly ($p < 0.001$) down-regulated joint inflammation as evidenced via reduction in the joint diameter, arthritic score and inflammatory cell infiltration.

Conclusions MO treatment were found to reduce pro-inflammatory cytokines (TNF- α , IL-6 and IL-1 β) and inflammatory mediators PGE₂ and COX-2 in a dose dependent manner. MO also down-regulated the NF- κ B in adjuvant immunised joint. Apart from these findings MO abrogated degrading enzymes, which was evident from down-regulated protein expression of MMP-3 and MMP-9. Our findings clearly indicate the anti-arthritis potential of MO via inhibition of NF- κ B pathway.

76 RASGRP4 EXPRESSION IN RHEUMATOID SYNOVIUM PLAYS A CRITICAL ROLE VIA RAS- MAPK PATHWAY

S Shimamura*, S Yasuda, Y Shimizu, M Kono, M Kato, K Oku, T Bohgaki, T Atsumi. Hokkaido University Graduate School of Medicine, Division of Rheumatology- Endocrinology and Nephrology, Sapporo, Japan

10.1136/lupus-2017-000215.76

Background and aims Ras activation as well as MAP kinase (MAPK) phosphorylation is known in the synovial tissues from patients with rheumatoid arthritis (RA). RasGRP4 is a guanine nucleotide exchange factor for small GTPase Ras and is expressed predominantly in the mast cells, monocytes and neutrophils. We previously identified ectopic expression of RasGRP4 in fibroblast-like synoviocytes (FLS) of a subset of RA patients, inducing proliferation of FLS (Kono M *et al.* Arthritis Rheumatol. 2015). Farnesyltransferase inhibitors (FTIs), prevent farnesylation of Ras, are known to prevent human tumour cell proliferation but the effect for proliferation of FLS is still unknown.

The aim of this study is to clarify the molecular mechanisms of how RasGRP4 induces proliferation of FLS and evaluate the effect of FTI on the proliferation of FLS.

Methods FLS or HEK293 cells were transfected with expression vector that encodes hRasGRP4. Phosphorylation of Raf, MEK, Erk, JNK and p38MAPK was evaluated in transfected cells using Western blotting. FLS were treated with tipifarnib, one of FTIs and cell proliferation was evaluated using BrdU Assay.

Results In HEK293 cells forced to express RasGRP4, Raf-MEK-Erk pathway as well as p38MAPK was readily phosphorylated at their steady state. FLS decreased RasGRP4 expression during multiple passages. RasGRP4 transfection into such cells recovered MAPK phosphorylations, especially of Erk and p38 MAPK. FLS treated with tipifarnib down-regulated their proliferation.

Conclusions RasGRP4 expression in FLS from RA patients contributes to the activation of Erk and p38MAPK signalling pathway. The inhibition of FLS proliferation by FTI was suggested as an alternative treatment in RA.