INTERRELATIONSHIP BETWEEN NICOTINIC ACETYLCHOLINE RECEPTOR AND CYTOKINE PRODUCTION NOTED FOLLOWING T-CELL ANTIGEN RECOGNITION AND ACTIVATION

Nicholas Manolios1,2,3, Kevin Hou4, Han-Shen Tae5, David Adams6,7.

1University Sydney; Westmead Hospital, Rheumatology, Sydney, Australia; 2The University of Sydney, Rheumatology, Camperdown, Australia; 3Westmead, Rheumatology, Westmead, Australia; 4Westmead, Rheumatology, Westmead, Sydney, Australia; 5University of Wollongong, Wollongong, Australia; 6University of Wollongong, Illawarra Health and Medical Research Institute, Wollongong, Australia

Background: T cells express muscarinic and nicotinic acetylcholine receptors (nAChRs) that increase intracellular Ca2+ [1] on stimulation. The expression of these receptors on macrophages and their activation by vagal stimulation has recently been focused for novel arthritis treatment [2].

Objectives: Our aim in the present study was to assess the effect of various peptides, on cytokine production and nAChRs inhibition.

Methods: nAChR heterologous subunits were expressed in Xenopus oocytes and the inhibitory activity of various peptides at ACh-evoked currents were assessed. The effect of these peptides on T-cell antigen recognition and subsequent cytokine production was assessed using an antigen presentation assay (APA). Briefly, the 2B4.11 murine T cell hybridoma recognizing cytokine c as the antigen was co-cultured with the antigen presenting B cell hybridoma line LK35.2 (αEβ2) and pigeon cytokine c in the absence or presence of peptide or several nAChRs antagonists, including mecamylamine (broad nAChR antagonist), vagnerin-1 (α1β1εδ), α-bungarotoxin (α7), Rgla (90kDa), Vc1,1 (90kDa) and dihydro-β-erythroidine hydrobromide (αβδ4 and α8β2). ELISA and real-time PCR were performed to measure cytokine protein levels and nAChRs T-cells mRNA express levels separately.

Results: At 10μM, peptide W32052 had modest 50–55% inhibition of human (h) α3β2 and h6091α2 nACHR subtypes, and 35% inhibition at h90910. W32052 greatly inhibited chimeric rat α1β1-mouse ε (∼85%) at 10μM. W32052 also inhibited IL-2, IL-6, TNF-α and GM-CSF production at 50μM in the APA. nAChRs antagonists, mecamylamine (100μM), Rgla (10nM), Vc1,1 (17.5μM) and dihydro-β-erythroidine hydrobromide (10μM) could decrease IL-2 production. However, vagnerin-1 and α-bungarotoxin did not affect IL-2 production in the APA.

Conclusion: W32052, an antagonist of nAChR, inhibits cytokine production following antigen recognition suggesting that there is a close link between T-cell antigen activation, ion channel regulation mediated by AChR and cytokine production. Further experiments are in progress.

REFERENCES

Disclosure of Interests: None declared


EFFECT OF SIDAGURI EXTRACT (SIDA RHOMBIFOLIA L) ON URINARY CARBOXY-TERMINAL TELEPEPTIDES OF TYPE II COLLAGEN IN OSTEOPOROTIC PATIENTS

Blondina Mapunda1, Sheena Dalmumute2, Joshua Patrick3, William Simanjuntak2.

1Universitas Sumatera Utara, Division of Rheumatology, Internal Medicine, Medan, Indonesia; 2Universitas Sumatera Utara, Division of Rheumatology, Internal Medicine, Medan, Indonesia

Background: Osteoporosis is one of the most common joint diseases in Indonesia and elsewhere. Assessment of the effectiveness of osteoporosis therapy with biomarkers should be developed. One of the biomarker that can be used to assess the activity of osteoporosis is Urinary Carboxy-Terminal Telepeptides of Type II Collagen. Indonesia is the center of world biodiversity, and Sida is one of the traditional plants that is believed to have many benefits including its anti-inflammatory effect and the ability to decrease level of uric acid. The β-sitosterol is an active component in Sida that has anti-inflammatory activity in osteoporosis.

Objectives: To compare the effect of sidaguri and meloxicam therapy with meloxicam alone in decreasing the levels of urinary Carboxy-Terminal Telepeptides Of Type II Collagen in osteoporotic patients.

Methods: This study was conducted on 24 patients with osteoporosis at H. Adam Malik General Hospital Medan from April to June 2018. Subjects were divided into 2 groups, namely placebo and Sidaguri group. Levels of uCTX II were assessed before and after intervention. T-test was used to analyze the data using SPSS version 22.

Results: 83.3% of osteoporosis patients in H. Adam Malik hospital who participated in this study were women with mean age 60.58 ± 9.74 years in the placebo group and 63.08 ± 6.14 years in the sidaguri group. The results showed that subjects receiving Sida showed significant decrease in uCTX II before and after intervention (p=0.046). Further, in the placebo group also found decreased levels of uCTX II but it was not statistically significant (286.17 ± 163.82 vs. 218.25 ± 75.05 ng/ml, p = 0.238). In addition, there was a significant difference between the mean of the two groups after the intervention (p = 0.046).

Conclusion: There was a significant decrease in uCTX II levels in osteoporosis patients who received Sidaguri extract for 30 days compared to the placebo group.

Disclosure of Interests: None declared


CAN DIFFERENT INTERLEUKIN LEVELS PREDICT RESPONSE TO BIOLOGICAL TREATMENT IN PATIENTS WITH RHEUMATOID ARTHRITIS?

Stephen McDonald1,2, Rachel Reed1,2, Ivona Baricevic-Jones3, Stephanie Ling1,5, Darren Plant5, Anne Barton5, University of Manchester, NIHR Manchester BRC, Manchester, United Kingdom; 2University of Manchester, Stoller Biomarker Discovery Centre, Manchester, United Kingdom; 3University of Manchester, Manchester Molecular Pathology Innovation Centre, Manchester, United Kingdom; 4University of Manchester, Division of Musculoskeletal and Dermatological Sciences Centre for Genetics and Genomics, Centre for Musculoskeletal Research, Manchester, United Kingdom

Background: The cytokine family interleukin IL-17 has an important pro-inflammatory role on adalimumab or etanercept and were designated good or poor EULAR responder status at 6-months, WILCOxon rank sum compared interleukin levels at pre-treatment and 3 months- according to EULAR classification by 6 months. Logistic regression was carried out adjusting for gender, baseline DAS28 and disease activity scores (DAS-28).

Methods: Data was collected from the Biologics in Rheumatoid Arthritis Genetics and Genomics Study Syndicate (BRAGGSS). Patients were followed up at pre-treatment (baseline), 3 months, 6 months and 12 months with bloods, questionnaires and clinical data obtained. Patients were eligible for inclusion if undergoing on adalimumab or etanercept and were designated good or poor EULAR responder status at 6-months. WILCOxon rank sum compared interleukin levels at pre-treatment and 3 months- according to EULAR classification by 6 months.

Objectives: To determine if pre-treatment or 3 month IL-17 IL-17 concentrations correlate with treatment response to anti-TNF drugs by 6 months of treatment.

Disclosure of Interests: None declared