(BET) family protein was reported to be a potential therapeutic target by inhibiting epigenetics interaction between bromodomains and acetylated histones.

Objectives: We aimed to investigate the effects of bromodomain-containing protein 4 (BRD4) inhibition on tumor necrosis factor (TNF)- α -stimulated rheumatoid arthritis fibroblast-like synoviocyte (RA-FLS) using BRD4 inhibitor, I-BET762.

Methods: We examined the effects of BET protein inhibitor on cytokine production and cellular proliferation in RA-FLS. RA-FLSs were treated with TNF- α (10 ng/ml) in the presence of I-BET762 for 48 h. The cell viability and proliferation were measured after 24, 48, and 72 h in I-BET762-treated RA-FLS using CCK-8 colorimetric assay. We then screened pro-inflammatory mediators by using the human inflammation antibody array (Abcam). The levels of interleukin (IL)-6 and IL-8 in culture supernatants of TNF- α -stimulated RA-FLS were measured by enzyme-linked immunosorbent assays (ELISA).

Results: I-BET762 had no significant effect on cytotoxicity and proliferation of RA-FLS. I-BET762 reduced the secretion of CXCL-10 and regulated upon activation, normal T cell expressed, and secreted (RANTES) from RA-FLS while increased the secretion of tissue inhibitor of metalloproteinase 2 (TIMP-2) in the antibody array. In addition, ELISA showed significantly decreased level of IL-6 and IL-8 in culture supernatant after treatment with I-BET762.

Conclusion: Inhibition of BRD4 by I-BET762 leads to down-regulation of pro-inflammatory cytokines and chemokines in RA-FLS. I-BET762 may have anti-inflammatory properties and provide a therapeutic target molecule in RA.

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AB0139

ASSOCIATION OF RS17004921 ADORA2A GENE POLYMORPHISM WITH EFFICACY OF METHOTREXATE IN PATIENTS WITH RHEUMATOID ARTHRITIS

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Background: Adenosine A2A receptors (ADORA2A) are part of the adenosine-mediated antiinflammatory pathway. These receptors are over-expressed in peripheral blood leukocytes of patients with rheumatoid arthritis (RA). Methotrexate (MTX), the gold standard for therapy, exerts its antiinflammatory effects via increased release of adenosine into the extracellular space. Adenosine binds to ADOR A2A and A3 and initiates an antiinflammatory response. Therefore, ADOR gene polymorphisms could have an impact on MTX therapy outcome.

Objectives: To examine the role of adenosine receptor 2A gene (*ADORA2A*, rs17004921) polymorphism on outcome of MTX treatment in RA.

Methods: A total of 123 patients with RA (mean age 56.5±10.73, 91 (74% female), treated with MTX for 6 months (mean dose 12.22±3.20/weekly) were enrolled in a prospective study. Genotyping within *ADORA2A* gene was performed using the KASP genotyping assays. MTX efficacy assessment was based on the changes in the Disease activity score (DAS28) after 6 months of treatment according to the EULAR response criteria. Patients with good and moderate response were classified as „responders“, whereas patients with poor response were considered „nonresponders“. Data of adverse effects were collected during this period. MTX efficacy and toxicity were compared among patients with different genotypes. All statistical analyses were performed by SPSS version 16.0.

Results: Median DAS 28 at the beginning of MTX treatment was 7.43±0.89. According to EULAR response criteria, 111 (90.2%) patients with RA were classified as responders. Among all RA patients, 97 (78.9%) had CC, 20 (16.3%) CT and 6 (4.9%) TT genotype. The distribution of *ADORA2A* genotypes in responders (CC 77.5%, CT 17% and TT 5.4%) was not significantly different from nonresponders (CC 91.7%, CT 8.3%), p>0.05. After 6 months, 26 carriers of T allele (CT +TT) had higher reduction DAS 28 (7.16 vs. 3.88) in comparison to other 97 patients (7.50 vs. 4.64, p=0.013). Adverse effects were reported in 24 (19.5%) patients. Most of patients had hepatotoxicity and nausea, 14 (58%) and 9 (37%) respectively. No statistically significant association between *ADORA2A* genotype and side events has been observed (p>0.05).

Conclusion: According to our results, T allele of *ADORA2A* rs17004921 polymorphism may have favourable influence on efficacy in RA patients treated with methotexate.

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Spondyloarthritis - etiology, pathogenesis and animal models

AB0150

IMMATURE GRANULOCYTES LEVEL IS A POTENTIAL BIOMARKER IN PERIPHERAL ENTHESTITIS

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Background: Immature granulocytes (IG) level in peripheral blood is used as early sign of infection. On the other hand, IG could be elevated in other conditions like inflammatory or cancerous diseases and in pregnancy. Similar to CRP, we have observed a series of cases of peripheral enthesitis associated increased level of IG and correlated with CRP elevation and clinical activity.

Objectives: To test the concept of IG as a biomarker in peripheral enthesitis, This observation might be a reflection to the innate immunity role in pathogenesis of enthesitis.

Methods: We have identified 13 cases over the last 12 months at the Rheumatology clinic in our centre who have shared two features (clinical enthesitis and elevated IG) those 13 cases are mainly presented with recurrent foot and ankle pain and swelling of enthesitis nature.

Results: The cohort is of equal gender distribution 46/54% respectively and age range 31-53 years (mean age 38.5), only 3 patients are known to have Psoriatic arthritis whilst the rest either undiagnosed or diagnosed Rheumatoid arthritis or gout prior to clinic visit. The rheumatologist clinical diagnoses are of enthesitis of foot, ankle, knee and hip area as shown on the table [1] apart from one patient who has spinal symptoms mainly. 4/13 patients have the history of psoriasis and after their visits we find them fit in the CASPAR criteria for psoriatic arthritis. All these cases are associated with increased absolute number of IG as well as differential (IG) number compare to 10/13 of these cases are having high CRP. The 3 cases with normal CRP do have relatively slight increase in (IG) number. The main correlation is of response to therapy and was seen in 7 cases who have followed up at the time of submission and it shows a 100% correlation between CRP, absolute (IG) and differential (IG) values. There are 3 patients who have elevated (IG) but normal CRP and it would possible indicate (IG) test has a better yield than CRP in peripheral enthesitis.

Conclusion: Immature granulocytes can be elevated in inflammatory disease and more notably in peripheral enthesitis of the lower limbs of inflammatory rather than mechanical nature and do correlate with CRP elevation as well as response to therapy. Larger studies are needed to assess the usefulness and validity of (IG) level in clinical practice.

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Table 1: The table shows the CRP and immature granulocytes

Case	Age	Response before therapy	CRP before therapy	IG before therapy	CRP after therapy	IG after therapy	CRP before therapy	IG before therapy	CRP after therapy	IG after therapy
M 40	40	Gout	Peroneal tenosynovitis	2	0.60%	0.04	Stavits	2	1.6*	5.9
M 40	40	Inflammatory arthritis	peroneal and Tibialis posterior tendinitis	19	0.90%	0.09	Stavits and MTX	10	0.50%	0.03
M 44	44	Undiagnosed	Peripartur enthesitis and spondylitis	20	0.70%	0.07	Methotrexate	awaited	awaited	awaited
F 51	51	Seronegative arthritis	Seronegative arthritis on Subpharyngeal	24	0.80%	0.04	Increased dose	17	0.2	0.01
F 41	41	Rheumatoid Arthritis/Psoriasis	Entesitis, Ant Talar, Achilles, plantar	17	1.50%	0.06	steroids and MTX	awaited	awaited	awaited
F 47	47	Rheumatoid Arthritis/Ebstein	plantar fasciitis bilaterally / ischial pain	15	0.70%	0.07	steroids	12	0.50%	0.03
M 33	33	Plantar fasciitis 13 years	Plantar fasciitis, high	16	1.00%	0.1	Adalimumab	1	0.70%	0.03
M 42	42	Plantar fasciitis	Plantar fasciitis / at rest	4	0.90%	0.05	Etanercept	awaited	awaited	awaited
F 31	31	Undiagnosed	Ankylosing Spondylitis/ Knees, plantar	30	0.50%	0.05	Secukinumab	awaited	awaited	awaited
M 32	32	Psoriasis /PSA	Psoriatic Arthritis / Dopl	4	1.00%	0.07	Acetate	awaited	awaited	awaited
M 33	33	PSO, PPA, Spinal disease	PSO, PPA, Spinal disease	13	0.50%	0.05	Secukinumab	awaited	awaited	awaited
F 42	42	PSO	PSA, Achilles and Plantar	21	1.00%	0.11	Golimumab	9	0.40%	0.04
F 35	35	PSO on Secukinumab	PSA, Knees tendinopathy	9	0.70%	0.07	to switch	awaited	awaited	awaited

* Values elevated due to renal unit

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