The current available therapies to treat RA target the immune response which in turn adversely affects the immunity of the patients.
**Objectives:** The presents study deals with the discovery of 1,3,5-triazine-thiazoles targeting immune and non-immuno synovitis by via dual inhibition of NF-κB and EGFR-TKs for possible benefit in rheumatoid arthritis.
**Methods:** The 1,3,5-triazine-thiazole hybrid derivatives were synthesized via cascade of nucleophillic and cyclo-condensation reaction. These inhibitors was screened for NF-kB transcriptional activity in RAW264.7 macrophages, whereas, EGFR-TKs inhibitor activity was assessed via kinase inhibition assay kit. The docking study was carried out with 3D-crystal structure of NF-κB and EGFR-TK to explicate the inhibitory action.
**Results:** The designed hybrid analogues showed excellent inhibitory activity against both NF-κB and EGFR-TK. Particularly, against NF-κB, methyl (5c) containing molecule showed most significant activity (respectively with relative NF-κB activity: 1.82±1.87). Docking study suggests that, 5c was deeply buried in the DNA binding domain of NF-κB interacting with Tyr57, Val58, Cys59, His141, and Val142. In EGFR-TK inhibitory assay, the synthesized molecules showed $IC_{50}$ ranging from 4.23–39.32μ M via interacting with Leu788, Met766, Lys745, Glu762 with 3D crystal structure of EGFR-TK.
**Conclusions:** These results demonstrate the feasibility of 1,3,5-triazine-thiazole as dual inhibitior of NF-κB and EGFR-TKs for the treatment of inflammatory disorders such as rheumatoid arthritis in more efficient way.
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## Rheumatoid arthritis - etiology, pathogenesis and animal models

### AB0076 PERIODONTAL MICROBIOTA IN EGYPTIAN RA PATIENTS AND THEIR RELATION TO SERUM AND GINGIVAL ANTI-CITRULLINATED PROTEIN ANTIBODIES AND OTHER DISEASE PARAMETERS

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**Background:** A possible infectious trigger for RA is suspected at the gingival site. Emerging data implicates the microbiome in RA pathogenesis. Mucosal sites exposed to a high load of bacterial antigens, such as the periodontium, may represent the initial site of autoimmune generation. If validated, these findings could lead to the discovery of potential biomarkers and therapeutic approaches in the pre-clinical and clinical phases of RA[(1)].
**Objectives:** To determine the organisms causing periodontitis in Egyptian RA patients and their relation to serum and gingival ACPA level and other disease parameters.
**Methods:** This study was carried out on 100 Egyptian RA patients fulfilling the 2010 ACR/EULAR classification criteria for RA and of less than 5 years disease duration, recruited from Rheumatology Unit, outpatient clinic and Dental clinic at Alexandria Main University Hospital. RA disease activity was assessed by applying DAS28 and functional state of the patients was assessed by applying HAQ score. Dental examination, serum RF, and ACPA in serum and GCF were done for all patients. X-ray of both hands to detect erosions and severity of the disease. Gingival Crevicular Fluid (GCF) culture was performed for all cases with periodontitis for the three micro-organisms most reported in the literature to produce periodontitis (Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Prevotella intermedia).
**Results:** Of the 100 patient, 66 patient had periodontitis, for them, GCF culture was performed and Porphyromonas gingivalis, Aggregatibacter actinomycetemcomitans, and Prevotella intermedia were found in 60.6%, 15.2%, and 30.3% of RA patients with periodontitis respectively. Gingival ACPA was detected in the 3 studied organisms, being of significant higher level with P.gingivalis than P.intermedia positive cases (p=0.047). No statistical significant difference detected on comparing P.gingivalis with A.actinomycetemcomitans or A.actinomycetemcomitans with P.intermedia. A. actinomycetemcomitans positive cases were associated with significantly higher level of CRP than P. intermedia positive cases (p=0.029), while no statistical significant difference was detected between P.gingivalis and A. actinomycetemcomitans or P. intermedia positive cases. There was no statistical significant difference between the three studied organisms regarding serum ACPA level, DAS 28, HAQ score, or X-ray findings of hands.
**Conclusions:** P.gingivalis is the most prevalent periodontal microbiota in Egyptian RA patients with periodontitis, that associated with significant higher level of gingival ACPA. None of the detected organisms correlated with the degree of RA activity or other disease parameters, apart from significantly higher CRP level with A. actinomycetemcomitans.
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### AB0077 INVESTIGATION OF THE INFLUENCE OF TERIFLUNOMIDE PLASMA CONCENTRATIONS ON DISEASEACTIVITY IN LEFLUNOMIDE-TREATED PATIENTS WITHRHEUMATOIDARTHRITIS

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**Background:** Leflunomide has become of increasing value for the treatment of rheumatoidarthritis (RA), and leflunomideisused via its active metabolite teriflunomide. The European League Against Rheumatism (EULAR) suggestedthatboth LEF and methotrexatewerefundamentalmedicines for the treatment of RA.
**Objectives:** To investigate the relationshipbetweenteriflunomideplasma concentrations and diseaseactivity in patients with RA.
**Methods:** This was a cross-sectional multicenter study (four rheumatology departments) over a four years period.Patients withRA on a stable and dailyleflunomide dose for >2 monthswereincluded.
Socio-demographic data and clinical data were recorded. Respectively, disease status and functional disability were assessed by disease activity score (DAS28) and Health Assessment Questionnaire (HAQ). Treatment response was evaluated according to the EULAR criteria (variation of DAS28).
Quantitative determination of teriflunomide (active metabolite of leflunomide) plasma concentrationswas carried out by high-performance liquid chromatography with ultraviolet detection.
**Results:** A total of 24 patients were enrolled; sex ratio =1. The mean age of the sample was 51,71 (±15,3) years; the mean disease duration at study baseline was 135,2 (±80,26) months; 70% of patients were RF positive, and 58% ACPA positive.The mean score on VAS pain was 43 mm (±22,92). Respectively, the mean swollen and tender joint counts (SJC-28, TJC-28) were4,3 (±6,1) and 2,8 (±3,09). The mean HAQ was 2,01 (±0,78). At baseline, the mean DAS28 score was 4,17 (±1,12); 56% weregood and moderate EULAR responders.
The mean leflunomide treatment duration was 34,94 months (±32,47). The meanteriflunomide plasma concentrations was 38,34 ug/ml (±24,92).
Residualteriflunomide plasma concentrations was significantly associated SCJ-28 and DAS28 decrease (p=0,0027). However, all these parameters (VAS pain, TJC-28, HAQ, C reactive protein, prescription duration of leflunomide and EULAR response) were not correlated with residualteriflunomide plasma concentrations.
**Conclusions:** This studyconcludedthatresidualteriflunomide plasma concentration isassociatedwithlow active disease.
**Disclosure of Interest:** None declared
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### AB0078 ROLE OF EXPERIMENTAL RESEARCH IN STUDY OF RHEUMATOID ARTHRITIS ETIOPATHOGENESIS

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**Background:** To study the pathogenesis, diagnosis and therapy of rheumatoid arthritis (RA) there are used numerous experimental *in vivo* and *in vitro* models. Topical issue of this problem is to study the causes of disorder and rehabilitation of immune tolerance mechanisms in RA. The concept about the role of different cells in central and peripheral tolerance formation in this pathology is often contradictory and not clear. A tolerogenic activity of products of fetoplacental complex has long been studied at the Cryopathophysiology and Immunology Department of the Institute for Problems of Cryobiology and Cryomedicine of NAS of Ukraine. The presence of a wide range of immunotropic substances in placenta is a premise to use placental cell suspension (PCS) for immunocompetent sphere recovery in autoimmune diseases.
**Objectives:** The research aim was to determine the possibilities and features of implementation of a tolerogenic activity by native and cryopreserved placental cells in experimental models of RA development: adjuvant arthritis (AA).
**Methods:** Research was carried out in CBA/H mice. The PCS was obtained via homogenizing the murine placenta to days 18–19 of gestation. The AA was induced by subplantar administration of the complete Freund's adjuvant. The AA development was expressed as the arthritis index. Either native (nPCS) or cryopreserved PCS were administered intravenously to day 7 after pathology induction. The PCS was cryopreserved under protection of either 10% dimethyl sulfoxide solution (suspension CD) or Propandiosakharol (suspension CP). A number of $CD4^+CD25^+$ T reg cells was determined by direct immunofluorescence