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Fig. 1. Dual-luciferase reporter assay with the regular 3'UTR of PRTN3 cloned into the pmir-GLO vector compared to empty vector (NTC). Significant effect for miR-184 (17.5 %), miR-708 no effect and let-7f small but not significant reduction in luciferase activity (12.3 %). Data represent 3 independent experiments with triplicate measurements. miR-184 was tested 6 times. * $P < 0.05$; ns = not significant; error bars display standard deviation.

Fig. 2. Dual-luciferase reporter assay with the alternative 3'UTR of PRTN3. Significant effects of let-7f (29.2 %) and miR-708 mimic (23.6 %) but no significant effects of miR-184 of luciferase activity. 3 independent experiments with triplicate measurements. * $P < 0.05$

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THU0026 CLONAL HAEMATOPOIESIS ASSOCIATED SOMATIC MUTATIONS IN RHEUMATOID ARTHRITIS

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Background: Clonal haematopoiesis of indeterminate potential (CHIP) occurs when somatic mutations arise in myeloid neoplasia driver genes of haematopoietic progenitor cells, in the absence of overt cytopenia or dysplasia. The prevalence of CHIP increases with age. The most common genes affected by CHIP mutations in unselected populations are DNMT3A, ASXL1, and TET2. The presence of CHIP is linked to increased basal level of inflammation and a high risk of cardiovascular disease and all-cause mortality. Rheumatoid arthritis (RA) is one of the most common and debilitating multi-system autoimmune disorders, affecting up to 1% of adults in developed countries. The role of somatic mutations in the pathogenesis of autoimmune diseases is an unexplored area; therefore, we aimed to test the hypothesis that clonal haematopoiesis (CH) is associated with the incidence and severity of RA.

Objectives: To evaluate the association of CH somatic mutation with severity of RA.

Methods: 163 RA patients were recruited from the following cohorts: (i) Early RA/ treatment naive (n=31), (ii) Refractory RA - non-responders to Disease-Modifying Anti-Rheumatic Drugs (DMARDs) and biologics (n=48), (ii) Flare (n=41) vs Remission patients (n=43) –patients treated with DMARDs and withdrawn from treatment on achieving remission. Six months later, 50% relapse and 50% sustain remission. Single molecule molecular inversion probes (smMIPs) were used to screen for somatic mutations in 40 loci known to carry clonal haematopoiesis driver mutations (CHDMs). Whole exome sequencing was also performed on Flare/Remission patients (n = 84) to screen for CHDMs and other somatic mutations. In-house bioinformatics pipelines were used to call mutations from both the datasets.

Results: We identified CH in RA with an overall prevalence of 14%. Twenty-four unique variants with a variant allele frequency (VAF) of 2-35% were found in ten genes including ASXL1, CBL, DNMT3A, GNAS, GNB1, PTPN11, PTPN12, SF3B1, TET2, and TP53. The number of unique patients carrying mutations in these genes are follows: **refractory:** n=12/48, **flare:** n=6/41, **remission:** n=4/43 and **early RA:** n=2/31. The majority of the mutations occurred in DNMT3A (n=6) followed by TP53 (N=4) and TET2 (n=3). Two variants with VAF of 15% were identified in two patients under the age of 30, both with clinically severe disease. In patients between the ages of 50-59 yrs., 60-69 yrs., and 70-79 yrs., CH was observed at 11% (4/35), 23% (11/46) and 17%(7/41), respectively.

Conclusion: We here report the prevalence of CH in RA, affecting more patients with clinically advanced/refractory disease compared to those with early/less severe disease.

Further study will be conducted to confirm the results.

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THU0027

THE ASSOCIATION OF THE RS35677470 DNASE1L3 GENE POLYMORPHISM WITH SLE, RA AND SSC: STRUCTURAL/BIOLOGICAL INSIGHTS

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Background: Genome-wide association studies (GWAS) have identified hundreds of autoimmune diseases-associated loci so far but much of the heritability of these diseases remains unknown. In an attempt to identify potential causal variants, various studies revealed that the missense variant rs35677470 at DNASE1L3 is associated with the development of systemic lupus erythematosus