according to functional analyzes reduce the function of the ABCG2 protein (2). Based on *in silico* prediction, the impact on reduced function is expected for variants p.M71V, p.G74D, p.M131I, p.R147W, p.I242T, p.F373C, p.T434M, p.S476P and p.S572R.

Conclusion: Our data suggest that the common variant p.Q141K and most of the rare variants in the *ABCG2* gene affect the function of the ABCG2 urate transporter and are a genetic risk factor for hyperuricemia and gout.

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POS0353 DEEP PHENOTYPING OF PSORIASIS BASED ON LIPID METABOLISM RELATED GENES BY INTEGRATIVE SYSTEMS ANALYSIS

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Background: Psoriasis is an immune-mediated inflammatory, genetic disease with numerous concomitant metabolic disorders¹. Patients with psoriasis experience substantial morbidity and increased rates of cardiometabolic diseases². Among the metabolic disorders, lipid disturbances are recognized as a very important part in the pathogenesis of psoriasis and psoriasis-associated cardiometabolic diseases^{3,4}.

Objectives: To characterize the molecular features of psoriasis by the development of a classification system that was based on the gene expression profile of lipid metabolism related genes.

Methods: We performed molecular subtyping and association analysis of psoriasis from Gene Expression Omnibus (GEO). The training sets includes GSE13355 cohort (N = 58), GSE14905 (N = 28) cohort and GSE30999 cohort (N = 81), while the GSE54456 (N = 92) was selected as the validation set. Energy metabolism-related genes were collected from MSigDB (version 7.0; <http://software.broadinstitute.org/gsea/msigdb/>). Based on these psoriasis lipid metabolism-related genes, we conducted consensus molecular subtyping with nonnegative matrix factorization (NMF). Finally, Gene set variation analysis (GSVA) was used to score individual subtypes against the metabolism-related gene sets, and each group got a GSVA index.

Results: Total 104 lipid metabolism-related genes were clustered into three subgroups (Figure 1A). GSVA revealed the lipid metabolism with the correlation in subtypes. There was no statistical difference was identified between the subtype 1 and subtype 2 ($P > 0.05$, Figure 1B), so we merged the two types as a new Sub1, another subtype was named as the new Sub2 (Figure 1C). We finally identified 2 distinct subtypes of psoriasis in GEO cohort that were characterized by significantly different lipid metabolic gene score. Sub1 was featured by higher metabolic gene score compared with that of Sub2 ($P < 0.001$; Figure 1D). The lipid metabolic subtype classification was successfully validated in another independent patient cohorts (GSE54456).

Conclusion: This study established a new classification based on the gene expression profiles of lipid metabolic genes, thereby furthering the understanding of the pathogenesis and psoriasis-associated diseases.

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Figure 1: Molecular typing of patients with psoriasis based on lipid metabolism-related gene expression profiles. (A, C) consensus clustering of 167 GEO samples by NMF, a heatmap displaying the expression pattern of the lipid metabolism related subtypes is shown. (B) comparison of lipid metabolic score levels among three subgroups. (D) comparison of lipid metabolic score levels between the final two subgroups. $^*P > 0.05$; $***P < 0.001$.

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POS0354 DETECTION OF ABCG2 VARIANTS IN ENCODING OF URATE TRANSPORTERS ASSOCIATED WITH THE HYPERURICEMIA IN HAEMODIALYSIS PATIENTS

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Background: Hyperuricemia is associated with gout, hypertension, cardiovascular diseases and renal disease. The presence of chronic kidney disease (CKD) is associated with low excretion of the uric acid as the homeostasis in maintaining of serum levels of uric acid is impaired. Progression of CKD is connected to hyperuricemia and lowering levels of the uric acid is one of the most important goals in clinical treatment. Dysfunctional variants of ATP-binding cassette transporter subfamily G member 2 (*ABCG2*), a major urate transporter in the kidney and intestine, are the major causes of hyperuricemia and gout.

A recent studies found that *ABCG2* is also a major transporter of uremic toxins and *ABCG2* dysfunctional variants are risk genetics factors for mortality in hemodialysis patients.

Objectives: The aim of the present study was to investigate the frequencies of *ABCG2* variants in cohort of hemodialysis patients.

Methods: In this retrospective one centre study 167 patients (age=79.8±11.03; female=74) with end-stage CKD (pre-dialysis n=86; dialysis n=79) were collected. Peak urate levels were 456.3±113.6 µmol/l in pre-dialysis and 572.93±114.56 µmol/l in dialysis. *ABCG2* coding regions were analyzed from genomic DNA, as we described previously (1). The reference sequence was defined as version ENST00000237612.7; the reference protein sequence was defined as Q9UNQ0. The chi-square goodness-of-fit test was used to compare minor allele frequencies (MAF), and the log-rank test was used to compare empirical distribution functions.

Results: In the CKD cohort, 15 intronic and seven non-synonymous allelic exonic variants were detected: two common (rs2231137/p.V12M; rs2231142/p.Q141K), five ultra rare and/or rare (rs142634180/p.R45Q, rs759726272/p.M131I, rs140207606/p.R236X, rs138606116/p.G354R, rs138892154/p.A607V), and one novel (p.E344D). Common variant p.V12M, previously reported as protective

allele, was detected in 12 heterozygous patients with. The p.Q141K variant, detected in the homozygous stage in three patients and in 31 patients as heterozygous variant. Heterozygous rare variants p.R45Q, p.G354R, p.A607V, and novel variant p.E344D were detected in one heterozygous patient each; heterozygous p.M131I and p.R236X in two patients.

Conclusion: In this study, significantly higher frequency of dysfunctional ABCG2 variants, common and rare, in comparison with common European population, were identified. On the other hand, the frequency of probably protective allele variant p.V12M was significantly lower in CKD cohort (MAF in our cohort = 0,036/MAF in the European population = 0,061). Further analysis of ABCG2 association with CKD events via ABCG2 inflammation role is necessary. In conclusions, our finding of one novel, five rare and two common non-synonymous ABCG2 allelic variants in a sample of 167 CKD patients suggests that the ABCG2 variants should be considered a risk factor for CKD.

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POS0355

ASSOCIATIONS BETWEEN HLA-DRB1 SHARED EPITOPES ALLELES AND ANTI-RA33 ANTIBODIES IN DIFFERENT SUBSETS OF RHEUMATOID ARTHRITIS IN MALAYSIAN POPULATION

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Background: The mechanisms affecting anti-RA33 antibody's involvement in RA pathogenesis is still unclear. Refining our understanding of anti-RA33's role in RA in relation to known RA-associated genes and serological elements is needed.

Objectives: We investigated the relationship between RA-associated HLA-DRB1 epitope (SE) allele and presence of anti-RA33 antibodies in different serological subsets of rheumatoid arthritis in a Malaysian population.

Methods: Serum samples from 550 RA cases comprising seronegative (negative for anti-CCP2, IgG and IgM, n=250), seropositive (triple-autoantibody positive, n=150), singular anti-CCP2 positive (n=100), and double RF positive RA (n=50) were chosen from the Malaysian Epidemiological Investigations of RA (MyEIRA) case-control study. Three hundred MyEIRA population controls were used for comparison. All serum samples were assayed using a commercial anti-RA33 ELISA kit. All genetic samples were genotyped for four-digit HLA-DRB1 alleles using the PCR-SSO method on Luminex platform.

Results: The proportions of anti-RA33 positive was 20.9% in all RA cases (i.e. 34% in RF only positive RA; 25% in seropositive RA; 18% in seronegative RA and 18% in anti-CCP2 only positive RA). The HLA-DRB1 shared epitope alleles were significantly associated with anti-RA33 positive in the seropositive RA subgroup (OR=6.9, 95% CI 1.4-34.8; p=0.02). We observed significant association between anti-RA33 negative and HLA-DRB1 SE alleles among the seropositive RA patients (OR=4.5, 95% CI 2.8-7.2; p<0.001) and among CCP only positive RA (OR=4.4; 95% CI 2.6-7.4; p<0.01). No association was observed between anti-RA33 status and HLA-DRB1 SE alleles in seronegative RA and RF only positive RA.

Conclusion: The HLA-DRB1 SE alleles increased the risk of seropositive and CCP only positive RA independent of anti-RA33 positivity.

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POS0356

THE RELATIONSHIP OF GENETICS AND CLINICALLY SUSPECT ARTHRALGIA IN RA DEVELOPMENT ASSESSED USING HC, CSA AND RA PATIENTS

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Background: The identification of a pre-RA stage of patients with clinically suspect arthralgia (CSA) has proven to be beneficial in the early detection of Rheumatoid disease. Similarly, genetic susceptibility studies have identified important genetic risk factors for the development of (CCP positive) RA.¹ The question that arises is whether these findings represent independent etiological pathways and could therefore be complimentary in the early diagnosis of RA.

Objectives: To corroborate the knowledge of genetic differences between HC and RA patients and extend it to include the CSA stage of disease.

Methods: We used three datasets sampled from the same region in the Netherlands: 1,085 healthy controls (HC), 530 CSA and 1,277 RA patients. CSA patients were monitored for a median of 2 years for conversion into clinically apparent inflammatory arthritis (CSAc) or not (CSAnc).² We assessed the association between HLA SE and disease stage using logistic regression. The analysis was repeated in the CCP positive and CCP negative strata of both the CSA and the RA populations.

Results: Consistent with previous studies, HLA SE was significantly enriched in RA patients compared to HC (OR 2.28) (Figure 1). HLA SE also differentiated HC vs CSAc (OR 1.69), CSAnc vs CSAc (OR 1.74), and CSAnc vs RA (OR 2.35). No difference was found in HC vs CSAnc and CSAc vs RA.

Conclusion: HLA SE is more prevalent in patients who developed (rheumatoid) arthritis than in both healthy controls and CSA patients who do not progress to arthritis. The results presented here seem to indicate a clear distinction between CSA patients who develop arthritis and those who do not. We therefore believe that known RA genetics play a role in the development of arthritis rather than the CSA symptoms. While this relationship varies by CCP status, an independent effect remains. Studies into the broader role of genetics beyond HLA SE are currently underway.

Figure 1. Distinguishing ability of HLA SE across HC, CSAc, CSAnc and RA in the full populations as well as in the CCP positive and negative stratifications. The arrowhead indicates the "case" status in each logistic regression. OR's (95% CI) derived from regression coefficients indicate the change in odds ratio attributable to HLA SE positivity.