for leukotriene A4 hydrolase, which converts LTA4 to LTB4; microsomal glutathione S-transferase, which converts LTA4 to LTC4; and gamma-glutamyltransferase (LTC4 >LTD4). In contrast, Tr14, but not diclofenac strongly induced Nrf2 mRNA at 12–36 hours.

Conclusions: Tr14 and diclofenac had very different effects on the COX/LOX synthetic pathway after cutaneous wounding. Tr14 allowed normal autoinduction of COX2 mRNA by PGE2, but suppressed mRNA levels for the key enzymes in the leukotriene synthetic pathway. A likely explanation for these effects is that Tr14 strongly induced Nrf2 mRNA, which is known to co-repress the leukotriene enzymes via transcription factor Bach1.

Disclosure of Interest: None declared

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THU0022 ANALYSIS OF 47 NON-MHC ANKYLOSING SPONDYLITIS SUSCEPTIBILITY LOCI REVEALS SHARED ASSOCIATED VARIANTS ACROSS CAUCASIANS AND CHINESE HAN

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Background: Genetic factors play a prominent role in AS pathogenesis. So far over 40 non-MHC Ankylosing Spondylitis(AS) susceptibility loci with genome-wide or suggestive significance have been initially reported in Caucasians, however, lack of association evidence of most loci was seen in Chinese Han and some results seemed controversial.

Objectives: Here, we present a systematic evaluation of 47 non-MHC AS susceptibility loci using GWAS datasets in Chinese Han.

Methods: Totally 1853 AS cases and 4048 newly matched controls in 4 cohorts were obtained, after imputation meta-analysis results of 93 589 variants within 47 reported loci were extracted. Best-guess genotype data were used for interaction analysis and weighted genetic risk score model construction which was then assessed by receiver operator characteristic analysis. Functional annotation was conducted using HaploReg, RegulomeDB and rVarBase Database.

Results: We revealed 14 AS-associated variants with nominal evidence in Chinese Han, including rs10865331(p=2.96E-9), rs10050860 (p=1.84E-4) and rs8070463(p=2.81E-4) and found potential associated variants within these loci. We then extracted variants in ERAP1 as well as HLA-B27 tag snp rs13202464 for HLA-B27-ERAP1 interaction analysis (figure 1). Epistatic association between ERAP1 (rs30187, rs10045403) and HLA-B27 (rs13202464) was confirmed. Among those 14 variants, rs30187 showed weaker risk effect in Chinese while rs10050860 and rs12504282 seemed to attribute more risk (Table 1). Genetic prediction model combining 14 variants in 11 loci with HLA-B27 achieved better discrimination ability(AUC=0.884, 95%CI=0.873~0.895) than HLA-B27 alone (p=2.17E-6). We also identified some likely functional variants at these loci.

Abstract THU0022 – Figure 1

Abstract THU0022 – Table 1. Comparison of 14 shared associated non-MHC SNPs across European and Chinese

Locus	SNP	Nearby Gene(s)	Risk allele	RAF% (CEU/CHN)	OR (CEU/CHN)	PARP% (CEU/CHN)
1 p36	rs6600247	RUNX3	C	0.50/0.69	1.16/1.15	7.41%/9.42%
2 p15	rs10865331	Intergenic	A	0.38/0.49	1.34/1.27	11.44%/11.60%
3 p24	rs10510607	CMC1	C	0.83/0.54	1.15/1.14	11.07%/7.03%
4q21	rs12504282	ANTXR2	T	0.54/0.91	1.14/1.20	7.03%/15.38%
5 p13	rs11742270	IL7R	G	0.73/0.84	1.11/1.14	7.43%/10.53%
5q15	rs30187	ERAP1	T	0.34/0.53	1.32/1.11	9.81%/5.47%
5q15	rs10045403	ERAP1	A	0.73/0.82	1.20/1.18	12.74%/12.92%
5q15	rs10050860	ERAP1	C	0.78/0.95	1.18/1.45	12.31%/30.01%
6q15	rs639575	BACH2	T	0.61/0.49	1.08/1.10	4.65%/4.69%
14q13	rs8006884	PPP2R3C	C	0.35/0.40	1.11/1.09	3.71%/3.44%
17q11	rs2297518	NOS2	A	0.19/0.16	1.13/1.11	2.41%/1.72%
17q21	rs9901869	NPEPPS	A	0.52/0.62	1.15/1.14	7.24%/7.95%
17q21	rs8070463	TBKBP1	C	0.51/0.44	1.14/1.16	6.66%/6.64%
21q22	rs2836883	Intergenic	G	0.74/0.83	1.19/1.16	12.33%/11.71%

Conclusions: Our results provided a detailed spectrum of non-MHC AS susceptibility loci in Chinese Han and highlighted 2 p15, ERAP1 and TBKBP1 may play a critical role in AS pathogenesis.

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THURSDAY, 14 JUNE 2018:

Adaptive immunity (T cells and B cells) in rheumatic diseases

THU0023 COMPLEX IMMUNOPHENOTYPING STRATIFIES PATIENTS WITH PRIMARY SJÖGREN'S SYNDROME, SYSTEMIC LUPUS ERYTHEMATOSUS AND SECONDARY SJÖGREN'S SYNDROME ASSOCIATED WITH SYSTEMIC LUPUS ERYTHEMATOSUS INTO DISTINCT CLINICALLY RELEVANT GROUPS WITH POTENTIAL THERAPEUTIC IMPLICATIONS

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Background: Similarities in the clinical and laboratory features of patients with primary Sjögren's syndrome (pSS) and systemic lupus erythematosus (SLE) have led to attempts to treat pSS and SLE patients with similar biologic therapeutics. However, the results of many clinical trials are disappointing and no effective treatments are available for pSS and few for SLE patients with refractory disease.

Objectives: To identify novel patient endotypes using in depth immune phenotyping that facilitates the selection of biological therapies for patients regardless of diagnostic labels.

Methods: Peripheral blood was collected from patients with pSS (n=55), SLE (n=38), SS/SLE (n=15) and age/sex-matched healthy controls (HCs) (n=34). In-depth phenotyping of peripheral B and T-cell subsets by flow-cytometry, followed by unsupervised cluster analysis were performed. ROC analysis identified immune signatures characteristic for every cluster (endotype).

Results: Patients with pSS, SLE and SS/SLE had both unique and shared defects in immune cell phenotype. Hierarchical clustering of CD19⁺ B-cells, CD4⁺ and CD8⁺ T-cells across the three disease groups identified five distinct endotypes spanning diagnostic boundaries. Three of the endotypes had distinct immune signatures, characterised by predominantly B-cell, T-cell memory or CD4⁺/CD8⁺ T-cell subset fingerprints respectively, while two clusters had no distinct immune profiles. Notably, clinical and disease features were not significantly different between clusters.