Objectives: The purpose was to detect the susceptibility genes of RP through whole-exome sequencing (WES) in a Chinese family and deepen our understanding of the pathogenesis of RP.
Methods: A 32 year-old Chinese female proband with RP and her family in which only her mother was RP patient were recruited in the current study. The genomic DNA of 6 human subjects was extracted from the peripheral blood monocyte cells (PBMCs) and then identified gene allele mutations using WES. Candidate variants with low frequency (<0.1%) in general population and predicted deleterious on gene function were identified. Sanger sequencing was then used to validate the analysis results of WES and further validated the gene variants in 12 human subjects.
Results: 38 genes mutated were confirmed by WES among RP patients. Of them, 10 gene mutated were validated by Sanger sequencing, including Collagen Type XXII Alpha 1 Chain (COL22A1) rs200464636, folliculin (FLCN) NM_144606: c.G838A: p.E280K, glycosylphosphatidylinositol anchor attachment 1 (GPAA1) rs201424010, DNA ligase 3 (LIG3) rs761808558, RecQ like helicase 4 (RECQL4) rs757703895, ring finger protein 207 (RNF207) NM_207396: c.T425C:p.I142T, coiled-coil domain containing 61 (CCDC61) rs777816675, Purkinje cell protein 2 (PCP2) rs144974437, tubulin alpha 3e (TUBA3E) rs749780020 and myosin heavy chain 15 (MYH15) NM_014981: c.G4462A: p.A1488T.
Conclusions: This study confirms that coinheritance of multigene mutated may contribute to the susceptibility to RP. The candidate genes mutated we discovered are potential targets for in-depth functional studies.

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

AB0023 SEX-BASED DIFFERENCES IN ASSOCIATION BETWEEN CIRCULATING T CELL SUBSETS AND DISEASE ACTIVITY IN UNTREATED EARLY RHEUMATOID ARTHRITIS PATIENTS

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Background: Genetic association studies strongly support the role of $CD4^+$ T cells in promoting RA pathology. In a cohort of untreated early RA patients, we recently demonstrated that the balance of helper T cell subsets in blood of ueRA patients is skewed towards Th2 cells relative to healthy controls.[1] RA has been shown to be a sexually dimorphic condition with current data suggesting that prevalence, disease course and treatment outcome varies between men and women.
Objectives: It is not known if sex-based disparities in immunological factors contribute to the disease process in rheumatoid arthritis (RA). Hence, we examined whether circulating T cell subset proportions and their association with disease activity differed in male and female patients with untreated early rheumatoid arthritis.
Methods: Proportions of T cell subsets were analysed in peripheral blood from 70 ueRA DMARD and prednisolone naïve patients with untreated early Rheumatoid arthritis (50 females and 20 males) and in 31 healthy age-matched controls. Broad analysis of helper and regulatory $CD4^+$ T cell subsets was done using flow cytometry. Disease activity in patients was assessed using DAS28, CDAI, swollen joint counts, tender joint counts, CRP and ESR.
Results: Multivariate factor analyses showed that male and female untreated early rheumatoid arthritis patients display distinct profiles of association between disease activity and circulating T cell subset proportions. In male, but not female, ueRA patients Th2 cells showed a positive association with disease activity and correlated significantly with DAS28-ESR, CDAI and tender joint counts. Likewise, proportions of non-regulatory CTLA-4^+ T cells associated positively with disease activity in male patients only, and correlated with DAS28-ESR. In contrast, there was a negative relation between Th1Th17 subset proportions and disease activity in males only. Proportions of Th1 and Th17 cells showed no relation to disease activity in either males or females. There were no significant differences in proportions of T cell subsets between the sexes in patients with untreated early rheumatoid arthritis.
Conclusions: In conclusion, our findings show sex-based differences in the association between T cell subsets and disease activity in ueRA patients, and that Th2 helper T cells may have a stronger role in the regulation of disease activity in male patients.

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AB0024 IGA-EXPRESSING BM PC ARE RESPONSIBLE FOR ENHANCED PHOSPHORYLATION OF BCR-ASSOCIATED KINASES AFTER BCR STIMULATION INDEPENDENTLY OF THEIR CD19 EXPRESSION

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Background: Plasma cells (PC) are considered key drivers of antibody mediated autoimmune diseases. Long-lived PC survive for years in their niches, preferentially in the bone marrow (BM) but also in inflamed tissues.[1 2] A subset of PC lacking expression of CD19 has been identified.[3] Better understanding of factors and pathways involved in survival and maintenance of long-lived PC is needed to find strategies to target PC in autoimmunity since targeting B cells or proliferating cells does not affect already existing PC.[4] B cell receptor (BCR) signalling is a critical mediator of B cell survival and it was shown before that IgA^+ and IgM^+ PC in the BM express a functional BCR suggesting a potential role for the BCR signalling pathway.[5]
Objectives: Expression of BCR associated molecules in BM PC and the response of $CD19^+$ and $CD19^-$ BM PC to BCR stimulation by anti-IgM/IgA/IgG was assessed to test whether these PC subsets are capable of responding to BCR mediated signals. We further investigated if the PC isotype has an impact on BCR signalling.
Methods: BM samples from patients undergoing routine total hip arthroplasty without systemic immune manifestations were stained for baseline expression of spleen tyrosine kinase (Syk) and Bruton's tyrosine kinase (Btk) as well as for the phosphosites pSyk (Y^{352}) and pBtk (Y^{223}). BM mononuclear cells have been isolated, stimulated with anti-IgM/IgA/IgG and the increase of fluorescence intensity of pSyk (Y^{352}) and pBtk (Y^{223}) was measured by intracellular flow-cytometric analyses. In some experiments, cells have been stimulated with anti-IgA alone and stained for the isotype additionally to the pPTK staining.
Results: Whole BM stainings revealed that both $CD19^+$ and $CD19^-$ PC express the PTKs Syk and Btk at baseline. Both PC subsets showed the ability to respond to BCR stimulation with enhanced phosphorylation of the PTKs with a clear trend to reduced responsiveness among $CD19^-$ PC. Ig staining revealed that IgA expression was identified on both membrane and intracellularly, whereas IgG was