disease-relevant pathways in the synovium that may point to possible combination therapies.

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Figure 1. Differentially expressed genes from collagen-injected versus naïve rat synovial tissue were identified over the course of disease and mapped to biological processes.

Disclosure of Interests: Debbie Ruelas Employee of: Gilead, Ruidong Li Employee of: Gilead, Christian Franci Employee of: Gilead, Victor Lira Employee of: Gilead, David Lopez Employee of: Gilead, Li Li Employee of: Gilead, Gundula Min-Oo Employee of: Gilead, Julie A. Di Paolo Employee of: Gilead
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THU0071 CD5L IN RHEUMATOID ARTHRITIS: PROTECTIVE OR PROMOTER?

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Background: Rheumatoid Arthritis (RA) is an aggressive auto-immune disease characterized by synovial hyperplasia and chronic inflammation. The main players of RA pathogenesis are T-cell and B-cell dependent pathways and some myeloid cells are also abundant in the synovial tissue. However, how inflammation is initiated, propagated and maintained remains controversial. Unbiased proteomic reports revealed an enrichment in the scavenger receptor CD5L, a component of serum and synovial tissues of arthritic patients. Upon secretion, this blood circulating glycoprotein represses pathogenic Th17 cells, promotes M2 polarization and binds and aggregates Gram-negative and -positive bacteria. However, its mechanisms of action has not been established either in health or disease.

Objectives: We intend to clarify whether CD5L is an immune component that helps resolving RA or a factor that aggravates the disease.

Methods: We analyzed by ELISA the presence of CD5L in samples from RA patients covering different stages of the disease, and correlated with other markers of RA. In parallel, we experimentally induced collagen induced arthritis (CIA) in CD5L knockout (KO) mice to evaluate the incidence and severity of the disease. The differences between the cellular groups in circulation vs the composition on secondary lymph organs using flow cytometry were also investigated in KO and WT mice. The histopathology of the joints was examined, while cytokine concentrations at several timepoints and total Ig levels were measured by ELISA and cytometric bead assays, respectively.

Results: The samples from RA patients showed increased CD5L levels concomitant with the severity of the disease and a direct correlation with Sharp RTG Score or IL-6 serum levels, and inversely correlated with COMP levels. However, these correlations did not clarify whether CD5L helps to resolve RA or is a component that aggravates the disease. To clarify this aspect, we provoked CIA in CD5L KO mice and observed a higher incidence of RA, higher severity and a much lower recovery rate when compared with WT mice. To corroborate

these data, the H&E staining of sagittal section of fore- and hindpaws revealed histopathology consistency with RA, with notable inflammatory signs especially in KO mice. WT animals with RA also showed higher levels of CD5L when compared with the control group, which confirms the observations obtained for human samples. Total serum IgG levels did not correlate with the disease severity but KO mice presented higher quantities of IgG and IL-6 when compared with WT mice.

Conclusion: Overall, these data imply that CD5L is not a promoter of the disease but rather a fundamental protective molecule against inflammation.

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THU0072 THE RELATIONSHIP BETWEEN INFLAMMATION AND COGNITIVE IMPAIRMENT IN RHEUMATOID ARTHRITIS

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Background: The pathophysiology of cognitive impairment remains unclear, however, several studies have demonstrated that pro-inflammatory cytokines such as Interleukin-6 (IL-6), Tumor necrosis factor- α (TNF- α) and lipocalin-2 (LCN2) are related with cognitive impairment by activation of microglia and astrocyte in brain. Rheumatoid arthritis (RA) is a representative inflammatory disease; however, the association of pro-inflammatory cytokines and LCN2 with cognitive impairment has seldomly been investigated in RA.

Objectives: Here, we determined the effect of pro-inflammatory cytokines and LCN2 on cognitive impairment in collagen-induced arthritis (CIA) mouse model. In addition, we studied the effect of TNF- α inhibitor (etanercept) on cognitive impairment.

Figure 1. Comparison of learning and memory abilities in CIA mice.

For the Morris water maze, the learning phase was conducted four times per day over 5 days. (A) Escape latency to reach the platform during the training session (days 1-4), (B) escape latency to reach the platform, (C) time spent in the target zone, (D) number of the target zone crossing and (E) tracking figures in the final trial of the last training day was also shown. Normal; Healthy group, CIA; collagen-induced arthritis group, CIA/Etanercept; collagen-induced arthritis and etanercept treatment group. Values are the means $\pm$ SEM (n = 10 mice per group). *, $p < 0.05$; **, $p < 0.01$; ***, $p < 0.001$ and ns=not significant.