Results: collected blood samples every two hours over a period of 24 hours. The absolute
with regular meals, allowed to eat snacks ad libitum and carry passive activities. We
either were (n=8) or, for comparison, were not (n=5) under current treatment with
ber was notably reduced in RA (Table 1). CD8+ T cells, CD14+ monocytes, and
and patients with RA in terms of circadian rhythms. We examined the effect of
ment strategies, we conducted a clinical study comparing healthy donors (HD)
and Versus Arthritis for providing infrastructure support through the Experimental
Arthritis Treatment Centre (grant number: 20022).

Disclosure of Interests: None declared.
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Table 1. Circadian rhythms in the cellular, gene, and protein levels in HD, RA, and RA with ongoing GC treatment

<table>
<thead>
<tr>
<th>Comparison</th>
<th>Circadian impact</th>
<th>Circulating immune cells</th>
<th>Clock genes in monocytes</th>
<th>Serum cytokines</th>
</tr>
</thead>
<tbody>
<tr>
<td>HD vs. RA</td>
<td>Non-circadian in HD and RA</td>
<td>-</td>
<td>CLOCK, CRY2, DBP, RORA</td>
<td>Fractalin, IFNγ, CXCL11, GM-CSF, MMP11, MMP3, IL-1β, IL-6, IL-8, IL-10, IL-12, IL-13, IL-17A, IL-21, IL-23, IL-23p19</td>
</tr>
<tr>
<td>RA</td>
<td>Circadian in HD and RA</td>
<td>CD3+*, CD4+, regulatory T cells</td>
<td>PER3</td>
<td>IL-10</td>
</tr>
<tr>
<td>RA</td>
<td>Circadian in RA</td>
<td>CD8+ T cells, CD14+ monocytes, CD15+ B cells</td>
<td>PER2, REVERB</td>
<td>MIP1α, MIP1β, IL-1β, IL-6, IL-8, IL-10, IL-12, IL-13, IL-17A, IL-21, IL-23</td>
</tr>
<tr>
<td>RA</td>
<td>Restorative effect of GC in RA</td>
<td>CD8+ T cells, CD14+ monocytes</td>
<td>PER3, CRY1, RORA</td>
<td>-</td>
</tr>
<tr>
<td>RA</td>
<td>Dampening effect of GC in RA</td>
<td>CD8+ T cells, CD15+ B cells</td>
<td>PER2, REVERB</td>
<td>-</td>
</tr>
</tbody>
</table>

Conclusion: In patients with RA, we found a certain loss of circadian rhythms and the establishment of “inflammatory” rhythms. GC treatment in patients with RA resulted in three different types of effects on circadian rhythms at immune cell level: restoration, amplification, and attenuation. In conclusion, these findings provide new insights into the pathophysiology of circadian rhythms in RA that could be used to optimize diagnosis and treatment.

REFERENCES:

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Background: Rheumatoid Arthritis (RA) is a chronic inflammatory disease, which is characterized by circadian inflammation resulting in bone and cartilage destruction. Crosstalk between activated fibroblast-like synoviocytes (FLS) and immune cells, such as CD4+ T cells, within the synovium might amplify synovial inflammation and joint destruction.

Objectives: To define the interaction profile of activated FLS and CD4+ T cells within an inflammatory setting and to elucidate its consequence on synovial inflammation.

Methods: To screen for factors that activate FLS in RA, isolated FLS were treated with different inflammatory cytokines and transcriptomic changes were measured with RNA-seq. Fluorescence activated cell sorting (FACS) purified naïve CD4+ CD45RO- T cells from the same patients were co-cultured with the cytokine pre-treated FLS. Automated fluorescence microscopy and downstream bioinformatic image analysis allowed visualization and quantification of cell-cell interactions. After co-culture T-cells were isolated and T-cell activation, proliferation and differentiation was determined by flow cytometry.

Results: To model the in vivo situation, FLS were pre-stimulated with different pro- and anti-inflammatory cytokines. RNA-seq revealed cytokine specific activation patterns of FLS. Correspondingly, we observed distinct CD4+ T cells – FLS interaction profiles depending on the cytokine used for FLS activation. In line with distinct interaction profiles, specific patterns in CD4+ T cells activation, proliferation and differentiation of naïve T cells into CD26+CD45RO+ memory T cells could be detected. Signatures of cytokine-stimulated FLS could be identified in transcriptomic data from synovial tissue samples.

Conclusion: Within this study, we describe how cytokine induced CD4+ T cells – FLS interactions impact on T-cell proliferation, activation and differentiation.

REFERENCES: