confirm several targets of HOXD10, -D11, and -D13 by qPCR, e.g. *NR4A1*, *ROR2*, *LIF*, *ATF3*.

Figure 1. Comparison of the genes which were differentially expressed after HOXD10-11-13 silencing

Conclusion: The expression of HOXD10, -D11 and -D13 in synovial fibroblasts and tissues strikingly overlaps with predilection sites for RA. Silencing experiments suggested that these embryonic HOX transcription factors have a crucial role in regulating fibroblast functions and might shape a joint specific environment that modulates the development and course of RA in specific joints.

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OP0021

IDENTIFICATION OF DIFFERENTIALLY EXPRESSED GENES IN EARLY RHEUMATOID ARTHRITIS PATIENTS RESPONDING TO TOCILIZUMAB

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Background: Tocilizumab (TCZ) is a monoclonal antibody that binds to the interleukin 6 receptor (IL-6R), inhibiting IL-6R signal transduction to downstream inflammatory mediators. TCZ has shown to be effective as monotherapy in early rheumatoid arthritis (RA) patients (1). However, approximately one third of

patients inadequately respond to therapy and the biological mechanisms underlying lack of efficacy for TCZ remain elusive (1). Here we report gene expression differences, in both whole blood and peripheral blood mononuclear cells (PBMC) RNA samples between early RA patients, categorized by clinical TCZ response (reaching DAS28 < 3.2 at 6 months). These findings could lead to identification of predictive biomarkers for TCZ response and improve RA treatment strategies.

Objectives: To identify potential baseline gene expression markers for TCZ response in early RA patients using an RNA-sequencing approach.

Methods: Two cohorts of RA patients were included and blood was collected at baseline, before initiating TCZ treatment (8mg/kg every 4 weeks, intravenously). DAS28-ESR scores were calculated at baseline and clinical response to TCZ was defined as DAS28 < 3.2 at 6 months of treatment. In the first cohort (n=21 patients, previously treated with DMARDs), RNA-sequencing (RNA-seq) was performed on baseline whole blood PAXgene RNA (Illumina TruSeq mRNA Stranded) and differential gene expression (DGE) profiles were measured between responders (n=14) and non-responders (n=7). For external replication, in a second cohort (n=95 therapy-naïve patients receiving TCZ monotherapy), RNA-seq was conducted on baseline PBMC RNA (SMARTer Stranded Total RNA-Seq Kit, Takara Bio) from the 2-year, multicenter, double-blind, placebo-controlled, randomized U-Act-Early trial (ClinicalTrials.gov identifier: NCT01034137) and DGE was analyzed between 84 responders and 11 non-responders.

Results: Whole blood DGE analysis showed two significantly higher expressed genes in TCZ non-responders (False Discovery Rate, FDR < 0.05): urotensin 2 (UTS2) and caveolin-1 (CAV1). Subsequent analysis of U-Act-Early PBMC DGE showed nine differentially expressed genes (FDR < 0.05) of which expression in clinical TCZ non-responders was significantly higher for eight genes (MTCOP12, ZNF774, UTS2, SLC4A1, FECH, IFIT1B, AHSP, and SPTB) and significantly lower for one gene (TND2P28M). Both analyses were corrected for baseline DAS28-ESR, age and gender. Expression of UTS2, with a proposed function in regulatory T-cells (2), was significantly higher in TCZ non-responders in both cohorts. Furthermore, gene ontology enrichment analysis revealed no distinct gene ontology or IL-6 related pathway(s) that were significantly different between TCZ-responders and non-responders.

Conclusion: Several genes are differentially expressed at baseline between responders and non-responders to TCZ therapy at 6 months. Most notably, UTS2 expression is significantly higher in TCZ non-responders in both whole blood as well as PBMC cohorts. UTS2 could be a promising target for further analyses as a potential predictive biomarker for TCZ response in RA patients in combination with clinical parameters (3).

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

OP0022

RHO EXPRESSION FACILITATES T CELL MIGRATION TO LYMPH NODES IN RESPONSE INFLAMMATION

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Background: Deficiency in geranylgeranyltransferase type I (GGTase-I) results in accumulation of active Rho family proteins RhoA, Rac1 and Cdc42, responsible for cell communication and migration. We reported that mice with GGTase-I deficient macrophages (GLC mice) develop a spontaneous and age-dependent arthritis, reproducing pathology of RA [1].

Objectives: We study how GGTase-I deficiency in Mø changes T cell phenotype to facilitate their translocation to joints and the development of arthritis.