

# SERUM COLLAGEN TRIPLE HELIX REPEAT-CONTAINING (CTHRC1) LEVELS IS ASSOCIATED WITH CIRCULATING STEM CELL FACTOR AND PRO-INFLAMMATORY CYTOKINES IN RHEUMATOID ARTHRITIS

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**Introduction:** Everyday monitoring disease activity of chronic inflammatory diseases such as Rheumatoid Arthritis (RA) is a tempting approach for every patient for attaining personalized treatment strategies. Still underdeveloped area of RA biomarkers needs sensitive and specific analytes. CTHRC1 was found earlier expressed in activated synoviocytes and present in circulation that makes it potential valuable RA marker.

**Materials and methods:** We collected serum and synovial fluid of RA patients (n=40) of the Republican Diagnostic Center, Astana, Kazakhstan to compare it with healthy samples. Rheumatoid factor (RF), C-reactive protein (CRP), anti-cyclic citrullinated peptide antibodies (ACPA), and CHRC1 were measured along with BioLegend proinflammatory cytokine multiplex immunoassay analytes. We were also first to show a high endogenous levels of CTHRC1 in vitro RA cell cultures using immunofluorescence with anti-CTHRC1 antibodies.

**Results and discussion:** Circulating peripheral CTHRC1 levels were significantly higher in RA when compared to normal individuals (6.3-folds,  $p < 0.0002$ ). CTHRC1 positively correlated with RA severity and duration. Analysis of the blood cellular composition indicated strong correlation between CTHRC1 and neutrophils and eosinophils. CTHRC1 correlated most strongly with INF $\gamma$ , IL-1 $\beta$ , IL-6 and IL-8 ( $r > 0.8$ ,  $p < 0.001$  for these cytokines). In line with the stromal cell origin and control of granulocytosis, CTHRC1 significantly correlated with Stem Cell Factor SCF ( $r = 0.56$ ,  $p < 0.05$ ). In healthy individuals, weaker correlation was observed and only for INF $\gamma$  and SCF. CTHRC1 expressed endogenously in RA synoviocytes showed near nuclear localization. More studies are required on co-localization of CTHRC1 with cellular organelles to elucidate the particular location.

**Conclusion:** Peripheral CTHRC1 protein levels strongly correlated with major RA cytokines, RF and neutrophils. Since CTHRC1 was initially found in the arthritic pannus, its peripheral concentration might indicate local pannus activity.

**Acknowledgments.** This study was supported by the Program "Translational and Personalized Medicine in Biomedicine Industry Development in the Republic of Kazakhstan" grant "Mechanisms of Cellular Polarization and Motility of Fibroblast-like Synoviocytes", Principal Investigator - VAA.