Annual meeting of the Croatian Immunological Society 2019

Rovinj
11-12.10.2019

Diamond Sponsor

THE EFFECT OF CCL2/CCR2 SIGNALING BLOCKADE ON BONE RESORPTION AND OSTEOCLAST PROGENITORS IN COLLAGEN INDUCED ARTHRITIS

Darja Flegar[1,2], Alan Šućur[1,2], Antonio Markotić[1,2], Maša Filipović[1,2], Nina Lukač[3,2], Dino Šisl[1,2], Nataša Kovačić[3,2], Tomislav Kelava[1,2], Vedran Katavić[3,2], Katerina Zrinski Petrović[3,2], Danka Grčević[1,2]

1 Department of Physiology and Immunology, University of Zagreb School of Medicine, Zagreb, Croatia
2 Laboratory for Molecular Immunology, Croatian Institute for Brain Research, Zagreb, Croatia
3 Department of Anatomy, University of Zagreb School of Medicine, Zagreb, Croatia

INTRODUCTION: Osteoclast progenitors (OCPs) originate from myeloid lineage precursors common to macrophages and dendritic cells. Their differentiation to osteoclasts, specialized bone resorbing cells, increases in rheumatoid arthritis (RA) and promotes joint destruction. We investigated effects of CCL2/CCR2 axis blockade on OCPs and osteoresorption in mice with collagen-induced arthritis (CIA), a mouse RA model.

METHODS: Male DBA and B6 mice were immunized with chicken type II collagen to induce CIA. DBA mice developing CIA (day 15-30 after immunization) were treated with methotrexate (MTX) (2mg/kg) and CCR2 receptor antagonist (CRA) (4mg/kg) every 48 hours. CIA severity was assessed by clinical scoring, and osteoresorption by fluorescence imaging using osteoclast-specific probe, micro-CT and histology. Spleen and distal tibia bone marrow (BM) cells were immunophenotyped for hematopoietic markers to assess effects on myeloid lineage cells and OCP frequency. Sorted OCP subsets were assessed for migration potential using Transwell system and osteoclast differentiation by culturing with M-CSF/RANKL.

RESULTS: Frequency of CD45+B220-CD3-NK1.1-Ly6G-CD11b-/loCD115+CCR2+ OCPs was significantly increased in arthritis. CIA severity score and osteoresorption, measured by fluorescence imaging and micro-CT analysis, were decreased in treatment groups. Frequencies of BM neutrophils, macrophages and CD45+B220-CD3-NK1.1-Ly6G-CD11b-/loCD115+CCR2+ OCPs were also decreased with tretment, particularly in CRA treated mice. Sorted OCPs from treated groups generate multinucleated TRAP+ osteoclasts less efficiently compared to untreated CIA group.

CONCLUSION: CCR2 blockade affects myeloid cell populations and OCPs. Therefore, additive therapeutic inhibition of CCL2/CCR2 signaling may help antagonizing enhanced osteoresorption in arthritis.

SUPPORT: Croatian Science Foundation projects IP-2014-09-7406, IP-2018-01-2414 and DOK-2018-09-4276.

Poster number 09