

EXPERIMENTAL RHEUMATOLOGY

Role of FcγRs in osteoclast differentiation and function

Clinical Relevance

Rheumatoid arthritis (RA) is an autoimmune disease that results in a chronic, systemic inflammatory disorder that may affect many tissues and organs, but principally attacks flexible (synovial) joints. It can be a disabling and painful condition, which can lead to substantial loss of functioning and mobility if not adequately treated. More than 150.000 people in the Netherlands suffer from RA and an additional 15.000 develop RA every year.

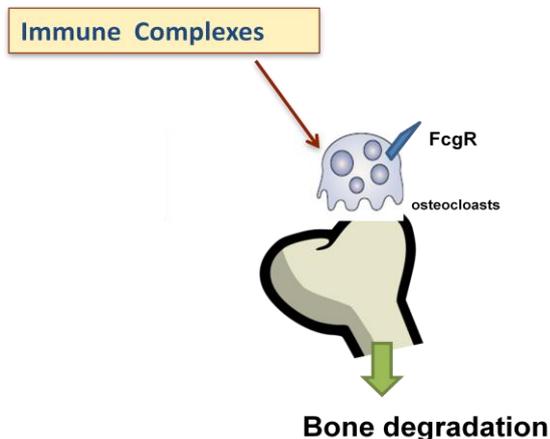
Background

RA is characterized by massive bone destruction in joints which is mediated by osteoclasts. These cells are derived from bone marrow derived precursors that migrate via the blood stream into the inflamed joint where they can differentiate into mature osteoclasts.

The presence of autoantibodies and immune complexes (autoantibody complexed with the self-antigen) have both been identified as possible important initiators and mediators of bone damage in RA. Immune complexes stimulate immune cells by signaling via Fcγ receptors. Various activating and one inhibiting FcγR have been described and the balance between them on the membrane of the immune cell determines their sensitivity for IC stimulation.

FcγR are expressed also on the osteoclast surface and experimental and clinical evidence suggests their role in regulation of osteoclastogenesis and function. Immune complexes present in high concentrations during RA, may stimulate osteoclast activity via binding to FcγRs and lead to the massive bone destruction as observed in RA.

Goal



The aim of our study is investigate the role of FcγRs in osteoclast differentiation and function.

For that primary bone marrow cells and ER-Hoxb8 progenitor cell line with wild type genetic background and FcγR I,II,III,IV $-/-$ will be used to obtain osteoclasts. Stimulation of wild type and FcγR I,II,III,IV $-/-$ osteoclast with immune complexes will be performed in order to mimic the situation present in RA.

We Offer

During this internship you will have the opportunity to learn a broad spectrum of molecular biological and immunological techniques: cell culture of osteoclasts, bone resorption assay immunohistochemistry, FACS analysis, and qPCR. You will be able also to develop your scientific thinking and expand your knowledge on immunology.

Contact

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