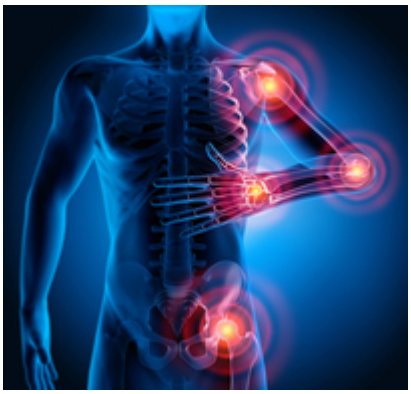
INNOVATION PARTNERSHIPS
UNIVERSITY OF MICHIGAN

A Small Molecular Compound for Arthritis and Bone Erosion Treatment

TECHNOLOGY NUMBER: 7656



Technology ID
7656

Category
Therapeutics and Vaccines
Life Sciences

Inventor
Andrew White
Joseph Holoshitz

Further information
Tiefei Dong
tiefeid@umich.edu

Learn more

OVERVIEW

A small molecule that decreased bone erosion in rheumatoid arthritis and periodontal disease

- Affects the reaction between the Shared Epitope and calreticulin in stimulating osteoclasts
- Oral delivery in a mouse model decreased arthritis by 50%

BACKGROUND

Inflammation and bone erosion are common complications of rheumatoid arthritis (RA) and periodontal disease, and they are associated with increased severity of these illnesses. Currently available rheumatoid arthritis treatments only target the end stages of the immunological responses that cause deleterious manifestations of the disease. And, given that these agents are fairly non-specific in their actions, their use can result in significant side effects. The protein HLA-DRB1 is associated with the Major Histocompatibility Complex and may contain a specific genetic marker that associates with a greater incidence and severity of RA. This "Shared Epitope" (SE) is present in up to 80% of patients with RA and interacts with Calreticulin (CRT) to drive inappropriate bone erosion. A need exists to discover a means to disrupt the SE/CRT interaction to mitigate bone loss in RA patients and minimize the effects of the disease.

INNOVATION

Researchers have discovered a small molecule called HL840 which inhibits the SE/CRT interaction to inhibit disease development, decrease arthritis severity, and prevent bone

destruction in mouse models. HL840 can be easily formed and isolated, and the resulting drug can be safely administered orally on a twice-per-week schedule. The medicine suppresses nitric oxide-mediated signaling pathways, ultimately leading to decreased differentiation and activation of osteoclasts, the cells responsible for the break down and reabsorption of bone tissue. This new technology elicits its activity by targeting a specific pathway important for early rheumatoid arthritis pathophysiology.

Experiments in arthritic mouse models demonstrate that the technology reduces the incidence of arthritis by greater than 50% and diminishes the severity of the disease in afflicted organisms. Notably, these results are heavily correlated with significant reductions in the degree of bone erosion. Owing to its specificity, the risk of side effects associated with its use are significantly lower than those related to existing medications. As such, the discovery may serve as a useful lead molecule for developing novel therapies for rheumatoid arthritis and periodontal disease.