

Summary of the PhD thesis No 24723, PhD in Immunology, Faculty of Veterinary Medicine, Urmia University.

The academic year: 2024-2025

Author: Farshad Yadollahi

Title of thesis: Effect of conditioned medium of peritoneal macrophages treated with estrogen in experimental model of rheumatoid arthritis.

Summary:

Objective: Anti-inflammatory macrophages help to prevent tissue damage and chronic inflammation. Estradiol (E2) reduces inflammatory cytokine expression in these cells. This study explored the impact of conditioned medium from E2-treated macrophages on Wistar rats with rheumatoid arthritis (RA) .

Materials and Methods: RA was induced by injecting complete Freund's adjuvant into the hind paw of each rat. Treatment began on day 4 in all RA rats and continued until day 24 when they were sacrificed. The rats were divided into five groups of 10: RA with Vehicle, RA with macrophage conditioned medium (M ϕ CM), M ϕ CM from E2-pulsed macrophages (M ϕ CM-E2), RA on prednisolone, and healthy controls. The lyophilized media, at 10 mg/ml protein concentration, were administered intraperitoneally on days 4, 12, and 20 at 1 mL each .

Results: The conditioned medium from E2-treated M ϕ showed increased IL-10, TGF- β , and IDO activity compared to untreated M ϕ . The mRNA expression levels of Egr2 and MR were higher in macrophages treated with E2 than in untreated macrophages. Treatment with M ϕ CM-E2 could reduce the severity of clinical and therapeutic symptoms of RA and enhance weight gain more significantly than treatment with M ϕ CM. Furthermore, M ϕ CM-E2 led to a notable decrease in antigen-specific proliferation index and serum levels of C-reactive protein, Myeloperoxidase, Nitric oxide, IL-1, and TNF- α more prominently than the similar results observed with M ϕ CM. The mRNA expression of RANKL and MMP-9 exhibited a significant reduction in rats with arthritis that received M ϕ CM-E2 compared to RA rats treated with M ϕ CM.

Conclusion: The secretome from estradiol-treated macrophages, containing a rich profile of anti-inflammatory and regulatory factors, represents a promising and advantageous cell-free therapeutic strategy for immunotherapy in rheumatoid arthritis .

Keywords: conditioned medium, estradiol, immunotherapy, macrophages, rheumatoid arthritis.