**Dr. Mohan R. Wani**

**The list of ten best papers of the candidate, highlighting the important discoveries/contributions described in them briefly (not to exceed 3000 words)**

Bone contains two distinct cell types, osteoblasts, essential for bone formation; and osteoclasts, essential for bone resorption (break-down). Co-ordinated activity of osteoblasts and osteoclasts is essential to maintain bone homeostasis and structural integrity of skeleton. Increased osteoclast activity and simultaneous decrease in osteoblast function result in pathological bone loss in musculoskeletal and autoimmune diseases. The present treatment prevents only the partial bone loss and does not induce new bone formation. Mohan Wani investigated the novel role of IL-3 in regulation of pathological bone loss and obtained following important research leads and publications.

1. Shruti M. Khapli, Latha S. Mangashetti, Yogesha S.D. and **Mohan R. Wani** (2003) IL-3 acts directly on osteoclast precursors and irreversibly inhibits receptor activator of NF-κB ligand-induced osteoclast differentiation by diverting the cells to macrophage lineage. ***The Journal of Immunology 171:142-151.***

We revealed that IL-3 acts directly on mouse osteoclast precursors, and inhibits receptor activator of NF-κB ligand (RANKL)-induced osteoclast differentiation and diverts the cells to macrophage lineage. IL-3 inhibits NF-κB activation and the inhibitory action of IL-3 on osteoclast differentiation was irreversible.

1. Yogesha, S. D., Shruti M. Khapli, and **Mohan R. Wani** (2005). Interleukin-3 and granulocyte-macrophage colony-stimulating factor inhibits (TNF)-α-induced osteoclast differentiation by down-regulation of expression of TNF receptors 1 and 2. ***Journal of Biological Chemistry 280:11759-11769.***

TNF-α is crucial to the pathogenesis of osteoporosis and rheumatoid arthritis. Further, we demonstrated that IL-3 inhibits TNF-α-induced osteoclast differentiation by inhibiting the expression of TNF receptors.

1. S. D. Yogesha, Shruti M. Khapli, Rupesh K. Srivastava, Latha S. Mangashetti, Satish T. Pote, Gyan C. Mishra and **Mohan R. Wani** (2008). IL-3 Inhibits TNF-α-Induced Bone Resorption, and Prevents Inflammatory Arthritis. ***The Journal of Immunology 182: 361-370.***

This work is highlighted In Research Highlight Section of ***Nature Reviews Rheumatology, 2009, 5:180.***

IL-3 also inhibits the TNF-α-induced bone resorption in presence of many pro-inflammatory cytokines such as IL-1α, TGF-β1, TGF-β3, IL-6 and PGE2. Interestingly, IL-3 prevents the development of inflammatory arthritis in mice, and protects cartilage and bone destruction

1. Navita Gupta, Amruta P Barhanpurkar, Geetanjali B. Tomar, Rupesh K. Srivastava, Satish T. Pote, Gyan C. Mishra and **Mohan R. Wani** (2010). IL-3 inhibits human osteoclastogenesis and bone resorption through down-regulation of c-Fms, and diverts the cells to dendritic cell lineage. ***The Journal of Immunology 185:2261-2272.***

This study was further extended to human osteoclast differentiation. Interestingly, IL-3 also inhibits human osteoclast differentiation and diverts the cells to dendritic cell lineage. Moreover, IL-3 inhibits bone resorption in osteoclast precursors of osteoporotic individuals

1. Rupesh K. Srivastava, Geetanjali B. Tomar, Amruta P Barhanpurkar, Navita Gupta, Satish T. Pote, Gyan C. Mishra and **Mohan R. Wani** (2011). IL-3 attenuates collagen-induced arthritis by modulating the development of Foxp3+ regulatory T cells. ***The Journal of Immunology 186:2262-2272****.*

In mouse model of RA, we demonstrated that IL-3 attenuates collagen-induced arthritis (CIA) by modulating the development of regulatory T (Treg) cells and production of pro- and anti-inflammatory cytokines in mice. IL-3 inhibits the development of pathogenic Th17 cells and increases the number of Treg cells in IL-2-dependent manner and ameliorates CIA in mouse model of human RA *(The Journal of Immunology- revised manuscript submitted)*.

1. Manasa G. Garimella,Supinder Kour, Vikrant Piprode, Monika Mittal, Anil Kumar, Lekah Rani, Satish T. Pote, G. Mishra, Naibedya Chattopadhyay and **Mohan R. Wani** (2015).Adipose-derived mesenchymal stem cells prevent systemic bone loss in collagen-induced arthritis**. *The Journal of Immunology 195:5136-5148.***

We have developed adult MSCs lines from bone marrow and adipose tissues of mice and human. We found that adipose tissue-derived MSCs prevent pathological bone loss, suppresses autoimmune T cell responses and promote immune tolerance by increasing the percentages of peripheral regulatory T and B cells in mice.

1. Amruta Barhanpurkar-Naik, Suhas T. Mhaske, Satish T. Pote, Kanupriya Singh and **Mohan R. Wani** (2017) Interleukin-3 enhances the migration of human mesenchymal stem cells by regulating expression of CXCR4. **Stem Cell Research and Therapy 8:168:1-15.**

In osteoporosis and RA, the osteoblast number is decreased and they are defective in synthesis of bone matrix. We found that IL-3 increases osteoblast differentiation and mineralization from human mesenchymal stem cells (MSCs) in both in vitro and in vivo conditions. Regeneration of bone requires recruitment of MSCs with increased potential for osteoblast differentiation. Interestingly, IL-3 enhances in vivo migration and wound healing abilities of MSCs*.*

1. Supinder Kour, Manasa G. Garimella, Divya A. Shiroor, Suhas T. Mhaske, Snehal R. Joshi, Kanupriya Singh, Subhashis Pal, Monika Mittal, B. Harikrishnan, Naibedya Chattopadhyay, Anil H. Ulemale and **Mohan R. Wani** (2016). IL-3 decreases cartilage degeneration by down-regulating matrix metalloproteinases and reduces joint destruction in osteoarthritic mice. ***The Journal of Immunology 196:5024-35.***

*This article is featured**In Research Highlight Section* of July 2017 issue of **Nature Reviews Rheumatology, *12:374-375****.*

We further demonstrated that IL-3 ameliorate degeneration of articular cartilage and subchondral bone in osteoarthritic mice, and also prevent degeneration of human cartilage*.*These findings are highlighted by Nature Reviews Rheumatology.

1. Kanupriya Singh, Vikrant Piprode, Suhas T. Mhaske, Amruta Barhanpukar-Naik, **Mohan R. Wani** (2017) IL-3 differentially regulates membrane and soluble RANKL in osteoblasts through metalloproteases and JAK2/STAT5 pathway, and improves RANKL/OPG ratio in adult mice. ***The Journal of Immunology 200:595-606****.*

Importantly, IL-3 helps in restoring decreased RANKL/OPG (osteoprotegerin) ratio in mice, which is observed in important skeletal disorders.

1. Anil Kumar, Lekha Rani, Suhas T. Mhaske, Satish T. Pote, Shubhanath Behera, Gyan C. Mishra and **Mohan R. Wani** (2020).  IL-3 receptor expression on activated human Th cells is regulated by IL-4; and IL-3 synergies with IL-4 to enhance Th2 cell differentiation.**The Journal of Immunology 204:819-831.**

We further investigated that the expression of IL-3R on T helper cells is modulated by IL-4; and IL-3 regulates the development and effector function of Th2 cells.

Overall, Dr. Wani’s research leads strongly suggest the potential of IL-3 to prevent pathological bone and cartilage loss in important diseases of clinical importance such as osteoporosis, osteoarthritis and rheumatoid arthritis.