

Signed statement from the applicant to the effect that the research work under reference has not been given any award in the past. (not to exceed 500 words)

Following research work was not considered for the previous three awards mentioned below:

- "National Bioscience Award for Career Development 2009" by DBT, Govt. of India, New Delhi.
- "B. M. Birla Award 2004" for outstanding research contributions in the field of Bone Remodeling and Medicine. This award was given by the B. M. Birla Science Centre, Hyderabad.
- Prof. B. K. Bachhawat International Award for Young Scientists for the year 2006 by Christian Medical College (CMC), Vellore, India.

#### A) IL-3 prevent pathological bone loss

- Importantly, IL-3 helps in restoring decreased RANKL/OPG (osteoprotegerin) ratio in mice, which is observed in important skeletal disorders (*Singh et al., 2018, The Journal of Immunology*).

#### B) IL-3 has important immunomodulatory role in rheumatoid arthritis

- In mouse model of RA, he 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 (*Srivastava et al., 2011, The Journal of Immunology*).
- 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*).
- He 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 (*Kumar et al., 2020, The Journal of Immunology*).

#### C) Tissue regenerative potential of IL-3

- In osteoporosis and RA, the osteoblast number is decreased and they are defective in synthesis of bone matrix. He found that IL-3 increases osteoblast differentiation and mineralization from human mesenchymal stem cells (MSCs) in both in vitro and in vivo conditions (*Barhanpurkar et al., 2012, Biochem Biophys Res Commun*).
- 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 (*Barhanpurkar-Naik et al. 2017 Stem Cell Research and Therapy*).
- He further demonstrated that IL-3 ameliorate degeneration of articular cartilage and subchondral bone in osteoarthritic mice, and also prevent degeneration of

human cartilage (*Kour et al., 2016 The Journal of Immunology*). These findings are highlighted by **Nature Reviews Rheumatology, 2016**).

#### **D) Stem cell applications in regenerative medicine**

- He has developed adult MSCs lines from bone marrow and adipose tissues of mice and human. He 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 (Garimella et al., 2015, *The Journal of Immunology*).

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 RA. His novel research work has featured in several high impact international journals and patents; and highlighted twice by *Nature Reviews Rheumatology*. His work is also recognized by three National Science Academies including National Academy of Medical Sciences (NAMS), Indian National Science Academy (INSA) and The National Academy of Sciences, India (NASI).



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