Brief Summary: Research Work

Title: *Bifidobacterium longum* Ameliorates Ovariectomy-Induced Bone Loss *via* Enhancing Anti-Osteoclastogenic and Immunomodulatory Potential of Regulatory B Cells (Bregs)

Disease Studying: Osteoporosis is a systemic skeletal illness that is principally distinguished by a loss of bone mechanical strength (BMS) and bone mineral density (BMD), which increases the risk of fragility-related fractures in the wrist, hip, and spine. It is the 4th most burdensome chronic disease after ischemic heart disease, dementia, and lung cancer, impacting over 500 million people globally. A frequent skeletal disorder that causes bone fractures and disability is postmenopausal osteoporosis. *The condition is primarily caused by the cessation of ovarian function, which triggers a period of accelerated bone loss by stimulating bone resorption and, to a lesser extent, bone synthesis. A growing body of evidence supports the notion that the disruption or loss of homeostatic balance of the osteoclastogenic (Th17) and anti-osteoclastogenic immune cells (Bregs and Tregs_ is what causes the bone deterioration seen in osteoporosis.* ***Our group is pioneer in discovering the role of immune system in osteoporosis i.e., Immunoporosis.*** We along with others have reported that a shift in the dynamic balance of "Bregs-Tregs-Th17" cell axis towards Th17 cells augments the inflammatory bone loss observed in case of osteoporosis.

Research Problem: Various pharmacological interventions used for the treatment and management of this bone pathology include the administration of anti-resorptive therapeutics involving the use of estrogen agonists/antagonists, estrogen, bisphosphonates, Denosumab, Romosozumab and/or osteoanabolic therapies, including teriparatide, to improve the process of bone genesis. However, the multitude of side effects related to these therapies has pushed us to seek alternative options such as probiotics and we explore the efficacy of *Bifidobacterium longum* for the treatment and management of post-menopausal osteoporosis (PMO) via modulating the immunoporotic potential of Bregs which in turn regulate the homeostatic balance of Tregs and Th17.

Findings: This study for the first time highlights the immunoporotic role of BL in skeletal homeostasis and emphasizes the probiotic BL as a novel osteoprotective agent for the treatment and management of osteoporosis. BL supplementation significantly enhances the BMD, bone strength, and micro-architecture of bones via modulating both the osteoclastogenesis and differentiation of Tregs, Bregs, and Th17 cells, thereby suggesting toward the pivotal role of the "Breg–Treg–Th17" cell axis in postmenopausal osteoporotic mouse models.