My laboratory investigates the role of vitamin D in modulating osteosarcoma pathobiology. Osteosarcoma (OS) is an aggressive bone cancer that occurs during childhood and adolescence. The overall disease burden of osteosarcoma is much higher compared to other cancers because of the affected target population i.e. children, adolescents and young adults. Despite multi-agent chemotherapeutic strategies and surgery, one third of the patients usually relapse with chemoresistant pulmonary metastatic lesions. Hence, there is a need for developing more efficacious therapies which when used alone or in combination therapy will significantly improve and enhance the survival rates in OS patients especially with metastasis. Cellular, preclinical and epidemiological evidence suggest the role of vitamin D in cancer chemoprevention/therapy. Studies investigating the role of vitamin D or vitamin D metabolism in modulating osteosarcoma are relatively unknown. Using the skills and expertise of a highly interdisciplinary research team, we investigate the role of vitamin D in modulating OS targeted to a three-tier system composed of cell lines, orthotopic mouse models, and human OS clinical samples. We have previously reported that human OS cells have vitamin D receptors and respond to vitamin D by undergoing changes at the cellular and molecular level leading to differentiation and apoptosis\(^1\),\(^2\). Currently experiments are ongoing to elucidate the molecular mechanisms underlying the antineoplastic effects of vitamin D in human OS. In addition, we have recently developed and characterized a bioluminescent orthotopic osteosarcoma mouse (BOOM) model which allows the tracking of tumor progression in real time. This model closely mimics the human disease, and the tumor tissue expresses clinically relevant OS biomarkers. We are using the BOOM model to evaluate the efficacy of vitamin D and other potential chemotherapeutic agents against human OS. Specifically we are interested in investigating the effects of vitamin D or chemotherapeutic agents on (a) OS growth and progression (direct effects), and/or (b) on the bone microenvironment and architecture (indirect effects). We are also interested in evaluating the prevalence of vitamin D deficiency or insufficiency among OS patients by determining serum 25(OH)D\(_3\) by ELISA. Finally, to understand the role of vitamin D metabolism in human OS, we plan to determine tissue concentrations of vitamin D and vitamin D metabolites, and measure the expression and activity of vitamin D regulating enzymes i.e. 1, \(\alpha\) hydroxylase and 24-hydroxylase. Our long term goal is to translate results obtained from the three-tier strategic system, and initiate Phase I and Phase II clinical trials against OS.

Research Projects:
The main research projects currently conducted in Garimella laboratory and in collaboration with other laboratories are:

1. Role of vitamin D in modulating osteosarcoma pathobiology
2. Drug repurposing and osteosarcoma
3. Role of extracellular membrane vesicles in bone health and diseases

Research Interests:
Bone and cartilage biology; bone morphogenetic proteins; bone microenvironment; bone-marrow dynamics; extra-cellular membrane vesicles; osteosarcoma: biology and experimental therapeutics; vitamin D and osteogenic/osteotropic cancers

Collaborators:
Osteosarcoma collaborators

*Intra-Institutional:* Drs. Anant, Anderson, Diaz, Iwakuma, Keighley, Perez, Rowe, Tawfik, Templeton, Vielhauer

*Inter-institutional:* Drs. Fullbright, Garg, Neville, and Rosenthal

I also serve as a collaborator on other research projects on leukemia (Dr. Aljitawi), multiple myeloma (Dr. Lipe), and mesenchymal stem cells and regeneration potential (Drs. Aljitawi, Detamore and Hopkins)
Funding:
Research support start-up funds (Medical Clinical Oncology)

Publications: