WORKSHOP
Normal and Neoplastic Osteogenesis Signaling: Targeted Therapeutic Opportunities
(In Collaboration with Musculoskeletal Tumor Society)

Organizers:
Francis Y. Lee, MD, PhD
Michelle Ghert, MD

Speakers:
Hicham Drissi, PhD
Bang Hoang, MD
2018 ORS/MSTS SPECIALTY SOCIETIES WORKSHOP

8:00 AM – 9:30 AM
Sunday, March 11, 2018
Room: Empire CD

Organizers

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Workshop Title
Normal and Neoplastic Osteogenesis Signaling: Targeted Therapeutic Opportunities

Name of BOS Society organizing workshop
Musculoskeletal Tumor Society (MSTS)
American Academy of Orthopaedic Surgeons

Speakers & Talk Titles

1. Introduction
Francis Y. Lee, M.D.

2. Normal Osteogenic Differentiation and Stemness
Hischam Drissi, Ph.D.

3. Aberrant Signaling in Neoplastic Osteoprogenitors & Therapeutic Targets
Bang Hoang, M.D.

4. Interactive Interpretation of Clinical and Scientific Data; Q & A
Speakers, Organizers, and Audience

Significance and Purpose:
In the era of Personalized Medicine and Post-Genome Sequencing, genetic profiling and molecular signaling data are readily available for human pathology samples. And yet, such big data are not readily utilized to treat altered bone properties and tumorigenesis. This workshop will highlight molecular signaling that distinguishes normal and neoplastic osteogenesis and stemness in order to discover new therapeutic opportunities to enhance bone health and cancer outcomes. The topic is highly relevant to the mission of the American Academy of Orthopaedic Surgeons, Musculoskeletal Tumor Society, and Orthopaedic Research Society.
Learning objectives:
1. To learn about normal proliferation and differentiation of osteoprogenitors that constitute skeletal competency
2. To learn about deregulated signaling in neoplastic osteoprogenitors
3. To learn about deregulated stemness of neoplastic osteoprogenitors
4. To identify therapeutic opportunities to preserve bone and to kill cancer cells
5. To interpret human pathology and signaling data through interactive discussions

Methods that will be used to measure educational outcomes:
1. Post-symposium survey
2. Interactive discussion with audience
3. Audience responses

Results and outcomes:
Participants (Speakers, Organizers, and Audience) will share state-of-the-art knowledge on developmental bone biology and tumorigenesis through interactive discussions.

Therapeutic areas to be discussed:
1. Bone development & structural competency of bone
2. Deregulated osteoprogenitors in benign and malignant osteogenesis
3. Deregulated stemness of osteoprogenitors in benign and malignant osteoprogenitors
4. Therapeutic targets and specific methods to restore bone quality and to control tumorigenesis

Learning outcome levels (based on Moore’s Level outcomes):

We anticipate Level 6 (patient health) / Level 7 (community health) by sharing clinical data, scientific analysis of patient-derived pathology specimens, and new therapeutic opportunities to restore normal bone physiology and target aberrant signals of neoplastic cells.

Clinical relevance:
This workshop will encompass essential knowledge on stemness, proliferation, and differentiation that govern normal and neoplastic osteogenesis. Knowledge gained from this workshop can be directly applied to treat bone dysplasias, benign bone tumors, and bone cancers by targeting specific molecular signaling. The topic is highly relevant to the mission of the American Academy of Orthopaedic Surgeons, Musculoskeletal Tumor Society, and Orthopaedic Research Society.

Objectives
This workshop will encompass essential knowledge on stemness, proliferation, and differentiation that govern normal and neoplastic osteogenesis. Knowledge gained from this workshop can be directly applied to treat bone dysplasias, benign bone tumors, and bone cancers by targeting specific molecular signaling. Trainees will gain access to
published and unpublished data on normal and neoplastic osteogenesis. Clinically relevant research ideas can be generated by interacting with orthopaedic surgeon scientists and developmental biologists.

**Summary**

In the era of Personalized Medicine and Post-Genome Sequencing, genetic profiling and molecular signaling data are readily available for human pathology samples. And yet, such big data are not readily utilized to treat altered bone properties and tumorigenesis. Furthermore, recent advances in bone developmental biology and signaling have been awaiting clinical application with respect to diagnosis and therapeutics. By bridging bone molecular biology and orthopaedic oncologic translational science, we are poised to rectify deregulated osteogenesis and to control pathologic deterrence of stemness of proliferation. Such opportunities will be presented by NIH-funded senior investigators from the Orthopaedic Research Society, American Academy of Orthopaedic Surgeons, and Musculoskeletal Tumor Society. Published data, work-in-progress, and human pathologic specimens will be shared through interactive discussions among speakers, organizers, and audience. The impact and educational outcomes will be high in that we are pinpointing critical issues related to pathologic bone formation and tumorigenesis. Audience will gain deep insights in normal and neoplastic osteogenesis and novel therapeutic ideas.

Osteosarcoma is the most common primary malignant tumor of bone. Osteosarcomas are mesenchymal tumors that arise from progenitor cells of the mesenchymal lineage. Present therapy consists of a multi-drug neoadjuvant treatment, however, despite advances in surgical management of the tumor the overall survival rate of the disease has not significantly improved in the past thirty years. New targets for therapeutic intervention are needed. Osteosarcoma tumors are thought to be maintained by a population of cancer stem cells that resemble both pluripotent and mesenchymal stem cells in that the osteosarcoma cancer stem cells express markers of both pluripotency as well as bona-fide markers of mesenchymal progenitor cells. The ability of these cells to differentiate into osteoblasts has been explored via specific targeting of pluripotency markers such as Sox2. Several signaling pathways play a role in maintaining the stem cell like phenotype of the osteosarcoma cancer stem cells. Most of the transcriptional control of osteosarcoma has focused on the master regulator of osteogenesis, Runx 2. Indeed, Runx2 has been shown to
play an important role in both normal and osteosarcoma differentiation. However, other members of the Runx family, Runx1 and Runx3 are increasingly implicated in the regulation of mesenchymal progenitor cells into the chondro/osteogenic lineage. Exploring parallel mechanisms that distinguish normal from aberrant cell differentiation and multipotency will be the object of this presentation. A specific emphasis on the Runx family of transcription factors will be discussed.