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# The 34th International Sun Valley Workshop on Skeletal Tissue Biology

## Foreword

### History

The Sun Valley Workshops on Skeletal Biology grew out of an NIDR-sponsored training program for dental students. It has always emphasized active participation of junior faculty and students (both graduate and postdoctoral), and continues to do so. The Workshop began in 1965 with support from the NIDR (Mineralized Tissues of Interest to Dentistry, 1964-1974) for summer workshops for dental students interested in doing dental-related research. The first workshop included six faculty (W.S.S. Jee, Harold Frost, Lent Johnson, Roy Talmage, Leonard Belanger and Richard Greulich) and 9 students. The following year, there were eight faculty (Jee, Frost, Jim Arnold, Robert Heaney, Roy Talmage, Harold Copp, Edgar Tonna and Howard Suzuki) with about 25 participants. In 2004, 110 students, academic and industry scientists, including both basic and clinical investigators, attended the Workshop.

Historically, these Workshops have had an impact on the study of skeletal physiology and disorders. They formed the genesis of such concepts and techniques as dynamic histomorphometry, the quantum concept of bone turnover, the BMU as the functional unit in bone, strain-feedback mechanisms, and cyclic treatments for osteoporosis, to name only a few. Relationships and concepts first presented and critiqued at these Workshops were subsequently incorporated into nearly every discipline that currently works on skeletal problems.

### Organization and Goals

The Workshops are unusual in that discussion time equals or exceeds time allotted for formal presentation. Formal presentations are purposely short (typically 20 minutes). Morning sessions (4 hours) are limited to 5-6 speakers; Evening sessions (2.5 hours) are limited to 3-4 speakers. This leaves 45-60 minutes at the end of the session for general discussion and synthesis. Additionally, time is set aside each day to allow informal exchanges among the participants.

The Workshops are also unusual in being truly interdisciplinary: participants at most of the last 20 Workshops included one or more anatomists, anthropologists, biomechanicians, biochemists, cell biologists, dentists and maxillofacial surgeons, endocrinologists, geneticists, gerontologists, internists, mathematicians, molecular biologists, orthopaedic surgeons, pathologists, pediatricians, pharmacologists, physicists, rheumatologists and sports medicine experts. They included one or more people involved in human, dental and veterinary medicine and research, and a good mix of students and senior investigators, both women and men. All Workshops have had active participation from representatives of the pharmaceutical industry, as well as both clinical and basic science university faculty.

It is widely recognized that the Sun Valley Workshops have had a major impact on scientific thinking in the field of skeletal biology particularly in areas related to histomorphometry, *in vivo* animal models, and biomechanics. The Workshop has a long and successful history of training of industry and academic scientists in the quantitative study of musculoskeletal diseases. It has been successful in promoting interdisciplinary and multidisciplinary communication, and has accomplished this because of its unique structure.

The 34th International Sun Valley Workshop on Skeletal Biology was held Aug. 1-4, 2004 in Sun Valley, Idaho. The goals of the Workshop were to:

(1) work toward a multidisciplinary basic and clinical synthesis of molecular, tissue and biomechanical processes in bone that help us to understand the pathogenesis of bone disease as well as its prevention and treatment
(2) apply basic science concepts to clinical problems, and develop a dialogue between basic and clinical investigators
(3) provide a forum for student training and the opportunity in a small group setting for junior scientists to talk with more senior scientists

**Program and Innovations**

One major innovation this year was to establish the ASBMR/Harold M. Frost Young Investigator Awards, a new Young Investigator Award in collaboration with the ASBMR. Six awards of $1,500 each were given based on competitive application and review by a committee appointed by the ASBMR and by the Workshop organizers. Those young investigators who won an award presented their work from the podium during the Monday evening session. This program is intended to stimulate young investigator participation by providing the opportunity for presentation of their results.

This year's program centered around therapies for osteoporosis (Sessions on *Calcium Receptors: Potential Targets for Novel Treatments for Skeletal Disease* and *What Constitutes a Cure for Osteoporosis?*) including a session on how to measure outcomes non-invasively (*Imaging of Bones and Joints*). In addition, orthopaedic applications of tissue engineering were explored (*Joint Regeneration Using Functional Tissue Engineering*). Following on a successful foray into the cancer area several years ago, a session on *Bone Metastases* explored the bone cell biology related to metastatic bone cancers.

The W.S.S. Jee Remodeling in Bone (RIB) Award this year was given to Dr. Bruce Martin, who discussed bone morphology in the context of an evolutionary and (biological) economic framework. Dr. Martin presented a unique and interesting perspective about bone structure and adaptive mechanisms, and his presentation generated lively discussion. The plenary lecture was followed by a poster session, which highlighted posters from students who received Alice L. Jee Travel Awards.

## 34th International Sun Valley Workshop On Skeletal Tissue Biology

August 1-4, 2004 Sun Valley, Idaho, USA

*Sunday Morning (8 am-Noon):*

**Imaging of Bones and Joints**
(Chair: **Babul Borah**)

(1) **T. Dufresne** (P+G) – Novel 3-D image analysis and microCT applications in musculoskeletal research
(2) **C. Peterfy** (Synarc) – Structural characterization of rheumatoid arthritis by MRI - applications in clinical research and in clinical practice
(3) **D. Gazit** (Hadassah) – Imaging using OC-luciferase
(4) **M. Thornton** (GE Healthcare) – Multi-modality imaging of musculoskeletal disease in small animals
(5) **M. Gray** (MIT) – Molecular (and functional) imaging of articular cartilage
(6) **C. Muehleman** (Rush) – Yes, you can see articular cartilage with X-rays

*Sunday Evening (7:30 pm-10 pm):*

**W.S.S. Jee Remodeling in Bone Award/Plenary Lecture**
**R. Bruce Martin** (Orthopaedic Research Laboratories, U of CA, Davis) – Vertebrate evolution and the economics of bone and muscle

At the end of the lecture and discussion, a wine and cheese reception was held in the poster area to allow attendees to view and discuss posters with the presenters.

*Monday Morning (8 am-Noon):*

**Bone Metastases**
(Chair: **Hank Donahue**)

(1) **T. Byzova** (Cleveland Clinic) – Integrins in bone matrix recognition and metastasis
(2) **H. Donahue** (Penn State Univeristy) – Molecular profiling of breast tumor metastasis models
(3) **P. Kosteniuk** (Amgen) – Revisiting the seed and soil theory of bone metastasis: New tools, same answer
(4) **S. Moseley** (Genentech) – Effect of anti-TGF-ß antibodies in syngeneic mouse models of metastasis
(5) **Y. Kang** (Sloan-Kettering Institute) – Breast cancer bone metastasis: Molecular basis of tissue tropism

*Monday Evening (7:30 pm-10 pm):*

**Presentations by ASBMR/Harold M. Frost Award Recipients**

(1) **R. Al-Qawasmi** (Indiana Univ) – Root resorption associated with orthodontic force in IL-1B knockout mice
(2) **W. Yang** (Univ of Missouri) – *In vitro* and *in vivo* study on osteocyte-specific mechanical signaling pathways
(3) **E. Gazzerro** (St. Francis) – Actions of extracellular bone morphogenetic protein antagonists in skeletal tissues
(4) **D. Novack** (Washington Univ) – Role of NIK in inflammatory arthritis
(5) **D. Harmey** (Burnham Insitute) – Therapeutic strategies to treat infantile hypophosphatasia
(6) **A. Schneider** (Univ of Michigan) – Increased bone turnover facilitates prostate cancer skeletal localization

*Tuesday Morning (8 am-Noon):*

**Joint Regeneration Using Functional Tissue Engineering**
(Chair: **Rick Sumner**)

(1) **A. Virdi** (Rush U) – Anabolic agents and gene expression around the bone implant interface
(2) **E. Schwarz** (U Rochester) – Bone implant interface, osteolysis and potential therapies
(3) **R. Sah** (UCSD) – Interfaces in the repair, regeneration, and replacement of articular cartilage
(4) **J. Lim** (Penn State) – Biomaterial characteristics important to skeletal tissue engineering
(5) **R. Guldberg** (Georgia Inst of Technology) – Functional integration of tissue-engineered constructs

*Wednesday Morning (8 am-12:30 pm):*

**What Constitutes a Cure for Osteoporosis?**
(Chair: **Steve Cummings**)

(1) **C. Turner** (Indiana University) – A cure for osteoporosis? How is a cure achieved? How do you reverse age-related changes in bone structure? How do you fix problems with bone quality?
(2) **M. Bouxsein** (BIDMC) – Non-invasive measurements of bone strength: promise and peril. What measurement is accurate, practical and affordable for determining how 'curative' treatment has affected risk of fracture in individual patients?
(3) **J. San Martin** (Eli Lilly) – How does PTH work in people? Mechanisms of anti-fracture effects; optimum duration of treatment?
(4) **D. Bauer** (UCSF) – Combination therapy for osteoporosis: anabolics and anti-resorptives - Do they work? How might anti-resorptives interfere with PTH bone forming effects? What is the best available strategy for increasing bone strength?
(5) **S. Cummings** (UCSF) – Curing osteoporosis: designing and testing the best approach. Design a trial: recommendations from audience for improvement of proposed design of a curative vs. current therapy.

*Wednesday Evening (7:30 pm-10 pm):*

**Calcium Receptors: Potential Targets for Novel Treatments for Skeletal Disease**
(Chair: **Edward F. Nemeth**)

(1) **W. Chang** (VAMC, UCSF) – Extracellular calcium-sensing in cartilage
(2) **E. Brown** (Harvard) – Calcium-sensing receptors in bone cells
(3) **E. Nemeth** (NPS) – Calcilytics: Potential anabolic therapy for osteoporosis
(4) **M. Peacock** (Indiana University) – Clinical effects of calcimimetics in hyperparathyroidism

Summaries of most of these talks are included in this issue of the JMNI, together with a synthesis of the main points, including those made in the discussion, provided by the session chair.

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