

Department of Orthopaedics & Traumatology



Queen Mary Hospital



The University of Hong Kong Medical Centre

TABLE OF CONTENTS

P.1

Editorial note

P.2

Should I Have Parathyroid Hormone Therapy Together With Bisphosphonates, Doctor?

P.3

Cutting Edge - How Does Strontium Reduce Bone Resorption?

P.4-5

Interview with Professor William Lu

P.6

Osteoporosis - DEXA scanning
AO course, Cairo

P.7

7th Hong Kong International Orthopaedic Forum

P.7-8

Announcements

EDITORIAL BOARD

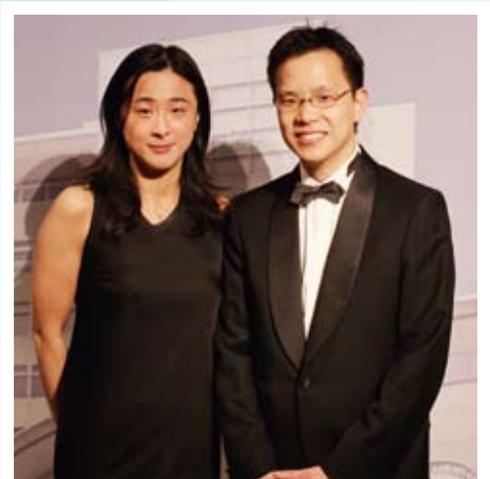
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Editorial note

We are happy to bring you this issue of the Ortho. Newsletter. Once again, we hope you will enjoy reading it as much as we had in preparing it. In this issue we hope to highlight a very important and integral “division” of our department, our post-graduate researchers and fellows, headed by Professor William Lu. While the articles focus on osteoporosis (a pressing and widespread issue), our researchers have many more projects and always welcome collaboration.

Many exciting events took place in the past few months. The 7th Hong Kong International Orthopaedic Forum “Common Orthopaedic Myths” started with a bang and finished with a roar, while the AO Course on “Advances in Paediatric Fractures and Minimally Invasive Osteosynthesis” was hugely popular as usual. Together with the Basic Orthopaedic Bioskill Workshop and the Basic Microsurgery Course, we hope to bring our expertise to future generation of orthopaedic surgeons in Hong Kong.

And last but not least, is our hearty congratulations to our successful fellowship examination candidates, Drs Margaret Fok and Christian Fang. Dr Fang captured another Gold Medal in the exit examination, and is the 5th gold medalist in our department!



***Congratulations to our 2010 orthopaedic fellowship examination candidates:
Dr Margaret Fok and Dr Christian Fang***

Should I Have Parathyroid Hormone Therapy Together With Bisphosphonates, Doctor?

Why concurrent therapy of anti-resorptive agents with parathyroid hormone does not show more effective results when treating osteoporosis?

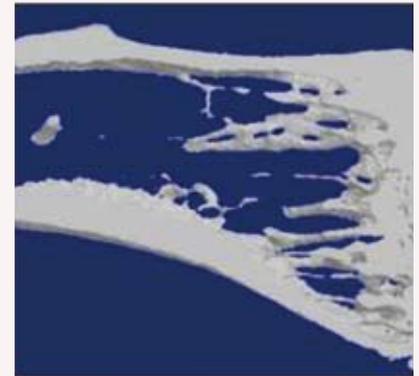
Osteoporosis is a disease of bone loss and fractures. It is a major age-related public health problem, affecting millions of people worldwide each year. The current treatment goal for osteoporosis is prevention of osteoporotic fractures via two pathways. One is by inhibiting osteoclastic bone resorption through use of anti-resorptive drugs, such as alendronate and risedronate, while the other is by stimulating osteoblastic bone formation using parathyroid hormone (PTH). Intuitively concurrent therapy of anti-resorptive agents with PTH may be a more effective treatment for osteoporosis by acting synergistically. However, clinical trials of the concurrent therapy have found that the anabolic effects of PTH are impaired by anti-resorptive agent alendronate, indicating that osteoclastic bone resorption is necessary for PTH-induced bone formation. It is, however, unclear how osteoclastic bone resorption is required for the anabolic effects of PTH on bone formation.

Bone is constantly remodeled in the adult skeleton with bone resorption by osteoclasts and bone formation by osteoblasts. A net bone loss is generated during aging or pathological situations when bone resorption exceeds bone formation. Bone formation occurs at new resorptive sites in remodeling cycles to maintain the bone microarchitecture and its mechanical properties. This is achieved by migration of bone marrow stromal/mesenchymal stem cells (BMSCs) to bone resorptive sites by active TGF- β 1 which is released during osteoclastic bone resorption. The TGF- β 1-mediated coupling process is essential for balancing bone resorption and formation.

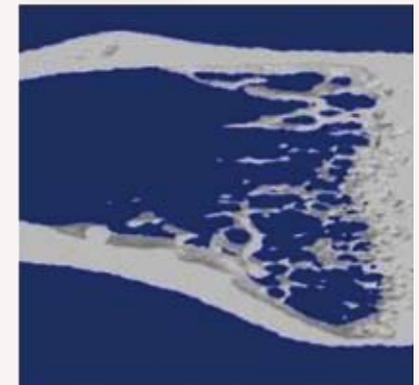
In this joint study, we investigated the cellular mechanism by which PTH-induced bone formation was inhibited during concurrent therapy with bisphosphonates. We found the release of active TGF- β 1 during osteoclastic bone resorption was inhibited by anti-resorptive drug alendronate in mice. As a result, the recruitment of BMSCs to bone remodeling sites by active TGF- β 1 was also reduced. The inhibition of active TGF- β 1 release and recruitment of BMSCs by alendronate were validated in the Tgfb1^{-/-} mouse model, in which the anabolic effects of PTH were diminished. In a transplantation experiment, PTH-stimulated recruitment of injected mouse Sca-1- and CD29-positive BMSCs was inhibited by alendronate. Thus, inhibition of active TGF- β 1 release by alendronate reduced the recruitment of BMSCs for bone remodeling, which ultimately impaired the anabolic action of PTH in bone. Our finding suggests that the additive effects may be achieved by PTH stimulation of anabolic bone formation first followed by anti-resorptive drug therapy.

Understanding the necessity of bone resorption for PTH-induced anabolic bone formation now provides a mechanistic rationale for use of PTH first and anti-resorptive drugs afterward for the effective treatment of osteoporosis.

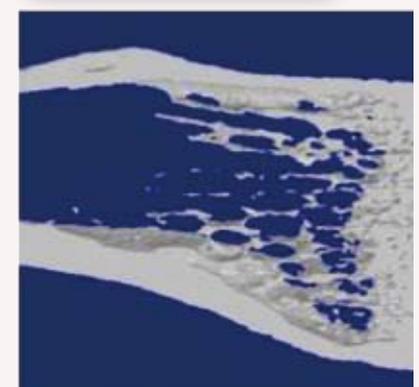
Joint study of Department of Orthopaedic Surgery, Johns Hopkins University School of Medicine USA and Department of Orthopaedics and Traumatology, the University of Hong Kong



PTH only



alendronate (Aln) only

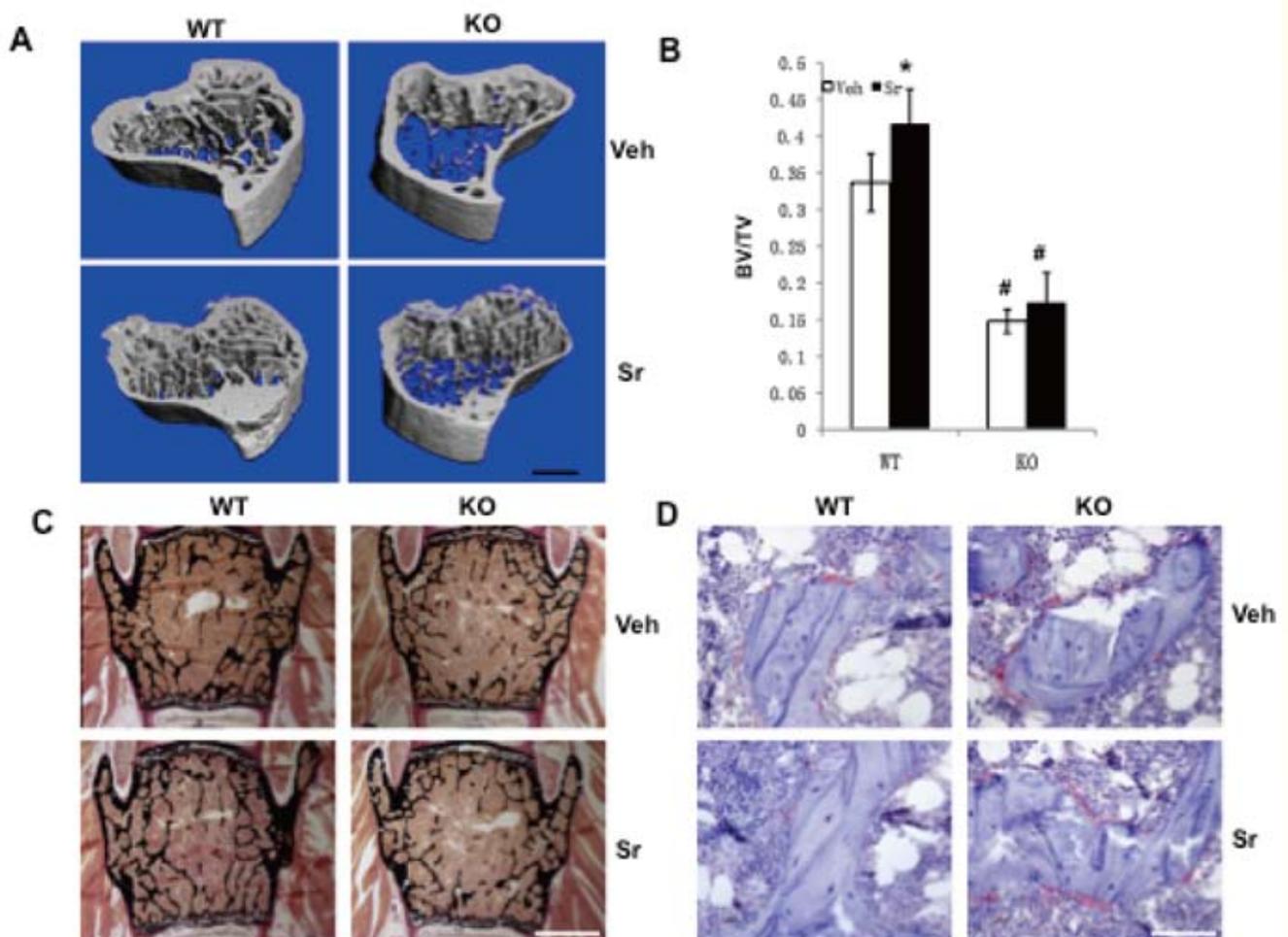


both (PTH+Aln)

Cutting Edge - How Does Strontium Reduce Bone Resorption?

Osteoprotegerin Deficiency Attenuates Strontium-Mediated Inhibition of Osteoclastogenesis and Bone Resorption

Osteoprotegerin (OPG) expression by osteoblasts plays an important role in regulating bone homeostasis by inhibiting osteoclastogenesis and bone resorption. Strontium (Sr) exerts an anabolic (anti-resorptive) effect on bone but the mechanism remains unknown. We evaluated the role of OPG in Sr-mediated inhibition of osteoclastogenesis and bone resorption. Six-week-old OPG knockout (KO) male mice (i.e. without OPG gene) and their wild type (WT) littermates were given oral Sr compound for 8 weeks. Bone mass and microstructure in lumbar spine and the proximal tibiae were analyzed with micro computed tomography (microCT). Bone remodeling was evaluated with serum biochemical analysis, static and dynamic bone histomorphometry. Osteoclasts differentiation potential and gene expression were analyzed in the bone marrow cells. Sr use resulted in greater bone volume and trabecular number compared with Vehicle (Veh) treatment in WT mice (fig. B). The anabolic response of trabecular bone to Sr treatment was attenuated in KO mice. (fig. A, C, D) Sr treatment decreased in vitro osteoclastogenesis and bone resorption in WT mice but the effect was reduced in KO mice. Sr treatment profoundly increased OPG gene expression in the tibiae and OPG protein levels in the serum in WT mice. Our data suggests that inhibition of osteoclastogenesis and bone resorption was associated with OPG up-regulation by Sr treatment.



A: Representative microCT images of bone microstructure in the proximal tibiae.

B: Quantification of bone volume (BV/TV) of trabecular bone from microCT images. Not significant in KO mice.

C: Representative images of lumbar vertebra by Von Kossa staining.

D: Representative images of osteoclasts in lumbar vertebra by TRAP staining.

Interview with Professor William Lu, Chairman of Departmental Research and Postgraduate Committee

Department of Orthopaedics and Traumatology, The University of Hong Kong

“...If you can help your students “expand” their minds and develop a proper pattern of thinking, then they will be successful in whatever they do.”

By Dr Samuel Wan

Department of Orthopaedics and Traumatology, QMH



Q: 16 years ago you decided to come to Hong Kong and work in the Orthopaedics and Traumatology Department (from here on called the Department) here at the University of Hong Kong (HKU). How did you come to make that decision?

A: I was in Canada from 1988 to 1994 working on my PhD in the field of biomechanics. The projects I worked on were related to improving automotive safety. This was when airbags were just becoming the next step up from seatbelts in the standard of safety, and cars were not quite as sophisticated as what we have today. It was considered quite advanced to have one driver's side airbag.

At the time, I was studying spinal injuries using crash dummies in simulated car crashes with the aim to develop better protection systems. With what some people may call serendipity, I learned of a position here at the research laboratory of the Department and was hired after several interviews. I flew to Hong Kong and stayed with a friend in Sha Tin. I still remember the long 1.5-hour journey with multiple bus transfers in order to get to the interview before 8 am!

I was very fortunate to have the chance to meet good people like Professor Ma Ho-kei, Professor John Leong, Professor Keith Luk, Professor Peter Chiu, Professor Kenneth Cheung and Dr Chien Ping. They decided that I was a good fit for the department, and I was hired as one of the first scientific officers at the O&T Department here at HKU in 1995.

Q: How did you arrive to your current focus of research?

A: In 1998 I was collaborating with a Fellow from Shanghai when we discovered the potential of Strontium in stimulating bone growth, and [thought of] the possibility of it being used in the prevention of osteoporosis. At the time vertebralplasty was not popular and we were searching for a material with bio-active and osteointegrative properties that we could use for application in spinal injuries and other bone fractures. Strontium seemed like a good fit and we've continued working with it since then.

Under sponsorships such as the private company Hantak Limited, we have been able to develop a series of new

strontium-containing hydroxyapatite bioactive bone cements used in many orthopaedic procedures today. We are currently working on understanding its underlying mechanism by collaborating with Johns Hopkins and Columbia University.

Q: What is your next big research idea?

A: I am still excited about the possibilities of Strontium, and am hoping to find out its underlying mechanism on bone metabolism. With that, I could then optimize strontium as a drug, which may take management of osteoporosis to another level.

Q: What vision do you have for the research department of O&T in HKU?

A: I have seen our research team grow and progress in the 16 years that I have been working here. We started off with having just part time MPhil and PhD students in 1995 and recruited our first batch of full time postgraduate students in 1996. Since then, our division has grown to 35 postgraduate students, two assistant professors, two research assistant professors and six post-doctoral fellows. All of this would not be possible without hard work, perseverance and good funding.

My vision for the research arm of the department is that it will become a world-renowned institute that produces high impact research and attracts high caliber international projects.

One example of our progress is winning the New Investigator Recognition Award this year, granted by the Orthopaedics Research Society. It is our first time winning this award, and we are honored to be one of the 10 winners from more than 20,000 participants among the orthopaedic community worldwide. Results like these are encouraging towards achieving our vision, and I hope to publish in journals like Nature in the future.

Q: What are the advantages and disadvantages of doing research here in Hong Kong?

A: I think our proximity to mainland China and our academic environment sets us apart from other laboratories. You

can look up any research journal today and see that about half of the authors are from China. Certainly, being geographically close to academic talent[s] gives us certain leverage in coming up with research topics.

Another advantage of working in Hong Kong is the high standard of academia and the good work ethic[s] that people have here. In my opinion, people here are harder working than people overseas, and this also plays a big part in our success. Professor Luk is a good example of [a] hard work[er] as he comes in tirelessly on Saturday mornings for his various duties and projects. [Editorial note: In fact, Professor Luk sends out multiple e-mails long past midnight. Though we believe he does not expect an immediate reply when it was already 3 a.m.]

In terms of disadvantages, our geographical location can also limit our work. Being away from major research hubs meant that it was more difficult for equipment and supplies to be delivered for our work. One example was the specific rat models that we used: the delivery process for overseas lab supplies took up to a month in contrast to deliveries made within the US that could be done overnight.

Q: In your opinion, what makes a great scientist and what advice would you give to younger researchers?

A: To me, true research means uncovering new ideas and applications for the future. The work that you do today should translate into something that is completely innovative and different from what we have currently. Merely aiming to improve or modify a certain way of doing things is not enough. We must dream big and aim high. For instance, there is a lot of research going on regarding fracture fixation. Great will be the day when we can use a material that is completely injectable and biodegradable, instead of using screws and metal implants.

With all that said, to younger researchers my advice would be to start early and take small steps when you begin. It is unrealistic to expect everybody to be a “star” researcher right away, but you must set small goals in order to get yourself moving. The work that you do will probably not get recognized immediately, but as you persevere and trust in your instinct, you will find success in your field of interest.

Q: You have been very prolific in your research work. Can you tell us how you keep yourself fresh with new ideas for your projects?

A: I love watching Hollywood movies and they give me the inspiration and drive to develop something new. I’m always impressed by how the writers and directors in Hollywood are able to sell and market something fictional to the general masses and [even] critical people like myself. Marketing something so removed from reality to something believable is no easy task, and I appreciate the creativity and innovation behind these productions. Some

of my favorite movies include Men in Black and Face Off. It is their “can-do” spirit and creativity that drives me to push boundaries in my research work. It is sad today to see less and less of that creativity in movies, but there are still some unique ideas that pop out every once in a while.

Q: What are your personal hobbies aside from watching movies?

A: I enjoy playing golf. I used to play more [often] a few years ago, but now [I] don’t get to play as much as I want to. I only picked up the sport two or three years ago, but I am a quick learner and I am fairly good at it now. I can usually score less than 100 in a typical 18-hole game. Nevertheless, I’m always trying to improve and trying to come up with new ways to play the game better. I always try to apply my spirit of research in everything I do, including golf.

Q: How do you balance between your busy career and family time?

A: I try my best to be involved in my family’s activities, and allow them to be involved in mine as much as possible. We love to play different sports together, including tennis and swimming. And I try to play with them as much as possible. In addition, I like to keep them as close to me as possible while I work. For example, if I have to travel for work, sometimes I try to bring my family with me. As surgeons you cannot bring your family into the operating room, but as a research scientist, I am lucky that I can bring them to conferences with me. I always give my kids something stimulating to work on during our travels so they’ll not be bored.

Q: Working in a University environment means that you will often have the opportunity to teach and mentor others, and I’m sure there is no exception in your work. Can you please tell us what you would consider the qualities of a good mentor or teacher?

A: A good teacher doesn’t just provide information, but is also one that can stimulate thinking and imagination. If you can help your students “expand” their minds and develop a proper pattern of thinking, then they will be successful in whatever they do. This doesn’t just apply to the medical and research fields, but in all different areas, and even to your own children. I always challenge my children to think no matter where they are so they can develop this habit. There was a time when we were stuck in traffic, and I asked my son to come up with ways to solve a traffic jam. We ended up having a great discussion. It is finding moments to stimulate and inspire [them] that can turn a dull routine into something meaningful.

Osteoporosis - DEXA scanning

By Anna Mak, Radiographer

Department of Radiology, MacLehose Medical Rehabilitation Centre

Osteoporosis is a widespread phenomenon, affecting millions of people worldwide. Various methods for measuring bone mineral density were devised in the past, including heel ultrasound, but the most reliable and acceptable method nowadays is Dual-Energy X-ray Absorption. Bone densitometry, or DEXA or DXA as it is commonly known, involves measuring the absorption of 2 x-ray beams of different energy levels over the lower (mainly lumbar) spine and hips. While it uses x-rays, the radiation dosage is only about 1/10 that of a regular chest x-ray. Furthermore, it should not be confused with a bone scan which involves injection of a radioactive isotope to identify sites of bony pathologies.

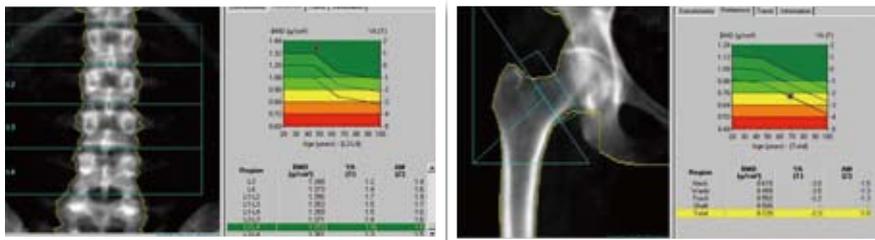
In general, women older than 65 and men older than 70 should get a scan. Other risk factors that should prompt for earlier DEXA scan include the following:

- prior fragility fracture
- steroid use (prednisolone \geq 5mg/day or equivalent for \geq 3 months)
- or other disease or medication use that may predispose to low bone mass or increased bone loss

DEXA is also used for monitoring progress of use of osteoporotic medication (e.g. bisphosphonates, Strontium and parathyroid hormone) However, it is not normally recommended for children or adolescents.

Some reports may use T-scores while some use Z-scores. T-score is obtained by comparing to a young normal adult average whereas Z-score is comparing someone of similar age group. As it is with reference to a "norm", the measurement is expressed as a standard deviation. T-score less than -2.5 is considered osteoporotic; from -1.0 to -2.5 is considered to have low bone mass.

Falsely high bone density readings are found in vertebral collapse fractures, prior spinal instrumentation with metal implants, Strontium adsorption, and sometimes even osteophytes.



Scans of hip & spine AP showing the corresponding T- & Z-scores

AO course, Cairo

By Dr Dennis Yee

Department of Orthopaedics and Traumatology, QMH

"Cairo? Why not Davos?" This was the first response when my colleagues knew I was going for my AO Trauma Course in Cairo. However it turned out to be the most educational and yet thrilling trip I have had for years.

The AO Trauma Course – Principles in Operative Fracture Management is a course that teaches all the basics in fracture management. It is considered the 'gold standard' in fracture management. All the lectures were delivered by experts in the field, including not only trauma surgeons in Egypt but also the whole Middle East, as well as international faculties. Saw bones were used to demonstrate principles and enable participants practical experience. Through discussion with my Egyptian classmates and teachers, I have gained more insight into the subject as well as friendship and information about the country that you won't find even on Lonely Planet.



Drs. Henry Fu & Dennis Yee risking fracture. Not part of the course curriculum!

I was deeply impressed by the quality of presentations by the speakers. Professor Kremli. He is the chairperson of AO Trauma Middle East, and was one of the principle speakers. He was not only an expert orthopaedic surgeon, but also an expert in teaching. He also showed great care to me and Henry who were the only participants not from the Middle East.

The pyramids and the Sphinx in Egypt were certainly amazing, but I was awed by much more in this journey!



My masterpiece and my tutor, Dr Van der Werken.

7th Hong Kong International Orthopaedic Forum “Common Orthopaedic Myths”

24-25 April 2010

Li Ka Shing Faculty of Medicine
The University of Hong Kong

This is one of our main events of the year and it took place on Apr 24th & 25th 2010. Many “myths,” principles and concepts fundamental to orthopedics were well discussed. We were pleased to see a further increase in attendance this year, as it has been year on year.

In addition to the brilliant presentations from our local experts, we also invited 3 overseas professors to enlighten us on their specialties: Professor Toshio Fujii (Japan) on pediatric orthopaedics, Professor Andrew Haig (USA) on spinal rehabilitation, Professor Daniel Berry (USA) on joint replacement. We were lucky to have Professor Jaro Karppinen (Finland), a rehabilitation specialist, join us as well.



Prof. Andrew Haig

The forum closed on a lighter note with a special dinner where many of our local doctors and overseas speakers and fellows could mingle. Many jokes and personal experiences were exchanged. Dr. David Fang shared his impressive opera talent despite a sore throat.



Prof. Jaro Karppinen



Forum Dinner



Prof. Daniel Berry



(from left to right): Prof. KY Chiu and Prof. Toshio Fujii

Announcements

Congratulations

Victor Leung was awarded the “Webster Jee Young Investigator Award” for a conference paper, 15th Annual Meeting of International Chinese Hard Tissue Society, New Orleans, Louisiana, USA

“Sox9 mediates gene expression specificity in growth plate chondrocytes via concomitant positive and negative regulation”

^{1,2,3}Leung, V Y; ¹Gao, B; ¹Melhado, I, ^{1,3}Leung, K K; ¹Wynn, S L; ^{1,3}Chan, D; ⁺^{1,3}Cheah, K S
Departments of ¹Biochemistry and ²Orthopaedics & Traumatology, ³Centre for Reproduction, Development &

Growth, The University of Hong Kong, Hong Kong SAR, China

Jason Cheung was awarded the “Best Paper Award” at the 23rd Hong Kong Society for Surgery of the Hand for the paper entitled: *“Prognostic Factors of Mycobacterium Marinum Infection of the Hand and Wrist”*.

Cheung JPY, Fung BKK, Ip WY, Department of Orthopaedics & Traumatology

Congratulations

Songlin Peng, X. Sherry Liu, Ting Wang, Zhaoyang Li, Guangqian Zhou, Keith Luk, X. Edward Guo, W. William Lu was awarded: New Investigator Recognition Award at 56th annual meeting of Orthopedic Research Society (ORS) in New Orleans, Louisiana, USA during March 6-9, 2010.

Poster titled: *"In vivo anabolic effect of strontium on trabecular bone was associated with increased osteoblastogenesis of bone marrow stromal cells"*

Once again to Dr Kevin Wong, who was conferred his orthopaedic fellowship on May 25th 2010. Kevin has recently transferred to Kwong Wah Hospital to further pursue his career in orthopaedics.



Dr Kevin Wong, wife Pamela and his parents Dr & Mrs Wong.

Drs Margaret Fok and Christian Fang for passing the orthopaedic fellowship examination in flying colors.

Donation

Anonymous - \$20,000 in support of research activities undertaken by Prof. Kenneth Cheung in the Division of Spine Surgery.

Recent Events

Basic Orthopaedic Bioskill Workshop, which forms basic building block for surgical training for our junior orthopaedic residents, two workshops took place on **Jan 8th & 9th and Jun 11th & 12th 2010**.



AO spirit of learning

AO Trauma Course on the **"Advances in Paediatric Fractures and Minimally Invasive Osteosynthesis"** was held between **Jan 29th - 31st 2010**. Overseas speakers included Dr. Chris Morrey (Australia), Dr. Chang-Wug Oh, (South Korea) and Professor Theddy Slongo (Switzerland). This included both saw bone and cadaveric workshops.



AO Trauma Course (front row) left to right: Aaron Ho, Dr Chang-Wug Oh, Assoc. Prof. Frankie Leung, Prof. Theddy Slongo, Dr. Chris Morrey

Basic Microsurgery Course was held in our 9/F Laboratory Block, Li Ka Shing Faculty of Medicine, Sassoon Road, Pokfulam, Hong Kong on **May 14th 2010**. Participants learned the handling and repair of minute soft tissue structures under the microscope under close supervision.

Upcoming Events

Basic Orthopaedic Bioskill Workshop course dates are: **Sep 10th - 11th, Oct 29th - 30th 2010**.

Basic Microsurgery Course organized by the Division of Hand & Foot Surgery. The course emphasizes hands-on experience with unmatched teacher-student ratio. Each time 1 tutor will supervise 2 students. To complete the course one would need to complete 6 sessions, and preferably within 3 weeks. For more information on course outline, course fee and arrangements (individual booking) please call Ms Doris Lau at 2255 4581 or e-mail lws835a@ha.org.hk

The **7th Dr. Tam Sai Kit Visiting Professor Lecture** by **Professor Hiroyuki Tsuchiya** is scheduled on November 2, 2010 in 5/F Lecture Theatre, Professorial Block, Queen Mary Hospital. Professor Tsuchiya is specialized in bone tumor surgery, limb reconstruction & lengthening and external fixation.

The **12th Dr. Yang Hsueh Chi Visiting Professor Lecture** by **Professor Gunnar B.J. Andersson** is scheduled on November 29, 2010 in 5/F Lecture Theatre, Professorial Block, Queen Mary Hospital. His clinical area of interest is spine while his research interests are disc degeneration, epidemiology and occupational biomechanics.