Berton Rahn Research Award

Prof Dr med Dr med dent Berton Albert Anton Rahn
(1939-2008)

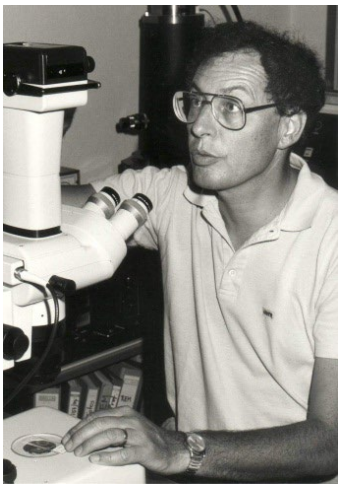
Background

The 'Berton Rahn Research Award' was established in recognition of Berton Rahn's immense contribution to the AO Foundation. The prize previously honored the best completed AO Start-up grant project of that year (based upon final reports and the publications resulting from all completed studies). Since 2017, the award is now open to any AO funded research. From August 2018, there is no longer an age limit for the award. The award consists of a keynote presentation at ARI's eCM conference (along with free registration, accommodation and travel to Davos) and a certificate.

Berton A Rahn

Here we inform you briefly about the Berton Rahn and his dedication to the Laboratory for Experimental Surgery Davos (LECD) and its continuation as AO Research Institute Davos (ARI), the AOCMF community and to the AO Foundation itself.

On March 26, 2008, Prof Dr med Dr med dent Berton Rahn passed away after a difficult illness. We as the AO Foundation family lost a friend, mentor and collaborator who dedicated himself to research for the Foundation in Davos. Berton was a highly respected scientist whose morphological-based bone histology is world-renowned and frequently used in AO courses, though often unperceived by those who use and benefit from it. At the 2009 Trustees Meeting in Chicago, the former AO Research Fund Prize Award, which annually honors the best external start-up research fund project, was renamed the Berton Rahn Research Fund Prize Award in honor of his many contributions to the AO Foundation.



Berton grew up in Schaffhausen, Switzerland and first studied dentistry in Zürich until 1964 and medicine in Berlin until 1968. In 1968 he then joined the Laboratory for Experimental Surgery (now ARI) in Davos under the Directorship of Prof Stephan Perren. Berton stayed with AO for over 37 years. Berton received his doctorate in dentistry in 1970, followed by one in medicine in 1973. He qualified as an assistant professor and in 1985 became an associate professor at the University of Freiburg in Germany. In addition to his lecturing responsibilities at the university, he gave lectures on bone healing mainly based on his own research work, at the AO Courses in Davos and worldwide. He also contributed chapters on bone biology and fracture healing to several respected books. His animal studies in sheep on healing of mandibular fractures (1970–1972) were extremely important because they showed that the healing pattern in craniofacial bones (membraneous bones) is the same as in postcranial bones.

Berton was extremely interested in the microscopic pathology (histology) of bone healing and developed polychrome sequence labeling for newly formed bone (1969), used today worldwide in bone research. This technique also led to a decrease in the number of animals needed for research models. Berton also had strong interest in all forms of microscopy and interactions of cells within tissues and with cells and tissues to implants. Berton made important contributions to the development of craniomaxillofacial surgery as well as to the important field of dental implantology. The correction of deformed and damaged maxillofacial structures using Illizarov's distraction method took some fundamental steps forward thanks to the clinical application of Berton Rahn's research. Berton was an active member of many societies and helped place AO Research on the world map. He was one of the original council members of the European Society for Biomaterials (ESB), helped organize their meeting in Davos in 1984 and 1993 and was chosen

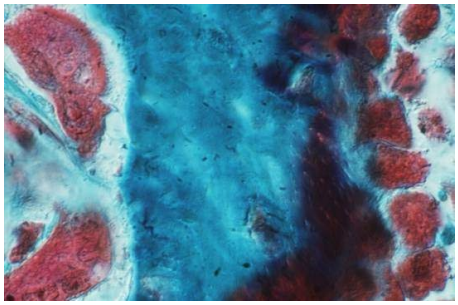
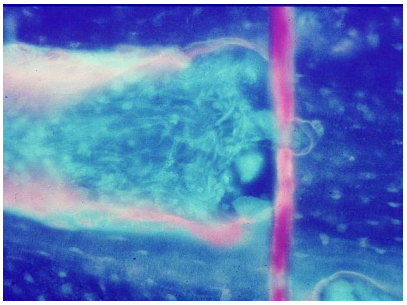
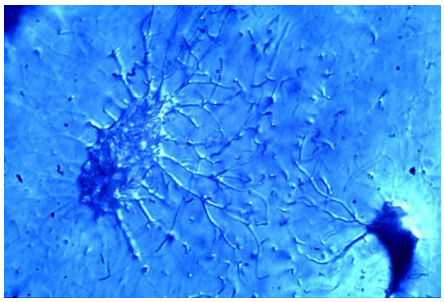
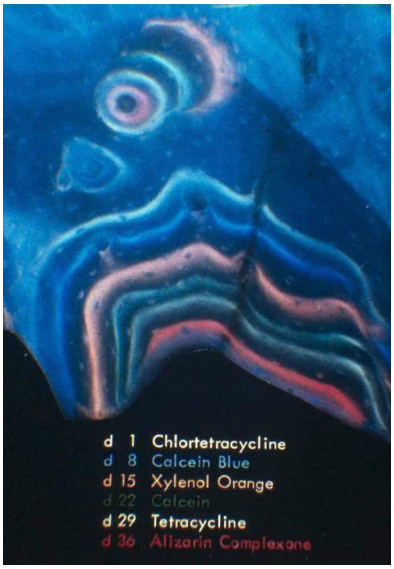
as an honorary member in 2003. Berton was an author of more than 150 papers and has had several dozens of students pass through his hands, many of them earning their doctoral degree with his help. He always listened to his student's problems and liked to help them to solve these issues through their own reasoning. His research was characterized by its creativity, and above all by the support he offered to young researchers (including Geoff Richards in the early 90's).

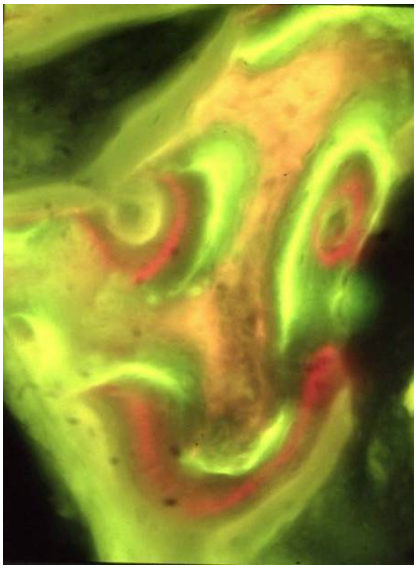
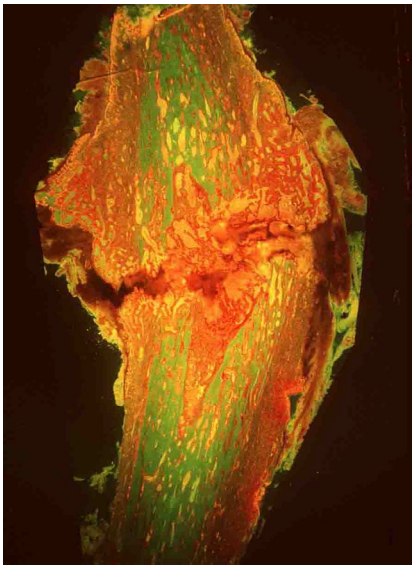
Berton was vice-director of the ARI (from 1975 onwards) and was intimately involved in the design and building of the AO Center on Clavadelerstrasse in Davos which opened in 1992.

Berton was a reserved, sensitive man, but one who in the right moment could surprise with his unique dry sense of humor. His profound humanity made being in his company a great pleasure. In his short duration of retirement, he served as a Scientific Advisor to ARI until the symptoms of his illness manifested themselves in his bones, the very part of the body that he had spent a lifetime studying.

Berton's influence throughout the formative years of the AO Research Institute Davos, and the AO Foundation as a whole, is remembered with deep gratitude.

Prof R Geoff Richards, Director AO Research & Development
Prof Dr med Stephan M Perren, Honorary & Founding Member AO Foundation, past Director LECD & ARI
Prof Dr med Joachim Prein, Honorary Trustee, AO Foundation

Berton Rahn Research Award Winner 2024:

Biographical Sketch

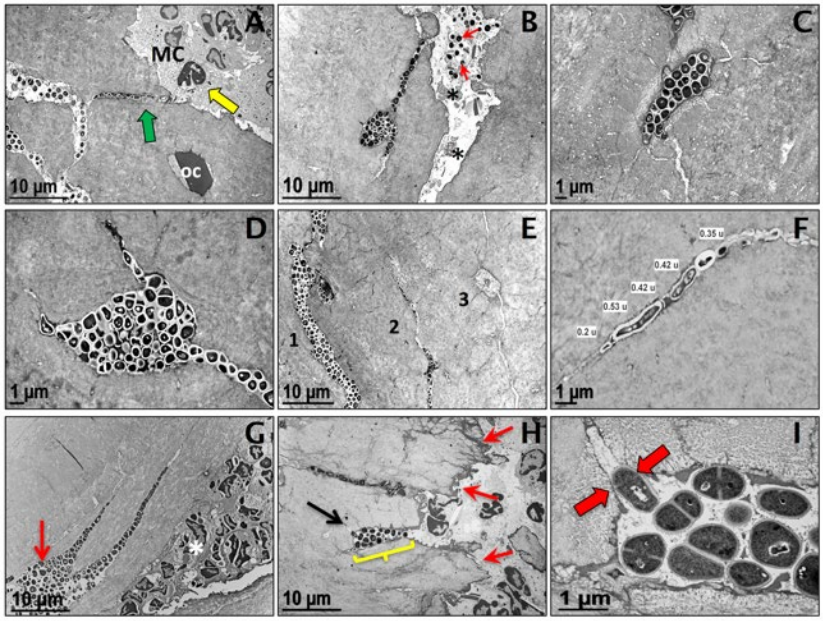
Edward M. Schwarz, Ph.D.

Dr. Edward Schwarz is the Burton Professor of Orthopaedics and Director of the Center for Musculoskeletal Research at the University of Rochester Medical Center, in Rochester, NY. He is a renowned Osteoimmunologist who has published more than 380 journal articles. He was funded by the Arthritis Foundation and National Multiple Sclerosis Society during his postdoctoral fellowship, has been continuously funded by the NIH since 1999, and served as Principal Investigator on R01, R21, R43, P01, P30 and P50 grants. He also served as Co-PI on the AO Trauma Clinical Priority Program – Bone Infection from 2012-2022. He served as Associate Editor of Arthritis Research & Therapy, Arthritis & Rheumatism, Journal of Bone & Joint Infection, and the Journal of Orthopaedic Research, and was just named Editor-in-Chief of JOR. His laboratory focuses on inflammatory bone loss, such as that seen in rheumatoid arthritis, infections, tumor metastasis and wear debris-induced osteolysis around loose prosthetic implants. Dr. Schwarz is also a leader in orthopaedic biologic therapy, for which his lab has developed a novel passive immunization for MRSA and bone targeted antibiotics. Dr. Schwarz's lab is also interested in developing translational in vivo imaging outcome measures include near infrared imaging of lymphatic flow to detect arthritic flare, cone beam CT to assess bone healing in patients with orthopaedic implants, and intravital microscopy of bone infections. Dr. Schwarz has been an ORS member since 1999. He received the ORS's Harris Award in 2003, the ORS/AAOS Kappa Delta Award in 2005, and the CORR/ORS Richard Brand Award for outstanding Orthopaedic Research in 2015. He served on the ORS Board of Directors from 2006-2008, 2010-2011and 2017-2019. He served the Orthopaedic Research and Education Foundation Study Section as a reviewer and Co-Chair from 2001-2007. He also served on many NIH Study Sections including Regular Membership and Co-Chair on Arthritis, Connective Tissue and Skin (ACTS, 2012-2016) and Musculoskeletal Tissue Engineering (MTE, 2017-2023). He has also served on the ORS Publications Committee as a member and Chair. Most recently he co-founded the ORS Musculoskeletal Infection (MSKI) Research Interest Group (RIG), Guest Edited JOR's Special Issue on MSKI, and Co-Chaired the ORS's 1st International Consensus Meeting (2023 ORS ICM on MSKI).

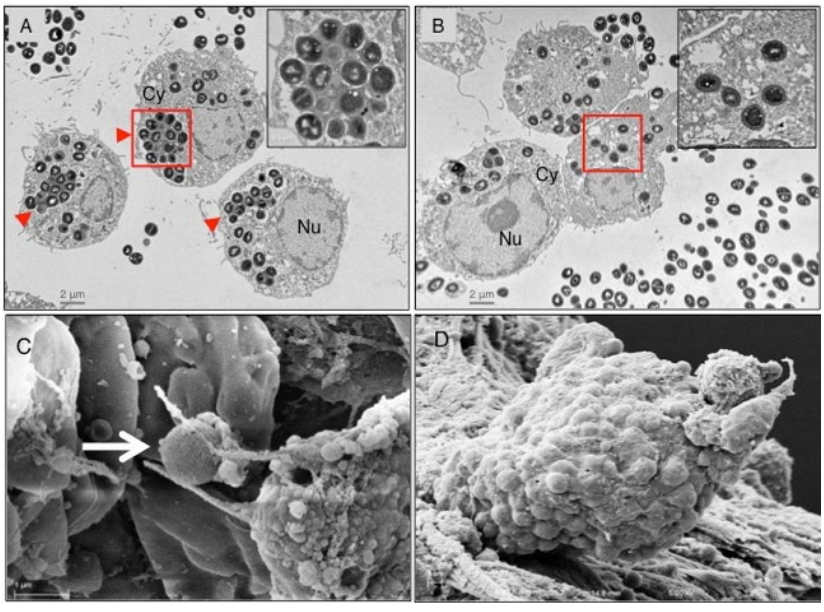
AO Funded Research

1. Discovery of S. aureus invasion and colonization of the osteocyte lacuno-canalicular network (OLCN) of cortical bone during chronic osteomyelitis. Figure: TEM evidence of submicron-elongated S. aureus in the osteocytic lacunar-canaliculi network of infected live bone tissue. Long bones from mice (n = 5) infected with a UAMS-1 contaminated tibial pin (A-F, H, I), or a USA300 infected femoral osteotomy (G), were harvested on day 14 post-infection for TEM. (A) Low magnification TEM image of UAMS-1 invasion of live bone tissue (note osteocyte OC) in a canaliculus (green arrow) communicating with the marrow cavity (MC). Also note the proximal neutrophils (yellow arrow) within the marrow. (B) Low magnification TEM image of UAMS-1 invasion of an osteocytic lacunar-canaliculus adjacent to a channel infected with S. aureus (arrows) containing necrotic cells (*). Higher magnification TEM images (C, D) of UAMS-1 colonization of osteocytic lacunae. (E) Low magnification TEM image of three parallel canaliculi in various states of colonization (1-severely infected, 2-moderately infected, and 3-uninfected) by the invading UAMS-1 within the live cortical bone. (F) Higher magnification TEM image measuring submicron-elongated

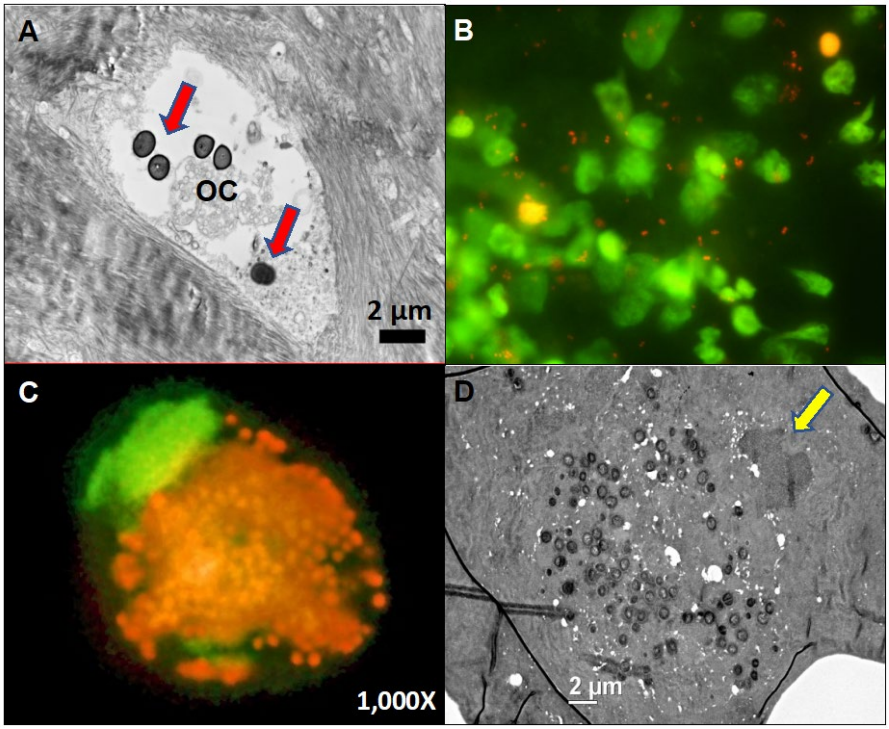
UAMS-1. (G) Similar bacterial invasion of canaliculi adjacent to the osteotomy (red arrow), and neutrophils in the marrow cavity (*) were observed in USA300 infected femurs, but not in long bones that received sterile implants (data not shown). (H) Low magnification TEM image documenting cortical bone damage adjacent to the infected tibia pin (red arrows), and a cavity filled with UAMS-1 (yellow bracket) that leads to a canaliculus (black arrow). (I) High magnification TEM of the infected cavity in H demonstrating mitotic S. aureus in the live cortical bone. Note that only the bacterium entering the canaliculus has an asymmetric septal plane (red arrows), which is aligned perpendicularly with the canaliculus orifice, perhaps to anchor and propel the emerging daughter cell into the submicron channel in the cortical bone during binary fission. (see de Mesy Bentley et al. J Bone Miner Res. 2017 May;32(5):985-90)



2. Passive immunization with anti-glucosaminidase antibodies protect mice from MRSA osteomyelitis. Figure: Anti-Gmd mAb significantly increases internalization of S. aureus and megaclusters. Ultrathin section TEM was performed on RAW cells after 4hr of culture with MRSA opsonized with 1C11 (A) or αT2m (B). Note the megaclusters (arrowheads in A) are connected by a thick matrix (boxed region in A), whereas intracellular S. aureus in the control cultures were mostly individual bacterium (boxed region in B). Quantification confirmed that 1C11significantly induced the % of internalized MRSA vs. aT2m (88.5 +/- 7.4 vs. 58.7 +/- 3.3; p<0.006; N=4 randomly chosen fields and the results are representative of duplicate experiments; Nu=nucleus; Cy=cytoplasm). Representative SEM of a macrophage phagocytosing a bacterium (arrow in C), and megaclusters inside of a macrophage (D), on the pins harvested on day 14 from 1C11 treated mice challenged with MRSA, which were not observed on pins harvested from PBS and ΔGmd treated mice. (see Varrone et al. J Orthop Res. 2014 Oct;32(10):1389-96)



3. Anti-IsdB antibodies mediate Trojan horse leukocyte formation, S. aureus dissemination, and septic death. Figure: The role of S. aureus intracellular infection as a virulence mechanism in chronic osteomyelitis. Extensive TEM analyses of S. aureus-infected human bone samples failed to identify significant evidence of viable bone cells (osteoblasts, osteoclasts, osteocytes) containing intracellular bacteria, while all S. aureus colonized OLCN contain necrotic osteocytes (OC) with extracellular bacteria (red arrows) within osteocyte lacunae (a, TEM). In contrast, an acridine orange-stained smears of blood, harvested post-mortem from a patient that died from septic multiorgan failure, demonstrates both extracellular bacteria (orange) and colonized leukocytes (yellow cells) via fluorescent microscopy (b). c A higher power fluorescent image of the blood smear reveals a "Trojan horse" macrophage with cytoplasmic S. aureus, and acentric nucleus (fluorescent green). dTEM of this Trojan horse macrophage was performed via a "pop-off" technique, which confirmed intracellular S. aureus cocci within the cytoplasm, adjacent to the nucleus (yellow arrow). (see Masters et al. Bone Res. 2019;7:20)



Publications for AO-funded research

Publications

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55. Jennings JA, Arts JJ, Abuhussein E, Alt V, Ashton N, Baertl S, et al. 2023 International Consensus Meeting on musculoskeletal infection: Summary from the treatment workgroup and consensus on treatment in preclinical models. J Orthop Res. 2023 Dec 9. Epub 2023/12/10.

56. Moriarty TF, Hickok NJ, Saeed K, Schaer TP, Chen AF, Schwarz EM. The 2023 Orthopaedic Research Society International Consensus Meeting on musculoskeletal infection. J Orthop Res. 2023 Oct 12. Epub 2023/10/12.

57. Schwarz EM, Archer NK, Atkins GJ, Bentley KLM, Botros M, Cassat JE, et al. The 2023 Orthopaedic Research Society's International Consensus Meeting on musculoskeletal infection: Summary from the host immunity section. J Orthop Res. 2023 Dec 16. Epub 2023/12/16.

58. Xie C, Ren Y, Weeks J, Rainbolt J, Kenney HM, Xue T, et al. Longitudinal intravital imaging of the bone marrow for analysis of the race for the surface in a murine osteomyelitis model. J Orthop Res. 2023 Oct 9. Epub 2023/10/09.

Leveraged extramural research grants that resulted from AO research funding.

Public Health Service, NIAMS, R21 AR081050 $577,500 7/1/22-6/30/24
Quantifying the Race for the Surface
Principal Investigator, Edward M. Schwarz, Ph.D.

Public Health Service, NIAID, Phase 2 SBIR R44AI155309 $2,791,540 7/1/22-6/30/25
Immunotherapy of MRSA Osteomyelitis
Paid Consultant, Edward M. Schwarz, Ph.D. (Integrated Biotherapeutics, Inc.)

Public Health Service, NIAID, Phase 1&2 SBIR R44 AI175069 $ 2,134,423 12/1/22-11/30/25 A
Novel Bone Targeted Antibiotic Therapy for the Treatment of Infected Fractures
Paid Consultant, Edward M. Schwarz, Ph.D. (Biovinc Inc.)

Public Health Service, NIAMS, P50 AR72000 $17,000,000 10/01/17 - 9/30/27
Translating the Osteoimmunology of Bone Infection
Contact PI, PI of the Administration Core and Project 2, Edward M. Schwarz, Ph.D.

Previous Berton Rahn Research Award Winners

2023

Ria Versus BMC as orthobiologic augments to allografts

Brett Crist Vice Chair of Business Development, Director of the Orthopaedic Trauma Service, Director of the Orthopaedic Trauma Fellowship, Director of the Limb Preservation Center, and is a tenured Professor of the Department of Orthopaedic Surgery at the University of Missouri Health, USA

2022

CRP Annulus Fibrosus Rupture (AFR) (ANNUMECH) Establish the functional requirements for next-generation annulus repair methods through iterative, parametric experimental and simulation studies, to develop methods for the fabrication of novel biomaterial-based repair devices, and to validate their mechanical and biological performance in organ models

Stephen Ferguson, Institute for Biomechanics, ETH Zurich, Switzerland

2021

3D printed constructs for osteochondral defect repair

Jos Malda, Department of Orthopaedics, University Medical Center Utrecht and the Department of Clinical Sciences, Faculty of Veterinary Medicine, University of Utrecht, The Netherlands

2020

Rapid Prototyping of Custom-Made Bone-Forming Tissue Engineering Constructs & Projects on 3D printing in collaboration with ARI consortia

Ling Qin, Musculoskeletal Research Laboratory, Department of Orthopaedics & Traumatology, The Chinese University of Hong Kong, China

2019

Projects on Fracture Related Infection in collaboration with AOTrauma Clinical Priority Program Bone Infection, ARI and AOTK

Willem-Jan Metsemakers, UZ Leuven, Department of Trauma Surgery, Leuven, The Netherlands

2018

CRP Annulus Fibrosus Rupture (AFR): (ANNUPHEN)

Characterization of intervertebral disc cells and identification on a suitable cell source for efficient tissue regeneration

Daisuke Sakai, Tokai University School of Medicine in Kanagawa, Japan

2017

CRP Acute Cartilage Injury (ACI): (HiCartia)

A novel platform for optimizing material design for cartilage tissue engineering and enabling drug discovery for cartilage restoration

Robert Mauck, University of Pennsylvania (USA)

2016

Project S-12-27S:

Targeting endothelial to mesenchymal transition in fibrodysplasia ossificans progressive

Gonzalo Sánchez Duffhues, Leiden University Medical Center (NL)

2015

Project S-10-07L:

Controlling nanotopography-ECM environment for enhanced bone formation with hMSCs

Jung Yul Lim, University of Nebraska-Lincoln (USA)

2014

Project S-10-62Y:

Stem cell mobilization for enhanced bone healing

Clare Yellowley, University of California Davis (USA)

2013

Project S-07-1C:

Can low intensity pulsed ultrasound accelerate osteoporotic fracture healing?

Wing-Hoi Cheung, The Chinese University of Hong Kong (China)

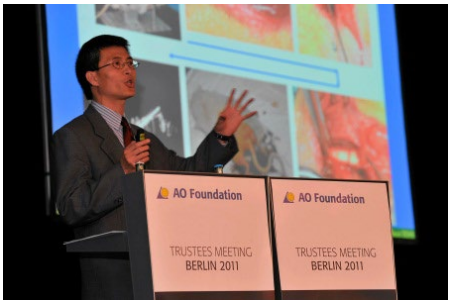
2012

Project S-05-95J:

In-situ crosslinkable osteoinductive poly(lactide) scaffold for bone regeneration

Esmaiel Jabbari, University of South Carolina (USA)

2011



Project F-07-43L:

A pilot study of interleukin-12 local delivery for infection prevention after a traumatic open fracture

Bingyun Li, West Virginia University (USA)

2010

Project 04-J44:

Skeletal effects of estrogen

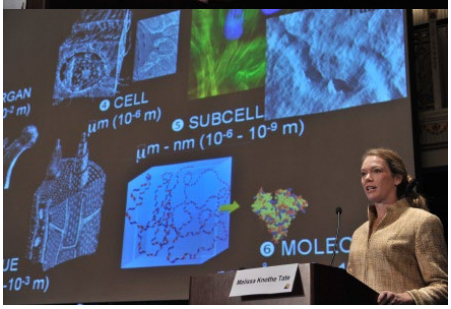
Teppo Järvinen, University of Tampere (Finland)

2009 (2 winners)

Project 04-I58:

Effects of cyclic compression on intervertebral disc cell metabolism

James C Iatridis, University of Vermont (USA)



Project 04-K3:

Unravelling endogenous mechanisms of bone regeneration through quantification of the interplay between bone cells and their environment

Melissa Knothe Tate, Cleveland Clinic Foundation (USA)