HKU International Symposium for 3D Bio-printing and Biomaterials

27 – 28 October 2016

Seminar Rooms 1 & 2, G/F, Laboratory Block,
LKS Faculty of Medicine, 21 Sassoon Road,
Pokfulam, Hong Kong

Program Rundown

Time	Topic	Speaker
27th Oct 2016	**3D Bio-printing Session 1 (Moderator: Dr. Kevlin Yeung)**	
8:50am	Opening Remarks	Prof. Kenneth Cheung (HKU)
9:00am	Plenary Lecture 1: Design and 3D Fabrication of Biomimetic Materials for Stem Cell-Based Tissue Engineering and Regeneration (40 mins)	Prof. Rocky Tuan (University of Pittsburgh)
9:40am	Plenary Lecture 2: The Micro/nano-Bioactive Glasses for Bone and Teeth Tissue Engineering (40 mins)	Prof. Xiaofeng Chen (SCUT)
10:20am	**Tea break**	
10:40am	Keynote 1: Low-temperature 3D printing technique for fabricating biodegradable composite materials with bioactive elements (25 mins)	Prof. Ling Qin (CUHK)
11:05am	Keynote 2: Biodegradable Zn based alloys designed for future orthopedic application (25 mins)	Prof. Yufeng Zheng (PKU)
11:30am	Keynote 3: Management of Larger Bone Defects Made Easy: Combination of Biomaterials and Distraction Osteogensis Techniques (25 mins)	Prof. Gang Li (CUHK)
11:55am	Keynote 4: One-stop 3D printing solution for biomedical innovations by HKPC (25 mins)	Ir Bryan So (HKPC)
12:20pm	Keynote 5: 3D Printing of biomaterials from structure design to multifunctional properties (25 mins)	Prof. Chengtie Wu (CAS Shanghai Institute)
1:00pm	**Lunch**	
	3D Bio-printing Session 2 (Moderator: Dr. Christian Fang)	
2:15pm	Plenary Lecture 3: Biodegradable Polymer Scaffolds and Biomimetic Matrices for Tissue Engineering Applications (40 mins)	Prof. Chen Guoping (NIMS)
2:55pm	Keynote 6: Lumbar intervertebral disc allografting (25 mins)	Prof. William Lu (HKU)
3:20pm	Keynote 7: Experience of 3d printing technology for management of post traumatic limb deformities (25 mins)	Dr. Christian Fang (HKU)
3:45pm	**Tea break**	
4:15pm	Keynote 8: Magnesium incorporated 3D Printed Scaffold for Bone Regeneration (25 mins)	Dr. Kelvin Yeung (HKU)
4:40pm	Keynote 9: Functional biopolymeric hydrogels for musculoskeletal tissue regeneration (25 mins)	Prof. Liming Bian (CUHK)
5:05pm	Keynote 10: Opportunity of 3D printing in sports medicine (25 mins)	Dr. WP Yau (HKU)

Time	Topic	Speaker
28th Oct 2016	**Biomaterials Session (Moderator: Dr. Kelvin Yeung)**	
9:00am	Plenary Lecture 4: Biomaterials for tendon/ligaments regeneration (40 mins)	Prof. Hongwei Ouyang (ZJU)
9:40am	Keynote 11: Biomaterials for Translational Regenerative Medicine (25 mins)	Prof. Xin Zhao (Xi'an JTU)
10:05am	Keynote 12: Construction of Drug and Ag Carrier System on Ti Implants (25 mins)	Prof. Shuilin Wu (Hubei University)
10:30am	**Tea break**	
10:50am	Keynote 13: Alkaline biodegradable implants for osteoporotic bone defects-importance (25 mins)	Dr. Xiaoli Zhao (CAS SIAT)
11:15am	Keynote 14: Annulus fibrosus regeneration: a multi-mode mechanomodulation and layer-by-layer assembly based strategy (25 mins)	Prof. Bin Li (Soochow University, Suzhou)
11:40am	Keynote 15: Bone tissue engineering and regenerative medicine 2.0 --Paradigm shift from "Proof-of-concept" to "Proof-of-value" (25 mins)	Prof. Zhiyong Zhang (SJTU)
12:05am	Closing remarks	Dr. Kelvin Yeung (HKU)

Design and 3D Fabrication of Biomimetic Materials for Stem Cell-Based Tissue Engineering and Regeneration

Rocky S. TUAN, PhD

Distinguished Professor and Director, Center for Cellular and Molecular Engineering, Department of Orthopaedic Surgery, University of Pittsburgh School of Medicine, Pittsburgh, PA 15219

Abstract: Degenerative joint diseases, the most prevalent cause of physical disabilities, affect up to 15% of the population, particularly the elderly. In osteoarthritis, the low, intrinsic reparative capacity of cartilage is a clinical challenge to effective treatment. Current treatments, such as anti-inflammatory drugs, are only able to provide short-term pain relief. Total joint arthroplasty remains the only effective procedure, but is ultimately limited by the finite life expectancy of the implant. Tissue engineering and regenerative medicine, an emerging scientific discipline encompassing translational application of cells, scaffolds, and biological signals, is a potentially promising approach to repair damaged/diseased tissues to restore joint function and mobility. Adult mesenchymal stem cells (MSCs), from tissue sources such as bone marrow, adipose, and skeletal muscle, exhibit multi-lineage mesenchymal differentiation potential, including chondrogenesis, and are considered a promising candidate cell type for cartilage repair. A critical component to successful cell-based cartilage tissue engineering is a biocompatible biomaterial cell-carrier scaffold that ideally also enhances proliferation and differentiation of the seeded cells. We have previously shown that electrospun biomimetic scaffolds that simulate the structure of native extracellular matrix, e.g., the nanoscalar fibrous nature of collagen, are effective in MSC-based skeletal tissue engineering, both in vitro and in vivo. We have recently custom-designed 3D-printed, photocrosslinked hydrogel scaffolds derived from natural and synthetic polymers, to achieve live cell encapsulation during fabrication, with high fidelity tissue infrastructure reproduction and excellent cell retention, viability, and differentiation, and generated robust cartilage and bone tissue constructs. Bioactivation of these biomimetic scaffolds by incorporating biologically targeted gene constructs results in transduction of both exogenous and endogenous host cells. These constructs may also be formed in situ, serving to both deliver cells and create custom-designed shapes for joint cartilage re-surfacing, potentially amenable to minimally invasive, arthroscopic procedures. Most recently, we have applied 3D-printing approach and a custom-designed microbioreactor to fabricate an MSC-derived microtissue analogue of the biphasic osteochondral junction of the articular joint, demonstrating functional biological crosstalk between the chondral/osseous components. This osteochondral microphysiological system is currently being used to model the pathogenesis of osteoarthritis, e.g., exposure to pro-inflammatory agents, and to study biological, hormonal, pharmacological, and mechanical influences, including exposure to microgravity, on osteochondral health. Adult stem cells, with their multi-differentiation potential and their recently discovered trophic activities, in combination with biomimetic scaffolds, present a powerful platform for regenerative, therapeutic, and disease modeling applications in biomedicine.

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Dr. Tuan (Ph.D., Rockefeller University; postdoctoral fellowship, Harvard Medical School) was a professor at the University of Pennsylvania and Thomas Jefferson University, before he was recruited to the NIH (NIAMS) as Chief of the newly created Cartilage Biology and Orthopedics Branch in 2001. In 2009, he joined the University of Pittsburgh as Founding Director, Center for Cellular and Molecular Engineering, and Arthur J. Rooney, Sr. Chair and Professor and Executive Vice Chair, Department of Orthopaedic Surgery, and Professor in the Department of Bioengineering. Currently, Dr. Tuan is the editor of the developmental biology journal *BDRC: Embryo Today*, and founding editor-in-chief of *Stem Cell Research and Therapy*. Dr. Tuan was the recipient of the Marshal Urist Award for Excellence in Tissue Regeneration Research in 2004. Since 2010, Dr. Tuan has served as Co-Director of the U.S. Armed Forces Institute of Regenerative Medicine, a multi-institutional consortium focused on developing regenerative therapies for battlefield injuries. In 2012, he became the Founding Director of the Center for Military Medicine Research and Associate Director of the McGowan Institute for Regenerative Medicine. In addition, Dr. Tuan was appointed a Distinguished Professor in 2014, and received the Chancellor’s Distinguished Research Award in 2015, and the Clemson Award and Carnegie Science Award in Life Sciences in 2016. An author of more than 450 research publications (>34,000 citations), Dr. Tuan directs a multidisciplinary research program focusing on the development, growth, function, and health of the musculoskeletal system, the biology of adult stem cells, 3D scaffold development, and the utilization of this knowledge to develop stem cell- and smart biomaterial-based technologies that regenerate and/or restore function to diseased and damaged musculoskeletal tissues.

The Micro/nano-Bioactive Glasses for Bone and Teeth Tissue Engineering

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Abstract: In the past few decades, various bioactive glasses (BGs) for bone and teeth restoration have been developed, including the melt-derived BGs and sol-gel BGs. However, for the melt-derived BG prepared under high temperature conditions, it is difficult to control the microstructure, and the materials has relatively low degradation rate. The sol-gel BG have made improvement with many advantages including mild processing conditions, controllable composition, high bioactivity and degradability, however, some problems are still unsolved, such as the severe agglomeration, and uncontrolled particle size, which would weaken their bioactivity and physicochemical properties when used for tissue regeneration and tissue engineering.

Due to the unique micro/nano-structure, human natural tissues show the absolute advantages of biological function when compared with the traditional synthetic materials. These remind us to synthetize the novel micro/nano-BG (MNBG) with controlled micro-morphology, structure and particle size. In recent years, our group have done some efforts and focused on the preparation, properties and potential applications of MNBG. These studies showed that introducing surfactants which act as templates into sol-gel process was an effective approach to synthetize MNBG with controlled shape, structure and size. The cell experiment showed that Si and Ca ions, released from MNBG particles, promote the expression of Runx 2 by MAPK pathway, including ERK and p38 pathway. ALP, OCN and other bone related genes and proteins are increased. The micro/nano bioactive glass that we developed, can be considered as a new candidate of bone repair materials which possess excellent gene activation properties.

Chen Xiaofeng is professor and Chairman of Department of Biomedical Engineering of South China University of Technology(SCUT), and vice director of National Engineering Research Center for Tissue Restoration and Reconstruction (NERCTRR), China. He is Fellow of Biomaterials Science and Engineering (FBSE), International Union of Society of Biomaterials Science and Engineering; Executive member of Chinese Society for Biomaterials; Secretary-general of Biomaterials Branch, Chinese Society of Biomedical Engineering.

Professor Chen has engaged in research on the bioactive materials for dental and orthopedic applications since 1988, such as: bioactive glasses, bioceramics and their composites with biomedical polymers. In recent years, his research directions have focused on: 1. Preparation and characterization of structure and properties of micro- and nano-bioactive glasses with function of the gene activation; 2. New type biomaterials and tissue engineering scaffolds for bone, teeth, cartilage and skin restoration; 2. Mechanism of bone tissue regeneration and restoration of the micro- and nano-biomaterials by activating osteo-genes through certain signal pathways. He has published more than 170 papers and been authorized 20 pieces of invention patent of China.

Low-temperature 3D Printing Technique for Fabricating Biodegradable Composite Materials with Bioactive Elements

QIN Ling, Ph.D.

Abstract: Three-dimensional (3D) printers can create complex structures based on digital models. Based on microCT data, we are able to design the interconnected porous scaffold materials for 3D printing. Tissue engineering principle can also be realized but it is stall away from clinical applications. Our current approach in translational roadmap is aiming at acellular concept by integrating especially exogenous growth factors from herbal and mineral sources using a unique low-temperature 3D machine. Apart from in vitro studies, the prove-of-concept studies are clinical disease-orientated by establishing relevant experimental models, such as steroid-associated osteonecrosis (SAON). In fact, SAON may lead to joint collapse and subsequent joint replacement. Poly lactic-co-glycolic acid/ tricalcium phosphate (P/T) scaffold providing sustained release of icaritin (a metabolite of Epimedium-derived flavonoids) was investigated as a bone defect filler after surgical core-decompression (CD) to prevent femoral head collapse in both quadrupedal or even more relevant in bipedal animal models, such as SAON animal model using emu (a large flightless bird). In conclusion, both efficacy and mechanistic studies show the potential of a bioactive composite porous P/T scaffold incorporating icaritin to enhance bone defect repair after surgical CD and prevent femoral head collapse in a bipedal SAON emu model.

Now there are a number of commercial available ‘bio-printing’ 3D devices with different specifications for our R&D. Before “tissue from printer” can be widely applied, further R&D on improving and optimizing printing techniques and biomaterials, identifying potential growth factors from external sources and knowledge on the development of printed constructs into living tissues will be essential for future clinical use. A functional restoration in skeletal tissue regeneration is also rely on consistent mechanical stimuli for making 3D constructs and their biointegration after its implantation into bone defects.

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Dr. Qin is Professor and Director of Musculoskeletal Research Laboratory in the Department of Orthopaedics & Traumatology, the Chinese University of Hong Kong (www.ort.cuhk.edu.hk). Dr. Qin also holds joint professorship in Shenzhen Institutes of Advance Technology (SIAT) of Chinese Academy of Sciences (CAS) and serves Director of the Translational Medicine Research & Development Center of Institute of Biomedical & Health Engineering of SIAT (www.siat.cas.cn). He received his B.Ed and M.Ed. in sports medical sciences at the Beijing University of Physical Education in China, and his Ph.D. at the Institute of Experimental Morphology at the German Sports University, Cologne, Germany and postdoc in AO-Research Institute, Davos, Switzerland. Dr. Qin was research scientist in the Department of Trauma & Reconstructive Surgery, University Clinic Rudolf Virchow, Free University Berlin (now known as Charite Medical University), Germany, before joining CUHK in late 1994.

Dr. Qin has been working on advanced diagnosis, prevention and treatment of bone metabolic disorders, especially osteoporosis and osteonecrosis, in collaboration with research and clinical scientists in medicine, geriatrics, rheumatologists, traditional medicine, and biomaterials. Dr. Qin is the past President of the International Chinese Musculoskeletal Research Society (ICMRS) (www.icmrs.net) and member of a number of journal editorial boards, including Editor-in-chief of Journal of Orthopaedic Translation (http://ees.elsevier.com/jot); Associate Editor of Clinical Biomechanics and Chinese Journal of Orthopaedic Surgery; editorial member of a number of international journals, including Journal of Bone and Mineral Research (www.jbmr.org) and International Journal of Sports Medicine (http://www.thieme.de/sportsmed). He holds memberships in several international and national orthopaedic and related research organizations, including collage fellow of American Institute of Medical and Biological Engineering (http://www.aimbe.org). As Principle Investigator, Dr. Qin has received over 30 competitive research grants (including CRF, GRF, ITF, HMRF, NSFC-RGC, and EU-NSFC, 12.5 and 13.5 Key R&D projects of the MOST) and over 30 research awards. Dr. Qin also holds 9 new invention or new utility patents.

Dr. Qin published 9 monographs as editor or associate editor, 5 conference proceedings, 80 book chapters, over 400 journal papers in English, German, and Chinese, including 300 SCI articles published in Nat Med, JBMR, Osteoporosis Int, Bone, A&R, Biomaterials, Acta Biomaterialia, Am J Sports Med, Int J Sports Med, etc. with citation >6500 and a H-index of 44.

Biodegradable Zn Based Alloys Designed for Future Orthopedic Application

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Abstract: In order to evaluate the feasibility of zinc alloys as future biodegradable bone implant materials, the mechanical properties, corrosion resistance, hemocompatibility, cell activity, proliferation and adhesion, *in vivo* animal implantation experiments have been employed. The experimental results show that the alloying element magnesium, calcium and strontium can significantly improve the mechanical properties of zinc alloys, and further deformation processes can further improve the mechanical properties of zinc alloys. Alloying elements can effectively control the corrosion rates of zinc alloys, adding magnesium, calcium and strontium elements can speed up the corrosion rate compared with the pure zinc alloy. The corrosion rates of zinc alloys are between the rates of magnesium and magnesium alloys and iron and iron alloys, which is more in line with the clinical demand. After being soaked in Hank's simulated body fluid, zinc and zinc alloys still remain the excellent mechanical properties, thus effectively avoid the problem of fast mechanical loss resulted from fast degradation of magnesium and magnesium alloys. Zinc and zinc alloys exhibit excellent hemocompatibility and the hemolysis rate is far lower than 5%. Less platelets adhered on the zinc and zinc alloy surfaces and the morphology of platelets maintained a healthy form at the same time, mostly spherical, without antenna or pseudopod extending. After adding alloying elements Mg, Ca and Sr, MG63 and ECV304 cell proliferation rate and activity increased significantly, while for VSMC cell, the influence of alloying elements effect is not obvious. Zinc alloy intramedullary pins can effectively promote the new bone formation, and after 2 months implanted in mice femur, they still maintained a relatively complete structure, indicating that they are able to provide enough mechanical strength and thus more conducive to bone tissue repair and healing.

Dr. Yufeng Zheng, received his Ph.D in materials science from Harbin Institute of Technology, China in 1998. From 1998 to 2004 he was Assistant Professor (1998-2000), Associate Professor (2000-2003), Full Professor (2003-2004) at Harbin Institute of Technology, China and since 2004 he has been a Full Professor at the Peking University in Beijing, China. Dr. Zheng has authored or co-authored over 300 scientific peer-reviewed articles, with the citation of over 7500 times, and a H-index of 42 (http://www.researcherid.com/rid/A-4146-2010). He served as the Editor-in-Chief of Bioactive Materials (http://www.keaipublishing.com/en/journals/bioactive-materials/), Editor of "Materials Letters" (www.journals.elsevier.com/materials-letters), Member of the editorial board of the Journal of Biomedical Materials Research-Part B: Applied Biomaterials (Wiley), "Journal of Biomaterials and Tissue Engineering" (American Scientific Publishers), "Intermetallics" (Elsevier), "Journal of Materials Science & Technology" (Elsevier), "Acta Metallurgica Sinica (English Letters)" (Springer) and Journal of Orthopaedic Translation (Elsevier). His areas of special interest include the development of various new biomedical metallic materials (biodegradable Mg, Fe and Zn based alloys, beta-Ti alloys with low elastic modulus, bulk metallic glass, ultra-fine grained metallic materials, etc). Dr. Zheng has received several awards including New Century Excellent Talents in University awarded by MOE of China (2007) and Distinguished Young Scholars awarded by NSFC (2012).

Management of Larger Bone Defects Made Easy: Combination of Biomaterials and Distraction Osteogensis Techniques

Gang LI, MBBS, DPhil (Oxon)

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Abstract: Introduction: Distraction osteogenesis (DO) techniques have been widely accepted and practiced in orthopaedics, traumatology, and craniofacial surgery over the last two decades, using DO methods, many previously untreatable conditions have been successfully managed with outstanding clinical outcomes. The major limitation of DO is relatively long period required for new bone consolidation. Here, we investigated whether the application of biomaterials, including polycaprolactone (PCL) and hydroxyapatite (HA) cylinder or composite microspheres could be used to reduce the treatment time and enhance bone formation in DO.

Study 1: A 1.0cm tibial shaft was removed in the left tibia of 36 rabbits and divided into three groups: Group A, the defect gap shortened for 1.0-cm; Group B, the defect gap was filled with 1.0-cm porous hydroxyapatite/tri-calcium phosphates (HA/TCP) cylindrical block; Group C, The 1.0-cm defect gap was reduced 0.5cm and the remaining 0.5-cm defect gap was filled with 0.5-cm HA/TCP block. The tibia was then fixed with unilateral lengthener; for groups A and C, lengthening started 7 days after surgery at a rate of 1.0 mm/day, in two steps. Group A received lengthening for 10 days and Group C for 5 days, there was no lengthening for Group B. All animals were terminated at day 37 following surgery. The excised bone specimens were subject to micro-CT, mechanical testing and histological examinations. Results: Bone mineral density and content and tissue mineral density and content, as well as the mechanical properties of the regenerates were significantly higher in Group C compared to Groups A and B. Micro CT and histological examinations also confirmed that the regenerates in Group C had most advanced bone formation, consolidation and remodeling compared to other groups.

Study 2: Pure PCL microspheres and composite PCL and 10% HA microspheres were synthesized using a modified solvent evaporation method. Bone mesenchymal stem cells isolated from green fluorescent protein rats (GFP-rBMSCs) were cultured with these microspheres in a rotary bioreactor system. The formation of the microstructures was confirmed by scanning electron microscopy (SEM). We confirmed that PCL/HA promotes osteogenic differentiation of rBMSCs in vitro. To investigate the effects of addition biomaterials on bone consolidation during DO process, PCL/HA (20 mg), PCL (20 mg), or PBS were then locally administered into the distraction gap in Sprague-Dawley male rat DO model towards to the end of distraction period and animals were allowed for bone consolidation for 4 weeks after the distraction completed and then terminated. Weekly x-rays, micro-computed tomography, mechanical testing, histology, and immunohistochemical examinations were performed to assess the quality of the newly bone. Results: The microspheres used were of the uniform size and monodisperse. After incubation with rBMSCs in culture, PCL/HA microspheres showed a better ability of cell adhesion and osteogenic differentiation comparing

to PCL microspheres. In the rat DO model, the bone volume/total tissue volume, bone mineral density, and mechanical properties of the newly formed bone were significantly higher in the PCL/HA group compared to the PCL and PBS groups. Histological and immunohistochemical analyses confirmed improved bone formation and vascularization in the PCL/HA group.

Conclusions: The combined use of biomaterials such as HA/TCP blocks or PCL/HA composite microspheres in distraction osteogenesis is a novel approach for promoting bone regeneration and consolidation in DO treatment, reducing the treatment time, pain and suffer of the patients.

Prof. Li Gang received his MBBS degree from the 4th Military Medical University, Xian, China (1985-1991). In 1997, he received D.Phil. degree from University of Oxford Medical School. After post-doctoral training at the MRC Bone Research Laboratory in the University of Oxford, he took up a lectureship (1998), Senior Lectureship (2001) and Readership (2004) in the School of Medicine, Queen's University Belfast, UK. Dr. Li is currently a Professor at the Department of Orthopaedics and Traumatology, The Chinese University of Hong Kong (2009-). His main research interests are on biological mechanisms of distraction osteogenesis, fracture healing, musculoskeletal tissue regeneration with emphasis on stem cell biology, tissue engineering and clinical applications. He has published more than 150 peer-reviewed SCI articles, 15 book chapters, edited 3 books on tissue engineering, distraction histogenesis, leg-lengthening and Ilizarov techniques. He has been invited to give keynote lectures in more than 30 countries including USA, UK, Russia, many European countries, Japan, Korea, Taiwan, etc. Prof. Li serves as an associate editor of Journal of Orthopaedic Translation; member of editorial board of Calcified Tissue International (2004-now); etc. He is an active member of American Society for Bone and Mineral Research (ASBMR), American Orthopaedic Research Society (ORS), International Society for Cell Therapy (ISCT), and International Chinese Musculoskeletal Research Society (ICMRS). He served as Honorary Treasurer of British Orthopaedic Research Society (2004-2006), Member of Program Committee of ORS (2006-2007) and currently is Chairman of China Branch, International Limb Lengthening and Reconstruction Societies (ILLRS) and Association from Study and Application of the Methods of Ilizarov (ASAMI); a council member of Chinese Orthopaedic Research Society, Chinese Medical Association; council member of Tissue Engineering and Regenerative Medicine Society, Chinese Association of Biomedical Engineering. Prof. Li holds honorary Professorship at Sichuan University, China; Shanghai Jiaotong University School of Medicine, China; Shanxi Medical University, China; China Medical University; South-East University Medical School, China; The Forth Military Medical University, China; Guangdong Medical College, China, Jilin University, China.

One-stop 3D Printing Solution for Biomedical Innovations by HKPC

Bryan SO

The presentation by Ir Bryan SO, Principal Consultant on Biomedical, Optical and Precision Engineering of HKPC, will highlight the biomedical projects and inventions that employed the 3D printing technology in HKPC.

Abstract: HKPC is a semi-government organization in Hong Kong, offers 3D printing one-stop solution to a wide spectrum of industry and professional sectors. With the 1st rapid prototyping technology center established in 1995, HKPC provides one-stop consultancy services on product development through 3D scanning, computer aided design (CAD), computer aided engineering (CAE), 3D printing, as well as other bureau services including PU duplication through silicone molding, small batch production through quick molding, opto-mechatronics design, precision machining towards compliance testing. With also the expertise in medical device quality management systems (e.g. GMP, ISO13485) and regulatory affairs, the biomedical engineering team in HKPC supports researchers, medical specialists and industrialists in design verification and validation through clinical trials support as a contract research organization, pre-market clearance (e.g. USFDA 510(k)) and submissions to regulatory authorities through their consultancy support services, leveraging the unique role of HKPC as the Secretariat of the Asian Harmonization Working Party (AHWP), with the objective to harmonize the medical device regulatory requirements in Asia and amongst the 26 member economies.

As a technology development & technology transfer agent in Hong Kong, HKPC owns patented technologies in various medical sub-specialties, including dentistry, orthopedics, dermatology, surgery, etc. With the new 3D printing center namely “3D Printing One” officially opened by the Chief Executive of the HKSAR government in August 2015, HKPC has further strengthened the 3D printing facilities and supports to the industry and professional sectors on innovative design and new technology development. This presentation will highlight the solutions available in 3D Printing One, with case sharing on the biomedical projects and technology inventions that applied 3D printing technology in HKPC.

Ir Bryan SO is the Principal Consultant of Biomedical, Optical & Precision Engineering Unit of the Hong Kong Productivity Council (HKPC), responsible for business & technology development on biomedical applied research, medical device regulatory affairs, quality management systems, opto-mechatronic systems, biomedical 3D printing & CAD/CAM, Bryan is a pioneer in biomedical technology development & leading investigator of government funded projects on biomedical R&D & industry best practices, covering projects on ISO14971 Risk Management for Medical Devices, Medical Device Good Distribution Practices; professional upgrade on Biomedical Engineering, Paediatric Dermatology, Optical Engineering; R&D on Dental CAD/CAM system, Artificial Finger Joint, Liquid Silicone Rubber Technology, Bio-Optics for Dermatology, Laparoscopic Surgery, etc. As an expert in medical device regulations, Bryan has developed the local pilot schemes of medical device risk management system & medical device good distribution practice, and authored the manuals for the two pilot schemes. Bryan has won recognitions & awards in professional engineering community, including the grand prize winner of HKIE Young Engineer of the Year Award, HKIE Innovation Awards for Young Members, HKPC Award for Distinguish Achievement. Bryan serves as Honorary Secretary of the Biomedical Division of HKIE, Executive Committee of IEEE EMBS HK Macau Joint Chapter, Executive Deputy Secretary General of Asian Harmonization Working Party (AHWP) on harmonization of medical device regulatory, Adjunct Associate Professor in Interdisciplinary Division of Biomedical Engineering in the Hong Kong Polytechnic University.

3D Printing of Biomaterials from Structure Design to Multifunctional Properties

Chengtie WU

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Abstract: For therapy and regeneration of tissue defects resulting from malignant bone/skin disease, it is of great importance to develop multifunctional biomaterials for tumor therapy and regeneration. Conventional biomaterials always lack multifunctional properties, limiting their application for treating and repairing bone disease (e.g. bone tumors)-initiated defects. How to design and prepare bioscaffolds with favorable microenvironments for disease therapy and tissue regeneration is one of interesting topics in the fields of biomaterials and tissue engineering. We developed several strategies, including harnessing nutrient elements, biomimetic structure and functional interface as well as thermo-therapy to construct multifunctional scaffolds by 3D-Pringting method for therapy and regeneration of bone and skin tissues. It is interesting to find that both nutrient elements and biomimetic structure of the printed bioscaffolds have important effect on the stimulation of osteogenesis and angiogenesis of stem cells, and thermotherapy plays an important role to treating tumors. Therefore, we put forward new concept that 3D-Printed bioscaffolds combined tissue therapy and regeneration could be a new direction of bone tissue engineering.

Prof. Chengtie Wu is now working in Shanghai Institute of Ceramics, Chinese Academy of Sciences (SIC, CAS). He completed his Ph.D in 2006, and then he worked in the University of Sydney, Dresden University of Technology, Germany and Queensland University of Technology where he was awarded Vice-Chancellor Research Fellow, APDI Fellow and Alexander von Humboldt Fellow. In 2012, Dr Wu has been recruited to work in SIC, CAS, as One-Hundred Talent Program of Chinese Academy of Sciences. Then he was awarded Recruitment Program of Global Young Experts of China (One-Thousand Young Talent Program), Shanghai Pujiang Talent Program and Shanghai Outstanding Academic Leaders. Prof Wu's research focuses on bioactive inorganic materials for bone tissue engineering. Up to now, Prof Wu has published more than 150 SCI peer-review journal papers, including Mater Today, Adv Funct Mater, Biomaterials, Chem Sci, Adv Mater Interface, Small, J Control Release, Acta Biomater, Carbon, J Mater Chem, ACS Appl Mater& Interface, Bone, Tissue Eng. etc. The papers have been cited more than 3600 times, H Index 36 via SCI, Web of Science. Prof Wu has been awarded 16 patents, in which 3 of them have been transferred to companies.

Biodegradable Polymer Scaffolds and Biomimetic Matrices for Tissue Engineering Applications

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Abstract: Tissue engineering has been developed as a promising approach in treating diseases and injuries by combining cells, biomaterial scaffolds and biologically active molecules. Many engineered tissues and organs such as skin and cartilage have been used for clinical applications. Biomaterials and scaffolds play an important role in tissue engineering by providing necessary interim support for cell adhesion, proliferation and phenotypic differentiation; offering biochemical and biophysical cues to modulate the new tissue formation. A number of scaffolds and biomimetic biomaterials have been prepared from biodegradable polymers and extracellular matrices to mimic the *in vivo* nano- and micro-environments surrounding cells. This lecture will highlight the latest progress, future trends and challenges of scaffolds and biomimetic matrices by focusing on a few typical scaffolds such as micropatterned scaffolds, hybrid scaffolds of biodegradable synthetic polymers and naturally derived polymers and biomimetic ECM scaffolds. The micropatterned scaffolds can be prepared by using ice particulates as a template. They have a unique pore structure with open pores on the top surface and interconnected inner bulk small pores within the matrix. The hybrid scaffolds can be prepared by forming collagen sponge or microsponge in the openings of porous skeletons of mechanically strong synthetic polymers. The hybrid scaffolds have the advantages of both types of polymers. Biomimetic ECM scaffolds can be prepared by 3D culture of cells in a template that can be selectively removed after cell culture. Autologous ECM scaffolds can be prepared by this method. Autologous ECM scaffolds have excellent biocompatibility and minimize host response for implantation. These scaffolds and matrices have been widely used for tissue engineering and controlling stem cell differentiation.

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Dr. Guoping Chen received his Ph.D. from Kyoto University in 1997 majoring in Biomaterials and did postdoctoral research until 2000. He became a researcher in 2000 and a senior researcher in 2003 at Tissue Engineering Research Center, National Institute for Advanced Industrial Science and Technology, Japan. He moved to Biomaterials Center, National Institute for Materials Science as a senior researcher in 2004 and was promoted to group leader in January, 2007. He was Principal Investigator and Unit Director of Tissue Regeneration Materials Unit from April, 2011 to March, 2015. He holds current position since April, 2015. He is also a Professor of Joint Doctoral Program in Materials Science and Engineering, Graduate School of Pure and Applied Science, University of Tsukuba. His research interests include tissue engineering, polymeric porous scaffolds, nonabiomaterials, biomimetic biomaterials, nano/micro-patterning and surface modification. He has authored more than 260 publications and holds 17 issued patents. He has given more than 140 invited lectures at conferences. He is an Associate Editor of Journal of Materials Chemistry B; an Editor of Science China Chemistry and Editorial Boards of Journal of Bioactive and Compatible Polymers and Tissue Engineering (Parts A, B and C)**.** He has received several awards such as Young Scientist Award from Japanese Society for Biomaterials in 2001, Original Award from Japanese Society of Artificial Organs in 2002, Tsukuba Award of Chemical and Bio-Technology from Tsukuba Foundation for Chemical and Bio-Technology in 2005, Best Research and Collaboration Award in 2010 and Best Presentation Award in 2012 from the Science Academy of Tsukuba in 2012. He was selected as a Fellow of the Royal Society of Chemistry in 2015.

Lumbar Intervertebral Disc Allografting

*Yong-Can Huang, Jun Xiao, Victor YL Leung, **William Lu**, Keith DK Luk*

Abstract: Our preliminary study in humans indicated that whole fresh-frozen intervertebral disc (IVD) transplantation may be an effective treatment for disc degenerative diseases, but signs of degenerative changes in the allograft were noted after the transplantation. The underlying mechanisms are not fully understood and remain a series of ongoing research in large animal model. Because of the ethically and economically accessible issues as well as the anatomical similarity with human disc, the goats were used to develop reliable surgical approaches for lumbar spine exposure and allograft disc transplantation. Out of 14 male goats, 3 goats were used in a pilot study of different surgical approaches for lumbar spine exposure and as IVD donors; the remaining 11 goats were used as allograft recipients. Radiographs were used to monitor the stability and healing of the grafts on day 0 and one month post transplantation, respectively. Compared with the retroperitoneal 'trans-psoas muscle' approach and the 'post-psoas muscle' approach with longitudinal skin incision, the 'post-psoas muscle' approach with transverse skin incision is the superior choice for the transplantation because of the broader surgical view and integrity of the psoas muscle. Preservation of the anterior longitudinal ligament and appropriate portion of the annulus fibrosus at the recipient site was crucial for satisfactory transplantation. In addition, a slightly reduced height of the disc allografts compared to that of the recipient slot may largely facilitate the transplantation owing to decreased incidents of dislodgement and endplate fracture. With the optimized approach, the IVD allograft can be steadily transplanted into the lumbar spine and matched well in goats.

Professor Lu obtained his PhD degree in biomechanics in 1994 from the University of Waterloo, Canada, receiving the Distinguished Graduate Award. The following year he joined HKU and established the Orthopaedic Research Centre in the Department of Orthopaedics & Traumatology. As director of the Centre since its founding, he has made significant research contributions in the fields of biomechanics, biomaterials, bio-nanotechnology, and applied clinical bioengineering. Today, he is the Ng Chun-Man Endowed Professor in Orthopaedic Bioengineering, and is widely acknowledged as one of the top 1% of scholars (2009-2015) according to ISI's Essential Science Indicators. He has been invited to hold honorary and visiting professor positions in internationally recognised universities and has conducted open lectures in more than 50 universities, including the Department of Bioengineering at Columbia University, the Department of Orthopaedics at Harvard Medical School, and the Biomedical Engineering and Research Center at the University of British Columbia. Professor Lu has a long track record of successful research fundraising for both basic and applied research, totaling over US$9M from major funding bodies in Hong Kong and mainland China. His research has led to numerous patents and startup companies, as well as over 240 peer-reviewed publications with >6000 citations and an H-index of 43.

Professor Lu has been nominated to serve as international conference chairman and conference committee member on more than 50 occasions. Recently he served as the chair of the 26th Interdisciplinary Conference on Injectable Osteoarticular Biomaterials and related Bone Repair procedures (GRIBOI 2016), held in Shenzhen, China, an organization with members from over 50 countries. This conference provided an “East-Meets-West” environment for experts from across disciplines of the world to share cutting-edge insights into the future of the biomaterials and clinical applications.

Professor Lu was a Founding Member and the Chairman of Hong Kong BME Division, (Honorary Secretary, 96-98, committee member 2008-2010, and Chairman 2010-2011) of The Hong Kong Institute of Engineers, and is also a co-convener of the BME-Nanotechnology Strategic Research Theme at HKU. He has developed wide collaborations with universities and research institutes throughout China, including the Peking Union Medical College Hospital, the Shenzhen Institute of Advanced Technology (SIAT), the Chinese Academy of Science, Beijing University, and Shanghai Jiaotong University. In 2012, he established the Research Center of Human Tissue and Organ Degeneration at SIAT with the Chinese Academy of Science. This research center was greatly expanded two years later, becoming the Institute of Biotechnology and Biomedicine and including over 45 PI, mostly recruited from overseas. Professor Lu is also a scientific advisor for medical device companies, including one of the leading orthopaedic device company in China, Weigao Orthopedic Device Co., Ltd.

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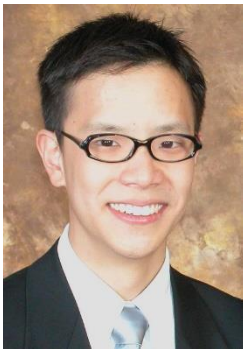
Experience of 3D Printing Technology for Management of Post Traumatic Limb Deformities

Christian FANG

Abstract: We all agree that 3D printing technology has numerous potential applications in the healthcare and biomedical science field. While many applications are still awaiting fruition as budding research projects, the technology is relatively mature and clinically applicable for the management of complex limb deformities. Under the concept of pre-operative 3d navigation, the technology is used in pre-operative planning, surgical simulation, implant templating and execution of surgical steps. We explore how 3d printing technology has been applied in daily clinical use in Queen Mary Hospital. We will look at the outcomes of some patients who has already benefited from the technology.



Christian Fang is the assistant professor and honorary associate consultant at the University of Hong Kong, Queen Mary Hospital and the University of Hong Kong-Shenzhen Hospital. His clinical practice, research and publications focus on trauma surgery, osteoporotic fractures, polytrauma, pelvic and acetabular fractures. He holds the Harry Fang gold medal award from the Hong Kong College of Orthopaedic Surgeons. He is a regional committee of the AO (Arbeitsgemeinschaft für Osteosynthesefragen) Foundation and has numerous teaching experience in international educational events for orthopaedic trauma surgery. He is well travelled and has received overseas training in Germany, Switzerland, China, Singapore, the United Kingdom and Australia.

3D Engineered Magnesium Biodegradable Scaffold for Segmental Bone Defect Treatment

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Abstract: Three-dimensional printing has driven a lot of technology advancements for regenerative medicine in particular to organ transplantation and tissue repair [1, 2]. The advanced 3D bio-printer has enabled a variety of choices of biomaterials, cell types, biomolecules and other supporting factors to build a complicated and functional 3D structure [3, 4]. In fact, the 3D-printed bone tissue scaffolds may utilize to regenerate bony tissues in patients suffering with segmental bone defect and the success of surgery depends on the osteogenicity, mechanical properties and the ability of revascularization of 3D printed scaffolds [5-7]. Our previous work demonstrated that appropriate amount of magnesium ions (i.e. 50-100ppm) could significantly stimulate new bone formation locally [8]. In this study, 3D bone scaffolds comprising biodegradable polymer polycaprolactone (PCL) and magnesium oxide (MgO) nano-particles have been developed by using our 3D bio-printer. The PCL/MgO hybrid scaffolds were surgically implanted in the rats with critical size bone defect for 2 months. Bone growth was monitored and quantified by X-ray and micro-CT up to 2 months, respectively. The results suggested that a larger amount of new bone formation was found on the hybrid scaffold as compared with pure PCL scaffold control. We believe that this osteogenic and cell-free scaffold is able to stimulate bone regeneration without the aid of implanted cells and growth factors. In summary, the current results have proposed that this economical and easily fabricated bio-scaffold may potentially apply in segmental bone defect treatment when the 3D microstructure and magnesium ion concertation are properly designed.

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Dr. Kelvin Yeung is passionate in orthopaedic biomaterial research for more than 15 years. His major research areas cover from the development of metallic and polymeric orthopaedic biomaterials, to bone implant design and development as well as musculoskeletal tissue engineering. He trained as materials scientist in his bachelor degree and then orthopaedic scientist in HKU Medical Faculty for his master degree and PhD, respectively. He is currently tenured associate professor in the Department of Orthopaedics and Traumatology, The University of Hong Kong. In addition to his more than 140 peer-reviewed journal papers published (h-index: 31, total citations: >3,200), 270 conference abstracts and 38 filed full patents in various countries, he has also co-founded the OrthoSmart Limited together with Dr Johnson Lau and Prof. Kenneth Cheung so as to translate their research findings to clinical use. He also serves as CEO in this company. During these years, he had received numbers of award and scholarship from local and regional competitions such as Young Scientist Award 2005 and Young Engineer Award 2009, respectively. The total amount of grants and sponsors directly arising from his projects in PI and Co-I capacity is over HK$46M.

Functional Biopolymeric Hydrogels for Musculoskeletal Tissue Regeneration

Liming BIAN

Abstract: Although biopolymer-based chemical hydrogels, with biopolymers covalently crosslinked, have been widely used as scaffolds for tissue engineering due to good stability, their permanent network structures and brittleness limit their applications in repairing load-bearing tissues, such as cartilage. In contrast, biopolymer-based supramolecular hydrogels, which are usually formed via self-assembly of physically interacting biopolymers, are usually weak as shown in "inverted vials" instead of freestanding 3D constructs and less stable than chemical hydrogels. Herein, we describe a novel host-guest macromer (HGM) approach for preparation of biopolymer-based freestanding supramolecular hydrogels. Host-guest macromers are formed by molecular self-assembly between adamantane functionalized hyaluronic acid (ADxHA) guest polymers and mono-acrylated beta-cyclodextrins (mono-Ac-CD) host-monomers. Supramolecular hydrogels are readily prepared by UV-induced polymerization of the pre-assembled host-guest macromers. Such hydrogels are solely crosslinked by in situ formed multivalent host-guest nano-clusters, and show significantly reinforced mechanical properties yet still retain desirable supramolecular features. They can self-heal and be re-molded into freestanding 3D constructs which afford effective protection on the encapsulated stem cells during the compression re-molding, making them promising carriers for therapeutic cells that can quickly adapt to and integrate with surrounding tissues of the targeted defects. We demonstrate that such hydrogels not only sustain extended release of encapsulated proteinaceous growth factors (TGF-beta1) but also support chondrogenesis of the human mesenchymal stem cells (hMSCs) and promote cartilage regeneration in a rat model. Lastly, we have developed a series of supramolecular hydrogels with unique properties such as resilient mechanical property, fast relaxation, self-healing, bioadhesiveness, injectability, and promoting recruitment of endogenous cells. These hydrogel properties are not only desirable for potential clinical applications of these hydrogels but also useful for studying the effect of microenvironmental mechanical cues on stem cell behaviors.

Dr. BIAN Liming received his B.Eng and M.Sc degree from the National University of Singapore in 2002 and 2004, respectively. Dr. Bian completed his Ph.D. study in Biomedical Engineering at Columbia University in 2009. Dr. Liming Bian then conducted his postdoctoral research in the Department of Bioengineering, the University of Pennsylvania from 2009 to 2012. In 2012, Dr. Bian joined the Chinese University of Hong Kong as an assistant professor. Dr. Bian's research focuses on the development of novel biomaterials for the regeneration of musculoskeletal tissues. Dr. Bian is also interested in developing biomaterial platforms to investigate the role of cell microenvironment factors including mechanical, chemical and cell-matrix interactions in stem cell differentiation.

Opportunity of 3D Printing in Sports Medicine

Wai Pan YAU

Dr. WP Yau is the Chief of the Division of Sports and Arthroscopic Surgery and the Clinical Associate Professor of Department of Orthopaedics and Traumatology in the University of Hong Kong.

Dr. Yau started his medical education in the Faculty of Medicine of the University of Hong Kong in 1987. Dr. Yau earned his medical degree in 1992. After completing his medical internship in 1993, Dr. Yau began his general surgical training in Queen Mary Hospital of Hong Kong and obtained the Fellowship of Royal College of Surgeons of Edinburgh in 1997. Dr. Yau was then enrolled in the Higher Orthopaedic Training in the Department of Orthopaedics and Traumatology, Queen Mary Hospital. He finished his orthopaedic residency training in 2000 and passed the fellowship examination in the same year with flying colour. Dr. Yau was awarded the Fellow of the Hong Kong College of Orthopaedic Surgeons and Fellow of the Hong Kong Academy of Medicine in 2001.

Dr. Yau joined the University of Hong Kong in 2007. He was appointed as the Chief of Division of Sports and Arthroscopic Surgery in Queen Mary Hospital in 2008. Dr. Yau was elected to be the Chapter President of Sports Medicine Chapter of Hong Kong Orthopaedic Association in 2012 and the Deputy Censor of Hong Kong College of Orthopaedic Surgeons in January 2013. Dr. Yau was appointed as the Clinical Associate Professor of the Department of Orthopaedics and Traumatology, the University of Hong Kong and the Honorary Clinical Consultant of Hospital Authority of Hong Kong in August 2013.

Dr. Yau specializes in Sports Medicine and Adult Joint Reconstruction Surgery. His major research interest lies in clinical outcome studies on these two areas. This had led to the publication of 56 peer-reviewed articles, 1 book chapter and over 80 conference papers. Dr. Yau has delivered more than 40 invited lectures, both locally and internationally, and given close to 100 presentations in both national and international conferences. Dr. Yau received the Author Yau Award of Hong Kong Orthopaedic Association in 1994 and 2004, David Fang Trophy of Hong Kong Orthopaedic Association in 2004, Harry Fang Gold Medal Award of Hong Kong College of Orthopaedic College in 2000 and Japan Orthopaedics and Traumatology Foundation Fellowship Award in 2008. Dr. Yau was selected to be the Ambassador of the Hong Kong Orthopaedic Association to Japanese Orthopaedic Association Annual Congress in 1995 and 2005, New Zealand Orthopaedic Association Scientific Meeting in 2003 and 2005, and Singapore Orthopaedic Association Annual Congress in 2006 and 2008.

Dr. Yau began his work in Computer Navigated Orthopaedic Surgery in 2004. He was invited to lecture in the “MIS Meets CAOS Symposium and Instructional Academy” in San Diego, United States in 2005, the Annual Meeting of Asian Society for Computer Assisted Orthopaedic Surgery in Taiwan in 2006 and in Hong Kong in 2008. Dr. Yau was also the organizing committee of the Annual Meeting of Asian Society for Computer Assisted

Orthopaedic Surgery held in Hong Kong in 2008. Dr. Yau was also one of the regular speakers in the Education Day of SICOT.

Dr. Yau was also very active in providing orthopaedic education to the orthopaedic trainees in Hong Kong. He was appointed as the Training Director of the Department of Orthopaedics and Traumatology, The University of Hong Kong since 2008. Dr. Yau also served as a member in the Education Subcommittee of the Hong Kong College of Orthopaedic Surgeons from then onwards. He was appointed as the Convener of the Basic Orthopaedic Bioskill Workshop under the Hong Kong College of Orthopaedic Surgeons in 2009 for a 5-year term. Dr. Yau was elected to be the Deputy censor of Hong Kong College of Orthopaedic Surgeons in January 2013.

Current Biomaterials and Scaffolld for Tendon and Ligament Regeneration

Hongwei OUYANG, Ph.D/MD

Dr. Li Dak Sum & Yip Yio Chin Center for Stem Cell and Regenerative Medicine

Key Laboratory of Tissue Engineering and Regenerative Medicine of Zhejiang Province

School of Medicine, Zhejiang University

Abstract: Tendon is a specific connective tissue composed of parallel collagen fibers, and is difficult to heal after injury. The topological structure, mechanical property, properties of raw materials and other material information constitute the structural microenvironment for stem cell, which influences the differentiation and migration of stem cells. At present, the research focus of biological scaffolds is shifted from simple physical scaffold function to biological induction function, especially requiring scaffold materials to have the biological function of promoting directed differentiation of seed cell towards expected direction. The research group makes series researches on the construction of biological scaffolds with the function of inducing tendon differentiation and its applications. Our research group investigated the effect of this tissue-specific matrix orientation on stem cell differentiation. It is found that parallel nanofiber can influence intracellular mechanical signal pathway, promote IPS and differentiation of tendon stem cells towards tendon system and inhibit bone differentiation. However, aligned scaffolds fabricated by the electrospinning procedure are nanoporous, and cells can only grow on the top of the scaffold, leading to low cell infiltration rates being observed in vivo. Or unwoven fibrous scaffold and gel system are adopted, but aforesaid scaffolds have poor mechanical property. The concept of an "internal-space-preservation" scaffold is proposed for the tissue repair under physical loading. In vivo and in vitro studies use induced human embryo stem cells, tendon stem cells,growth factor and scaffolds to construct tissue engineering tendon and apply them in tendon regeneration, which can promote tendon repair.In addition, our group developed a macroporous 3D aligned biomimetic collagen/silk scaffold for functional tendon repair by inducing aligned supracellular structures similar to natural tendon, which in turn enhanced cellular infiltration and tenogenic differentiation.For future: 3D-printed gel system with kintted silk scaffold and 3D-printed atsttrin-incorporated alginate/hydroxyapatite scaffold might be used for tendon/ligament and tendon/ligament-bone junction.

Hong Wei Ouyang

Professor in Sports medicine & Stem Cells and Regenerative Medicine
Director for School of Basic Medical Science, Zhejiang University
Vice-Dean for College of Mecine, Zhejiang University
Awardees of the National Science Fund for Distinguished Young Scholars（Jie-Qin）
Awardees of National "1000-talent"plan (Qian-Ren)
The “Qiu-shi” Distinguished Professor, Zhejiang University

Professor Ouyang focuses on the research of tissue engineering and regenerative therapy of tendon and cartilage. With the development of a functional silk scaffolds as well as the stepwise differentiation of embryonic or adult stem cells with the combination of biochemical and mechanical strategies, Prof Ouyang’s researches improved structural and functional tendon and cartilage regeneration significantly in vitro and in vivo. He has filed fifteen national patents applications (eight approved) and published more than sixty original research papers in the international journals. These papers corresponded by Professor Ouyang were published in the leading journals of particular fields, such as Stem Cells, Biomaterials, Cell Transplantation. In 2008, authorized by State Food and Drug Administration, he was involved in drafting the Guide for in vivo assessment of implants for cartilage repair and regeneration YY/T 0606.10-2008, Chapter 10 of Tissue Engineering Medical Products, Pharmaceutical Industry Standard of People’s Republic of China. In 2009, he was again involved in formulating the Provisions for Therapeutic Transplantation of Engineered Tissues announced by the Ministry of Health (MOH). In March of 2010, under the new regulations of the Ministry of Public Health in China, Prof Ouyang established a standard approach for tissue engineered cartilage (TEC) transplantation, and set up the clinical application network of cartilage tissue engineering technology in orthopedics from five third-grade class-A hospitals in Zhejiang.

Biomaterials for Translational Regenerative Medicine

Xin ZHAO

Abstract: Translational medicine is a new clinical medicine-oriented discipline that bridges basic medical research and clinical treatment. As a branch of translational medicine, regenerative medicine aims to achieve regeneration of diseased or damaged tissues using biomedical materials. The emphasis of this talk is placed on how biomaterials can be used to fabricate various scaffolds to reconstruct hard tissues such as bone as well as soft tissues such as skin and tendon. In detail, this talk will cover Dr. Zhao's several research projects, including "photocrosslinkable hydrogels for bone/skin regeneration", "injectable and degradable bone cement" and "anti-adhesion tendon regeneration membrane".

Xin Zhao is currently appointed as an associate professor at China's leading university, Xi'an Jiaotong University. Prior to starting her current appointment, she worked as a postdoctoral research fellow at Harvard University, Harvard-MIT Health Science & Technology (HST) under supervision of Prof. Ali Khademhosseini and School of Engineering of Applied Sciences (SEAS) under supervision of Prof. David Weitz. Her research interest is to use multi-disciplinary approach including material science, microfluidics, cell biology and molecular biology, to develop microscale and nanoscale technologies with the ultimate goal of generating tissue-engineered organs and controlling cell behaviors for addressing clinical problems. So far, she has published over 40 peer-reviewed journal articles including leading journals such as *Advanced Functional Materials*, *Materials Today*, *Biomaterials*, *Small*, etc.

Construction of Drug and Ag Carrier System on Ti Implants

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Keywords: Titanium; Implants, Surface Modification; Drug Carrier, Antibacterial; Ag nanoparticle.

Abstract: Titanium-based alloys are commonly used in orthopedic implants because of their desirable mechanical strength, corrosion resistance, and biocompatibility. Bacterial infection often induces the implant failure. Surface modification is the best way to not only improve the biocompatibility but also enhance the antibacterial performance of metallic implants. In the work, one-dimensional nanostructures including TiO_2 nanotube and titanate nanowire were constructed on the surface of Ti alloys. The former prepared by anodization method was used for drug loading with antibacterial polymer sealing while the latter produced by hydrothermal method was employed as carriers for Ag nanoparticles. Drug release tests disclosed that the drug release profile could be tuned to achieve the optimal therapeutic action throughout the treatment time by varying the thickness of the polymer film. SEM and TEM examinations showed that Ag nanoparticals could also be well carried by one dimensional titanate nanowires. Antibacterial tests revealed that the antibacterial activity increased with the increase of initial concentration of silver nitrate solution.

Prof. Wu Shuilin received his M.S. in Materials Surface Engineering from Tianjin University in 2003 and Ph.D in Biomaterials Engineering from City University of Hong Kong in 2007, respectively. After graduation, he worked as a Research Associate, Senior Research Associate and Research Fellow in Plasma Laboratory from August 2007 to October 2012 at City University of Hong Kong. Currently, he is a Professor of Materials Science and Engineering at Hubei University. His publications include 5 book chapters and over 90 journal papers including *Progress in materials Science, Materials science and engineernig r-reports, advanced functional materials, Nano Letters, Biomaterials, Journal of Biomedical Materials Research Part A, Acta Biomaterialia, Acta Materialia, ACS Applied Materials & Interfaces* and etc. His current research focuses on the design and synthesis of novel biomimetic scaffolds for biomedical applications.

Alkaline Biodegradable Implants for Osteoporotic Bone Defects-importance of Microenvironment pH

Xiaoli ZHAO

Abstract: The biocompatibility and bioactivity of orthopaedic implant materials are directly influenced by the local microenvironment generated after implantation. The microenvironment pH (μe-pH) is critical to the effectiveness of the implants in repairing osteoporotic bone defects, but has seldom been discussed. The purpose of this study was to determine the μe-pH for some orthopaedic implant materials in vivo, and to investigate its effect on the bone defect healing process. Ovariectomized rat bone defects were filled with one of three materials (β-tricalcium phosphate, calcium silicate, 10% strontium-substituted calcium silicate), and μe-pH was measured by pH microelectrode at various intervals post-surgery. The specific tissue responses, new osteoid and Tartrate-Resistant Acid Phosphatase (TRAP)-positive osteoclast-like cells were visualized by histological staining. Results from parallel in vitro experiments were consistent with the in vivo outcome. The intermediate layer between implants and new bone area was studied using energy-dispersive X-ray spectroscopy (EDX). Regardless of material, higher initial μe-pH was associated with more new bone formation, late response of TRAP-positive osteoclast-like cells, and the development of an intermediate 'apatitic' layer in vivo. EDX suggested that residual material may influence μe-pH even 9 weeks post-surgery. In vitro, weak alkaline conditions stimulated osteoporotic rat bone marrow stromal cell (oBMSC) differentiation, while inhibiting the formation of osteoclasts. Thus, the μe-pH of implanted materials directly affects their effectiveness in healing bone defects. We therefore propose for the first time to determine specifically the μe-pH for implants as part of the design of orthopaedic implant materials to improve their bioactivity and efficacy.

Dr. Xiaoli Zhao, Ph.D, is associate professor and supervisor of postgraduate in Shenzhen institutes of Advanced Technology, Chinese Academy of Science. She got the Overseas High-Caliber Personel Level C of Shenzhen. She is the key member of Shenzhen Peacock Innovation Team, vice director of Shenzhen Key Laboratory of Marine Biomedical Materials, member of the first committee of orthopedic research society SICOT China Chapter. She got PhD degree from The University of HongKong, and did research in Hopkins University as a visiting scholar. Research interest is focusing in orthopaedic biomaterials, including hydrogel, bone cement, drug and gene delivery, also involve in bone signaling and stem cell study.

Annulus Fibrosus Regeneration: A Multi-mode Mechanomodulation and Layer-by-layer Assembly Based Strategy

Bin LI

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Abstract: Degenerative disc disease (DDD) is the leading cause of low back pain, a serious global health problem which contributes to healthcare costs significantly. While it is promising to repair degenerated intervertebral discs (IVDs) using tissue engineering techniques, such an approach largely relies on the effective construction of annulus fibrosus (AF), a major load-bearing component of IVD. However, because of the tremendous cellular, biochemical, microstructural, and biomechanical heterogeneity of AF tissue, it remains challenging to fabricate AF replacements that are biologically and functionally comparable to native AF tissue. Recently, we started to employ a tissue engineering strategy based upon layer-by-layer assembly and multi-mode mechanomodulation in order to mimic the layered structure and to address the heterogeneity feature of AF tissue as well. In brief, we isolated multipotent AF-derived stem cells (AFSCs) for AF tissue engineering. We then synthesized a series of biodegradable polyurethanes and hydrogels with similar elastic modulus as AF tissue. We found that the biochemical and biomechanical profiles of AFSCs were markedly affected by the elastic modulus of scaffolds, implying the feasibility to induce differentiation of AFSCs into cells at different regions of native AF tissue. We also obtained AFSC sheets, i.e., cell monolayers together with the underlying matrix, using novel cell sheet culture techniques. Further, we applied dynamic mechanical stimulation to AFSCs and found that their anabolic and catabolic metabolisms were significantly dependent on the magnitude, frequency and duration of mechanical stimulation. Following these, we will assembly engineered AF tissue, through a layer-by-layer approach, using AFSC sheets primed with substrates of various elasticity and conditioned with appropriate mechanical stimulation. Findings from these studies may provide new insights toward developing engineered AFs whose biological features and mechanical functions approximate those of native AF tissue.

Keywords: intervertebral disc degeneration, annulus fibrosus, tissue engineering, annulus fibrosus-derived stem cells, mechanical stimulation

Professor Bin Li received the bachelor degree in Polymeric Materials Science and Chemical Engineering from the Department of Chemical Engineering of Tsinghua University in 1996. He received the PhD degree in Materials Science from Tsinghua University in 2001. He then worked as a Research Associate at the Institute of Materials Research and Engineering, Singapore from 2001 to 2004. After that he pursued postdoctoral training at the Department of Orthopaedics, University of Pittsburgh School of Medicine in USA from 2005 to 2009. He also completed two short-term trainings as a visiting research scientist at Carnegie Mellon University in 2004 and Harvard University in 2009, respectively. He joined Soochow University in 2009 as a Specially Appointed Professor and director of the Biomaterials and Cell Mechanics Laboratory (BCML) of Orthopedic Institute. He is the recipient of a number of awards such as the Orthopaedics Research Award (1st class) from Chinese Orthopaedic Association, Xu Guangqi Program from the French Embassy in China, and France Talent Innovation from the Consulate General of France in Shanghai. He currently serves as the chair of China Development Committee of the International Chinese Musculoskeletal Research Society (ICMRS). He is a fellow of Chinese Orthopaedic Research Society (CORS), Chinese Association of Orthopaedic Surgeons (CAOS), Chinese Association of Rehabilitation Medicine (CARM), and International Society of Orthopaedic Surgery and Traumatology (SICOT). He is also a member of the Orthopedic Research Society (ORS), Tissue Engineering and Regenerative Medicine International Society (TERMIS), Society For Biomaterials (SFB), Chinese Society for Biomaterials (CSBM), and Chinese Materials Research Society (CMRS). He serves on the editorial board of several journals, including *Journal of Orthopaedic Translation*, *International Journal of Orthopaedics*, *Chemical Sensors*, *Soochow University Journal of Medical Science*, and *Chinese Journal of Tissue Engineering Research*, and is the reviewer for over 30 journals. He was the organizing committee and executive chair of the Inaugural ICMRS-ASBMR International Chinese Musculoskeletal Research Conference (Suzhou, 2013). He has delivered more than 50 invited talks and is the author of over 80 journal articles and book chapters. His research interests include biomaterials for orthopaedic applications, degenerative disc disease, stem cells and tissue engineering, smart molecular recognition and controlled release, surface modification and functionalization, cellular biomechanics and mechanobiology.

Bone Tissue Engineering and Regenerative Medicine 2.0

--Paradigm Shift from “Proof-of-concept” to “Proof-of-value”

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Abstract: Large bone defect treatment remains a major clinical challenge, requiring effective bone grafts to achieve healing. Bone tissue engineering (BTE) strategy provides a promising approach to address this ever-pressing clinical need. Despite its first clinical application report in 2001, BTE strategy still stays as a laboratory technique rather than a regular clinical practice, with very limited clinical impact so far. In order to understand the major bottlenecking factors that hinder the fast clinical translation of BTE technology, in the first part of this talk, I would like to compare the development of tissue engineering technology with computer technology in order to illustrate the influence of “Proof-of-concept (POC)” and “Proof-of-value (POV)” oriented research strategy on the translation of new technology. Generally, it can be regarded as the BTE 1.0 development stage for the past thirty-year’s R&D effort, ever since the introduction of the BTE concept in 1980s. BTE 1.0 stage is the POC oriented with the goal to prove the scientific feasibility and clinical efficacy and safety of BTE concept. In order to facilitate its wider clinical application and the final translation from a lab technique into a routine clinical therapeutic practice, we believe, in the subsequential BTE 2.0 stage, the focus of our research should be shift from POC to POV, whose mission is to improve and achieve sufficient clinical and commercial value of BTE strategy to replace the current technique. I will discuss and illustrate the Low-Value points of current BTE strategy, such as unavailability off-the-shelf, high cost, complicated manufacturing process and so on and share with you our POV research efforts and thoughts on how to conquer these problems one by one. We believe, similar to the development of computer industry, the next stage of POV-orientated R&D effort (BTE 2.0 stage) will be the most critical and essential stage in order to boost up the final translation of BTE strategy into the real clinical technique, and facilitate the commercialization and maturation of the new industry of tissue engineering and regenerative medicine.

Professor ZHANG Zhi-Yong, PhD

Professor in Shanghai 9th People's Hospital, School of Medicine, Shanghai Jiao Tong University, P.R. China;

Principle Investigator and Group Leader in National Tissue Engineering Center of China & Shanghai Key Laboratory of Tissue Engineering;

Awardee of National "1000 Young Talent" plan, P.R. China;

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Professor Zhang Zhiyong received his B.Sc. degree in biology from Xiamen University of China in 2004 and PhD degree in bioengineering from National University of Singapore in 2009. From 2010 to 2012, he held an adjunct position in Fourth Military Medical University as Associate Professor. In 2012, he joined Shanghai Jiao Tong University and National Tissue Engineering Center of China as Professor and Group Leader; meanwhile he was granted National "1000 Young Talent" Award by the central government of China and appointed as "Eastern Scholar" Distinguished Professor by Shanghai government.

Trained as a bioengineer at multidisciplinary interfaces, Prof. Zhang holds great passion for translational research of bone tissue engineering and regenerative medicine (TERM). He is pioneering in the use of allogenic fetal mesenchymal stem cell source for TERM application and successfully developed an off-the-shelf bone TERM strategy with the integrated use of stem cell, scaffold, and bioreactor. Currently, the first-in-man clinical trial of this strategy has been approved by the Health Sciences Authority of Singapore (the regulatory agency counterpart of US FDA). He has filed more than 10 patents, published more than 30 academic papers in the prestigious international journals such as Stem Cells, Biomaterials, Cell Transplantation and Tissue Engineering (Average IF: 5.3 per paper) and authored five bookchapters. He has given plenary, keynote, invited presentation in more than 30 international conferences and been granted 12 scientific awards including the Natural Science Award of Ministry of Education of China (the First Prize, 2014) and so on. In addition, he has successfully secured 10 research grants with more than 10 million RMB research grants in China and serves in more than 10 academic societies. His research effort has also led to the successful commercialization and clinical translation of a unique bioreactor device and 3D printed surgical guide for total knee replacement surgery. Recently he was invited to become the committee member of Tissue Engineering Technical Committee in Standardization Administration of China (SAC, the counterpart of ISO) and helps to draft three industry standards for bone tissue engineered products.