



4th Annual Conference and Expo on **Biomaterials**

February 25-26, 2019 | London, UK

Posters

Biomaterials 2019

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Development of wearable sensor device using biodegradable microneedle patch**Eunjin An, Chang Yub Sung, Jung Dong Kim, Jung Hyun Bae, Keun Ho Lee, Moon Su Lee, Tae Hyung Kim, Seong Jin Kim, Geum Chae Jang, Yoonsik Kang and Do Hyeon Jeong**
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The microneedle-mediated transdermal delivery system has been developed to provide minimal invasive self-administration method. Droplet-born air blowing (DAB) method has great advantages in stability with precise dose control because DAB provide quick manufacturing process with ambient temperature. Also, microneedle (MN) array is stamped on the skin, and interstitial fluid (ISF) is obtained. MNs are designed to collect dermal interstitial fluid containing biomarkers without the risk or pain needed for collecting blood. This study suggests the novel dissolving microneedle fabrication method, droplet-born air blowing (DAB), which provide gentle temperature and fast manufacturing process with precise dose control. Microneedle fabricated by DAB method. Briefly, biodegradable polymer such as HA (hyaluronic acid) were dissolved in water with active ingredients. The mixture was dropped to a patch, and each droplet is shaped to the microneedle. The loaded amount of active ingredients was analyzed by ELISA or HPLC/UV system. Skin permeability of microneedle was confirmed by OCT (optical coherence tomography) and delivered amount into the skin was analyzed using Franz diffusion cell (Logan, FDC-6T). We optimized the DAB process parameters and scaled up without applying any heat. Various ingredients were loaded within microneedles approximately 100% compared to theoretical values independent of microneedle length. In vitro and ex vivo studies using Franz diffusion cell showed excellent delivery efficiency compared to topical solution. In vivo OCT images clearly showed that whole length of microneedles could penetrate into human skin. DAB technology suggests a way to solve the problems of conventional molding method to fabricate dissolving microneedle. Based on the method, we have successfully developed mass production system to manufacture microneedle-arrayed patch. We loaded lots of active ingredients with precise dose control, and confirmed the delivery efficiency of labile ingredients within microneedles. Also, we can access to biomarkers in dermis and future medical diagnostic and monitoring applications.

Recent Publications:

1. J D Kim, M Kim, H Yang, K Lee and H Jung (2013) Droplet-born air blowing: novel dissolving microneedle fabrication. *Journal of Controlled Release* 170(3):430-436.
2. S P Sullivan, D G Koutsonanos, M P Martin, J W Lee, V Zarnitsyn, S O Choi, N Murthy, R W Compans, I Skountzou and M R Prausnitz (2010) Dissolving polymer microneedle patches for influenza vaccination. *Nature Medicine* 16:915-920
3. Kolluru C, Williams M, Chae J and Prausnitz M R (2019) Recruitment and collection of dermal interstitial fluid using a microneedle patch. *Advanced Healthcare Materials* 1801262.
4. Kim H K, Lee S H, Lee B Y, Kim S J, Sung C Y, Jang N K and Lee S (2018) A comparative study of dissolving hyaluronic acid microneedles with trehalose and poly (vinyl pyrrolidone) for efficient peptide drug delivery. *Biomaterials Science* 6(10):2566-70.
5. Kim J H, Shin J U, Kim S H, Noh J Y, Kim H R, Lee J and Kim H K (2018) Successful transdermal allergen delivery and allergen-specific immunotherapy using biodegradable microneedle patches. *Biomaterials* 150:38-48.

Biography

Eunjin An received her bachelor's degree in Department of Chemistry. Also, she received her Master's degree in Department of Pharmacy from Duksung Women's University, Republic of Korea. Her research interests are biomaterial polymer materials and devices for effective drug delivery systems. And now her studying microneedle patch for transdermal drug delivery system and wearable device at Raphas Co. Ltd. Raphas Co., Ltd. is engaged in the research and development of cosmetics, medical devices and pharmaceuticals.

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Antimicrobial nano-fiber structures development to rejuvenate injured dura mater in brain surgery

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Statement of the Problem: Nosocomial pathogens such as *Staphylococcus epidermidis*, *Staphylococcus aureus*, *Escherichia coli* and *Pseudomonas aeruginosa* have been linked to surgical site infections. Inefficiency of surgical technique of the brain or spinal cord could greatly damage the duramater layer of the meninges. Hence, with it being non-regenerative in nature and with continued unsuccessful attempts to produce a well-maintained substitute, biomaterials incorporated with antimicrobials are the novel focus now. Silver salts have shown no harm when inserted in vitro and are emerging in many medical antimicrobial applications. Despite few scaffolds being proposed, a biomaterial with smooth integration and optimal properties has not yet been confirmed.

Aim: The purpose of this project is to attempt to close this gap by synthesizing polyacrylonitrile nanofibers, using the electrospinning technique and dip-coating them in polyethylene glycole solutions with dissolved silver acetate, behenate or citrate in hopes of inducing antimicrobial properties and creating optimal structures for such applications.

Methodology & Theoretical Orientation: Nanofibers were synthesized and tested using scanning electron microscopy. Also, antimicrobial efficacy assays, well diffusion assays and time kill assays were done to test the minimal concentration of each of the silver salts required to inhibit the 5 nosocomial pathogens *S. aureus*, *S. epidermidis*, *E. coli* K10, *E. coli* 10418 and *P. aeruginosa*.

Findings: The optimum minimum inhibitory concentration for the three silvers was found to be 0.8%. Both silver acetate and citrate at 0.8% showed potent antimicrobial activity; however, silver acetate coated nanofibers were the most potent amongst the three salts. Of the pathogens tested, gram-positive bacteria were proved, using CFU/ml viable count, to be most resistant to both silver salts despite efficient antimicrobial activity against them at 0.8%.

Conclusion & Significance: Based on these initial, yet interesting findings, future directions would be finding most appropriate scaffold sizes and diameters through varying flow rates and asking surgeons about biocompatibility, size of an optimum scaffold and easiness or best way of surgical insertion. Lastly, non-medical aseptic applications could be considered for testing on other microorganisms thus furthering experimentation with scaffolds.

Recent Publications:

1. Alamri A, El Newehy M and Al Deyab S (2012) Biocidal polymers: synthesis and antimicrobial properties of benzaldehyde derivatives immobilized onto amine-terminated polyacrylonitrile. *Chemistry Central Journal* 6(1):111.
2. Călina D et al. (2016) Antimicrobial resistance development following surgical site infections. *Molecular Medicine Reports* 15(2):681-688.
3. Dolina J, Jiříček T and Lederer T (2013) Membrane modification with nanofiber structures containing silver. *Industrial & Engineering Chemistry Research* 52(39):13971-13978.
4. Gopiraman M et al. (2016) Silver coated anionic cellulose nanofiber composites for an efficient antimicrobial activity. *Carbohydrate Polymers* 149:51-59.

Biography

Eunjin An received her bachelor's degree in Department of Chemistry. Also, she received her Master's degree in Department of Pharmacy from Duksung Women's University, Republic of Korea.

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Plasma electrolytic oxidation of titanium to biofunctionalize surfaces of ventricular assist devices**Eduardo GP Bock**
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Ventricular assist devices (VAD) are prescribed for congestive heart failure patients to stabilize their hemodynamics until recovery or alternative therapy. The devices are essentially machined in commercially pure titanium (Ti cp) a biomaterial capable of providing stable biological integration without compromising implant biofunctionality or patient well-being. The promotion of biofunctional surfaces for VAD became possible through surface modification of VAD components in order to improve the interface between biomaterial and assisted organ. A process was developed using plasma electrolytic oxidation (PEO) technique to form a textured oxide layer in Ti cp. Scanning electron microscopy was used to certify the effectiveness of texturing. A methodology was elaborated to assess the feasibility of endothelialization by in vitro cellular growth with human umbilical vein endothelial cells (HUVEC). PEO process was able to provide a textured oxide coating in Ti cp; in which the micrograph, scaffolding characteristics, has a proportional size to circulating blood cells and endothelial. Magnesium incorporation has shown to be promising since extracellular membrane proteins of adherent cells need this element to exert their function. In vitro procedure indicated endothelialization in modified surface as the HUVEC adhered three times more on coated titanium oxide compared to the observed in the experiment with pure polished titanium. Endothelialization in VAD tends to occur in vivo during circulatory assistance; the presence of a thrombosis-resistant neointima at the interface between implant/circulating blood aims to reduce the induction of heparin as anticoagulant thus assigning lower hemolysis due to higher absorption of tensions shear per flow to the surface of VADs.

Recent Publications:

1. Bock E G P (2016) Review of introductory tests to in vivo evaluation, prototypes assembling and anatomical position studies after five years. *International Journal of Advanced Robotics and Automation* 1:1-3.
2. Bock E G P et al. (2016) Left ventricle failure and blood flow estimation for centrifugal blood pumps. *Journal of Mechanics Engineering and Automation* 6:162-166.
3. Lopes G, Bock E G P and Gómez L (2017) Numerical analyses for low Reynolds flow in a ventricular assist device. *Artificial Organs* 41(6):E30-E40.
4. Uebelhart B et al. (2013) Study of a centrifugal blood pump in a mock loop system. *Artificial Organs* 37(11):946-949.
5. Bock E G P et al. (2011) Implantable centrifugal blood pump with dual impeller and double pivot bearing system: electromechanical actuator, prototyping, and anatomical studies. *Artificial Organs* 35(5):437-442.

Biography

Eduardo G P Bock holds a Degree in Mechanical Engineering from Sao Judas Tadeu University (2003); a Masters (2007) and PhD (2011) in Mechanical Engineering from the State University of Campinas – Unicamp, Brazil respectively. He is currently an Associate Professor (class D-IV) in the Laboratory of Bioengineering and Biomaterials (BIOENG) of the Department of Mechanics at Federal Institute of Technology (IFSP), Sao Paulo (Brazil). He has experience in the field of biomedical engineering with emphasis on bioengineering, working mainly in the following subjects: biomaterials, tribology, numerical simulation, artificial organs, artificial heart, circulatory assistance, left ventricular assistance and extracorporeal circulation.

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Development of Biomimetic Scaffolds for Controlled Release of Bioactive Agent**Farah Alwani Azaman, Margaret E. Brennan Fournet, Maria del Mar Blanes Martinez and Declan M.Devine**
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Osteogenic factors are a must have feature of bone regeneration scaffolds. Here we present a biomimetic delivery scaffold that is directly translatable to clinical applications, integrating multiple intricate factors in an orthopaedic implant that is easy to fabricate and adopt in the surgical setting. The straightforward preparation of a microporous bio-active scaffold designed for sustained bio-agent release is presented. Chitosan, combined with osteoconductive bio-ceramics form the basis of the scaffold architecture. The sustained release of growth factors (GF) for bone repair after trauma or non-union fractures is demonstrated. An in situ crosslinking step provides a unique route to overcome the low GF stability and short half-life challenges under physiological conditions. High initial burst release is prevented with effective prolonged delivery demonstrated. The scaffold crosslinking reaction, mechanical properties and degradation profile characterization will be described. The bioactive bone regeneration implant presents a substantial list of essential criteria including biocompatibility, biodegradability, micro/nano-architectural physical cues and holds a great promise for therapeutic bone tissue repair.

Recent Publications:

1. Declan M. Devine, Eilish Hctor, Jessica S. Hayes, Eoin Sheehan, Christopher H. Evans, "Extended release of proteins following encapsulation in hydroxyapatite/chitosan composite scaffolds for bone tissue engineering applications", *Materials Science & Engineering C*, 1, 84, 281-28 (2018)
2. C.J.D. Bergmann, J.C.E. Odekerken, T.J.M. Welting, F. Jungwirth, D. Devine, L. Bouré, S. Zeiter,
3. L.W. Van Rhijn, R. Telle, H. Fischer, P.J. Emans. Calcium phosphate based three-dimensional cold plotted bone scaffolds for critical size bone defects. *BioMed Res Intern.* 201, (2014)
4. J.A., Killion, S., Kehoe, L.M., Geever, D.M., Devine, E., Sheehan, D., Boyd, C.L., Higginbotham. Hydrogel/bioactive glass composites for bone regeneration applications: synthesis and characterisation. *Mat. Sci & Eng. C*, 33(7), 2013, 4203-12.
5. M Canillas, GG de Lima, MA Rodríguez, MJD Nugent, DM Devine, 2016. Bioactive composites fabricated by freezing-thawing method for bone regeneration applications. *J Polym Sci Part B: Polym Phys.* 54(7):761-773.

Biography

The research team has extensive experience and participates in a number of international collaborator research activities in the bone tissue regeneration field. In particular the team is focused on the development of variety of biomaterials which may be used to treat different ailments related to bone including, biomimetic bone graft substitutes and biodegradable polymers with tailored properties and degradation profiles.

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Notes:



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Accepted Abstracts

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Chitosan-based hydrogels as biomaterials for controlled releaseJacques Desbrieres¹, Marcel Popa² and Catalina Peptu²¹University of Pau and Pays de l'Adour, France²Gheorghe Asachi Technical University of Iași, Romania

Because of its favorable properties chitosan has been studied as a biomaterial and as a pharmaceutical excipient in drug formulations. For this, chitosan has to be crosslinked either chemically using covalent agents, or physically with ionic agents. The use of crosslinking agents is imposed by the properties of the non-crosslinked gels, such as lack of shape and mechanical stability. It is well-known that the covalent crosslinking agents present a certain toxicity leading to cytotoxic formulations. To reduce this toxicity original concepts were developed. The first one to be described was double-crosslinking consisting in a mixture of covalent (glutaraldehyde was used in a minimum amount to ensure the system stability) and ionic (sodium or magnesium sulphate, sodium tripolyphosphate) crosslinking agents. A second concept is the use of natural non-toxic crosslinking agents such as tannic acid. Due to hydrogen interactions able to form with the polysaccharides, tannic acid is able to prepare hydrogels able to load and deliver drugs or biologically active matter. These materials can be prepared under different forms such as hydrogels, particles and capsules. Their properties depend on some initial preparation parameters, the aqueous solution concentration, the process conditions, etc. Specific tests were performed in order to prove the ability of these biomaterials to be used in different areas of medicine. But drug release studies on these materials show, in many cases, a burst effect phenomenon. A great quantity of active principle is released in the first minutes before release rate stays constant. This effect leads to a great initial drug concentration in the body and decreases the lifetime of the system. According to applications it may be desired (wound dressing) or, very often, negative. To overcome this problem liposomes dispersed in the hydrogel were used playing the role of supplementary barrier against early drug release. Complex systems capable of prolonged and controlled drug release kinetics were prepared based on chitosan hydrogels and drug loaded liposomes. Calcein release from polymeric hydrogels has been retarded from several days to weeks after calcein inclusion in small phosphatidylcholine unilamellar and multilamellar vesicles entrapped subsequently in hydrogels. The calcein release kinetics of complex systems was compared to simple systems (control hydrogels) and important changes were observed proving that the mechanism of the process increases in complexity. Kinetic constants obtained from Higuchi or Korsmeyer-Peppas models were compared and discussed. Moreover, it is demonstrated that liposomes' stability can be greatly improved by inclusion in polymer matrices.

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***In situ* tissue engineering using an induced adipose tissue to regenerate bone**

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It is known that disturbances of the balance between osteogenesis and adipogenesis lead to metabolic diseases such as osteoporosis. Several studies have reported that induction of adipose tissues in bone marrow leads to decreased bone mass and bone formation suggesting that bone marrow osteogenesis and adipogenesis are inverse processes.

In this preliminary study we were testing the hypotheses of induction of adipose tissue to form bone using bioceramic material, rat mesenchymal stromal (rMSCs) cells and bone morphogenetic protein-2 (BMP-2) in ex vivo experiments. hMSC-TERT cell line was used to test the interconversion cell process. Osteogenic and adipogenic trans-differentiation was assessed for the same culture cell line. The osteogenic and adipogenic differentiation were confirmed by applying the following assays: ALP staining, Nile Red Staining & Quantitative Real Time PCR (qRT-PCR). For in vivo, 5 bone cement constructs were prepared, using injectable calcium sulphate/hydroxyapatite of 60% calcium sulfate, 40% hydroxyapatite powder (CS/HA) and 0.13 mg of bone cement of bone morphogenetic protein-2 (BMP-2), then injected bilaterally at abdominal fat tissues in Sprague Dawley male rats (n=5). Eight weeks postoperative histological assessment for the harvested adipose tissues showed, immature bone formation with osteocyte was noted. Area of cartilage tissues and chondrocytes were found with close approximation to the injected bone cement CS/HA formation. The findings indicate osteogenic differentiation of fat cells occurs under the effect of bio-ceramic and bone morphogenetic protein which were injected in situ. Interestingly, presence of chondrocytes and premature cartilage tissue could indicate endochondral bone formation. This study confirms the in vivo trans-differentiation of adipose tissues and suggests novel strategies for bone regeneration.

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Tribocorrosion behavior of Ti-10Nb alloy for biomaterial applications

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Ti and Ti6Al4V alloy are widely used to replace hard tissues due to their higher biocompatibility, corrosion resistance and suitable mechanical properties. There is a concernment about the long-term release of harmful ions, as aluminum and vanadium by dissolution from the Ti6Al4V alloy. These metals have a poor wear performance, and higher coefficient of friction that restrict to the applications in the biomedical area. Besides, wear debris can result in inflammatory reactions that cause pain and the loss of implants by osteolysis. In order to replace these materials, new beta alloys composed by non-toxic elements, as Nb, Ta, Mo, have been proposed, which are corrosion resistant and have mechanical properties suitable for biomaterials applications. After implantation into bone, implants can be exposed to tribocorrosion conditions, i.e., process combined of corrosion and wear. However, research about the tribocorrosion behavior of new beta Ti alloys is still very limited. In this study, tribocorrosion properties pure Ti and Ti-10Nb alloy for biomedical applications in phosphate-buffered saline solution were investigated. The tests were done by reciprocating tribometer against Al₂O₃ ball, electrochemical tests and scanning electron microscope images. The results, during the sliding, of open circuit potential demonstrated that the Ti-10Nb alloy was more resistance to corrosion than pure Ti. The coefficients of friction obtained were 0.48 and 0.57 to Ti-10Nb alloy and Ti, respectively. These metals showed a similar wear rate ($\sim 0.66 \cdot 10^{-3} \text{ mm}^3/\text{Nm}$). The images of worn tracks revealed abrasive, adhesive and oxidative wear for all samples. The results disclosed that the coefficient of friction was influenced through microstructure of Ti-10Nb alloy. Neither mechanics of wear nor wear rate were dependent on the material microstructure. Therefore, in comparing to pure Ti, the addition of beta stabilizer element in the Ti-10Nb alloy improves the corrosion resistance and the coefficient of friction.

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Investigating dynamic biological processes with high-speed, high-resolution correlative AFM-light microscopy**Heiko Haschke, Florian Kumpfe and Torsten Müller**
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The ability of atomic force microscopy (AFM) to obtain three-dimensional topography images of biological molecules and complexes with nanometer resolution and under near-physiological conditions remains unmatched by other imaging techniques. However, the typically longer image acquisition times required to obtain a single high-resolution image (~minutes) has limited the advancement of AFM for investigating dynamic biological processes. While recent years have shown significant progress in the development of high-speed AFM (HS-AFM), the ability to scan faster has typically been achieved at the cost of decreased scanner range and restricted sample size. As such, these HS-AFM systems have mainly focused on studying single molecule dynamics and have been very limited in their ability to conduct live cell imaging. The novel NanoWizard® ULTRA Speed AFM not only enables high-speed studies of time-resolved dynamics associated with cellular processes, it's latest scanner technologies and compact design also allow full integration of AFM into advanced commercially available light microscopy techniques. Thus, fast AFM imaging of several frames per second can be seamlessly combined with methods such as epifluorescence, confocal, TIRF, STED microscopy, and many more. We will present how the latest advances in the ULTRA Speed AFM are being applied to study a wide-range of biological samples, from individual biomolecules to mammalian cells and tissues. We will also describe how this unique system is enabling new research opportunities with high-speed, high-resolution correlative AFM-light microscopy.

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Development of few new materials for microminiaturization of electronic circuits used for various applications

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A large demand has been placed on miniaturization of electronic applications, especially in the last two decades. Ferrite materials are recognized as more important and essential for the further development of electronics than before, and it is believed that the production of ferrites will increase year by year as their applications become more diverse. They are used in fabrication of multilayer chip inductors (MLCIs) as surface mounting devices (SMDs) for micro-miniaturization of electronic circuits. The tendency to miniaturize electronic components began in the 1990s. Concurrently, progress also occurred in surface-mounting technology, and attempts have been made to accomplish high density, incorporation of ferrite inductors into a printed circuit board. This has a result, allowed development of various types of multilayer ferrite chip inductors. The present chip inductor features make the miniaturization process very easy chip inductors are one of the passive surface mounting devices (SMD). The flux is entirely free from leakage because the coil is shielded with a ferrite material. Hence it is expected that the demand for the chip inductors will increase more and more in the future. Recently, the surface mounting devices (SMD) have been rapidly developed for micro inductor applications which have great demand in electronic applications. MLCIs as the key component of electronic devices are confronting new challenges. The dominant materials for MLCIs are soft ferrites materials. These studies revealed the development of new materials for the multilayer chip inductors and concluded that these ferrites possess good electromagnetic properties and can be exploited as core material for micro inductor applications.

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Biodegradable copolyester based blends: Properties and applications**Shanta Pokhrel**

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Biopolymers extracted from renewable resources such as plants, marine animals, insects have limited applications in large scale plastic production. Among various synthetic polymers, aliphatic aromatic copolyester i.e. poly(butylene adipate-co-terephthalate) (PBAT) has made its own place due to its good thermal, mechanical properties and biodegradability. It can be used in several applications, such as packaging materials (trash bags, food containers, film wrapping), hygiene products (diaper back sheets, cotton swabs), biomedical fields, industrial composting. PBAT's compostability is its major advantage which contrasts to polylactic acid (PLA) where industrial fermentation conditions (60°C) are required. Biodegradable polymers are modified for broadening their potential applications by various means such as blending and composites forming, which lead to new materials having unique properties including high performance, low cost, and good process ability. This lecture will highlight the properties and various applications of PBAT based biodegradable blends.

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Microfluidics fabrication of ECM-based microstructures and their 3D printing

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Soft microtissues comprising living cells and the supportive matrices have been attracting growing research attention by their potential as in vitro organ models that acquires the patient's heterogeneity, as well as building blocks for artificial organs or regenerative tissues. To recapitulate the native tissue structures and functions in vivo, the engineered microtissues shall recapitulate the mechanical and biological properties of the matrices in their native counterpart tissues. Using extracellular matrix (ECM) or ECM-derived materials is an option. However, the structural components of natural ECM are low in modulus (usually less than 1000 Pascal) and slow-gelling (generally taking tens of minutes to gel at 37°C), which may challenge the structural integrity in engineering and raise limitation in the production rate. Microfluidics has been known for its capability to produce monodisperse microstructures in high-throughput. This talk summarizes our progress on microfluidics fabrication of ECM-based microstructures and soft microtissues, and the challenges still faced by this technique. It also covers the chemical and physical functionalization of ECM-like materials to render higher compatibility with biomanufacturing, without sacrificing their biological competence.

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2D and 3D cell cultures systems in biomedical studies

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Development of cell culture systems are indispensable for advancing in basic biology and clinical translations. Breakthroughs have been discovered using 2D with defined and controlled physical properties such as stiffness and geometry, evidencing that signals that cells receive from the physicality of their microenvironment are absolutely essential for their survival and to direct their fate. These results go far beyond the limit of the classically preferred culture model, 2D cell monolayers cultured on adhesive rigid and flat plastic petri dish substrates. However, cells grown in vivo within a complex 3D soft microenvironment and 3D cultures have been more recently introduced for in vitro studies, showing structurally and functionally different behavior of embedded cell aggregates or organoids. At the meeting, I will introduce examples of engineered biomaterials and microenvironments to control cell-behavior using mechano-transcriptional regulators, YAP and TAZ, as molecular beacon of the cell response. The use of chemically defined biomaterials for the preservation of pancreatic progenitor traits ex-vivo, 2D hydrogels with controlled rigidity and micropatterned substrates to control cell behavior, will be presented. The engineering of in vitro 2D and 3D culture microenvironments still requires efforts to develop reproducible and chemically/physically defined biomaterials, in particular hydrogels, and to use microfabrication techniques to generate controlled shapes and microenvironment, which more closely mimics key aspects of the natural environment of cells. New opportunities in these directions will be discussed

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Collagen 3D matrix regulates osteoblastogenesis and osteoclastogenesis in bone: A novel model for bone homeostasis

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Collagen is the extracellular matrix protein in bone that regulates ossification and bone resorption through modulating the paracrine cues of bone cells, and has been used for the treatment of bone disorders due to its bio-mimic properties. However, the biological activity of collagen depends on the interactions with other biomolecules such as minerals and glycosaminoglycan in bone. Considering the above perceptions, collagen was crosslinked with calcium apatite (CA) and chondroitin sulphate (CS), to produce a natural bone like 3D-structure and evaluated its effect on bone homeostasis using bone marrow mesenchymal stem cells, osteoblast and bone marrow macrophages (BMM). The arrangement of CA crystallites in collagen-CA-CS (CCACS) 3D-matrix was confirmed by XRD spectra. Micro-CT hierarchical structure confirmed the three-dimensional structure of matrix and the structure resembles as trabecular bone. The stimulatory osteoblastogenic and exploitive osteoclastogenic activity of CCACS 3D-matrices were identified by the high level of bone biomarkers (collagen, ALP, and minerals) in differentiated-osteoblasts and decreased mCSF-RANKL or rPTHr11 induced TRAP⁺ osteoclasts from ovariectomized-mice-BMM, respectively. Besides, paracrine cues of osteogenic progenitors for BMM-derived osteoclastogenesis by CCACS 3D-matrix disclose that the differentiated osteoblast secreted higher level of RANKL to support osteoclastogenesis and the effect was down-regulated by CCACS 3D-matrix. The present empirical evidence proved the osteogenic stimulatory and osteoclastogenic inhibitory effect of CCACS 3D-matrix. From that we hypothesize, the morphological features of CCACS 3D-matrix resembles as a trabecular bone, enhances bone growth and limits bone resorption.

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Freeze-dried platelet as a natural source of essential growth factors for periodontium regeneration

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Periodontitis is a common disease that starts with gingival inflammation and may end with the formation of periodontal pocket with loss of attachment and destruction of the supporting structures. This eventually leads to functional and esthetic problems. Several limitations in the current treatment modalities restrict the reach for full periodontium regeneration. The utilization of the science of tissue engineering and regenerative medicine offers the opportunity to overcome these limitations. Platelet concentrates have been used to deliver a high dose of growth factors that can aid in the healing and regeneration of wound defects. However, fresh prepared platelet concentrate has a shelf life of only 4-5 days and frozen platelet concentrate loses a lot of its benefits. In addition, delivered growth factors have a short half-life in vivo (within hours) due to rapid clearance which makes it difficult to maintain a therapeutic dose at the defect site throughout the healing period. Therefore, it was hypothesized that incorporating freeze-dried platelets in high amounts with their load of many growth factors in a hydrogel carrier can control their delivery and provide a sustained therapeutic dose for a longer period. In addition, an antimicrobial easy-applicable hydrogel scaffold was used for better regeneration.

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3D-Printing of Bio ceramics for Bone Regeneration Applications**Rainer Gadow**

University of Stuttgart, GerAbstract

Bone degradation and fractures represent a significant concern to human health and to the increased population life expectancy. When such defects overcome a certain critical size, body induced autorepair cannot restore lost skeleton functionality. Medical treatment involves bone grafting, a common surgical procedure with more than 2.0 million grafting procedures performed worldwide each year. Autologous bone grafts are currently the golden standard treatment but are associated with donor-site complications, risk of infection and size and shape limitations. Artificial scaffolds with tailored geometry, porosity, architecture and composition present an alternative to autologous grafts and are excellent 3D templates to provide structural support for ingrowth of the newly formed bone. The use of bioceramics like calcium phosphates (Hap, TCP) or bioactive glasses for the regeneration of critical bone defects is intensively researched worldwide. The advantages of additive manufacturing technology make it possible to process these ceramic materials into customized patient-specific implants. In this work the process chain of powder-based inkjet-3D-printing is presented. This includes the production of bioceramic suspensions from bioglass, calcium phosphates and composites and spray dry granulation to obtain flowable granulates. 3D-printing is performed from CAD-modelling to post-processing of the printed structures. Printed components are sintered and characterized with respect to mechanical properties and in vitro biocompatibility. After sintering the scaffolds show high porosity (about 70 %) and high surface roughness (Ra about 25 μm , Rz up to 200 μm) which is beneficial for the colonization of bone cells. In vitro tests using MG-63 stem cells showed an effective growth of cells on the outer and inner surface of the scaffolds and the formation of reinforcing secondary hydroxyapatite crystals.

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Development of a novel chitosan based biocompatible and self-healing hydrogel for controlled release of hydrophilic drug**Swati Sharma, Shere Afgan, Ashok Kumar, Deepak and Rajesh Kumar**
Banaras Hindu University, India

Smart polymeric hydrogels of chitosan and acryloyl-phenylalanine having potential of fast intrinsic shape memory properties (self-healing), non-toxic, biocompatible with moderate mechanical strength have been developed. The hydrogel has been formed by linking its network with flexible pendant side chains of chitosan and acryloyl-phenylalanine (exhibiting optimal balance of hydrophilic and hydrophobic moieties). The non-toxic and biocompatible behavior of the synthesized chitosan based hydrogel reveals its potential use towards the biomedical field. The side chain of hydrogel consists of amine and carboxylic acid groups and these moieties allow non-covalent interactions (H-bonding) across its interface. Thus, synthesized hydrogel shows very good self-healing property. Further, it has shown remarkable swelling (at different pH viz.- 2, 7, 9), cell viability (HEK-293 cells up to 200 µg/mL), cell proliferation, and controlled drug release and thus found multi-responsive.

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4th Annual Conference and Expo on **Biomaterials**

February 25-26, 2019 | London, UK

Nanoparticles as new emerging antibacterial: Potential and Limitations

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Now days, microbial strains become resistant to the antibiotics and thus become serious public health problems that increase the need to develop novel antimicrobial agents that can cope with these problems. The field of nanotechnology has generated numerous novel antimicrobial options as the minute size of the nanoparticles is very appropriate for carrying out antimicrobial biological operations medicinal sector. Metals such as silver, zinc, copper and iron nanoparticles types have shown tremendous potential as bactericidal and fungicidal elements, demonstrating their potential as efficient antibiotic reagents in wound care and related medical issues. These nanomaterials showed a positive effect as an antimicrobicide against various pathogenic species. Today, Nanomaterials are found as a promising platform for unconventional measures to control microbial infections as they offer prolonged antimicrobial efficacy with insignificant toxicity, when compared with small molecular antimicrobial agents that shows short term activity as well as environmental toxicity.

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Bioconjugation studies of GO/Fe₃O₄ nanocomposites hollow/porous magnetite

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In this paper, we have synthesized reduced graphene oxide/magnetite (rGO-Fe₃O₄) nanocomposites by chemical co-precipitation method for a comparative Raman spectroscopic study. The nanocomposites along with its pristine GO and Fe₃O₄ counterpart were modified covalently with a fluorescently labeled protein. The modification was confirmed using confocal fluorescence microscopy. The GO, Fe₃O₄ and rGO-Fe₃O₄ samples were characterized by different spectroscopic and microscopic techniques before and after protein conjugation. A significant enhancement in Raman peaks obtained in case of protein modified rGO-Fe₃O₄ nanocomposites compared to pristine GO and Fe₃O₄ explains active Surface Enhancement Raman Spectroscopy (SERS) effect. An unusual phenomenon of GO to rGO conversion and vice-versa was noted as a result of covalent protein attachment.

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