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Innovative Biomaterials and Crossing Frontiers in Biomaterials and Regenerative Medicine

Final Program

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P-MON-B-073 **Deposition of Calcium Phosphate Coating on TiO2 Nanotube Arrays (ID: 3519)**
Ana Lúcia Amaral Escada (Unesp - São Paulo State University, BRAZIL)

P-MON-B-074 **The Role of Peptide in the Remineralization for Artificial Carious Enamel (ID: 671)**
Hsiu-Ying Chung (Feng Chia University, CHINESE TAIPEI), Chia-Chan Hsu

P-MON-B-075 **Effect of Cell Density on Osteogenic Differentiation of Stem Cells Cultured on PVA-micropattened Polymer Surfaces (ID: 2708)**
Naoki Kawazoe (National Institute for Materials Science, JAPAN), Wei Song, Hongxu Lu, Guoping Chen

P-MON-B-076 **Effect of Alkali and Heat Treatment on Bioactivity of Micro-arc Oxidized Titanium (ID: 2421)**
Xiaojing Lou (Nanjing University of Science and Technology, CHINA), Sen Yang, Jun Li

P-MON-B-077 **Cytotoxicity Evaluation of Chitosan/Apatite/Vitamin E Hybrid Films (ID: 3506)**
Wladymyr Jefferson Bacalhau Sousa (Ufcg, BRAZIL), Marcus Vinicius Lia Fook, Marcio Jose Batista Cardoso, Katilayne Vieira Almeida, Thiago Fideles

P-MON-B-078 **Immobilization of Bisphosphonates on the Nanotube Surface of Titanium Discs for Bone Implants (ID: 2686)**
Zhi-Cai Xing (Kyungpook National University, KOREA), Inn-Kyu Kang, Tae-Hyung Koo, Yong-Suk Shin, Seung-Jin Han, Sungmo Moon, Yongsoo Jeong

P-MON-B-079 **In-vitro and In-vivo Studies of a Novel Biodegradable Polycaprolactone-magnesium Hybrid Scaffold for Orthopaedic Implantations (ID: 1564)**
Hoi Man Wong (The University of Hong Kong, HONG KONG), Paul Chu, Keith Luk, Kenneth Cheung, Kelvin Yeung

P-MON-B-080 **Reinforcement of Carbonate Apatite form by Coating with Poly-l-lactic Acid Containing Carbonate Apatite Granules (ID: 3315)**
Kanji Tsuru (Kyushu University, JAPAN)

P-MON-B-081 **PEG-HA Composite Hydrogel for Bone Tissue Engineering (ID: 1345)**
Seunghee Lee (Seoul National University, KOREA), Hyoun-Ee Kim, Jinsang Kim

P-MON-B-082 **CaP Glass nanoparticles/PLA hybrid Fibers for Angiogenic Applications (ID: 3481)**
Oscar Castano (Institute for Bioengineering of Catalonia, SPAIN), Miguel Angel Mateos-Timoneda, Blandine Contreras, Arlyng Gonzalez, Aitor Sanchez, Elisabeth Engel, Josep Anton Planell

P-MON-B-083 **Poly(l-lactide-co -glycolide) Scaffolds Modified with Hydroxyapatite or Collagen: Physicochemical Properties and in vivo Evaluation (ID: 1399)**
Elzbieta Pamula (Agh University of Science and Technology, POLAND), Elzbieta Menaszek, Maciej Orzelski, Lucja Rumian, Piotr Malisz, Piotr Dobrzynski, Piotr Silmanowicz

P-MON-B-084 **Biodegradable Novel Polymeric Nanocomposite-studies on Interfacial Stability (ID: 308)**
Jayabalan Muthu (Sree Chitra Tirunal Institute for Medical Sciences & Technology, INDIA), Ganesan K, Epple M

P-MON-B-085 **In situ Formation of Hyaluronic Acid Hybrid Hydrogel for Mimicking of Bone Mineralization (ID: 1394)**
Xia Yang (Uppsala University, SWEDEN), Sultan Akhtar , Klaus Leifer, Jöns Hilborn, Dmitri Ossipov

P-MON-B-086 **The Preparation and Characterization of the Injectable Chitosan-Hydroxyapatite Microspheres As Microcarrier in Cell Culture (ID: 1890)**
Xiaomeng Liang (Shandong University, CHINA), Guancong Wang, Hong Liu

P-MON-B-087 **Multilayer Composite Membrane Based on Collagen, PLA, and PCL by Electrospinning for Development of a Dura Substitute Material (ID: 508)**
Yu-Fei Wang (Third Military Medical University, CHINA), Da-jun Ying

P-MON-B-088 **Induction Time Studies of Calcium Carbonate in the Presence of Silk Sericin (ID: 3174)**
Xiangdong Kong (Zhejiang Sci-Tech University, CHINA), Shao Ding

P-MON-B-089 **Effectives of Structural Properties of Electrospun TiO2 Nano-fiber Meshes on Their Osteogenic Potential (ID: 3568)**
Xiaokun Wang (Peking University, CHINA), Rolando Gittensi, Rosemary Song, Rina Tannenbaum, Rene Olivares-Navarrete, Zvi Schwartz, Haifeng Chen, Barbara D. Boyan

P-MON-B-090 **Composites Membranes Stymulate Mineralization in Bone Cell Culture (ID: 3404)**
Izabella Rajzer (University of Bielsko-Biała, POLAND), Elzbieta Menaszek

P-MON-B-091 **Preparation and Bio-mineralization Behavior of Bioactive Glass Micro-spheres (ID: 2271)**
Naru Zhao (National Engineering Research Center for Tissue Restoration and Reconstruction, CHINA), Yingjun Wang, Xiaofeng Chen, Xuan Wei

In-vitro and *In-vivo* studies of a novel biodegradable polycaprolactone-magnesium hybrid scaffold for orthopaedic implantations

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Introduction

Synthetic grafting materials made of ceramics and polymers offer an alternative solution to regenerate diseased or damaged bone tissue[1]. However, due to their poor mechanical properties, composite materials were developed instead. Polycaprolactone (PCL) is one of the suitable candidates to be used to form composite material since it has slow degradation rate and relatively low melting point when compared with other polymers. Therefore, it allows sufficient time for bone healing and easy shaping for the scaffolds. However, the low mechanical strength and intrinsic hydrophobic properties of polymers may inhibit its use[2]. Hence, our group has recently fabricated a biodegradable polymeric-metallic hybrid made of PCL and magnesium (Mg) to solve the problems[3]. Mg is chosen since it possesses higher mechanical properties than polymers. However, in order to reduce rapid corrosion and further enhance the mechanical properties of Mg, silane coupling agent (TMSPM) surface treatment was applied on the Mg granules prior hybrid fabrication. This study aims to investigate the mechanical, *in-vitro* and *in-vivo* properties of the newly developed hybrid.

Materials & Methods

The PCL-Mg hybrids were prepared by incorporating 9% Mg granules with 2 different particle sizes (i.e. 45µm and 150µm), respectively by thermal method.

Compression test was conducted to study the mechanical properties of the hybrids with the use of Material Testing System (MTS). MTT and ALP assays using MC3T3-E1 pre-osteoblasts were conducted to test the cytotoxicity and osteoblastic differentiation properties of the PCL-Mg hybrids.

For the *in-vivo* studies, two of each of the pure PCL and PCL-Mg hybrids were implanted into six 2-month old Sprague-Dawley rats, respectively. The animals were monitored and examined by micro-computed tomography at week 1 to week 4 and week 8 of post-operation.

Results & Discussion

Figure 1 shows the compressive moduli of the PCL and PCL-Mg hybrids. The compressive moduli were significantly increased from 249MPa of pure PCL to approximately 344MPa and 331MPa of the hybrids with only 0.1g of 150µm and 45µm Mg granules, respectively. The results suggested that the mechanical properties of pure PCL can be enhanced by incorporating the Mg granules, and were also similar to the mechanical properties of cancellous bone (0.3-2.1GPa)[4]. However, no significant difference was between the composites made from the different sized Mg granules. From the MTT assay, similar cell viabilities were found when cells were cultured on pure PCL and PCL-Mg composites (Figure 2). This showed that the amount of Mg ion released from the hybrids were at a safe level with no toxic effects to the MC3T3-E1 pre-osteoblasts. In addition, significantly higher specific ALP activities were found on the PCL-Mg hybrids as compared to pure PCL on both Day 7 and Day 14 (Figure 3), which suggested that the PCL-Mg composites favour osteoblastic differentiation. This was possibly due to the effect of Mg ion release. In our previous studies, we reported that a low level of Mg ions (i.e. 50ppm) is able to stimulate the growth and differentiation of osteoblasts. This also explained why more new bone was found on the PCL-Mg hybrids than pure PCL after 2 months (Figure 4).

Conclusion

We report here that with the incorporation of Mg into polymer, a novel polymeric-metallic hybrid which is biodegradable, injectable, bioactive and with suitable mechanical properties comparable to human bone can be fabricated. However, further studies include the mechanical test during degradation is still needed.

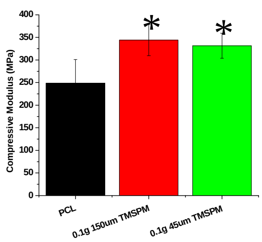

Figure 1. Compressive moduli of pure PCL and PCL-Mg hybrids. The addition of Mg is able to enhance the compressive moduli of pure PCL. (*$p<0.05$)

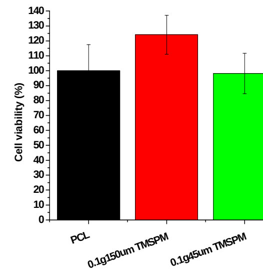

Figure 2. Cell viabilities of pure PCL and PCL-Mg hybrids. No toxic effect was found as the hybrids have similar cell viabilities as pure PCL.

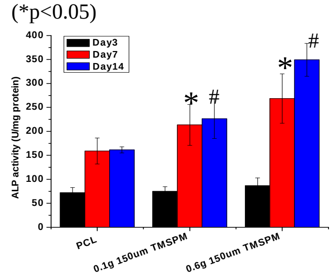

Figure 3. Specific ALP activities of pure PCL and PCL-Mg hybrids. Significantly higher activities were found on the hybrids on days 7 and 14 than pure PCL. (*#$p<0.05$)

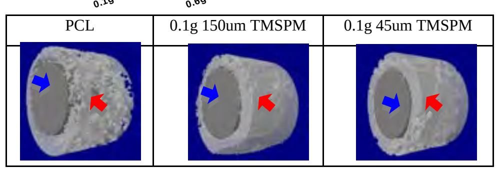

Figure 4. 3D models of the newly formed bone (red arrows) around the implants (blue arrows). More new bone was found around the PCL-Mg hybrids as compared to pure PCL.

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