Introduction: In the previous study, we aim to study whether titanium affinity biomimetic peptide DOPA-BMP-2 could promote the osteogenesis of bone marrow mesenchymal stem cells (BMSCs) in vitro and accelerates the osseointegration of titanium screws in vivo in osteoporotic rats.

Methods: Titanium sheets and titanium screws were dual-functionalized by soaking to graft DOPA-BMP-2 and DOPA-RGD bioactive polypeptide. The physicochemical properties was explored and the optimal concentration of DOPA-BMP-2 polypeptide and DOPA-RGD polypeptide (promoting cell adhesion) were studied to promote the osteogenesis of BMSCs in vitro. Then, titanium screw coated with dual peptides were implanted into the osteoporotic rats to comprehensively evaluate the osseointegration.

Results: The results of X-ray photoelectron spectroscopy, water contact angle and atomic force microscopy displayed that the DOPA-BMP-2 and DOPA-RGD polypeptides were successfully grafted onto the titanium surface. QRT-PCR, ALP staining and alizarin red staining results further confirmed that the ratio of BMP-2 and RGD at 3:1 (BMP-2:RGD = 3:1) had the strongest bone-promoting of BMSCs in vitro. In bone-implant contact (BIC) area of the osteoporotic rats, quantitative parameters of Micro CT showed that the bone volume/tissue volume, trabecular bone number, trabecular bone thickness of dual-functionalized group were higher than other groups, trabecular bone separation and trabecular pattern factor were decreased. The toluidine blue staining and the anchorage force test showed that the dual-functionalized titanium affinity biomimetic peptide promoted osseointegration in vivo.

Conclusions: Biomimetic active peptides and dual-functionalized strategies have successfully promoted osseointegration of titanium implants in osteoporotic rats.

Abstract 1745

PEPTIDE TARGETED CORE CROSS-LINKED MICELLES FOR DOX DELIVERY TO HER2 EXPRESSING CANCER CELLS

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In this study, we prepared a novel targeted and extra stable micellar nanocarrier that can facilitate intracellular drug release. First, ((N-3-sulfopropyl-N, N-dimethylammonium)ethyl methacrylate was synthesized by RAFT polymerization, and it was followed by copolymerization of macroCTA with AEM in the presence of an acid-degradable cross-linker. Then, a peptide estimated by phage display for HER-2 recognition was incorporated into these core cross-linked micelles with carbodiimide reaction. Following this, DOX was loaded to the micelle nanocarriers by dialysis method in varying amounts to reach optimal loading. The resulted formulations were characterized in terms of size and zeta potential values. For polymer characterization, 1H-NMR, 13C-NMR, FTIR, and GPC were used. Size and morphological characterizations of the micelle nanocarriers were performed by Zeta Sizer and TEM, respectively. Analyses demonstrated that micelles with very low size distribution with sizes below 100 nm were obtained successfully. Then, pH-triggered DOX release was achieved due to the acid-degradable cross-links. Afterward, the efficiency of drug-loaded and targeted micelles on SKBR-3 cell lines was determined by using cell viability assay with the healthy breast cells as control (MCF-10A). Drug loaded micelles interacted with SKBR3 and MCF-10A cell lines for toxicity and drug efficiency, and the results were evaluated. According to the in vitro studies, the cytotoxicity of DOX loaded, peptide conjugated micelles were higher than free DOX at the same drug concentration, which indicates the high efficiency and selectivity of a peptide targeted smart nanocarrier system to HER2 positive breast cancer cells. Acknowledgment: This work is supported by the Scientific and Technological Research Council of Turkey(-TÜBİTAK), Project Number: 216S639

Keywords: core cross-linked micelles; breast cancer; HER2 targeting

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Abstract 1746

EGGSHELL MEMBRANE AS A BIOACTIVE AGENT IN POLYMERIC NANOTOPOGRAPHIC SCAFFOLDS FOR ENHANCED BONE REGENERATION

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A bone regeneration scaffold is typically designed as a platform to effectively heal a bone defect while preventing soft tissue infiltration. Despite the wide variety of scaffold materials currently available, such as collagen, critical problems in achieving bone regeneration remain, including a rapid absorption period and low tensile strength as well as high costs. Inspired by extracellular matrix protein and topographical cues, we developed a polycaprolactone-based scaffold for bone regeneration using a soluble eggshell membrane protein (SEP) coating and a nanotopography structure for enhancing the physical properties and bioactivity. The scaffold exhibited adequate flexibility and mechanical strength as a biomedical platform for bone regeneration. The highly aligned nanostructures and SEP coating were found to regulate and enhance cell morphology, adhesion, proliferation, and differentiation in vitro. In a calvaria bone defect mouse model, the scaffolds coated with SEP applied to the defect site promoted bone regeneration along the direction of the nanotopography in vivo. These findings demonstrate that bone-inspired nanostructures and SEP coatings have high potential to be applicable in the design and manipulation of scaffolds for bone regeneration.

Abstract 1747

NANOSCALE TOPOGRAPHIES TO ENHANCE MESENCHYMAL STEM CELL ADHESION AND REDUCE BIOFILM FORMATION

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Post-operative infection is a major complication in patients recovering from orthopaedic surgery. As such, there is a clinical need to develop biomaterials for use in regenerative surgery that can promote mesenchymal stem cell (MSC) osteospecific differentiation and that can prevent infection caused by biofilm-forming pathogens. Nanotopographical approaches to pathogen control are being identified, including in orthopaedic materials such as titanium and its alloys. These topographies use high aspect ratio nanospikes or nanowires to prevent bacterial adhesion but these features puncture adhering cells, thus also reducing MSC adhesion. Here, we we will describe a number of approaches that can enhance MSC interaction without losing reduction in bacterial adhesion. An example is using poly(ethyl acrylate) (PEA) polymer coatings on titanium nanowires to spontaneously organise fibronectin (FN) and to deliver bone morphogenetic protein 2 (BMP2) to enhance MSC adhesion and osteospecific signalling. This nanotopography when combined with the PEA coating enhanced osteogenesis and reduced adhesion of Pseudomonas aeruginosa in culture. Using a novel MSC–Pseudomonas aeruginosa co-culture, it can also be shown that the coated nanotopographies protect MSCs from cytotoxic quorum sensing and signalling molecules. Such approaches may be useful in development of improved orthopaedic fixation.