Novel nanostructured materials accelerating osteogenesis

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Osteoporosis is a disease in which the mineral density of the bone is reduced, its microarchitecture disrupted, and the expression profile of non-collagenous proteins altered. Regular fracture treatment is a complicated, multistage process, affected by cell evidence and regulated by local and systematic factors.

In osteoporotic patients, the incidence of fracture non-unions and mal-unions with poor functional outcomes is up to 20% [1], caused by poor fixation of the implant in the mechanically weak bone and progressive implant loosening at a rate faster than bone callus formation. Although the vast majority of hip fractures occur in osteoporotic patients, these fractures are fixed with implants designed for the fixation of normal healthy bone, thus ignoring the special needs of porous bone. No fracture fixation implants currently available were specifically developed for the fixation of fragility fractures. Many of these fractures, including femoral neck, proximal humerus, and knee fractures are now treated with prostheses generally fixed with bone cement. However, as acrylic fixation requires good quality cancellous bone, typically absent in the osteoporotic population, the incidence of prosthesis loosening and revision surgery is high.

The objective of the study was to develop new bioactive nanostructured materials in both acellular and autologous cell-seeded forms to enhance bone fracture fixation and healing thought creating highly porous structures, which will promote angio- and osteogenesis.

The approach to developing highly effective scaffolds for counteracting the effects of osteoporosis followed the initial lines of inquiry and involved the comparative investigation of the performance of different systems: (a) metal surfaces coated with hydroxyapatite (by micro-arc oxidation method) and/or nanodiamonds (NDs) (b) synthetic and biological polymer chemistry, by using of thermal gelling polymer and thermoplastic aliphatic polyesters, polyacrylamide, and polyethylene glycols, and copolymers; (c) genomic and proteomics analysis; (d) experiments with cell models (endothelial progenitor cells (EPS) and adult human adipose-derived cells MSCs (hADMSCs)).

The results showed that ultradispersed NDs applied on different implant materials or as UCND-coated implants can enhance the mineralization and differentiation of EPS and hADMSCs. NDs incorporated in “intelligent” gel matrixes have functioned as scaffolds attracting calcium ions and inducing hydroxyapatite crystals growth.

Further investigations demonstrated that in vitro EPS transformation to osteoblasts and long-term functions (as measured by intracellular and extracellular matrix protein synthesis and calcium-containing mineral deposition) were enhanced in an osteoprogenitor medium. In vitro and in vivo experiments of the three different micro-arc oxidation coatings prove high biocompatibility towards adult stem cells and in vivo biocompatibility.

These results provide initial evidence that synthetic nanomaterials may exhibit specific properties that are comparable to natural ones, and the nanomaterial architecture may serve as a superior scaffolding for promoting the EPS and adult stem cells differentiation and biomineralization.

We are grateful to the National Science Fund of Bulgaria (Grant Agreement KP-06-Russia/20) for their financial support

References

[1] . Nicholson, N. Makaram, A. Simpson, JF Keating, Injury 52S2 (2021) S3–S11.