HUMANIZED TRANSGENIC PIG - AS A PRECLINICAL MODEL FOR *IN VIVO* STUDIES OF CARTILAGE INJURIES AND TREATMENTS WITH NEW GENERATION OF BIOMATERIALS AND STEM CELL POPULATIONS - PRELIMINARY RESULTS

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Introduction

Civilization diseases such as obesity and type 2 diabetes and accompanying them complications, including musculoskeletal disorders, such as osteoarthritis (*osteoarthrosis*), are a challenge for modern pharmacology and regenerative medicine [1]. Modern innovative therapeutic treatments includes the use of stem cells and biomaterials. The biomaterials are based on innovative polymers and graphene modifications as scaffolds for human mesenchymal stem cells (MSCs) for the regeneration of cartilage or bone injuries. To introduce mentioned treatments in regenerative medicine practice, an adequate research models are required, e.g. transgenic pigs with modification of the immune system that allows for xenogeneic transplants, e.g. human tissues.

Materials and Methods

The planned studies assume the use of approximately 70 transgenic pigs. On the selected transgenic pigs preclinical studies of a new treatment of cartilage injuries will be performed. Transgenic pigs were obtained using the Zinc Finger Nuclease technology (ZFN) in combination of microinjection procedure. In the established research model, cartilage of the knee joint of transgenic pigs was surgically injured. Subsequently, human mesenchymal stem cells (MSCs) were injected into the knee joint. Clinical observation was performed after the treatments.

Results and Discussion

To date, 21 transgenic animals have been obtained. After MSCs injection into the knees of transgenic pigs with surgically performed knee cartilage injuries, no clinical adverse effect were observed following the transplantation, while the regenerative effects are being investigated. Transgenesis is one of the biotechnology directions that allows obtaining animals with modified genotypes. Genetically modified animals, especially pigs are very useful preclinical trials research models for regenerative medicine. In the presented project, transgenic pigs with α 1,3-galactosyltransferase knockout are used as a research model. Acute phase rejection of the xenograft take place by humoral reaction of natural antibodies directed specifically against galactose-α1-3galactose epitopes α Gal. Epitopes α Gal occur on the surface of the vascular endothelium in most species (eg. pigs) except humans, apes and old world monkeys. In turn, humans, apes and old world monkeys have natural antibodies against epitopes α Gal. The knockout of porcine GGTA1 gene coding alfa 1,3-galactosyltransferase will reduce the immunologic reaction of graft rejection of human origin. Transgenic pig model with knockout of GGTA1 gene makes possibilities to perform preclinical trials treatments of cartilage injuries using human mesenchymal stem cells (MSCs).

Conclusions

The use in presented research of transgenic pig model is an innovative approach and so far have not been used in this type of research. The obtained preliminary results indicate that the used model is optimal for assessing procedures in treatments of knee cartilage injuries with use of human mesenchymal stem cells (MSCs)

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