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SMALL NON-CODING RNAS AS TOOLS FOR REGENERATIVE MEDICINE

MiRNAs and pi-RNAs are small non-coding RNAs (sncRNAs), is a class of small regulatory molecules with length <200 nucleotides. SncRNAs is a respectable family of non-protein coding regulatory RNAs, which modifies genetic program of cells. One part of sncRNAs acts in nucleus; another part regulates extranuclear processes. Using the combination of sncRNAs with different mechanisms of action may results in full reprogramming of any type of cells. The main regulatory mechanisms are: RNA interference with silencing of specific target genes; Mobile genomic transposable elements repression; Supporting of genome stability after cancer cell transformation (suppression of NAHR – non-allelic homologous recombination, regulation of DNA methylation and histone modification); Reversible post-transcriptional gene inhibition of specific genes by sncRNAs. Some sncRNAs are expressed ubiquitously, but many are tissue and differentiation stage-specific. SncRNAs have been aptly referred to as" rheostats" because their regulatory role is generally to fine-tune, but not abolish, protein expression. Most piRNAs are complementary to transcripts of and able to inhibit expression of retrotransposon mRNAs and represses the mobile genomic transposon elements (TE) to protect the integrity of the genome. Piwi protein is a typical suppressor of position effect variegation, similar to other key epigenetic factors such as HP1 and interacts with other key epigenetic factors. Piwi deficiency results in global loss of methylation of histone 3 at lysine 9 and the delocalization of HP1 from polytene chromosomes and loss of euchromatic features at a sub-telomeric region of chromosome 3R. Piwi and its homologs are key components of an epigenetic regulatory complex required for euchromatin/heterochromatin assembly. Moreover, miRNAs can modify cellular proliferation, differentiation and death. Results: In the recent studies, were investigated influences of separated micro-RNAs (miRNAs) and their antago-miRNAs, piRNAs and antago-piRNAS (more than 40 sequences) on the morphology and genetics of leukemic cells, colorectal adenocarcinoma cells, lung cancer cells, neuroblastoma, glioblastoma, skin adenocarcinoma cells. We firstly observed transformation of cancer cells into different types of mature cells. These transformations were obtained after modification of cancer cells into intermediate stem-like stage. Modified cells were identified morphologically, phenotypically, and genotypically. For transfection of cells, were used nanosized polymer complexes with any sncRNAs. Selected polymer-sncRNAs complexes has some advantages, such as: long period of biodegradation (more than 40 days), early beginning of transfection changes of cells (7–10 days), minimal toxic effects in optimal concentrations range (experiments with mice), high transfection efficiency (90-97%) with minimal concentration of sncRNAs, possibility to sterilization.

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MOLECULAR ASPECTS OF BONE REMODELING

Introduction. About 33.8% of women and 26.9% of men over 50 years suffer from osteoporosis in the Russian Federation (according to the Institute of Rheumatology of the Russian Academy of Sciences). Idiopathic postmenopausal or senile osteoporosis is most common (85% of cases), resulting in bone remodeling disorders. Therapy of osteoporosis requires a deep understanding of the basics of physiological regeneration of bone tissue. Purpose. Identification of the key links in the regulation of bone tissue remodeling. Materials and Methods. Analysis and systematization of literary sources. Results. It was revealed that sclerostin indirectly blocks the effects of bone morphogenetic proteins (BMPs) via the Wnt – signaling cellular pathway. In people with impaired formation of sclerostin, sclerosteosis develops (a pathological proliferation of the bony tissue of the facial skeleton). It is also known that the RANKL (receptor activator of nuclear factor kappa – B ligand) – OPG (osteoprotegerin) – the cytokine system plays a key role in conjugation of the remodeling phases. Numerous cytokines and hormones stimulate or inhibit the effects of RANKL and OPG. Some interleukins, prostaglandins E and E2, TNF (tumor necrosis factor), M – CSF, GM – CSF (macrophage and granulocyte – macrophage colony – stimulating factors) are local factors of bone resorption; interferon gamma, transforming growth factor beta (TGF – beta) are local factors of bone osteogenesis. Several factors have been studied separately or together in a number of investigations in vivo and in vitro, but with conflicting results. Regulation of calcification of bones is actively studied. According to recent data, inorganic pyrophosphate can act as a calcification inhibitor. The inhibitory effect of pyrophosphate is eliminated by pyrophosphatase during mineralization, which is found in bone tissue. Conclusion. The recent scientific data on the regulation of bone tissue regeneration, that showed good results in clinical trials, made it possible to develop new directions in the therapy of osteoporosis: the use of antibodies to RANKL (Denosumab) and antibodies to sclerostin (Romosozumab).

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THE BIOMATERIAL SYSTEMS ON THE BASIS OF MESOPOROUS TITANIUM DIOXIDE COATINGS FOR A HUMAN MESENCHYMAL STEM CELLS STUDY

Porous titanium dioxide (TiO_2) coatings provide an ingrowth of bone-tissue extracellular matrix into a metal surface to improve an osteointegration between a bone and a metal [1–3]. Porous coatings can serve