water and a greater amount of fat mass, compared to men, also presenting decreased parameters compared to those of reference.

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P214 (ND)

Search for epigenetic markers of osteoporosis formation

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Background/Introduction: There are data on the possible role of polymorphic variants of microRNA target sites in genes of bone metabolism in the development of osteoporosis (OP). However, research findings are inconsistent across populations.

Purpose: The objective of our study was to search for associations of rs11540149, rs6854081, rs10098470, rs10793442, rs1054204, rs1061947, rs1042673, rs9659030, rs1031820, rs5854, rs198470, rs1712, rs2745426 in microRNA target sites and rs2910164, rs11614913 in microRNA genes in postmenopausal women and men over 45 years of age with a low level of BMD and the risk of osteoporotic fractures.

Methods: DNA samples of 663 postmenopausal women and 508 men over 45 years old from the Volga-Ural region of Russia were studied. Genotyping was carried out by competitive allele-specific PCR KASP™. The search for associations of polymorphic variants with OP endophenotypes was carried out using the Pearson $\chi 2$ criterion.

Results: There was a significant association of Allele A of polymorphic variant rs11540149 with fractures in general ($p=0.043$) and spinal fractures ($p=0.016$), allele G rs6854081 with hip fractures ($p=0.00632$) and fractures in general ($p = 0.042$), C allele rs2910164 with low BMD in the lumbar spine ($p=0.000102$), T allele rs10098470 with fractures in general ($p=0.039$), allele A rs10793442 with low BMD in the general sample ($p=0.041$). In men: A allele rs11540149 is associated with fractures ($p=0.041$) and low BMD in the general sample ($p=0.002$), as well as with fractures of the radius ($p=0.00374$), T allele rs11614913 with fractures in general ($p=0.03275$), G allele rs6854081 with femoral neck fractures ($p=0.02469$), GG genotype at locus rs1054204 with low BMD in the general sample ($p=0.03$).

Conclusion(s): The association of polymorphic variants of miRNA target site with a low level of BMD and the risk of fractures in genes that are involved in the regulation of bone metabolism was revealed.

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P215 (ND)

Sympathectomy as well as β2-adrenoceptor deficiency lead to exacerbation of subchondral bone changes in experimental osteoarthritis

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Background/Introduction: Recent *in vitro* studies demonstrated that the sympathetic nervous system (SNS) and its major neurotransmitter norepinephrine might contribute to OA progression mediated by α1/2 or β2-adrenoceptors (ARs). Several AR subtypes are expressed in all joint tissues.

Purpose: To unravel their role during OA pathogenesis *in vivo we* examined the progression of surgically-induced OA in sympathectomized (Syx) and β2-AR-deficient ($Adrb2^{-/-}$) mice.

Methods: OA was induced by destabilization of the medial meniscus (DMM) in wildtype (WT), Syx and $Adrb2^{-/-}$ mice. 8 weeks after DMM or sham surgery, subchondral bone was analyzed by μCT and the severity of OA by histological scoring.

Results: Bone volume fraction (BV/TV, Fig.1) (WT 0.787 ± 0.021, Syx 0.885 ± 0.025, $Adrb2^{-/-}$ 0.942 ± 0.025), trabecular thickness (WT 0.249 ± 0.033 μm, Syx 0.323 ± 0.043 μm, $Adrb2^{-/-}$ 0.506 ± 0.085 μm) and subchondral bone plate thickness (WT 107.7 ± 3.1 μm, Syx 128.5 ± 3.5 μm, $Adrb2^{-/-}$ 160.0 ± 14.3 μm) were significantly increased in Syx and $Ardb2^{-/-}$ compared to WT mice after DMM, while there were no significant differences between WT, Syx and $Adrb2^{-/-}$ animals after sham surgery. The progression in cartilage degeneration and synovial inflammation was comparable in WT, Syx and $Ardb2^{-/-}$ DMM mice without significant differences.

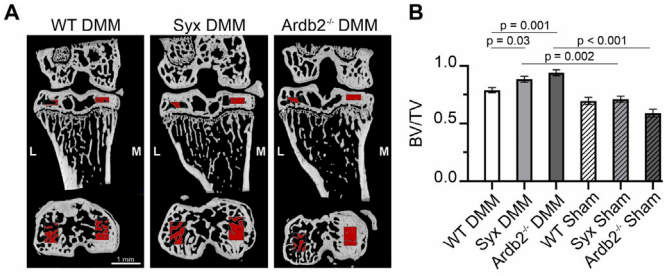

Fig.1: μCT analysis of subchondral bone microarchitecture (A) representing the volume of interest (M = medial, L = lateral) and (B) the analysis for BV/TV.

Conclusion(s): The increased bone mass in Syx and Adrb2-/- DMM mice suggests that there are synergistic effects of the SNS and OA in subchondral bone, mainly through β2-AR deficiency. Taken together, the β2-AR plays a major role in OA-related subchondral bone changes and is therefore an attractive target for novel therapeutic avenues.

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Cripto favours chondrocyte hypertrophy via TGF-beta SMAD1/5 signaling in experimental osteoarthritis

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Background/Introduction: Osteoarthritis (OA) is a painful and disabling condition of the joints affecting millions of people, for which effective biomarkers and therapies are desperately required. OA