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## EXPERIMENTAL MODELS *IN VIVO* ARE THE BASIS OF TRANSLATIONAL MEDICINE

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In the first set of experiments we evaluated recombinant human fibroblast growth factor 18 (rhFGF18) treatment of cerebral ischemia in the Wistar rat middle cerebral artery occlusion model of stroke. We found that this biotherapy led to a decrease in the fraction of neurons with abnormal morphology (chromatolysis, pyknotic nuclei, somal degeneration). Acetylcholinesterase-positive fiber density and activity increased over time in the rhFGF18 group. rhFGF18 treatment appears promising in promoting recovery following cerebral ischemia injury.

In the second set of experiments we evaluated the combined genetically engineered plasmid construct pcDNA\_VEGF165/Ang-1 in conditions of simulated chronic limb ischemia in the Wistar rat. A single local administration of pcDNA\_VEGF165/Ang-1 into the ischemic skeletal muscle of animals starting from the 14th day after therapy stimulates the formation of microcirculatory bed vessels with a statistically significant increase in the number of capillaries. The use of the gene thera-

peutic substance pcDNA\_VEGF165/Ang-1 allows for complete restoration of impaired blood supply in the muscles of the thigh and lower leg of the rats by the 28th day of observation, creates conditions for maintaining a long-term positive effect until the end of the experiment (42nd day) while maintaining the number of blood vessels in one muscle fiber not lower than the healthy tissue indicator. The use of the developed combined plasmid construct is accompanied by a pronounced antinociceptive effect as evidenced by increased in the values of the threshold of the nociceptive reaction, the area and intensity of the imprint of the operated limb of the animal. The positive dynamics of regression of symptoms of chronic ischemia of the operated limb after using the genetically engineered construct in the experiment indicates a high potential as a prototype of the first domestic combined gene therapy agent.

**Key words:** ischemia, experiment, rats, biotherapy