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# Is Multiplex Genome Modification of Astrocytes a Novel Candidate Therapy of Chronic Ischemic Stroke in the Rat?

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**Background and Aim:** Stroke is an enervating injury to the brain happening. The most common type is hemorrhagic There are no definitive FDA-approved treatments for chronic ischemic stroke without any side effects. Therefore the search for new therapies is vital. The main goal of this hypothesis is to improve the complications of chronic ischemic stroke in induced SDrat model by intraluminal suture MCAo utilizing combining cell and gene therapy. Based on the Stroke Treatment Academic Industry Roundtable, stroke is one of the most complex illnesses. Therefore, we offer to make a new version of astrocytes by making some changes in their multiple functions.

**Results:** A gene profile including IL-38 which is the most modern anti-inflammatory agent , BRAG-1 as an anti-apoptotic gene, complementary scaffold RNAs for theirs expression by deadCas9(dCas9), complementary scaffold RNAs of LZK and MST-1 for theirs deletion and, dCas9 gene. LZK is responsible for astrogeliosis. So it may be beneficial to omit LZK. The inhibition of MST-1 can help in preventing hypoxic death of cells with BRAG-1 and natural angiogenesis of astrocytes by secreting VEGF. The last gene, dCas9 gives us the opportunity of simultaneous activation and suppression of different genes by extended single guide RNAs or scaffold RNAs with the least off-targets. Moreover, astrocytes have a crucial role in the regulation of plasminogen activation in CNS by providing a surface for tissue plasminogen activator and fibrinolysis which prepare the ischemic area with the inhibition of LZK for the natural migration of NSC which can enhance motor function improvement.

**Conclusion:** In conclusion due to the using of dCas9 it is not expected to have some off-targets but if there are some side effects it is possible to switch it off by anti-CRISPR proteins.