SECRETOMES OF APOPTOTIC MONONUCLEAR CELLS AMELIORATE NEUROLOGICAL DAMAGE IN RATS WITH FOCAL ISCHEMIA

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The incidence of stroke is projected to rise within the next decades. The pursuit of targeting multiple pathways in the ischemic cascade is suggested to emerge as a possible treatment option. Here we examined the regenerative potential of conditioned medium derived from rat and human apoptotic mononuclear cells ("apoptotic MNC-secretomes") in a rat model of ischemic stroke.

We performed middle cerebral artery occlusion on Wistar rats and administered apoptotic MNC-secretomes intraperitoneally in two experimental settings (rat MNC-secretomes – 40 min after ischemia; human virusinactivated MNC-secretomes – 40 min, and 24 h after cerebral ischemia). The effects on ischemic lesion volumes were determined after 48 h. Neurological evaluations were performed after 6, 24 and 48 h. In vitro immunoblot analyses were conducted to characterize the influence of human MNC-secretomes on neuroprotective proteins in Astrocytes and Schwann cells.

Apoptotic MNC-secretomes significantly reduced ischemic lesion volumes by 32% ($p=0,0002$) in the first and 26% ($p=0,0175$) in the second setting compared to controls. Neurological examinations revealed a statistically significant improvement after stroke in the treatment groups, whereas the control group showed no change over time. In addition, co-incubation of Astrocytes and Schwann cells with apoptotic MNC-secretomes resulted in an upregulation of several protective proteins, such as CREB, HSP27, Akt, and Erk1/2.

These data indicate that MNC-secretomes elicit neuroprotective effects on rats that have undergone stroke.