STROKE

Looking for common ground in treating stroke

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Strokes can happen fast, but distinguishing between the subtypes often just takes too long. Ischemic strokes – which occur when blood flow to the brain is blocked by a clot – *can* be treated with thrombolysis *if* the clot-dissolving treatment can be applied – ideally – within about four and a half hours following the onset of symptoms. Thrombolytic therapy won't however help those experiencing a hemorrhagic stroke, in which a blood vessel has burst and is bleeding in the brain. These are rarer but more deadly than ischemic strokes and require a different course of treatment to drain the pooling blood and alleviate pressure on the brain. Completing the scans to determine the difference often pushes patients past that recommended window to begin thrombolysis for those experiencing ischemic stroke.

As strokes are the second leading cause of death worldwide, finding common treatment ground between the two types of stroke is of immense clinical importance; however, there has yet to be clinical success. Writing in *Science Translational Medicine*, researchers in China present a potentially promising peptide that they tested in two preclinical species: mice and rhesus macaques.

The synthetic peptide, called Tat-cold-inducible RNA binding protein (Tat-CIRP), disrupts the function of Toll-like receptor 4 (TLR4), a molecule involved in inflammation, apoptosis, and necroptosis, by way of perturbing its accessory protein, myeloid differentiation factor 2 (MD2). The authors show MD2 to be elevated in mouse and primate brain tissue following stroke, suggesting that impeding its function could minimize cell death.

Tat-CIRP appears to be a capable neuroprotectant across species and stroke types. The authors show that Tat-CIRP was able to successfully and safely cross the blood brain barrier in mice, and that it was protective in mouse models of both ischemic and hemorrhagic stroke, with Tat-CIRP treated animals experiencing better neurological outcomes than saline controls for up to 28 days.

Moving from mice to monkeys, the team then administered Tat-CIRP to rhesus macaque models of ischemic stroke. As was observed in the mice, the treatment reduced the brain infarct in the macaques; treatment also appeared to improve neurological outcomes over the coming month in the animals. "To some extent, these results bridge the biological gap between rodents and higher-order brains, thereby facilitating Tat-CIRP translational research from bench to bedside," the authors write.

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