Bench to Bedside

Neuroprotection after stroke

Stroke is major cause of morbidity and death in the elderly population. Although a small proportion of patients who experience stroke arrive at hospital early enough for reperfusion therapy, for most patients the treatment options are limited. Neuronal death as a result of inflammation and apoptosis continues after the initial ischemic insult. New research reveals a potential target that might help to limit neuronal death.

A molecule called NF-κB is known to have antiapoptotic effects in nonneuronal cells. Oliver Herrmann and colleagues targeted an enzyme called IKK2 that regulates the activation of the NF-κB protein. The scientists created 2 strains of mice: one that lacked IKK2 in neurons and another in which IKK2 was always turned on in the same cells. They found that, after induced cerebral ischemia, mice lacking IKK2 had reduced infarct size compared with mice in which IKK2 was activated (*Nature Med* 2005; doi:10.1038/nm1323).

The results suggest that pharmacologic inhibition of IKK2 might be successful in the treatment of stroke. Several IKK2 inhibitors already exist. Herrmann and colleagues found that administration of a known IKK2 inhibitor after cerebral ischemia in mice reduced the volume of cell death by 60%. This effect worked for up to 4.5 hours after the stroke, which may bode well for human patients who require time to reach a hospital.

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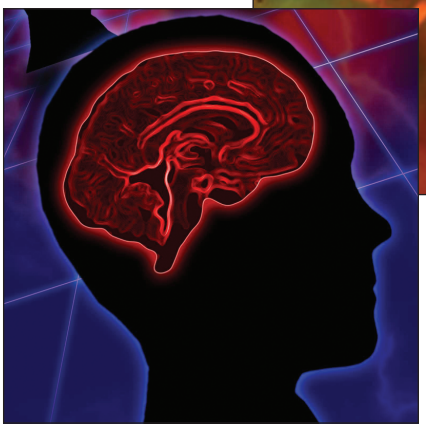

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HIV stalled by St. John's Wort

St. John's Wort, a widely used herbal remedy for depression, has been recently shown to contain a component that inhibits HIV replication. Although the findings are preliminary and the protein, named p27^{SJ}, is far from being recommended as a treatment for HIV infection, the findings suggest the possibility of alternative therapeutic strategies for HIV infection.

Nune Darbinian-Sarkissian and colleagues recently discovered p27^{SJ} while looking at the effects of plant extracts from St. John's Wort on the behaviour of brain cells in culture. Such extracts have received attention over the years as potential antiseptics, spasmolytics, diuretics and antidepressants.

To determine its antiviral properties, the authors extracted p27^{SJ} from cultured cells of the St. John's Wort plant and found that, in human cells infected with HIV-1, the extract suppressed the transcription of the viral genome. The scientists determined that p27^{SJ} is able to do this by interacting with 2 key proteins involved in HIV replication. When injected into microglial cells along with HIV-1, p27^{SJ} reduced viral replication by almost 50% (*Gene Ther* 2005; doi:10.1038/sj.gt.3302649).

St. John's Wort is widely available as an herbal supplement. Whether commercially available preparations contain p27^{SJ} is unclear, and their use as alternative therapy for HIV infection is not recommended. Rather, the findings should be interpreted as hypothesis generating. — Compiled by David Secko, Vancouver

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