Prion therapy

Prion proteins can protect the brain from injury after stroke, according to a study in rats in the 28 September issue of *The Journal of Neuroscience* (**25**, 8967–8977).

The prion protein PrP^C is perhaps best known for converting to a toxic form during prion disease. But it may also have important functions in nondiseased cells. For example, previous cell-culture studies suggested that PrP^C has a role in neuronal survival. So Woei-Cherng Shyu *et al.* asked whether PrP^C is neuroprotective in rats after ischemic stroke.

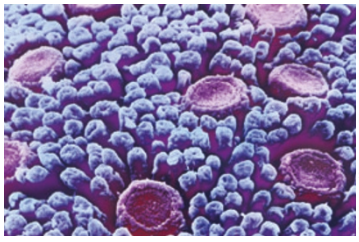
The investigators found that overexpressing PrP^C in the brain after blocking cerebral blood flow decreased brain damage and improved locomotor activity. The protective function of PrP^C was mediated by ERK1/2, a protein kinase, as ERK1/2 inhibitors blocked the ability of PrP^C to protect against the effects of stroke.

Next, the investigators found that endogenous PrP^C expression was increased after hypoxia. This increase was mediated by ERK1/2, operating through a transcription factor that has binding sites on the promoter of the gene that encodes PrP^C. Deletion of these binding sites blocked the increase in PrP^C expression induced under hypoxic conditions.

Precisely how increases in PrP^C expression protect the brain against stroke remains unclear.—*EC*

A new taste sensation

We taste food with five types of chemoreceptors that perceive salty, sour, bitter, sweet, and umami (glutamate). Now Fabienne Laugerette *et al.* make the case for another flavor—fat. In the November issue of *The Journal of Clinical Investigation* the researchers (115, 3177–3184) identify a fat sensor in the mouth.



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Sixth sense: animals taste fat through receptors on taste buds located in the large papillae of the tongue.

Previous studies showed that rodents have a preference for the taste of fat, specifically of long-chain fatty acids such those found in vegetable oil. But how the animals detected fat was unclear. A clue was the presence of the protein CD36 in the region of the taste buds on the tongue. CD36 can transport fatty acids in addition to acting as a scavenger receptor that can bind to a wide variety of proteins and lipoproteins.

The investigators refined the locale of CD36 to the apical side of taste bud cells, where it would be well positioned to sense dietary fat. They then showed that mice lacking this protein no longer showed a preference for dietary fat. Moreover, the investigators found that fat deposited in the mouth of mice and rats caused changes in biliary and pancreatic secretions that would aid digestion; these changes also required CD36.

Exactly how an interaction between long-chain fatty acids and CD36 contributes to the perception of fat by taste bud cells is not yet clear. But understanding why fat tastes so good could conceivably offer another route toward fighting obesity.—*MB*

Written by Michael Basson, Jasmine Bhatia, Eva Chmielnicki, Randy Levinson and Juan Carlos López

Gene for Tourette syndrome

A gene defect has been tied to Tourette syndrome, a neurological disorder characterized by involuntary motor tics.

The underlying brain defect in Tourette syndrome is poorly understood; most studies have pointed to dysfunctions of dopamine-mediated neurotransmission as the likely culprit. But association studies had suggested that the syndrome has a genetic component.

A gene called *SLITRK1* caught the attention of Jesse Abelson *et al.*—in part because of its location in a genetic inversion in an individual with Tourette syndrome. In the 14 October *Science*, the researchers report that *SLITRK1* mutations occurred in 3 of 174 people with the disease.

The researchers found that a binding site for a microRNA in *SLITRK1* was affected in two of the individuals, and showed that wild-type, but not mutant, *SLITRK1* enhanced neurite outgrowth in culture. The relationship of these observations to Tourette syndrome remains to be determined.—*JCL*

Smallpox preparedness

An experimental oral compound shows promise as an agent against smallpox, report Guang Yang *et al.* in the October issue of the *Journal of Virology* (**79**, 13139–13149).

The researchers found that the compound, ST-246, targeted a pox enzyme required for the formation of extracellular virus particles. ST-246 reduced the severity of disease in mice preinfected with vaccinia virus, used to make the smallpox vaccine. The drug could also prevent the onset of infection if given to mice before inoculation with vaccinia virus—and the compound seemed to be well tolerated by the animals.

The researchers suggest that ST-246 itself did not directly protect mice from infection; instead the drug may have fought off the virus long enough for the mice to mount a protective immune response.

Currently, only one drug, cidofovir, is approved by the US Centers for Disease Control and Prevention as an emergency treatment for a smallpox outbreak, but viral resistance can occur. ST-246 was active against a cidofovir-resistant strain of cowpox virus, although whether it would work in humans is not clear.—*JB*

Digestion complete

A signal that keeps bile acids flowing at the right levels from liver has been discovered.

Bile acids released from the liver aid in digestion, but they are also harsh detergents, so levels must be tightly controlled. Once in the small intestine, bile acids are recycled back to the liver, but any lost during resorption must be replaced by *de novo* synthesis in the liver. Although it was known that bile acids can regulate their own synthesis, exactly how was unclear.

In the 11 October *Cell Metabolism* (2, 217–225) Takeshi Inagaki *et al.* explore this feedback mechanism. In line with previous research, the researchers found that bile acids cross into gut epithelial cells, where they bind the nuclear hormone receptor FXR. This binding, they found, prompts the expression of the protein FGF15.

FGF15 can leave the gut and travel to the liver, where it signals the downregulation of a key liver enzyme involved in bile acid synthesis. If not enough bile acids are absorbed in the gut, then less FGF15 is made and sent to the liver, resulting in more bile acid synthesis.

These findings close the loop on the signaling pathway between the gut and the liver. They also identify a new biological role for FGF15, previously thought to have a role in development but never known to act as a hormone.—*RL*