NEURODEGENERATIVE DISEASE

RBM3, a protein upregulated during hibernation, provides new insights into neurodegeneration

A protein that is induced in the mammalian brain during hibernation and hypothermia might ameliorate neurodegenerative disease by reducing loss of synapses, according to research published in *Nature*. Giovanna Mallucci and colleagues found that the cold-shock protein RBM3 (RNA-binding protein 3) restored synaptic plasticity and

beneficially modified the disease course in mouse models of prion disease and Alzheimer disease (AD).

In a *Nature* interview, Mallucci explains that hibernation is a state in which an animal prepares to go without energy. “One of the obvious ways to stop energy transmission is to stop synaptic transmission, so one of the notable things that happens in hibernators’ brains is that they dismantle their synapses,” she says.

By cooling mice to 16–18 °C, the core body temperature reached by small mammals during hibernation, Mallucci’s team showed that reassembly of synapses on rewarming depended on induction of RBM3 expression. In the prion disease and AD models, synapse loss coincided with a reduction in the capacity to upregulate RBM3 in response to cooling.

Elevation of hippocampal RBM3 levels in the mouse disease models, accomplished either by cooling the animals early in the disease course or by

overexpressing the protein via a lentiviral vector, prevented loss of synapses and alleviated behavioural and memory impairments. In addition, survival times were improved in the prion disease model. In both of the models, knockdown of RBM3 through RNA interference increased synapse loss, accelerated disease progression and reduced survival.

“We already use hypothermia therapeutically in brain damage,” Mallucci points out. “What RBM3 gives us is a way of intervening without cooling.” The next steps will be to examine the role—if any—of RBM3 in the human brain, and to explore whether the cold-shock pathways can be harnessed for the prevention and treatment of neurodegenerative disease.

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