Life-extending protein can also have damaging effects on brain cells

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Proteins widely believed to protect against aging can actually cause oxidative damage in mammalian brain cells, according to a new report in the July *Cell Metabolism*, a publication of Cell Press. The findings suggest that the proteins can have both proaging and protective functions, depending on the circumstances, the researchers said.

" Sirtuins are very important proteins," said Valter Longo of the University of Southern California, Los Angeles. "Overexpression can protect in some cases, and in other cases, it may do the opposite. It has to do with the fact that they do so many things."

Sirtuins, or Sir2 family proteins, are found in organisms from bacteria to humans. Sir2 controls aging and life span in yeast, the worm C. elegans, and Drosophila fruit flies, earlier studies have shown.

Studies have also implicated Sir2 in the life-extending effects of a calorie restricted diet in some, though not all, organisms. Notably, Longo's lab showed that lack of Sir2 in yeast further extended the life span of calorie-restricted cells.

SirT1, the mammalian version of yeast Sir2, controls numerous physiological processes including glucose metabolism, DNA repair, and cell death, the researchers added. In mammalian cells, SirT1 also controls several stress-response factors.

Now, the researchers show that cultured rat neurons treated with a SirT1

inhibitor more often survived treatment with oxidative stress-inducing chemicals. They further show evidence to explain the mechanism responsible for that effect.

They also found lower oxidative stress levels in the brains of mice without SirT1. However, those SirT1 knockout mice didn't live as long as normal mice do on either a normal or a calorie-restricted diet.

" [Such drugs] could have beneficial effects for certain diseases, but again, these proteins do a lot of things," he said. "I would say the idea that there is a conserved action of sirtuins to cause major life span extension—the foundations for that are weak or very weak. Until we have more data to show that chronic treatment to increase SirT1 activity does not do damage, I don't think it's a good idea."

Source: Cell Press