New finding about rapamycin may help slow aging

A study outlines a new understanding of how a compound called rapamycin works that may help address neurologic damage such as Alzheimer's disease.

"It's possible this could provide a new therapeutic approach to neurologic disease," said Viviana Perez, an assistant professor in the Department of Biochemistry and Biophysics in the Oregon State University (OSU) College of Science.

In a study published in Aging Cell, the researchers said they have identified two mechanisms of action of rapamycin. One was already known. The newly-discovered mechanism is what the researchers say might help prevent neurologic damage and some related diseases.

"The value of rapamycin is clearly linked to the issue of cellular senescence, a stage cells reach where they get old, stop proliferating and begin to secrete damaging substances that lead to inflammation," said Perez, an expert on the biological processes of aging. "Rapamycin appears to help stop that process."

The secretion of damaging compounds creates a toxic environment called senescence-associated secretory phenotype, or SASP, disrupting the cellular microenvironment and altering the ability of adjacent cells to function properly, compromising their tissue structure and function. And this broad process is believed to be linked to aging.

"The increase in cellular senescence associated with aging, and the inflammation associated with that, can help set the stage for a wide variety of degenerative disease, including cancer, heart disease, diabetes and neurologic disease, such as dementia or Alzheimer's," Perez explained. "In laboratory animals when we clear out senescent cells, they live longer and have fewer diseases. And rapamycin can have similar effects."

It had been observed, prior to this research, that there was one mechanism of action for rapamycin in this process. And it was believed that rapamycin helped to increase the action of Nrf2, a master regulator that can "turn on" up to 200 genes responsible for cell repair, detoxification of carcinogens, protein and lipid metabolism, antioxidant protection and other factors. In the process, it helped reduce levels of SASP.

The new study showed that rapamycin could also affect levels of SASP directly, separately from the Nrf2 pathway and in a way that would have impacts on neurons as well as other types of cells. "Any new approach to help protect neurons from damage could be valuable," Perez was quoted as saying in a news release.

A natural compound first discovered from the soils of Easter Island in the

South Pacific Ocean, Rapamycin has already been intensively studied because it can mimic the valuable effects of dietary restriction, which in some animals has been proven to extend their lifespan. Laboratory mice that have received rapamycin have demonstrated more fitness, less decline in activity with age, improved cognition and cardiovascular health, less cancer, and a longer life.

Through its ability to help prevent SASP-related cellular damage through two pathways, one involving Nrf2 and the other more directly, rapamycin will continue to generate significant interest in addressing issues related to aging, Perez said. However, the use of rapamycin in humans has so far been constrained by an important side effect, an increase in insulin resistance that may raise the risk of diabetes.