Buck Institute's Pioneering Drug Fights Diabetic Macular Edema

Buck Institute

Diabetic macular edema (DME) is caused by an accumulation of fluid in the eye causing progressively impaired vision. More than 2.6 million people with diabetes have DME which is one of the leading causes of impaired vision in the United States. But an innovative treatment developed at the Buck Institute for Research on Aging is improving vision in patients with DME by neutralizing the so-called “zombie cells” partially responsible for the damage.

One hallmark of many chronic diseases is the accumulation of senescent cells, which are living cells that no longer function normally and cannot multiply, but remain and send out potent inflammatory signals (hence the “zombie cells” nickname). These signals transform the larger environment around them into a maladaptive one that weakens the immune system and promotes aging of muscles and organs, generating even more senescent cells. In people with DME, senescent cells contribute greatly to this disease, causing swelling and vision loss that can be severe and can even lead to blindness.

Researchers at the Buck Institute pioneered a new type of drug technology called senolytics, drugs that kill senescent cells without harming normal cells around them. A senolytic drug candidate called UBX-1325, which is designed to fight

DME and other age-related eye diseases, is being developed by Unity Biotechnology under a patent license. The company was co-founded by Buck Institute Professor Judith Campisi.

By eliminating the zombie cells, senolytic therapies can help restore aging or damaged tissues as the pro-inflammatory signals abate. One important feature of senolytics is that they selectively target only the senescent cells, leaving healthy cells intact. This is an advantage over the current standard of care for DME, anti-VEGF (vascular endothelial growth factor) therapy, which can alter critical blood supply of both diseased and healthy tissues. In addition, anti-VEGF therapy requires maintenance doses every eight weeks, which is disruptive, painful and costly for patients.

In a recent phase two clinical trial of patients with DME, a single injection of the UBX-1325 senolytic therapy was associated with significantly improved vision that lasted for 48 weeks. By comparison, the patients with DME who received a sham injection had minimal improvement in their vision. All patients in the study had been receiving anti-VEGF therapy for at least six months before the trial; more than half of the patients who received the treatment were able to stop their anti-VEGF therapy completely during the 48-week follow-up period, compared with just 22% of those who received the sham injection.

Because of the positive 48-week findings, a new trial is now under way to directly compare UBX-1325 to aflibercept, an anti-VEGF therapy.

Campisi, chief researcher at the Buck Institute, founded the institute's Campisi Lab in 2002 specifically to research age-related diseases. Campisi started her career at the Lawrence Berkeley National Laboratory as a senior scientist in 1991. Three decades later, through partnership with scientists at the Mayo Clinic and with funding from the National Institutes of Health, the senolytic drug was born.

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