



SENOLYTICS: TARGETING “ZOMBIE” CELLS

As a young assistant professor at the Dana Farber Cancer Institute, Judith Campisi, PhD received an AFAR Research Grant for Junior Faculty in 1990. Soon after, she first encountered senescence, the process by which cells are unable to proliferate further. Many believed senescence protects us against cancer.

“In the face of myriad types of stresses, cells will enter a state in which they no longer divide,” says Dr. Campisi, now a Professor at The Buck Institute for Research on Aging. “When that happens, cells are protected from becoming cancerous. The whole process is designed to suppress cancer, and it does a pretty good job.”

During senescence, cells also begin to secrete molecules that alert surrounding tissue to potential danger and repair cellular damage.

However, research has also confirmed a link between senescence and multiple age-related diseases.

Dr. Campisi admits she was initially skeptical of the connection, but her research led her to believe that the molecules produced by senescent cells “really could be a driving force behind aging. So, as with most science, you go where the data leads you, not the other way around.”

The data led Dr. Campisi to found Unity Biotechnology Inc. with Jan Van Deursen, PhD of the Mayo Clinic. Today, Unity is at the forefront of efforts to develop senolytics: drugs that have been shown in mice to target age-related chronic diseases by killing senescent cells.

The Link to Chronic Inflammation

Senescent cells may protect against cancer and repair damaged tissue, but there is a reason they are sometimes referred to as “zombie cells.”

“The problem with senescent cells is they tend to not die,” Dr. Campisi says. “And consequently, they increase with age. When people begin to accumulate them above certain thresholds, their secretions can drive what we term chronic inflammation. And chronic inflammation is a part of virtually every major age-related disease, from neurodegeneration to, ironically, late-life cancer.”

Unity—under the vision of its CEO Nathaniel “Ned” David, PhD—as well as other biotech companies are working on getting senolytic drugs into clinical trials with specific disease indications, such as osteoarthritis and glaucoma.

“Then the drugs, if approved, will be used off label by other researchers, and it’s going to take time before the senolytics are recognized as hitting multiple age-related diseases,” Dr. Campisi says. “I know Unity would like to have something at least in the first stages of a trial within a year. So we’re not talking decades down the road. I think most people who are thinking about drug interventions are thinking about it in terms of a couple of years—not a couple of decades.”

Dr. Campisi is an excellent example of why AFAR’s support for promising young scientists with a passion for understanding the biological processes of aging is so crucial. She says: “AFAR’s support at the beginning of my career fueled my passion for basic biological research and set me on the path to this fascinating and potentially life-changing work with senolytics.”

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