UC SANTA BARBARA

THE Current

August 27, 2003
Eileen Conrad

Discovery of Cell Survival Gene May Lead to New Treatments for Degenerative Diseases and Cancer

Our cells are constantly making life and death decisions.

A new gene that controls this life or death switch and protects cells from dying has been discovered by researchers at the University of California, Santa Barbara, as reported in the August 28 edition of the scientific journal Nature.

The discovery may provide scientists with new means for identifying drugs that combat degenerative diseases such as Lou Gehrig's disease (ALS), the destructive effects of stroke and heart diseases, autoimmune diseases, and cancer.

Chilling though it sounds, our cells are poised on the brink of death.

Yet the ongoing death of some of our cells is actually essential for us to live.

"Death, that is to say cell death, is a key player in biology and medicine," said Joel Rothman, professor of Molecular, Cellular and Developmental Biology, and leader of the UCSB research team.

"Cells often commit suicide so that others may live.

This is the ultimate example of altruism at the cellular level."

Why would a cell kill itself off?

"Programmed cell death is one of the first lines of defense against cancer and infection by invaders such as viruses," notes Rothman.

"Ironically, the failure of a wayward cell to die can actually lead to death of the individual."

By killing itself off, a malignant or infected cell can prevent the disease from spreading.

However, the throttle on cell death must be carefully set.

"While death is a necessary part of our survival, too much cell death is disastrous," said Rothman

"That is what happens in degenerative diseases."

The gene identified by Rothman and UCSB postdoctoral researchers Tim Bloss and Eric Witze is called ICD-1 (inhibitor of cell death gene 1).

It prevents normal cells from committing suicide.

"As often happens in research, we were looking into an entirely different process when we stumbled across this cell death gene," said Witze.

"We were startled to find that elimination of ICD-1 gene function causes lots of good cells to die by the same type of programmed suicide used to kill off harmful or defective cells, such as cancer cells."

However, there is a twist.

Although the aberrantly suicidal cells use some of the same cellular components to do themselves in, their path to death takes a somewhat divergent course from that used by cells whose normal fate is to commit suicide. "This was a completely unexpected outcome," Witze said.

"We had assumed that suicide we observed would use the same machinery as is used in cells that normally commit suicide."

This discovery indicates that there are alternative avenues for the programmed death of cells in some circumstances.

It is possible that such alternative routes are also used when cells inappropriately die in degenerative diseases.

The researchers discovered that the protein coded by the ICD-1 gene normally hangs out in a compartment within the cell called the mitochondrion.

"That was a gratifying discovery: the ICD-1 protein works in the organelle that is pivotal for the programmed suicide of cells," said Bloss.

"Within the mitochondria, ICD-1 may keep the instruments of death that are loaded up in that organelle safely stowed away."

The ICD-1 gene was discovered by studying a tiny roundworm called C. elegans.

This worm was in the international spotlight last fall when the Nobel Prize in physiology or medicine was awarded to three scientists who pioneered its use for understanding normal development and programmed cell death in particular.

The ICD-1 gene found in this animal is very closely related to a gene in humans, raising the possibility that its function may be altered in human degenerative diseases or cancer.

"Hyperactivation of the human ICD-1 gene might well lead to tumor formation," notes Bloss, who was supported in part by a post-doctoral research fellowship from the Cancer Center of Santa Barbara.

The findings have also allowed Rothman's team to discover other genes that act similarly to keep a check on the suicide of normal cells.

Discovery of such genes could lead pharmaceutical companies to develop drugs for the treatment of cancer and degenerative diseases.

The personal side of neurodegenerative diseases does not escape Rothman, who lost a family member to ALS a few years ago.

"Our human state, including our ability to move, to feel emotion, and to be self-aware, all require an exquisitely honed nervous system," he said.

"Progressive loss of our nerve cells chips away at who we are as humans."

Physicians currently have very limited tools to combat such degenerative diseases.

Discovering the genes that keep cells from committing suicide is likely to lead to new treatments for these devastating illnesses.

The death of cells is also believed to contribute to aging.

By ensuring cell survival, genes such as ICD-1 may help to prolong lifespan and decelerate the aging process.

The research was also funded by the National Institute on Aging and The National Cancer Institute.

About UC Santa Barbara

The University of California, Santa Barbara is a leading research institution that also provides a comprehensive liberal arts learning experience. Our academic community of faculty, students, and staff is characterized by a culture of interdisciplinary collaboration that is responsive to the needs of our multicultural and global society. All of this takes place within a living and learning environment like no other, as we draw inspiration from the beauty and resources of our extraordinary location at the edge of the Pacific Ocean.