Researchers warm to practical way of freezing tissue 1998-07-29

Category: News

Media contact	Email
Pre-2000	

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By Leila Belkora

As a graduate student at the Massachusetts Institute of Technology, Jens Karlsson was intrigued by efforts to develop an artificial liver by researchers at nearby Harvard Medical School.

Karlsson was interested to learn that, even if the project were successful, existing technology could not preserve the organ for shipping or storage before transplantation.

Now Karlsson, an assistant professor in mechanical engineering and bioengineering, directs UIC's new Biothermal Sciences Laboratory.

His research group is studying techniques for freezing and thawing living cells and tissue, paving the way for the preservation of organs in medicine, agriculture and biotechnology.

"With the emerging tissue engineering industry, cryopreservation will be a critical technology," Karlsson said.

"Maintaining cells in a state of 'suspended animation' by freezing would also be beneficial for other applications involving medical transplants, or banking of valuable biological materials such as genetically engineered cell lines or livestock reproductive cells."

The Whitaker Foundation of Rosslyn, Va., a private organization that supports biomedical engineering research, recently awarded one of 27 new grants to Karlsson.

The grant, $203,000 over three years, will support his work to improve the processes of freezing and thawing skin grafts for treatment of burn injuries.

Karlsson's goal is to develop cryopreservation techniques that avoid the often severe cell damage which can occur during freezing and thawing.

"Many laboratories have standard procedures for freezing and thawing cells, developed by trial and error," he said.

"That usually works well enough, because it may not be a problem if they destroy 50 percent of their cells; they can simply wait for the cells to grow back in culture.

"Survival of the cells is more critical in certain applications, however. If we take an artificial tissue out of the freezer, thaw it, and half of it is gone, that's a problem. If a patient comes in with a burn injury, we don't have time to wait for the cells to grow back."

There are several factors affecting the survival of cells -- how rapidly they are cooled or warmed, or what chemical agents are added to samples before freezing, for example. Karlsson and his group are seeking an engineer's "rational design" solution to determine the best possible conditions.

"We're trying to develop a more rigorous, methodical approach to the whole optimization process. By developing theoretical models of what physically happens to cells during freezing and thawing, we can predict the best method for cryopreserving a particular cell type," he said.

One of the instruments in Karlsson's laboratory is a specially designed cryomicroscope for viewing samples during freezing and thawing. The temperature of the sample is controlled by balancing liquid nitrogen cooling against the heat generated by passing an electric current through a resistor in the sample holder.

A computer measures the sample temperature continuously and adjusts the current, allowing the experimenter to set the temperature of the sample to any level.

To study the effect of freezing or thawing on the structure of a cell, Karlsson can program the cryomicroscope to change the sample temperature at a given rate, say, cooling by 10 degrees Celsius per minute.

As the temperature drops, ice forms in the liquid surrounding the cells. Because the ice is pure water, the remaining unfrozen liquid becomes more concentrated with salts and proteins, and this higher concentration in turn tends to draw water out from the cells, in an attempt to restore osmotic balance.

If the cooling is rapid, the cell doesn't have time to lose water, and water freezes inside the cell. Under the microscope, a freezing cell appears to turn black because the ice crystals deflect or scatter light.

"Ice formation inside cells is usually correlated with destruction or damage to the cell," said Karlsson. "This will happen if we cool too rapidly. On the other hand, if we cool too slowly, the cells become dehydrated."

Using a video camera mounted on the cryomicroscope, Karlsson records the behavior of the cells during the experiment. With digital image processing techniques, he analyzes what happens to cells under different conditions.

His previous research on egg cells from mice was the first demonstration that rational design could be successful in a practical freezing procedure.

Karlsson likes interdisciplinary research -- it allows him to combine his background in mechanical engineering and physics with the tools and techniques of biology and chemistry.

"Bioengineering is about trying to bring quantitative analytical methods to bear on biological systems," he said.

"I think of biology as one of the last frontiers of science. There is still so much unknown, a lot to be done.

"As engineers, we have exciting opportunities to make valuable contributions by adding new tools and a fresh perspective to the field."