SALT LAKE CITY, November 22, 2010 — Researchers from Huntsman Cancer Institute (HCI) at the University of Utah report that they have identified a previously undiscovered trigger mechanism for a quality control checkpoint at the very end of the cell division process in a paper to be published in the November 29 issue of The Journal of Cell Biology and online today. This trigger mechanism monitors whether the cell’s nucleus, where the DNA resides, has the proper structure and delays cell division if the structure is not correct. Previously discovered triggers have been associated with improper DNA division and distribution, but not the nuclear structure.

“Much cancer research centers on the question ‘How does cancer start?’ And it’s usually when some normal process that’s vital for cell division is somehow not carried out correctly,” says Katharine Ullman, Ph.D., professor in the Department of Oncological Sciences, HCI investigator, and senior author on the paper. “Mistakes in this stage of quality control and this particular trigger could be one of the contributing factors to the initiation of cancer. It’s not going to be the only one, but it will help us ask additional important questions about how cancer forms.”
Research in the Ullman Lab focuses on the nuclear pore complex (NPC), a cellular structure that is embedded in membranes that enclose the nucleus. NPCs serve as gateways for material moving between the nucleus and the rest of the cell, and they are also important to nuclear organization. More recently, roles for NPC components are emerging in cell division. Cell division requires duplication of the cell’s DNA, dissolution of the nucleus—including NPCs themselves—regrouping the duplicated DNA into two identical packages, and reformation of the two new nuclei before cell separation occurs. In this study, the researchers examined cells that had been depleted of a component of the NPC called Nup153.

“We found that in its absence, a set of architectural elements at, and associated with, the nuclear pore weren’t being put back together correctly during nuclear reformation,” says Ullman. “At the same time, we saw another protein, Aurora B, stopping the cell cycle from proceeding.” She continues that other experimental strategies that interfered with reformation of this aspect of nuclear architecture similarly affected Aurora B. Aurora B has been widely studied as a target for new chemotherapy drugs. When activated, it conveys signals beginning and ending many steps of cell division.

“The connection we recently found is specific to the last stage of cell division called abscission. Abscission is the point of no return in the process of one cell becoming two,” says Ullman. “Although Aurora B needs to be activated and inactivated throughout the cell division process, the impact of the missing Nup153 protein occurred only at this very late stage.”

Ullman plans to pursue further research into the details of the molecular pathway between Nup153 and Aurora B. “At present, we can see that the two connect, but we do not understand the steps of the pathway,” she says. Douglas R. Mackay, Ph.D., and Masaki Makise, Ph.D., both postdoctoral fellows in the University of Utah Department of Oncological Sciences, co-authored the study. Funding support was provided by the American Cancer Society, the National Institutes of Health, the Leukemia and Lymphoma Society, and Huntsman Cancer Foundation.

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*The mission of Huntsman Cancer Institute (HCI) at The University of Utah is to understand cancer from its beginnings, to use that knowledge in the creation and improvement of cancer treatments, to relieve the suffering of cancer patients, and to provide education about cancer risk, prevention, and care. HCI is a National*
Cancer Institute-Designated Cancer Center, which means that it meets the highest national standards for cancer care and research and receives support for its scientific endeavors. HCI is also a member of the National Comprehensive Cancer Network (NCCN), a not-for-profit alliance of the world’s leading cancer centers that is dedicated to improving the quality and effectiveness of care provided to patients with cancer. For more information about HCI, please visit www.huntsmancancer.org.