IBT researchers find link that leads to cancer

(HOUSTON) — Researchers at the Texas A&M Health Science Center (TAMHSC) Institute of Biosciences and Technology have established a link between the regulation of autophagy and the suppression of genomic instability and carcinogenesis in a model of liver cancer, a finding that could eventually help in the development of prevention of cancer.

The results emerged from a series of studies from the research team led by Leyuan Liu, Ph.D., assistant professor in the Center for Cancer and Stem Cell Biology at the TAMHSC-Institute of Biosciences and Technology. The most recent will appear in the Dec. 15 issue of Cancer Research. The editors of the specialty journal Autophagy noted the work and invited the researchers to contribute a summary of their findings in their prestigious section Autophagy Punctum, which covers the most significant breakthroughs in the autophagy field.

Autophagy, controlled self-digestion, is a cellular garbage disposal and recycling system for dysfunctional aggregated proteins and worn-out organelles essential to normal cellular functions. Mitochondria are the organelle that fuel cell functions but are highly toxic and cause cell death when damaged or worn out.

Autophagy is activated when cells are stressed out, serving to break down cellular components to their basic building blocks and reshuffle them into essential components aimed at surviving the particular situation. Any defects in the autophagy process will lead to accumulation of those cellular wastes that in turn enhances oxidative stress and causes genome instability that is thought to underlie all cancers.

In their study, Dr. Liu and his colleagues tested two-week-old mice with a single dose of the chemical carcinogen diethylnitrosamine, tracking the changes in the amount of proteins related to autophagy and the intensities of DNA damage from early stages before any tumor foci could be seen to later stages when the tumor foci were able to be easily detected.

The researchers found that levels of MAP1S, a protein identified earlier in their lab as a key regulator of autophagy, is dramatically elevated to activate the autophagy machinery to remove the damaged proteins or organelles immediately upon exposure to the carcinogen. Such response is defective in a MAP1S-deficient mouse model created in the group so that the mice accumulate a lot of waste and develop larger and more malignant tumor foci.

As a result, Dr. Liu said this study not only established a link between the regulation of autophagy and the suppression of genomic instability and carcinogenesis but also possibly reveal the impact on cancer patients.

The number and malignance of tumor foci detected in later stages have already been determined in early stages immediately after exposure to the carcinogen, and the genome of the exposed mice have been seriously damaged long before any tumor foci can be detected.

“The results reveal both good and bad news,” Dr. Liu said. “The good news is that we may still have a chance to prevent cancer development as early as immediately after carcinogen exposure. The bad news is that we cannot restore the genome back to normal after cancer is detected because any cells in tissues with the messed up genome have the ability to develop into cancer. Unfortunately, the situation in mice may be similar in humans.”

Further, data from this study has helped solve a long-term “chicken-egg” relation about genome instability in tumor development, Dr. Liu said.

Some researchers believe genome instability causes tumor development, but others argue genome instability is the result of tumor development. This experiment detected a wide range of genome instability before any tumor foci are visible, strongly suggesting genome instability is the origin of tumors.