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HSC-Institute of Biosciences and Technology researchers uncover potential mechanism that may prevent cancer at its origin

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Texas A&M Health Science Center Marketing and Communications

HSC-Institute of Biosciences and Technology researchers uncover potential mechanism that may prevent cancer at its origin

(HOUSTON) — Researchers at the Texas A&M Health Science Center Institute of Biosciences and Technology in Houston have uncovered a potential mechanism that could prevent cancer at its origin.

Their study is in the September issue of the journal *Cellular Oncology*.

Based on the theory that all cancers begin with a random error during cell division – one of the most fundamental processes of life – HSC-Institute of Biosciences and Technology researchers discovered a mechanism that may exist in nature to reduce the frequency of random error that gives rise to cancers.

At the cell level, DNA is duplicated and packaged into duplicate units called chromosomes, which normally divide equally into two cells. On rare occasions by chance, when cells – the building blocks of life - divide into two cells, chromosomes are divided unequally. One cell then will have too many chromosomes, the other too few in a condition called aneuploidy.

Seen in all cancers, aneuploidy creates hundreds of small changes in the effects of normal unmutated genes. This imbalance normally is so stressful that the cells cannot survive. But sometimes, these aneuploid cells live and outgrow normal cells. The increased cell division then increases the chromosome imbalance, eventually leading to continuously occurring mutations observed in diverse cancers that enable them to change, adapt and even evade treatment.

"Enhancing this mechanism that senses and stops an aneuploid cell division by mitotic cell death before it happens may be the ultimate in cancer prevention," said Wallace McKeenan, Ph.D., executive associate director of the HSC-Institute of Biosciences and Technology and study senior author. "Since aneuploidy is the one feature common to cancers at all stages, the findings – once completely understood – may also be of value for slowing cancers at all stages of progression."

In their study, Dr. McKeenan, J.S. Dunn Professor and director of the Center for Cancer and Stem Cell Biology at the HSC-Institute of Biosciences and Technology, and Leyuan Liu, Ph.D., assistant professor in the center, reasoned if a random error in partition of chromosomes during cell division causes aneuploidy and underlies the earliest origin of cancers in general, then nature may have evolved a mechanism to keep the consequences of this random event to a minimum.

Years ago, the research group discovered a novel complex of proteins that communicate between microtubules and mitochondria during cell division. Microtubules dynamically grow and shrink to provide the "muscle" for separating the two pairs of chromosomes into two new cells. Like batteries in a series, the mitochondria aggregate to combine their energy to power cell division, then shrink to recharge or be recycled.

The new *Cellular Oncology* study findings show a microtubule-associated protein (*C19ORF5*) can sense that a perfect separation of chromosomes is failing and prevents the mitochondria from shrinking, recharging or being recycled. The irreversibly blocked mitochondria then turn lethal, killing cells in a process called mitotic cell death. The cells are killed even before they can divide into two potential cancer-causing aneuploid cells with an uneven number of chromosomes.

Graduate students Rui Xie and Chaofeng Yang in the Center for Cancer and Stem Cell Biology at the HSC-Institute of Biosciences and Technology contributed to the *Cellular Oncology* study.

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The Texas A&M Health Science Center provides the state with health education, outreach and research. Its seven colleges located in communities throughout Texas are the Baylor College of Dentistry in Dallas; the College of Medicine in Bryan-College Station, Corpus Christi, Houston, Round Rock and Temple; the College of Nursing in College Station; the Graduate School of Biomedical Sciences; the Institute of Biosciences and Technology in Houston; the Irma Lerma Rangel College of Pharmacy in Kingsville; and the School of Rural Public Health in College Station. Regional efforts include the Coastal Bend Health Education Center in Corpus Christi and the South Texas Center in McAllen.

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