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Researchers discover mechanism that explains how cancer enzyme winds up on ends of chromosomes

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Human cancer cells divide and conquer. Unless physicians can control that division with surgery, chemotherapy or radiation, the wildly dividing cells will eventually destroy a person's life.

Researchers have known for some time that an enzyme called telomerase is crucial to cancer's progress. Now, for the first time, researchers at the University of Georgia's Franklin College of Arts and Sciences have shown a mechanism that explains how two essential components of human telomerase—normally active only in early prenatal development but turned back on during cancer growth—are "recruited" from distinct sites in the cell to the telomere, an area at the end of a chromosome that normally protects it from destruction.

"Telomerase is reactivated in more than 90 percent of human cancers," said Michael Terns, professor of biochemistry and molecular biology and genetics at UGA, "and the fact that telomerase keeps these telomeres growing when it should be inactive is crucial for the proliferation of cancer. That makes telomerase a very promising target for a potential drug to stop cancers from spreading."

The research was just published in the journal *Molecular Biology of the Cell*. Other authors on the paper were Rebecca Terns, a senior research scientist also in UGA's department of biochemistry and molecular biology (Michael and Rebecca Terns are a husband-wife team); Rebecca

Tomlinson, a former doctoral student in the Terns Lab; Eladio Abreu, a current graduate student in the Terns lab; Tania Ziegler, also a former member of the Terns lab, now pursuing an M.D. degree; Hinh Ly of Emory University; and Christopher Counter of Duke University Medical Center. Rebecca and Michael Terns are also members of the University of Georgia Cancer Center.

The two essential components of human telomerase are telomerase RNA and telomerase reverse transcriptase. They are "recruited" to telomeres during what is called the "S phase" (for synthesis) of the cell cycle when DNA replication or synthesis occurs.

"What we have found is that during the remainder of the cell cycle, telomerase RNA is found primarily in rather mysterious and, until recently, little-understood structures called Cajal bodies," said Rebecca Terns. "Though science has known about Cajal [pronounced Ca-HAHL] bodies for more than a hundred years, what we have discovered is that the localization of telomerase RNA to Cajal bodies and telomeres is specific to cancer cells where telomerase is active."

The new research shows for the first time that the trafficking of telomerase RNA to both telomeres and Cajal bodies depends on the presence of telomerase reverse transcriptase.

The Terns lab took advantage of the differences between normal and cancer cells of many kinds to better understand the trafficking of telomerase RNA.

"We examined a variety of factors that differ between normal and cancer cells in order to identify factors that impact human telomerase localization," said Michael Terns. "Our results indicate that human reverse transcriptase is a key determinant in human telomerase trafficking and is essential for the localization of telomerase RNA both

to Cajal bodies and telomeres."

While all this jargon-filled science may sound difficult to understand, the discovery could lead to new ways to attack cancers by blocking their ability to grow. While that is years down the road, the new understanding of how this crucial biological action in the human body takes place will at the very least open new avenues of investigation into why and how cancer cells continue to grow and take the human toll they do every day.

Source: University of Georgia