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Study may suggest new strategies for myelodysplastic syndromes treatment

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A study revealing fresh insight about chromosome "tails" called telomeres may provide scientists with a new way to look at developing treatments or even preventing a group of blood cell disorders known as myelodysplastic syndromes (MDS).

Researchers at The University of Texas MD Anderson Cancer Center have discovered a direct link between telomere degeneration and MDS. Telomeres, found at the tail ends of chromosomes, are sometimes described as similar to plastic shoelace tips because they prevent chromosome ends from fraying, causing genetic havoc.

Degrading telomeres can sometimes lead to MDS, also thought to be associated with age, gender (more common in men), smoking, previous cancer treatment with radiation or chemotherapy, and family history. MDS is one of the more common blood disorders in the elderly with 90 percent of cases affecting people over age 60.

"MDS risk correlates with advancing age, therapy-induced DNA damage, and/or shorter telomeres, but whether telomere erosion directly causes MDS is unknown," said Simona Colla, Ph.D., assistant professor of Leukemia. "Our study provided genetic evidence that DNA damage caused by telomere loss is linked to this disorder."

Findings by Colla, fellow first co-author Derrick Ong, Ph.D., Odyssey fellow of Genomic Medicine, and corresponding author Ron DePinho, M.D., professor of Cancer Biology and MD Anderson president, are

published in the May 11, 2015 issue of *Cancer Cell*.

The team's mouse and human cell study found that DNA damage caused by dysfunctional telomeres resulted in repressed expression of a gene called SRSF2. SRSF2 is a RNA splicing gene that plays a role in cellular processes. This change impacted blood cells named CMPs (common myeloid progenitors), affecting their ability to differentiate or fully mature.

"This study established an intimate link across telomere biology, aberrant RNA splicing and CMP differentiation," said DiPinho. "This may suggest that strategies to mitigate this DNA damage may be useful for preventing and/or treating MDS."

Colla added that their findings "were consistent with long-standing observations that poor prognosis in MDS correlates strongly with short telomeres and elevated DNA damage in CMP cells."

"This improved understanding should provide highly specific risk biomarkers for preventing and treating this incurable disease," said Colla.

Provided by University of Texas M. D. Anderson Cancer Center