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RNA spurs melanoma development

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Traditionally, RNA was mostly known as the messenger molecule that carries protein-making instructions from a cell's nucleus to the cytoplasm. But scientists now estimate that approximately 97 percent of human RNA doesn't actually code for proteins at all. A flurry of research in the past decade has revealed that some types of non-coding RNAs switch genes on and off and influence protein function. The best studied non-coding RNAs are the microRNAs. Now, researchers led by Dr. Ranjan Perera at Sanford-Burnham Medical Research Institute (Sanford-Burnham) in Lake Nona and collaborators at the University of Queensland in Australia, have discovered that levels of a relatively understudied group of RNAs – long, non-coding RNA (lncRNA) – are altered in human melanoma. Their study, published online May 10 by the journal *Cancer Research*, shows that one lncRNA called SPRY4-IT1 is elevated in melanoma cells, where it promotes cellular survival and invasion.

"Non-coding RNA used to be considered cellular junk. But we and others have been asking the question – if it doesn't code for proteins, then what does it do in the cell?" said Dr. Perera, associate professor at Sanford-Burnham. "We're especially interested in determining what roles microRNAs and lncRNAs play in the genesis and development of human melanomas."

Melanoma is one of the rarest forms of skin cancer, but it is also the most deadly. Dr. Perera and his team compared lncRNAs in several laboratory cell-lines of melanoma and normal skin cells, as well as in 30 different human patient samples. They found that levels of one lncRNA,

SPRY4-IT1, were particularly high in melanoma cells, but not in normal skin cells. To further probe the function of this lncRNA, they looked at what happens in a melanoma cell-line where SPRY4-IT1 levels are significantly reduced. Cellular growth was impaired and cell death was increased in these SPRY4-IT1-deficient melanoma cells, as compared to melanoma cells with fully functioning lncRNAs. What's more, the ability of melanoma cells to invade the extracellular matrix (an early step in cancer cell metastasis) was reduced in cells lacking SPRY4-IT1.

"The elevated expression of SPRY4-IT1 in melanoma cells, its accumulation in the cell cytoplasm and effects on cell dynamics all suggest that increased SPRY4-IT1 may play an important role in the molecular underpinnings of human melanoma," said Dr. Perera. "Based on this information, we believe SPRY4-IT1 could be an early biomarker for the detection of melanoma."

In a separate study recently published in the journal *PLoS ONE*, Dr. Perera's group also reported that melanoma cells have lower levels of a different non-coding RNA, called miR-211. Together, these two studies give researchers a better understanding of melanoma development, which in turn could help them design new diagnostics and therapeutics for this often fatal disease.

Provided by Sanford-Burnham Medical Research Institute

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