Study traces possible role of damaged DNA in tumor development

March 4 2011

DNA provides the instruction manual for all life forms. Occasionally, instructions are not carried out properly, and bad messages are sent leading to the creation of mutant proteins and possible tumor development.

Paul Doetsch, PhD, professor of radiation oncology and biochemistry and associate director for basic research at Emory's Winship Cancer Institute and Damien Brégeon, PhD, at Institut de Génétique et Microbiologie in Paris, have outlined the role this process – known as transcriptional mutagenesis – might play in tumor development in a *Nature Reviews Cancer* article published on February 24, 2011.

"The majority of human cells do not multiply continuously but are slow-replicating and devote a large part of their energy to transcription," say the authors. "DNA damage can miscode at the damaged site and produce mutant transcripts. This process is transcriptional mutagenesis and could lead to the production of mutant proteins and may therefore be important in tumor development."

Transcriptional mutagenesis occurs when cells with damaged DNA produce bad messages during transcription, which leads to the creation of mutant proteins. Scientists already have learned that some genetic damages may block the transcription process, which is a signal for DNA repair molecules to move in and correct the mistake. When certain types of DNA damage are present, however, the non-dividing cells are capable of continuing transcription through the damage despite the erroneous

coding messages. This problem can be exacerbated when cells have defects for repairing DNA damage.

As Doetsch and Brégeon note, data on this process are accumulating in several laboratories around the world, and evidence is mounting that transcriptional mutagenesis could have an important role in tumor develop¬ment and other biological outcomes, including the development of drug resistance. However, at this point there is not enough evidence to know the extent to which transcriptional mutagenesis is involved in tumor development.

"One will have to follow the progeny of a single cell to determine whether cancerous growth can be initiated by the transient expression of oncogenic pro¬teins or the disruption of signaling pathways," the authors say. "Future studies addressing these issues will provide additional insights into the mechanisms and consequences of transcriptional mutagenesis and further establish the role of this process in tumor development."

Provided by Emory University