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Post-transcriptional gene regulation in colorectal cancer

Colorectal cancer is mediated through genetic alterations that result in overexpression of oncogenic factors. In the normal intestinal epithelium, oncogenic gene expression is controlled through AU-rich mRNA elements (AREs) that target mRNA for rapid decay. However, mRNA turnover of these transcripts is compromised during colon tumorigenesis. The status of RNA-binding proteins that promote mRNA stability and rapid decay was evaluated for changes in expression during tumorigenesis. In normal tissue, the stability factor HuR was present in the nucleus at low-levels, whereas increased levels of the decay factor TTP was observed. By contrast, increased HuR expression and cytoplasmic localization was observed in 76% of adenomas and 94% of adenocarcinomas, while TTP expression was lost in >75% of tumor tissue. Similar results were obtained for HuR and TTP mRNA expression in normal and staged tumor samples. To determine the functional significance of HuR overexpression *in vivo*, a tissue-specific HuR-transgenic mouse (HuR-Tg) was created which overexpressed HuR in the epithelium of the small intestine and colon. To test if HuR overexpression can promote colon cancer, crosses between HuR-Tg mice and the APC^{Min/+} mouse, a genetic model of gastrointestinal tumorigenesis, were performed to initiate tumorigenesis. HuR-Tg/APC^{Min/+} lines display a 2- to 4-fold increase in tumor burden and size in both the colon and small intestine compared to APC^{Min/+} control mice. These findings indicate that HuR functions during colon tumorigenesis downstream of a tumor-initiating event to stabilize ARE-containing mRNAs and identify this RNA binding protein as a new molecular target for therapeutic intervention..

Biography

Dan A. Dixon is an completed his Ph.D. at Northwestern University Medical Center and postdoctoral studies from the University of Utah and Vanderbilt University Medical Center. He is an Associate Professor of Biological Sciences and Associate Director of the Colon Cancer Research at the University of South Carolina. He has published more than 50 manuscripts in reputed journals and serving as an editorial board member of repute. His laboratory now currently resides in the Department of Cancer Biology at the University of Kansas Cancer Center.

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