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Measurement of DNA repair enzymes as cancer biomarkers

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DNA damage continuously occurs in living organisms. Unless repaired, DNA damage can lead to mutations and consequently to genetic instability, a hallmark of cancer. DNA damage is repaired by various pathways involving numerous proteins. Evidence suggests that tumors may increase their DNA repair capacity, causing resistance to therapy. Knowledge of expression levels of DNA repair enzymes may help predict and guide treatments. These enzymes are emerging as predictive, prognostic and therapeutic cancer biomarkers. DNA repair inhibitors are being developed to increase the efficacy of therapy when used alone or together with chemotherapy or radiation therapy. There are inhibitors of several enzymes in development and Phase I-II clinical trials are being conducted. One of these enzymes is apurinic/apyrimidinic endonuclease 1 (APE1), which plays a crucial role in DNA repair and possesses other functions. Evidence points to the predictive and prognostic value of APE1 expression and subcellular localization in cancers. Increased APE1 expression in cancers is associated with resistance to therapy. The accurate measurement of APE1 levels in tissues is necessary for using APE1 as a biomarker. We developed methodologies using mass spectrometry that permits accurate measurement of APE1 *in vivo*. Levels of APE1 were measured in nuclear and cytoplasmic extracts of human normal and cancer cell lines. We found greater expression levels of APE1 in cancer cells and differences in its subcellular localization. We also showed the identification of APE1 variants in the human population. The developed novel approach may help define the role of APE1 in cancer and treatment responses.

Biography

Miral Dizdaroglu has studied DNA damage and repair for more than 30 years. He developed methods and standards for the measurement of numerous lesions formed in DNA *in vitro* and *in vivo* using mass spectrometric techniques to understand mechanisms of DNA damage and specificities of DNA repair enzymes. His latest work involves the measurement of DNA repair enzymes in human tissues as the knowledge of expression levels of these enzymes may help predict and guide treatments in cancer. He has published more than 200 peer-reviewed papers and received numerous awards for his work.