"DNA Damage, Repair and Disease" Course in TurkHeltox Congress

October 21-24, 2015 in Cesme-Izmir

Speaker: Prof. Dr. Miral Dizdaroğlu
National Institute of Standards and Technology, Gaithersburg, Maryland, USA

DNA damage constantly occurs in living organisms. In the oxygen-rich atmosphere, reactive species are derived from oxygen endogenously and cause damage to DNA by a variety of mechanisms. Exogenous sources such as UV- and ionizing radiations, carcinogenic compounds and environmental toxins, to name a few, also generate oxygen-derived species in living cells. Oxidative damage to DNA caused by such reactive species leads to multiple products including DNA base and sugar products, single- and double-strand breaks, tandem lesions, clustered sites and DNA-protein cross-links. Accurate measurement of DNA lesions is essential for thorough understanding of the mechanisms, cellular repair and biological consequences of DNA damage. Many of DNA lesions are mutagenic and cytotoxic. If they are not repaired before DNA replication, these lesions can cause genetic instability, which may lead to disease processes including carcinogenesis. Elaborate DNA repair mechanisms exist in living organisms that include multiple pathways to repair DNA lesions. Proteins involved in such pathways possess different, but sometimes overlapping substrate specificities. DNA repair systems are affected by mutations and polymorphisms in DNA repair genes. Such defects are associated with cancer. In addition to the role of DNA repair in carcinogenesis, mounting evidence suggests that cancer tissues develop greater DNA repair capacity than disease-free tissues by overexpressing DNA repair proteins. Increased DNA repair in malignant tumors is a major mechanism for development of resistance to therapy. As a result, DNA lesions formed in tumors by therapy are removed before they become toxic to cancer cells, affecting patient survival. Thus, DNA repair capacity may be a predictive biomarker for patient response to therapy. Knowledge of DNA protein expressions in normal and cancerous tissues may help predict and guide development of treatments, and yield the best therapeutic response. DNA repair proteins constitute targets for inhibitors to overcome the resistance of tumors to therapy. Inhibitors of DNA repair for combination therapy or as single agents for monotherapy are being developed globally to help eradicate cancer.

<u>The course will address the following topics:</u>

1. Mechanisms of oxidative DNA damage and its cellular repair
2. Measurement of DNA lesions and DNA repair proteins by mass spectrometric techniques
3. Biological consequences of oxidatively induced DNA lesions
4. DNA repair and cancer
5. Question time: open discussion