Redox regulation of genome stability by effects on gene expression, epigenetic pathways and DNA damage/repair.

Abstract: Reactive oxygen and nitrogen species (e.g. H2O2, nitric oxide) confer redox regulation of essential cellular signaling pathways such as cell differentiation, proliferation, migration and apoptosis. In addition, classical regulation of gene expression or activity, including gene transcription to RNA followed by translation to the protein level, by transcription factors (e.g. NF-κB, HIF-1α) and mRNA binding proteins (e.g. GAPDH, HuR) is subject to redox regulation. This review will give an update of recent discoveries in this field, and specifically highlight the impact of reactive oxygen and nitrogen species on DNA repair systems that contribute to genomic stability. Emphasis will be placed on the emerging role of redox mechanisms regulating epigenetic pathways (e.g. miRNA, DNA methylation and histone modifications). By providing clinical correlations we discuss how oxidative stress can impact on gene regulation/activity and vice versa, how epigenetic processes, other gene regulatory mechanisms and DNA repair can influence the cellular redox state and contribute or prevent development or progression of disease.