Preface

This special issue in *Cytogenetic and Genome Research* designated “DNA Repair, Genomic Instability and Cancer” addresses hot topics in the field, with an emphasis placed on preclinical and clinical implications. With cancer remaining a leading cause of death across the globe, biomedical research which addresses the endogenous and exogenously induced sources of genomic DNA damage, the mechanisms of mutagenesis and productive DNA damage and repair, and consequences for human health and tumorigenesis remains as important as ever. In this special issue, these topics are addressed with unique perspectives and experimental approaches.

DNA damage and unusual nucleic acid structures pose detrimental effects in distinct ways dependent on their chromosomal locations. While there has been a long history of studies in the DNA damage and DNA repair fields, more recently the alternatively arranged conformations of DNA or RNA have attracted considerable interest. One such structure known as the G-quadruplex (G4) forms in guanine-rich regions of the genome such as ribosomal DNA (rDNA). rDNA G4 poses an obstacle to smooth replication and/or transcription which can have dire consequences for genomic stability, gene expression, and cellular senescence. In a review from the Kormuth (Bethany College) and Brosh (National Institute on Aging, NIH) labs, G4 assembly at rDNA loci and its importance in disease pathogenesis and cancer are discussed. A perspective of rDNA G4 stabilization in cancer therapy via synthetic lethality is presented.

The Fang lab at the Norwegian Centre on Healthy Ageing and the University of Oslo discusses molecular and clinical aspects of the accelerated aging disorder Werner syndrome mutated in the *WRN* gene. In this innovative perspective piece, the authors address experimental evidence supporting the emerging hypothesis that impaired mitochondrial function contributes to the metabolic anomaly characteristic of the genetic disease with defects in a DNA helicase-nuclease that together with its protein interactions appears to have pleiotropic roles in nucleic acid metabolism that regulate cellular homeostasis. Modulation of autophagy by NAD⁺ manipulation provides insight into potential clinical therapies.

WRN is only one of five human RECQ helicases, all of which are important for genomic stability with unique but sometimes partially overlapping roles. Dr. Balajee at the Oak Ridge Associated Universities contributes a review article to the special issue that addresses the involvement of the *RECQL4* gene, linked to three apparently distinct hereditary disorders (Rothmund-Thomson, RAPADILINO, and Baller-Gerold syndromes), in cancer. A distinctively new perspective on *RECQL4* as a cancer therapeutic target is discussed.

Susan Bailey of Colorado State University has had a longstanding interest and reputation in chromosome bi-

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ology and the influence of DNA damage on the integrity and functional capacity of mammalian cells. In their review article, she and her colleagues contribute insights into the negative effects of ionizing radiation on chromosome stability. Given the environmental prevalence of ionizing radiation, as well as its clinical applications in cancer therapy, the outcome for chromosomal structural rearrangements mediated by inflicted strand breaks is significant. Bailey and her colleagues address the apparent consequences of ionizing radiation for microscopically detectable structural chromosome changes.

Aside from cancer therapy, radiation exposure due to detonation of nuclear devices is of worldwide and societal concern that needs to be addressed at a very mechanistic level. Turner and colleagues at Columbia University present their experimental findings relating to cytogenetic damage caused by neutron and gamma exposure in human lymphocytes using a hematopoietically humanized mouse model. The innovative model and detailed analysis enable the authors to determine the effects of neutrons and X-rays on clustered DNA damage in an organismal model.

A broader perspective of molecular and genetic defects contributing to cancer and implications for therapeutic strategies is provided in a perspective article by Proietti-De-Santis and collaborators at the University of Tuscia. In this review, the authors consider evolutionary pathways of carcinogenesis that might be exploited to achieve the highly desirable personalized medicine required to combat cancer heterogeneity.

Malignant brain tumors pose a unique challenge in therapy options. To achieve better treatment options, research hypotheses must be addressed in defined and manipulatable experimental systems. The Sakamoto-Hojo

lab at the University of São Paulo has assessed the unique involvement of the E2F1 transcription factor in glioblastoma cells grown either as a monolayer or as neurospheres. Their findings are compelling, as they suggest a critical role of E2F1 in the maintenance of glioblastoma multiforme stem cells.

In addition to the direct roles of transcription factors in gene expression, epigenetic regulation modulates processes of tumorigenesis which has an impact on clinical prognosis. Zhongwei Lv, Dan Li, and collaborators at the Tongji University School of Medicine addressed by new experimental studies the importance of DNA methylation on gene expression in embryonic carcinoma and seminoma derived from germ cell neoplasia. Differentially expressed genes and DNA methylation status between the two cancer types were demonstrated, suggesting they are a significant contributing factor to pluripotency and genomic stability. These findings have potential importance for cancer development and serve as a model for studies of other tissue-derived tumors.

We are highly pleased to present the readers a collection of articles in this special issue of *Cytogenetic and Genome Research* dedicated to the subjects of DNA repair, genomic instability and cancer. We anticipate the research articles and reviews will spark discussion, a greater understanding of chromosomal maintenance pathways, and new hypotheses focused on the molecular pathogenesis of cancer.

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