Preface

Recent advances in our knowledge of DNA repair mechanisms and DNA damage responses have led to understanding in great detail how these processes operate at several different organizational levels ranging from single molecules to chromatin supra-macromolecular complexes. This volume comprises 11 chapters that span a range of topics addressing a number of major issues in the areas of DNA repair and the orchestration of the DNA damage response. The chapters and topics are presented as a progression from prokaryotic to eukaryotic cellular models and experimental strategies designed to interrogate the operational features of the major DNA damage management systems.

Kad and Van Houten, in the first chapter, illustrate the successful application of single molecule approaches to unravel how several hundred copies of nucleotide excision repair (NER) proteins can scan an entire bacterial (*Escherichia coli*) genome and target damage with amazing specificity. This is followed by an up-to-date review by Ganesan *et al.* of how *E. coli* transcription-coupled repair, a subpathway of NER, achieves its function to prioritize the repair of various classes of DNA damage in actively expressed genes. We move from here to mismatch repair (MMR) in *E. coli* where Guarné reviews recent functional and structural studies aimed at defining the multiple functions of the MutL endonuclease and how its activity is regulated by other repair factors. In the fourth chapter by Prakash *et al.*, the subject switches to the base excision repair (BER) pathway in bacteria where the key initiating DNA glycosylases of the Fpg/Nei family are highlighted in terms of their structural features, substrate specificities, and how they search for their DNA damage targets.

The chapters that follow then review recent advances in knowledge of DNA damage management in eukaryotic systems. Swartzlander *et al.*, in the fifth chapter, address the issue of BER regulation in *Saccharomyces cerevisiae* via dynamic localization from cytoplasm to nucleus and mitochondria of an initiating DNA glycosylase (Ntg1) in response to oxidative stress. The theme of BER regulation continues in the sixth chapter by Hegde *et al.*, where the DNA glycosylases operating in the early steps of BER and single strand break repair are reviewed in terms of their structurally disordered regions and posttranslational modifications. Another critically important repair pathway involves the utilization of homologous recombination (HR) for repair of DNA double strand breaks. Amunugama and Fishel, in the seventh chapter, provide a timely review of the components and mechanics of HR in eukaryotes.

Following the seventh chapter, the topics move toward discussions of how chromatin structure and modifications impact DNA repair and DNA damage response processes. In the eighth chapter, Williamson *et al.* provide a succinct review of histone modifications associated with the major DNA repair processes mentioned above including NER, BER, MMR, HR, and nonhomologous end joining (NHEJ). This sets the stage for the ninth chapter by Chambers and Downs where they address the issue of how chromatin remodeling enzymes (RSC and INO80) in *S. cerevisiae* pave the way for sites of DNA damage to be accessed by the repair machinery in the context of HR and NHEJ for repair of DNA double strand breaks. In the tenth chapter, by Xu *et al.*, the focus of attention moves to the DNA damage response circuits that involve the master regulator of dsb repair, the ATM protein kinase, as well as histone methylation codes in human cells. These events, when corrupted, have important implications for the acquisition of genomic instability and the development of cancers. Finally, Morandell and Yaffe, in the eleventh chapter, discuss several recent examples of how synthetic lethal interactions (with an emphasis on p53) between DNA damage signaling and cell cycle checkpoint control can be exploited to kill tumor cells, illustrating how knowledge of damage response and repair pathways is being exploited for new therapies in cancer patients.

Thus, the complex landscapes of DNA repair processes and DNA damage responses are punctuated with timely examples of how the latest investigations are informing a detailed understanding of mechanistic processes.

PAUL W. DOETSCH
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