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From the Editor

DNA Repair: A Reinvigorated Therapeutic Target

With at least 165 genes involved[1], the human genome is conserved and repaired in sequential, carefully timed processes matched to the specific type of damage that has been wrought, whether from an endogenous or exogenous insult. Despite the fact that DNA is the target, directly or indirectly, for a large number of our cancer chemotherapeutics, and the obvious importance of DNA damage in determining success or failure of that therapy, the complexity and redundancy of its repair have made its components less attractive targets for cancer drug development. Indeed, the success of imatinib targeting Bcr-Abl in chronic myeloid leukemia led many to hope, for a moment in time, that the DNA damaging agents could become a treatment of the past. Our growing understanding of the mutational complexity of most solid tumors makes it clear that DNA will remain among the most important therapeutic targets for the foreseeable future. That point has been reinforced in recent months by clinical data showing activity of PARP inhibitors in breast cancer in patients who have loss of *BRCA1*, an important gene in homologous recombination, a double-strand break DNA repair pathway. This issue of *CCR Focus* is aimed at increasing our understanding of some of the more translational aspects of DNA repair. Guest Editor Eddie Reed, writing in the overview, details the repair pathways and highlights the first clinically validated biomarker, ERCC1, which proved that avid DNA repair could be a detriment to successful cancer therapy. Annunziata and O'Shaughnessy summarize the exciting data showing the activity of PARP inhibitors in breast cancer; Plummer describes the many other drugs in development that target DNA repair; and Pommier and colleagues discuss efforts to validate other biomarkers of DNA repair. Finally, to increase our understanding of DNA repair in the broader cellular context, Côté and colleagues review the involvement of epigenetics while Bristow and colleagues discuss the impact of cellular hypoxia in DNA repair. As with every issue of *CCR Focus*, it is hoped that this issue will inform the interested non-expert but also challenge and encourage those working in the field.

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Reference

1. http://sciencepark.mdanderson.org/labs/wood/DNA_Repair_Genes.html.

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