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Sommario/riassunto	<p>This Special Issue of International Journal of Molecular Sciences (IJMS) is dedicated to the mechanisms mediated at the molecular and cellular levels in response to adverse genomic perturbations and DNA replication stress. The relevant proteins and processes play paramount roles in nucleic acid transactions to maintain genomic stability and cellular homeostasis. A total of 18 articles are presented which encompass a broad range of highly relevant topics in genome biology. These include replication fork dynamics, DNA repair processes, DNA damage signaling and cell cycle control, cancer biology, epigenetics, cellular senescence, neurodegeneration, and aging. As Guest Editor for this IJMS Special Issue, I am very pleased to offer this collection of riveting articles centered on the theme of DNA replication stress. The blend of articles builds upon a theme that DNA damage has profound consequences for genomic stability and cellular homeostasis that affect tissue function, disease, cancer, and aging at multiple levels and through unique mechanisms. I thank the authors for their excellent contributions, which provide new insight into this fascinating and highly relevant area of genome biology.</p>