In every growing cell, the DNA replication and transcription machineries are routinely in conflict with each other. Replication-transcription conflicts have various negative outcomes, including slowing of DNA replication forks, and breaks in the DNA. Survival, despite the existence of conflicts, depends on essential conflict resolution factors that all organisms harbor. In this seminar, I will highlight some of the new insights we have gained regarding the multi-faceted effects of these encounters on key parameters of cellular function. I will discuss the impact of conflicts on DNA replication, mutagenesis, survival of environmental stress, and evolution of stress response and virulence. I will specifically focus on how 1) transcription disassembles the replication machinery every cell cycle and 2) three stranded nucleic acid structures called R-Loops contribute to the severity and detrimental outcomes of replication-transcription conflicts.