Chromosomal DNA replication is achieved by an assembly of multi-protein complexes at the replication fork. DNA sliding clamps play an important role in this assembly and are essential for cell viability. Inhibitors of bacterial (\(b\)-clamp) and eukaryal DNA clamps, proliferating cell nuclear antigen (PCNA), have been explored for use as antibacterial and anti-cancer drugs, respectively. Inhibitors for bacterial \(b\)-clamps include modified peptides, small molecule inhibitors, natural products, and modified non-steroidal... In this review, studies in the use of both bacterial and eukaryotic sliding clamps as therapeutic targets are summarized.