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Sommario/riassunto	DNA replication, a central event for cell proliferation, is the basis of biological inheritance. Complete and accurate DNA replication is integral to the maintenance of the genetic integrity of organisms. In all three domains of life, DNA replication begins at replication origins. In bacteria, replication typically initiates from a single replication origin (oriC), which contains several DnaA boxes and the AT-rich DNA unwinding element (DUE). In eukaryotic genomes, replication initiates from significantly more replication origins, activated simultaneously at a specific time. For eukaryotic organisms, replication origins are best characterized in the unicellular eukaryote budding yeast Saccharomyces cerevisiae and the fission yeast Schizosaccharomyces pombe. The budding yeast origins contain an essential sequence element called the ARS (autonomously replicating sequence), while the fission yeast origins consist of AT-rich sequences. Within the archaeal domain, the multiple replication origins have been identified by a predict-and-verify approach in the hyperthermophilic archaeon Sulfolobus. The basic structure of replication origins is conserved among archaea, typically including an AT-rich unwinding region flanked by several short repetitive DNA sequences, known as origin recognition boxes (ORBs). It appears that archaea have a simplified version of the eukaryotic replication apparatus, which has led to considerable interest in the

archaeal machinery as a model of that in eukaryotes. The research on replication origins is important not only in providing insights into the structure and function of the replication origins but also in understanding the regulatory mechanisms of the initiation step in DNA replication. Therefore, intensive studies have been carried out in the last two decades. The pioneer work to identify bacterial oriCs in silico is the GC-skew analysis. Later, a method of cumulative GC skew without sliding windows was proposed to give better resolution. Meanwhile, an oligomer-skew method was also proposed to predict oriC regions in bacterial genomes. As a unique representation of a DNA sequence, the Z-curve method has been proved to be an accurate and effective approach to predict bacterial and archaeal replication origins. Budding yeast origins have been predicted by Oriscan using similarity to the characterized ones, while the fission yeast origins have been identified initially from AT content calculation. In comparison with the in silico analysis, the experimental methods are time-consuming and labor-intensive, but convincing and reliable. To identify microbial replication origins in vivo or in vitro, a number of experimental methods have been used including construction of replicative oriC plasmids, microarray-based or high-throughput sequencing-based marker frequency analysis, two-dimensional gel electrophoresis analysis and replication initiation point mapping (RIP mapping). The recent genome-wide approaches to identify and characterize replication origin locations have boosted the number of mapped yeast replication origins. In addition, the availability of increasing complete microbial genomes and emerging approaches has created challenges and opportunities for identification of their replication origins in silico, as well as in vivo and in vitro.

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Sommario/riassunto	Biologically active small molecules have increasingly been applied in plant biology to dissect and understand biological systems. This is evident from the frequent use of potent and selective inhibitors of enzymes or other biological processes such as transcription, translation, or protein degradation. In contrast to animal systems, which are nurtured from drug research, the systematic development of novel bioactive small molecules as research tools for plant systems is a largely underexplored research area. This is surprising since bioactive small molecules bear great potential for generating new, powerful tools for dissecting diverse biological processes. In particular, when small molecules are integrated into genetic strategies (thereby defining "chemical genetics"), they may help to circumvent inherent problems of classical (forward) genetics. There are now clear examples of important, fundamental discoveries originating from plant chemical genetics that demonstrate the power, but not yet fully exploited potential, of this experimental approach. These include the unraveling of molecular mechanisms and critical steps in hormone signaling, activation of defense reactions and dynamic intracellular processes. The intention of this Research Topic of Frontiers in Plant Physiology is to summarize the current status of research at the interface between chemistry and biology and to identify future research challenges. The research topic covers diverse aspects of plant chemical biology, including the identification of bioactive small molecules through screening processes

from chemical libraries and natural sources, which rely on robust and quantitative high-throughput bioassays, the critical evaluation and characterization of the compound's activity (selectivity) and, ultimately, the identification of its protein target(s) and mode-of-action, which is yet the biggest challenge of all. Such well-characterized, selective chemicals are attractive tools for basic research, allowing the functional dissection of plant signaling processes, or for applied purposes, if designed for protection of crop plants from disease. New methods and data mining tools for assessing the bioactivity profile of compounds, exploring the chemical space for structure-function relationships, and comprehensive chemical fingerprinting (metabolomics) are also important strategies in plant chemical biology. In addition, there is a continuing need for diverse target-specific bioprobes that help profiling enzymatic activities or selectively label protein complexes or cellular compartments. To achieve these goals and to add suitable probes and methods to the experimental toolbox, plant biologists need to closely cooperate with synthetic chemists. The development of such tailored chemicals that beyond application in basic research can modify traits of crop plants or target specific classes of weeds or pests by collaboration of applied and academic research groups may provide a bright future for plant chemical biology. The current Research Topic covers the breadth of the field by presenting original research articles, methods papers, reviews, perspectives and opinions.