The plasmid Col E1 in Escherichia coli was found to replicate extensively when protein synthesis was inhibited by exposure of cells to chloramphenicol. During the first two to four hours there was an exponential increase in plasmid DNA while chromosomal replication was shut down. Over a period of 10 hours plasmid DNA increased from 24 to 3,000 copies per cell. [The SCI® indicates that this paper has been cited in over 1,075 publications.]

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In 1970 I joined the faculty at the University of Michigan as an assistant professor after having spent three years as a postdoctoral fellow in Don Heilnski's laboratory at the University of California, San Diego (UCSD). At UCSD I had been involved in analyses of the plasmid Col E1 in Escherichia coli and was successful in isolating a plasmid DNA-protein complex that we referred to as "relaxation complex." The supercoiled plasmid could be triggered in vitro to undergo a protein-promoted nick that resulted in a relaxation of the DNA to an open circular configuration. The complex was later shown to relate to the ability of the plasmid to be conjugatively mobilized.1, 2 We also showed that when cells were exposed to chloramphenicol (a protein synthesis inhibitor) the amount of relaxation complex remained constant while noncomplexed plasmid DNA accumulated.3

Upon moving to Michigan, I initially focused on a characterization of Col E1 replication in the presence of chloramphenicol with the idea that such a system might be useful in studying the effects of various inhibitors of DNA replication. The above-cited paper chronicles these efforts. A somewhat surprising result concerned the extent to which replication occurred under these conditions. Whereas the use of chloramphenicol shut down replication of the plasmid DNA, it actually increased the amount of unremoved RNA (used for priming), presumably because of a gradual breakdown of the RNA removal system during the lengthy inhibition of protein synthesis.4

The above-noted paper is frequently cited in connection with studies where investigators have used vectors that are related to Col E1. Many of the commonly used cloning vectors are derivatives of, or are related to, Col E1 and thus replicate extensively in the presence of chloramphenicol. Ironically, at the time the paper was submitted for publication, its value in this regard was totally unforeseen.