GENETICA POLONICA
Vol. 25 1984 No. 3

GENETIC REGULATION OF THE BACTERIOPHAGE λ DNA REPLICATION (A MINIREVIEW)[1]

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Summary. The current state of studies and perspectives of research into the control of DNA replication of bacteriophage λ and λ-plasmid are presented.

Immediately after penetration of the phage λ DNA into the cell of its bacterial host, *Escherichia coli*, the linear molecule of this double-stranded DNA becomes circular. Following the transcription/translation of the "early" viral genes, the circular DNA starts to replicate, exploiting most of the bacterial proteins, which normally take part in the replication of the host chromosome. In the development leading to the production of the phage progeny (lytic pathway), DNA replication occurs according to the Theta (circle-to-circle) mode, or the Sigma (rolling-circle) mode. Rolling-circle replication produces long concatemeric molecules which are cut and packaged into pro-heads of progeny phages. Of course, it is this type of replication that predominates late after infection. On the other hand, the Theta replication occurs early after infection. There is an inveterate belief that the parental circular DNA replicates once or twice to form daughter circles, and only later a switch to the rolling-circle replication may happen. Although the molecular mechanism of this switch is still obscure, the participation of phage *red* genes was implicated (Skalka, 1977).

The recent work by Better and Freifelder (1983) throws new light on several aspects of this process. For the first time a method was applied, by which all λ DNA molecules (circles, Theta forms and Sigma forms) could be isolated from infected cells without a selective loss. This made it possible to use electron microscopy to examine the total intracellular pool of molecules at a variety of times after infection. It appeared that responsible for the exponential accumulation of intracellular molecules is the circle-to-circle replication: it starts early and after 5-6 rounds

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[1] Paper delivered at Symposium VIII of the Polish Genetics Society (Łódź, 1983, September 14-16). Work has been supported by the Polish Academy of Sciences under Project 09.7.

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of replication, it results in about 50 circles per cell in 16th minute at 42°C, and is then turned off. The apparent doubling time is approximately 2-3 minutes. A comparison of this value to the expected replication time of one λ unit (30 seconds at 42°C) leads to the conclusion that there is a delay (of about 2 minutes) between the completion of one round of replication and the initiation of another. After 20th minute at 42°C the number of molecules is kept practically at the same level, although DNA synthesis proceeds further — it consists in the growth of the tails of 2-3 rolling circles per cell. The most important finding of the work by Better and Freifelder was that the Sigma replication is initiated at roughly the same time as in the Theta replication, indicating that the rolling-circle is not solely a late replicating form. This means that the rolling-circle replication may start from the parental circle. Contrary to the previous opinion, it was demonstrated that the initiation of rolling circles is independent of λ *red* genes. These genes (involved in the phage recombination) were only responsible for the production of oligomeric circles late in infection. It appears, therefore, that the long search for a specific phage gene product which triggers the Sigma replication remains without success.

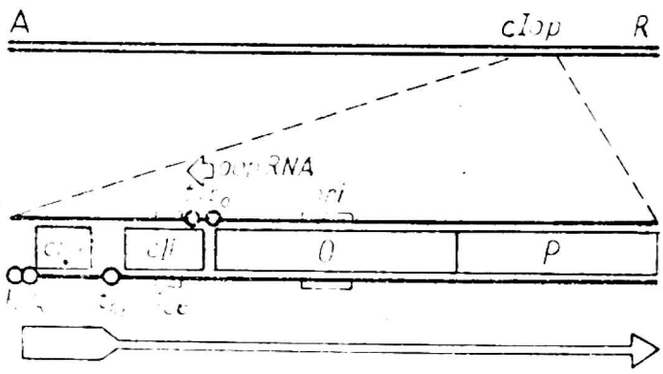

Fig. 1. Structure of the λ-phage and λ-plasmid genomes. The position and width of the structural genes *cro*, *cII*, *O*, *P*, as well as *ice* (inceptor) and *ori* (origin) sites are drawn approximately to scale. The *oop* and *cro* transcripts, starting at promoters p_o and p_R, respectively, are shown as arrows. Inefficient termination at the terminator t_{R1} is indicated by continuation of the *cro* transcript, which allows for the synthesis of the λ replication proteins, the *O*- and *P*-gene products. The operator o_R is a site of action of the repressor Cro

The region of λ DNA encompassing all genes and signals necessary for an autonomous replication and its control is called the replication region (Fig. 1). Following excision and circularization (*in vivo* or *in vitro*), this DNA fragment can replicate in the *E. coli* cell as a plasmid, called λdv or λ-plasmid (Matsubara, 1981). Here the replication seems to be restricted to the Theta mode. The bacterial cell harbours approximately 50 λ-plasmid copies which replicate on average once per cell generation. The molecular mechanism of this autoregulation (which will be presented later) seems also to account for the inhibition of the exponential circle-to-circle replication of phage λ DNA in the infected cell. Comparing a λ-phage infected cell with one harbouring the λ-plasmid, one is tempted to speculate that the very event of the

phage DNA injection and the following exponential Theta replication change the delicate balance of regulatory cellular proteins, which in turn provokes the initiation of the rolling-circle replication.

Regulation of the λ DNA replication conforms to the general rule — it occurs at the level of initiation of this process. Most of what we know of the initiation of replication of λ DNA concerns the circle-to-circle mode. It predominates early in infection, seems to be exclusive for λ-plasmids and recently has been shown to occur in *in vitro* systems.

The essential elements of the initiation of λ DNA replication are: 1) the presence of the specific nucleotide sequence, *ori*, where the bi-directional Theta replication starts, 2) the synthesis of *O*- and *P*-gene products, which supplement the set of bacterial replication proteins and 3) the still mysterious activation of *ori* due to the transcription of this site or a DNA region nearby.

Replication is initiated at a unique site of DNA called *ori* and proceeds bi-directionally. A region around 500 base pairs to the left of *ori* was cloned by Lusky and Hobom (1979 a, b) and shown to be necessary for the replication of a recombinant plasmid containing *ori* λ. This region was called *ice* and, according to the last Hobom's interpretation (1981), it may serve as a signal for the formation of the primosome involved in initiating the lagging strand synthesis. According to Hobom's hypothesis, the leading strand synthesis starts from *ori* leftwards, resulting in a temporary single-strandness of the *ice* region — at that time the primosome may be assembled. However, a recent work by Tsurimoto and Matsubara (1982, 1983) demonstrates that *ice* is dispensable in the *in vitro* system of replication of

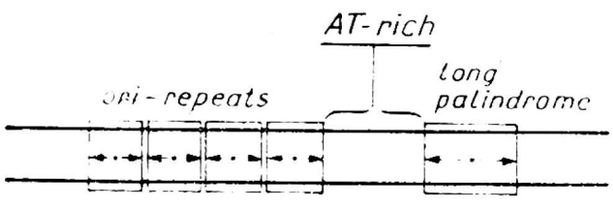

Fig. 2. Structure of the origin of λDNA replication. The "minimal *ori*" of λ plasmid DNA which functions in vitro covers four 19 base pairs repeating sequences (each revealing dyad symmetry), the *ori*-repeats, and the AT-rich segment (Tsurimoto, Matsubara 1982, 1983). *Ori*-repeats bind specifically the λ*O* protein. The nucleotide sequence of the AT-rich segment is reminiscent of that of the primase action site in the genome of phage G4 and is oriented leftwards

λ-plasmid DNA. Moreover, these authors have shown that the "long palindrome" (Fig. 2) is also dispensable in their *in vitro* system. Their "minimal *ori*" consists of only four characteristic 19 base pairs repeating sequences arranged tandemly, and an AT-rich segment. Each repeat has a region of dyad symmetry. *Ori*-repeats bind specifically one of the λ replication proteins, the *O*-gene product, recently purified to homogeneity (Tsurimoto, Matsubara, 1981). The nucleotide sequence of the AT-rich segment is reminiscent of that of the primase action site in the genome of

phage G4 and is oriented leftwards. The discrepancies of the results of two groups (headed by Hobom and Matsubara) may reflect the difference between the *in vivo* and *in vitro* conditions. It is possible that an autonomously replicating DNA carries many accessory structures that enhance or control its replication. Nevertheless, further experimental evidence to support the importance of *ice in vivo* is required.

The only phage-coded proteins taking part directly in the initiation of the replication of λ DNA are the *O*- and *P*-gene products. There is evidence from genetic studies that *ori* is the action site of O-protein. The purified O-protein protects the *ori*-repeats against Exo III and DNase I digestion (Tsurimoto, Matsubara, 1981); at a low concentration the O-protein protects only two inner *ori*-repeats. These experiments were performed, however, only with linear or circular-relaxed DNA. The ratio of added O-protein to *ori*-DNA needed in order to maximally initiate DNA replication in vitro was roughly the same as that needed for saturating the four *ori*--repeats in binding studies. If the dyad symmetry of each *ori*-repeat were responsible for dimer binding, as in the case of *cI* and Cro repressors, then the *ori* region would bind up to eight monomers.

Genetic studies (Tomizawa, 1971) and biochemical studies (Żylicz et al., 1984) suggest that the O-protein interacts with the P-protein which, in turn, is the target for action of several host proteins such as the *dnaB*-gene product. It seems, therefore, that the O-protein meets the criteria of an initiator protein: it recognizes the origin of replication and directs to this site the replication machinery of the host via the co-operating P-protein.

It has been known for a long time that the O-activity is unstable (Wyatt, Inokuchi, 1974). We (Lipińska et al., 1980), and others (Kuypers et al., 1980; Gottesman et al., 1981) have shown that this phenomenon is due to a rapid proteolytic degradation of the O-protein. It is possible, therefore, that the synthesis rate of this protein controls the initiation frequency of the Theta replication. It seems, that the O-protein is rapidly degraded only in the free form, and is much more stable when present in the DNA-protein complex. The experiments with temperature-sensitive *O*-gene product, performed by Klinkert and Klein (1978) suggest that the O-protein persists as a part of the replication complex, at least during the rolling-circle replication. It appears, therefore, that the O-protein is necessary not only for the initiation, but also for the maintenance of replication, i.e. for the fork movement. Most probably the replication complex dissociates (at least partly) after the termination of one round of Theta replication and has to be reassembled at the initiation of the next round of replication.

The suggestion that the bacterial *dnaA*-gene product performs the same function for the *ori* of the *E. coli* chromosome (*oriC*) as *λO* for the *oriλ* appears very often in the literature (Kornberg, 1982). The *dnaA*-protein seems to belong to a few bacterial replication proteins which are dispensable in λ phage DNA replication: λ grows well on *dnaAts* bacteria at 42°C. The *dnaA*-protein acts very early in the initiation of replication from *oriC*, and the purified protein binds in vitro specifically to *oriC* (Chakraborthy et al., 1982; Fuller et al., 1983). Besides, there is recent genetic

evidence that the role of *dnaA*, as in the case of *λO*, is not restricted to the initiation of replication (Walker et al., 1982; Blinkowa, Walker, 1983). However, there are several observations which contradict the functional resemblance of the *E. coli* *dnaA*-gene product to the λO protein. Sakakibara, Yuasa (1982) have found that *dna*A-protein (identified on the two-dimensional gel electrophoregrams) is stable and present in an amount exceeding that required for the initiation of chromosome replication. It is therefore unlikely that the *dna*A-protein is a regulatory factor that controls the timing of the initiation. Kellenberger-Gujer, Podhajska (1978) showed that the *P*-gene product of the λ-plasmid suppresses certain defect in the *dnaA* gene. This functional interaction could mean that the function of *dnaA* is necessary for λ-plasmid replication. Our preliminary experiments (Kur, Górska, Taylor) support this hypothesis suggesting, that *dna*A is involved in the termination of λ-plasmid replication. Assuming that the Theta mode of λ DNA replication (specific for λ-plasmids) is *dnaA*-dependent, how can we explain the well-known *dnaA*-independence of the λ phage growth? Taking into account the results of Better and Freifelder (1983), we postulate that when *dna*A activity is missing, the parental circle may initiate the rolling-circle replication which is sufficient to yield phage progeny.

Now let us turn to the λP-protein. It is regarded to as an analogue of the bacterial *dnaC*-gene product, since λP, as well as *dna*C-protein, inhibits the DNA-independent ATPase activity of the *dna*B-protein in *in vitro* assays (Wickner 1978; Klinkert, Klein 1979; Klein et al. 1980). In this context it is worth while to present the recent view on the activity of *dna*C (Nüsslein-Crystalla et al. 1982), which may be summarized as follows. The *dna*C-protein is absolutely necessary for the assembly of the primosome, a protein complex containing at least *dna*B and primase. The two primosomes functioning in the bi-directional Theta replication should be assembled at *oriC*; this function of *dna*C-protein in the initiation is revealed by the "slow-stop" phenotype of some *dnaC* mutants. The primosome travels along DNA in the direction of fork movement, priming the lagging strand synthesis (Kornberg 1982). This process does not require the action of *dna*C-protein. If, however, the primosome is damaged on the long way along the bacterial chromosome, the presence of *dna*C-protein is required again for the reassembly of the primosome. Some *dnaC* mutants revealing rather a "quick-stop" phenotype seem to reflect this function of *dna*C-protein in fork movement (elongation). By analogy, it is probable that the λP-protein is engaged in the assembly of the primosome at *ori λ*. The experiments with the temperature-sensitive *P*-gene product showed that the rolling-circle replication is *P*-independent (Klinkert, Klein 1978). It seems, therefore, that once-formed the primosome is not disassembled on its relatively short way along the λ concatemeric DNA.

There is genetic evidence that the P-protein may interact with six bacterial proteins involved in λ DNA replication, the products of genes: *dnaA* (Kellenberger-Gujer, Podhajska, 1978), *dnaB*, *dnaJ*, *dnaK* (Yochem et al., 1978), *grpD* and *grpE* (Saito, Uchida 1977) but till now the physical interaction of purified proteins has been demonstrated only for λ P-*dna*B (Klein et al. 1980) and λ P-*dna*K

(Żylicz, Georgopoulos 1983; Żylicz et al. 1983b). The recently purified *dna*K-protein is a DNA-independent ATPase and this activity is inhibited by the P-protein (Żylicz et al. 1983b). It is interesting that the purified λO stimulates the ATPase activity of the *dna*K-protein, which also indicates their physical interaction (Żylicz et al. 1983b). The physical interaction of λP-protein with other bacterial proteins, called *i*, *n*, *n'* and *n''* awaits further investigation. Recently McMacken's group (Wold et al. 1982) has demonstrated by the use of specific antisera that *n*, *n'* and possibly *i* do take part in the λ-plasmid DNA replication *in vitro*.

The origin of λ replication must be activated by transcription passing along or occurring nearby (Furth et al. 1982). This phenomenon called transcriptional activation is independent of the production of phage replication proteins. Its implication is not clear. There have been postulated transcription-induced changes in the intracellular location of *oriλ*, or in an *ori* secondary structure. The last-mentioned hypothesis is especially attractive, because the primosome assembly may occur only on the single-stranded DNA.

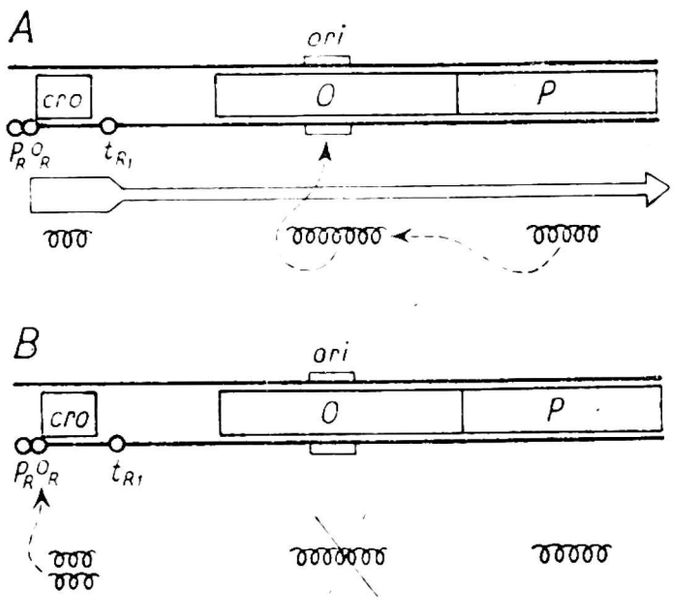

Fig. 3. Control of λ-plasmid replication

A — The rightward transcription starting at p_R simultaneously (1) activates *oriλ* and (2) provides O- and P-proteins, which results in initiation ; O-protein recognizes *oriλ* and directs to this site the replication machinery of the host via the co-operating P-protein

B — The initiation of the next round of replication cannot follow, because (1) the concentration of the repressor *Cro* attains the level at which it is blocking the operator o_R, consequently making impossible transcriptional activation of *oriλ* and the synthesis of O-protein, (2) the previously synthesized *λO* decays proteolytically

The regulation of the λ-plasmid replication (Matsubara, 1981) depends upon the rightward transcription starting from the promoter p_R (Fig. 3). This transcription plays a dual role: it activates *oriλ* and provides O- and P-proteins, which results in the initiation. There may occur one round of circle-to-circle replication, but the initiation of the next round cannot follow due to two reactions taking place in the meantime which eliminate *λO* and make impossible the activation of *oriλ*: 1) the concentration of the repressor *Cro* attains the level at which it is blocking the oper-

ator o_R, consequently making impossible the transcription of the *cro-O-P* operon, 2) λO decays proteolytically. Only when the concentration of *Cro*-repressor decreases due to cell growth, may the new round of replication start. The above-presented mechanism of regulation of the λ-plasmid DNA replication explains that the daughter cells contain roughly the same amount of λ-plasmid copies as that found in the parental cell.

It is reasonable to think that the Theta replication of the phage λ DNA is also based on the negative autoregulation of *Cro* and the lability of the initiator protein *λO*. The average number of λ-plasmid copies in a cell amounts to about 50, hence the concentration of the *Cro*-repressor is relatively high. On the other hand, in a phage-infected cell the initial concentration of *Cro* is low. This may explain the high frequency of initiation of the Theta replication occurring early in a λ-infected cell. The inhibition of the Theta replication, occurring later, may be due to a rise in *Cro* concentration, and more specifically, to a rise in the concentration of *Cro*-dimers, which varies with the square of the monomer concentration.

The role of the *Cro*-mediated inhibition of the Theta replication in the initiation of the rolling-circle replication awaits further studies and may only be the subject of speculations at present. Hobom claims that there is a second replication system in λ which is independent of the O-protein and *ori* (Lusky, Hobom, 1979a; Hobom, 1981). The main element of this "mini-system" is *ice* activated by the leftward transcription from p_0; λ mini-system is *P*-dependent. The mini-system is normally repressed by the O-protein — *ori* interaction characteristic of the "maxi-system". Herskowitz and Hagen (1980) suggest that Hobom's mini-system might be used for the rolling-circle replication and that the switch from Theta to Sigma replication could be mediated indirectly by *Cro*: the *Cro*-repressor would derepress the mini-system by eliminating the O-protein — *ori* interaction. Since the initiation of the rolling-circle replication may occur early after infection, one has to supplement the above hypothesis with the assumption that the temporary *Cro*-mediated inhibition of the Theta replication of an individual circle may occur early; this does not seem improbable, taking into account the proximity of the *cro*-gene to o_R, the target of the *Cro*-repressor. Even the modified model of Herskowitz and Hagen does not explain the absence of the rolling-circle replication of λ-plasmids, since they persist in the cell in the *Cro*-repressed form nearly all the time. Here again one has to return to the idea already presented in this article, that the processes which occur specifically in a λ-infected cell (as compared with a cell harbouring the λ-plasmid) namely λ DNA penetration and the rapid circle-to-circle replication, may indirectly take part in the switch to the rolling-cicrle replication.

The recent success in the development of *in vitro* systems for λ-plasmid DNA replication, which do not contain membranes (Anderl, Klein 1982; Wold et al. 1982; Tsurimoto, Matsubara 1982) raises doubt as to whether cell envelopes play any role in this process *in vivo*. No one has yet found a mutation affecting both the initiation of replication and the binding of *oriλ* to the membrane. There are only indirect indications as to the role of the membrane in the λ DNA replication. Previously we presented evidence suggesting that phage replication proteins, especially

the *P*-gene product, are associated with the cell membrane in λ-infected minicells (Żylicz, Taylor 1981). This was confirmed by the Matsubara group (Tsurimoto et al. 1982) who had to use 4M urea in order to extract P-protein from the membranes to start their isolation procedure. Recently, we have displayed the membrane-affinity of the *dnaJ*- and *dna*K-proteins (Żylicz et al. 1983a). If we assume that λ P and *dna*K are membrane-associated, and that both these proteins interact with the O-protein, the fact that O binds to *oriλ* suggests the possibility that the λ DNA becomes bound, at least temporarily, to the bacterial membrane. Membrane-binding of *oriλ* may present an advantage in the formation of appropriate complexes by the hydrophobic and membrane-associated replication proteins. It should be much easier for them to find each other by lateral diffusion on the two-dimensional surface of the fluid membrane rather than in the three-dimensional cytoplasm. Besides, membrane-binding may facilitate the separation of plasmid copies arising due to replication and may be crucial in the partition of plasmid copies to daughter cells. These processes may be coupled with replication.

REFERENCES

1. Anderl A., Klein A. (1982). Replication of *λdv* in vitro. Nucleic Acids Res., 10: 1733 - 1740.
2. Better M., Freifelder D. (1983). Studies on the replication of *Escherichia coli* phage λ DNA. I. The kinetics of DNA replication and requirements for the generation of rolling circles. Virology, 126: 168 - 182.
3. Blinkowa A., Walker J. R. (1983). Interactions of DNA replication factors in vivo as detected by induction of suppressor alleles of *dnaA* into other temperature-sensitive *dna* mutants. J. Bacteriol., 153: 535 - 538.
4. Chakraborty T., Yoshinaga K., Lother H., Messer W. (1982). Purification of the *E. coli dnaA* gene product. The EMBO Journal, 1: 1545 - 1549.
5. Fuller R. S., Bertsch L. L., Dixon N. E., Flynn J. E., Kaguni J. M., Low R. L., Ogawa T., Kornberg A. (1983), Enzymes in the initiation of replication at the *E. coli* chromosomal origin. In Cozzarelli N. (ed.) Mechanisms of DNA replication and recombination. UCLA Symposia on Molecular and Cellular Biology, v. 10. Alan R. Liss, Inc, New York.
6. Furth M. E., Dove W. F., Meyer B. J. (1982). Specificity determinats for bacteriophage λDNA replication. III. Activation of replication of λri^c mutants by transcription outside of *ori*. J. Mol. Biol., 154: 65 - 83.
7. Gottesman S., Gottesman M., Shaw J. E., Pearson M. L. (1981). Protein degradation in *E. coli*: the *lon* mutation and bacteriophage lambda *N* and *cII* protein stability. Cell, 24: 225 - 233.
8. Herskowitz I., Hagen D. (1980). The lysis-lysogeny decision of phage λ: explicit programming and responsiveness. Annu. Rev. Genetics, 14: 399 - 445.
9. Hobom G. (1981). Replication signals in procaryotic DNA. Curr. Top. Microbiol. Immunol., 94/95: 93 - 142.
10. Kellenberger-Gujer G., Podhajska A. J. (1978). Interactions between the plasmid *λdv* and *Escherichia coli dna*A mutants. Mol. Gen. Genet., 162: 17 - 22.
11. Klein A., Lanka E., Schuster H. (1980). Isolation of a complex between the P protein of phage λ and the *dna*B protein of *E. coli*. Eur J. Biochem., 105: 1 - 6.
12. Klinkert J., Klein A. (1978). Roles of bacteriophage lambda gene products O and P during early and late phases of the infection cycle. J. Virol., 25: 730 - 737.
13. Klinkert J., Klein A. (1979). Cloning of the replication gene *P* of bacteriophage lambda:

Effects of increased P-protein synthesis on cellular and phage DNA replication. Mol. Gen. Genet., 171: 219 - 227.

14. Kornberg A. (1982). 1982 Supplement to DNA Replication. W. H. Freeman, San Francisco.
15. Kuypers B., Reiser W., Klein A. (1980). Cloning of the replication gene *O* of *E. coli* bacteriophage lambda and its expression under the control of the *lac* promoter. Gene, 10: 195 - 203.
16. Lipińska B., Podhajska A., Taylor K. (1980). Synthesis and decay of λDNA replication proteins in minicells. Biochem. Biophys. Res. Commun., 92: 120 - 126.
17. Lusky M., Hobom G. (1979a). Inceptor and origin of DNA replication inl ambdoid coliphages. I. The λDNA minimal replication system. Gene, 6: 137 - 172.
18. Lusky M., Hobom G. (1979b). Inceptor and origin of DNA replication in lambdoid coliphages. II. The λDNA maximal replication system. Gene, 6: 173 - 197.
19. Matsubara K. (1981). Replication control system in lambda dv. Plasmid, 5: 32 - 52.
20. Nüsslein-Crystalla V., Niedenhof I., Rein R. (1982). *dnaC*-dependent reconstitution of replication forks in *Escherichia coli* lysates. J. Bacteriol., 150: 286 - 292.
21. Saito H., Uchida H. (1977). Initiation of the DNA replication of bacteriophage lambda in *Escherichia coli* K12. J. Mol. Biol., 113: 1 - 25.
22. Sakakibara Y., Yuasa S. (1982). Continuous synthesis of the *dnaA* gene product of *Escherichia coli* in the cell cycle. Mol. Gen. Genet., 186: 87 - 94.
23. Skalka A. M. (1977). DNA replication — Bacteriophage lambda. Curr. Top. Microbiol. Immunol., 78: 201 - 237.
24. Tomizawa J-I. (1971). Functional cooperation of genes *O* and *P*. In Hershey A. D. (ed.) The bacteriophage lambda, pp. 549 - 552. Cold Spring Harbor Laboratory, New York.
25. Tsurimoto T., Matsubara K. (1981). Purified bacteriophage λ O protein binds to four repeating sequences at the λ replication origin. Nucleic Acids Res., 9: 1789 - 1799.
26. Tsurimoto T., Hase T., Matsubara H., Matsubara K. (1982). Bacteriophage lambda initiators: preparation from a strain that overproduces the O and P proteins. Mol. Gen. Genet., 187: 79 - 86.
27. Tsurimoto T., Matsubara K. (1982). Replication of λdv plasmid in vitro by purified λO and P proteins. Proc. Natl. Acad. Sci. U.S., 79: 7639 - 7643.
28. Tsurimoto T., Matsubara K. (1983). Replication of bacteriophage λDNA. Cold Spring Harbor Symp. Quant. Biol. 48 (in press).
29. Walker J. R., Ramsay J. A., Haldenwang W. G. (1982). Interaction of the *Escherichia coli dna*A initiation protein with the *dnaZ* polymerization protein in vivo. Proc. Natl.Acad. Sci. U.S., 79: 3340 - 3344.
30. Wickner S. H. (1978). DNA replication proteins of *Escherichia coli* and phage λ. Cold Spring Harbor Symp. Quant. Biol., 43: 303 - 310.
31. Wold M. S., Mallory J. B., Roberts J. D., LeBowitz J. H., McMacken R. (1982) Initiation of bacteriophage λDNA replication in vitro with purified λ replication proteins. Proc. Natl. Acad. Sci. U.S., 79: 6176 - 6180.
32. Wyatt W. M., Inokuchi H. (1974). Stability of lambda *O* and *P* replication functions. Virology, 58: 313 - 315.
33. Yochem J., Uchida H., Sunshine M., Saito H., Georgopoulos C. P., Feiss M. (1978). Genetic analysis of two genes *dnaJ* and *dnaK* necessary for *Escherichia coli* and bacteriophage lambda DNA replication. Mol. Gen. Genet., 164: 9 - 14.
34. Żylicz M., Taylor K. (1981). Interaction between phage λ replication proteins, λDNA and minicell membrane. Eur. J. Biochem., 113: 303 - 309.
35. Żylicz M., Nieradko J., Taylor K. (1983a). *Escherichia coli dnaJ*- and *dnaK*-gene products: synthesis in minicells and membrane affinity. Biochem. Biophys. Res. Commun., 110: 176 - 180.
36. Żylicz M., Georgopoulos C. (1983). Properties of the purified *dnaK* gene product of

Escherichia coli. In Cozzarelli N. (ed.) Mechanisms of DNA replication and recombination, v. 10. Alan R. Liss, Inc., New York.
37. Żylicz M., LeBowitz J., McMacken R., Georgopoulos C. (1983b). The *dnaK* protein of *Escherichia coli* possesses an ATPase and autophoshorylating activity and is essential in an in vitro DNA replication system. Proc. Natl. Acad. Sci. U.S. 80: 6431 - 6435.
38. Żylicz M., Górska J., Taylor K, Georgopoulos C. (1984). Bacteriophage λ replication proteins. Formation of a mixed oligomer and binding to the origin of λ DNA. Mol. Gen. Genet. 196 : 401 - 406.

GENETYCZNA REGULACJA REPLIKACJI DNA BAKTERIOFAGA λ

Streszczenie

Przedstawiono aktualny stan badań oraz perspektywy badawcze w dziedzinie kontroli replikacji DNA bakteriofaga λ i λ-plazmidu.

ГЕНЕТИЧЕСКАЯ РЕГУЛЯЦИЯ РЕПЛИКАЦИИ ДНК БАКТЕРИОФАГА λ (МИНИРЕВЬЮ)

Резюме

В работе представлено актуальное состояние исследований и их перспективы относительно контроля репликации ДНК бактериофага λ и λ-плазмида.