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Interaction between the *min* Locus and *ftsZ*

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In *Escherichia coli*, distinct but similar minicell phenotypes resulting from mutation at the *minB* locus and increased expression of *ftsZ* suggested a possible interaction between these genes. A four- to fivefold increase in FtsZ resulting from increased gene dosage was found to suppress the lethality of *minCD* expressed from the *lac* promoter. Since increased MinCD did not affect the level of FtsZ, this suggested that MinCD may antagonize FtsZ to inhibit its cell division activity. This possibility was supported by the finding that alleles of *ftsZ* isolated as resistant to the cell division inhibitor SulA were also resistant to MinCD. Among the *ftsZ*(Rsa) alleles, two appeared to be completely resistant to MinCD as demonstrated by the lack of an effect of MinCD on cell length and a minicell phenotype observed in the absence of a significant increase in FtsZ. It was shown that SulA inhibits cell division independently of MinCD.

The formation of anucleate minicells in *Escherichia coli* can be induced by three apparently quite different mechanisms: mutation at the *minB* locus (1, 5, 11), overproduction of FtsZ (22), or interference with DNA segregation (9, 10, 19). This suggests that the cell pole is a potential division site that is normally masked but can be unmasked in a number of different ways.

The minicell mutant was isolated by Adler et al. (1), and minicell production has been shown to be due to a mutation at the *minB* locus (5). Detailed molecular analysis of the *minB* locus revealed the existence of three genes, designated *minC*, *minD*, and *minE* (6). Expression of these genes independently or in combination revealed that the products of *minC* and *minD* act in concert as an inhibitor of cell division that is topologically regulated by the *minE* gene product. At physiological levels, the MinCD inhibitor in the presence of MinE acts selectively at the poles; however, if MinCD is in excess, it can inhibit division at all sites, polar and nonpolar. The minicell phenotype caused by mutation at the *minB* locus presumably results from loss of the inhibitor function, making the polar site accessible to the division machinery. Deletion of the entire *minB* locus also results in the same phenotype, indicating that this locus is not an essential component of the septation machinery but ensures that the septation machinery is not used at the poles.

The division event that produces a minicell appears to be a product of the normal cellular division machinery and under normal growth regulation but is not properly placed (8). Examination of the cell length distribution of the minicell mutants led to a hypothesis that the polar sites compete with nonpolar sites for a limited division potential, resulting in a population of cells with an increased heterogeneous cell length (20). Increasing the level of FtsZ in the minicell mutant three- to fivefold restored the cell length distribution back to normal, demonstrating that a small increase in FtsZ can suppress this aspect of the *min* phenotype and supporting the suggestion that FtsZ is rate limiting for division (2). The increased level of FtsZ results in more division events per mass doubling, compenstating for the availability of the polar sites.

The *ftsZ* gene is thought to code for an essential component of the cell's division machinery (17). An increase in the level of FtsZ of three- to sevenfold in wild-type strains induces a minicell phenotype (22). This phenotype is quite distinct from that observed with the *min* mutant in that minicell formation is not accompanied by an increase in the average length of nucleated cells. Thus, it was suggested that the level of FtsZ regulates the frequency of cell division and that increasing the level of FtsZ can override the inhibition imposed by the *min* system at the cell poles (15, 22). Since this inhibition is now known to be due to the *minCD* gene products (6), this suggested that FtsZ and MinCD may interact.

FtsZ is the target of a cell division inhibitor, SulA, that is produced as part of the SOS response (3, 12–14). The evidence for this is largely genetic and consists of the finding that mutations that make cells refractory to SulA map in the FtsZ gene. These mutations, designated *ftsZ*(Rsa) (for resistance to SulA) appear to decrease the interaction between SulA and FtsZ (3, 13).

In this report we provide further evidence for an interaction between FtsZ and MinCD.

MATERIALS AND METHODS

Bacterial strains and media. The bacterial strains used in this investigation are listed in Table 1. LB broth (18) was used in all experiments and was supplemented with spectinomycin (25 μg/ml) for the growth of strains containing pGB2 (4) or its derivatives. To induce *minCD*, which was fused to the *lac* promoter contained on λDB173, isopropyl-β-D-thiogalactopyranoside (IPTG) was added to a final concentration of 0.5 mM. To assess the sensitivity of *lon* mutants to SOS induction, nitrofuantoin was added to a final concentration of 2.5 μg/ml (14).

Plasmids. The plasmids used in this study consist of chromosomal fragments encompassing the *ftsZ* gene cloned into pBR322 or the low-copy-number vector pGB2 (4). pZAQ contains the *ftsQ*, *ftsA*, and *ftsZ* genes on a *Pst*I-*Cla*I fragment cloned into pBR322 (22). pZAQ28 is a derivative of pZAQ containing pZAQ (*ftsZ*::Tn*5*) (16). pBS58 and pBEF0 contain the wild-type *ftsZ* gene but differ in the level of expression. pBEF0 contains the upstream *ftsA* gene and part of the *ftsQ* gene. pBS58 contains the *ftsA* gene and an additional 783 base pairs of upstream DNA that includes an intact *ftsQ* gene and results in a twofold increase in expres-

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TABLE 1. Bacterial strains

Strain	Relevant marker	Other markers	Source or reference
PB103		*dadR1 trpE61 trpA62 tna-5*	6
PB114	Δ*minB*	As for PB103, but Δ*minB*::Kan^r	6
PB114(λDB173)	Δ*minB*		6
BEF1	*lon-146*::ΔTn*10*	As for PB103	P1(SG20322) × PB103
BEF2	*lon-146*::ΔTn*10*	As for PB114	P1(SG20322) × PB114
BEF2(λDB173)			This study
W3110		Prototroph	Laboratory collection
SG20322	*lon-146*::ΔTn*10*	*cps-11*::*lac* Mu dl	3
BS101	*lon-146*::ΔTn*10*		P1(SG20322) × W3110
TKF12	*ftsA12*(Ts)	*thr leu thi pyrF thyA ilvA his arg lac tonA tsx*	17

sion of *ftsZ* over pBEF0 (2, 23). Other plasmids used containing mutant alleles of *ftsZ* are similar in construction to pBEF0 and are described in the accompanying article (3).

Determination of the level of FtsZ. The level of FtsZ in PB114(λBD173) was determined by quantitative immunoblotting as described previously (22). Samples from exponentially growing cultures that had been treated with IPTG and an untreated control were mixed with an equal volume of 10% ice-cold trichloroacetic acid. After sitting on ice for at least 15 min, the samples were pelleted in a microcentrifuge, and the pellets were washed with ice-cold acetone. The pellets were dissolved in sodium dodecyl sulfate sample buffer (62.5 mM Tris hydrochloride [pH 6.8], 2.3% sodium dodecyl sulfate, 10% glycerol, 5% β-mercaptoethanol, 0.01% bromophenol blue). Samples were heated at 100°C and then electrophoresed on 12.5% polyacrylamide gels. Proteins were transferred to nitrocellulose, and FtsZ was visualized with a rabbit polyclonal antiserum against FtsZ and goat anti-rabbit immunoglobulin G antibodies coupled to horseradish peroxidase (Immuno-Blot assay; Bio-Rad Laboratories).

Photomicroscopy. Samples from exponentially growing cultures treated with IPTG (0.5 mM) for 4 h or untreated controls were fixed with 10% formaldehyde and spotted on microscope slides covered with a thin film of 1% agarose.

RESULTS

Increased level of FtsZ can suppress lethality of increased *minCD* expression. Increasing the level of FtsZ three- to sevenfold above the physiological level is known to lead to a minicell phenotype, with the extent of minicell formation increasing with the level of FtsZ within this range (16, 22). This observation, along with the observation that MinCD acts as an inhibitor of cell division, suggested that increasing the level of FtsZ can overcome the MinCD inhibitor. pZAQ, a plasmid that is known to increase the level of FtsZ about sevenfold (22), can suppress MinCD inhibition (7). The system used to test the effect of MinCD was a strain deleted for the *minB* locus and containing *minCD* under *lac* promoter control carried on a λ transducing phage, λDB173. This strain [PB114(λDB173)] filamented in the presence of IPTG and could not form colonies on L-agar containing IPTG (efficiency of plating [EOP], 10^{-4}; Table 2). Using this system, we confirmed that pZAQ could suppress the sensitivity of this strain to IPTG and also found that pZAQ28, a derivative of pZAQ that contains a Tn*5* insertion in the *ftsZ* gene, could not suppress the IPTG sensitivity (data not shown). This latter result demonstrated that an intact *ftsZ* gene on pZAQ was necessary for suppression and that the presence of *ftsQ* and *ftsA* was not sufficient. We also observed that the level of FtsZ expressed from several different plasmids containing the *ftsZ* gene was the same in *min* strains as in a wild-type control, demonstrating that loss of the *min* locus did not affect *ftsZ* expression (2).

To determine the level of FtsZ that is required to suppress MinCD lethality, we used several plasmids that result in different levels of FtsZ production when introduced into cells. In addition to pZAQ, we used pBS58 and pBEF0, which increase the FtsZ level about four- to fivefold and threefold, respectively (2). These plasmids have a lower copy number than pZAQ, and pBEF0 has less DNA to the 5′ side of the *ftsZ* gene than pBS58, resulting in less FtsZ. Although pBEF0 had little effect on the IPTG sensitivity of PB114(λDB173), pBS58 was able to suppress it completely (Table 2). Thus, a plasmid that resulted in a four- to fivefold increase in FtsZ was sufficient to suppress MinCD lethality in this test system, whereas a plasmid that resulted in a threefold increase was unable to do so.

Induction of MinCD does not affect the level of FtsZ. Among the possible mechanisms to account for the suppression of MinCD lethality by an increased gene dosage of *ftsZ* are two that involve direct MinCD and FtsZ interaction: (i) increased MinCD could lead to a lower level of FtsZ through inhibition of expression of the *ftsZ* gene or destabilization of FtsZ, and (ii) MinCD might interact with FtsZ, antagonizing its essential cell division function. To examine the first possibility, we examined the level of FtsZ 4 h after the addition of IPTG to PB114(λDB173). At this time, all division is blocked and the cells are very filamentous. As shown in Fig. 1, we observed that MinCD had no effect on the level of FtsZ even at this late time after induction. This rules out the first of the above two possibilities.

Suppression of MinCD lethality by *ftsZ*(Rsa) mutations. Recently, a number of mutations that are located in the *ftsZ* gene and make cells refractory to the SOS-inducible cell

TABLE 2. Survival of PB114(λDB173) on IPTG plates containing plasmids with various alleles of *ftsZ*[a]

Plasmid	Relevant genotype	Relative EOP on Spc + IPTG
pGB2		1.10×10^{-4}
pBEF0	*ftsZ*$^+$	2.40×10^{-4}
pBS58	*ftsZ*$^+$	0.65
pBEF9	*ftsZ9*(Rsa)	0.89
pBEF1	*ftsZ1*(Rsa)	0.73
pBEF2	*ftsZ2*(Rsa)	0.91
pBEF3	*ftsZ3*(Rsa)	0.44
pBEF100	*ftsZ100*(Rsa)	1.00
pBEF103	*ftsZ103*(Rsa)	0.84

[a] The EOP of PB114(λDB173) containing each of the plasmids listed was determined on plates containing 0.5 mM IPTG plus 25 μg of spectinomycin (Spc) per ml.

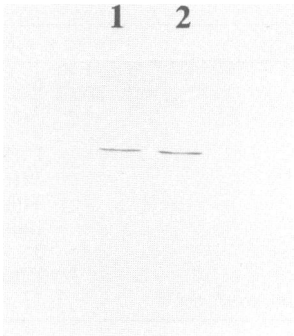

FIG. 1. Induction of MinCD does not affect the level of FtsZ. A culture of PB114(λDB173) growing exponentially in LB was split in two. To one of these cultures, IPTG was added to a final concentration of 0.5 mM. Four hours later, samples were taken from each culture and the FtsZ content was determined by immunoblotting. Lane 1, No IPTG; lane 2, with 0.5 mM IPTG.

division inhibitor SulA, designated *ftsZ*(Rsa), were isolated and sequenced (3). To obtain more direct genetic evidence that FtsZ is the target of MinCD, we examined these mutations to determine whether any of them could protect cells from induction of MinCD. Each of the *ftsZ*(Rsa) alleles was cloned onto a low-copy-number vector by using a *Bam*HI site on the 5′ side of the *ftsZ* gene within the *ftsQ* gene. Thus, each of the resultant plasmids is similar to pBEF0 and should result in the same increase in the level of FtsZ. Measurement of the survival of PB114(λDB173) in the presence of IPTG revealed that each of the *ftsZ*(Rsa) mutations suppressed the sensitivity to IPTG and overcome the lethality of MinCD induction (Table 2). To confirm that the suppression was due to the presence of an altered FtsZ and not to an increased level of FtsZ somehow brought about by the mutations, the level of FtsZ was determined by quantitative immunoblotting. The level of FtsZ was the same for each plasmid (data not shown). These results suggest that SulA and MinCD inhibit cell division through a common target, FtsZ.

Morphological examination of PB114(λDB173) cells containing the *ftsZ* plasmids following induction of *minCD*. The measurement of survival in the presence of IPTG demonstrated that all of the *ftsZ*(Rsa) mutations protected the cell from MinCD lethality. To determine whether there was any difference in resistance to MinCD between the various mutations, cell morphology was examined following *minCD* induction. As controls, we first examined cells containing the plasmids pGB2, pBEF0, and pBS58. The presence of pBEF0 had little effect, and cells were as filamentous as with the vector pGB2 (Fig. 2b and d). Cells containing pBS58, which completely protected from MinCD lethality, were somewhat filamentous, indicating that MinCD inhibition was not completely suppressed (Fig. 2f).

Examination of cells containing plasmids with the various *ftsZ*(Rsa) mutations revealed that the *ftsZ*(Rsa) mutations could be divided into two classes; one class appeared to be fully resistant, since MinCD induction had little or no effect on cell length, and a second partially resistant class, in which MinCD induction caused an intermediate filamentous phenotype. Mutations *ftsZ1*(Rsa), *ftsZ9*(Rsa), *ftsZ100*(Rsa), and *ftsZ103*(Rsa) belonged to the partially resistant class, and *ftsZ2*(Rsa) and *ftsZ3*(Rsa) belonged to the fully resistant class. Figures 2h and j contain photographs of cells containing pBEF9 [*ftsZ9*(Rsa)] and pBEF2 [*ftsZ2*(Rsa)], respectively. The morphology of cells containing pBEF9 was similar to that of cells of the somewhat filamentous phenotype observed with pBS58. Cells containing pBEF2 were slightly elongated in the absence of MinCD induction, which is thought to be the result of negative complementation by the *ftsZ2*(Rsa) allele. Following induction of MinCD, the average cell length actually appeared to decrease slightly, indicating complete resistance to MinCD.

TABLE 3. SulA inhibits cell division independently of MinCD

Strain	Relative EOP on Tet + IPTG[a]	Relative EOP on Tet + NF[b]
BEF1(*lon-146*::ΔTn*10*)	0.78	2.11×10^{-6}
BEF2(Δ*min lon-146*::ΔTn*10*)	1.13	6.64×10^{-6}
BEF2(λDB173)(Δ*min lon-146*::ΔTn*10*)	3.21×10^{-4}	3.57×10^{-5}

[a] The EOP of BEF1, BEF2, and BEF3 was determined on plates containing 0.5 mM IPTG plus 12.5 μg of tetracycline (Tet) per ml.
[b] EOP was determined on plates containing 2.5 μg of nitrofurantoin (NF) plus 12.5 μg of tetracycline (Tet) per ml.

Inhibitor SulA does not act through MinCD. Since mutations in *ftsZ* that confer resistance to SulA also confer resistance to MinCD, this raised the question of whether SulA inhibited cell division by acting through MinCD, e.g., by inhibiting *minE* or combining with MinC or MinD to form an inhibitor independent of *minE*. De Boer and Rothfield (6) have shown that the reciprocal is not true, that is, MinCD does not inhibit division by acting through SulA. To test this possibility, a *lon* mutation was introduced into the minicell mutant and the resultant strain was examined for sensitivity to the mild SOS-inducing agent nitrofuantoin. If SulA acts through MinCD, the double mutant should be resistant; but if SulA inhibits independently, then it should be sensitive. Table 3 shows that the *lon min* double mutant was as sensitive to nitrofurantoin as the *lon* mutant, indicating that SulA does not require the presence of MinCD in order to inhibit division. This indicates that the two inhibitors, SulA and MinCD, act independently but share FtsZ as a common target.

Minicell formation. Since *ftsZ2*(Rsa) and *ftsZ3*(Rsa) appeared to be quite resistant to MinCD, introduction of these alleles in single copy might be expected to yield a minicell phenotype similar to that of the minicell mutant. However, we have shown previously that the *ftsZ3*(Rsa) allele cannot support cell growth and have been unsuccessful at recombining *ftsZ2*(Rsa) from the plasmid onto the chromosome, indicating that this mutation may also affect the cell division activity of the *ftsZ* gene (3). Therefore, we assessed this possibility by examining the frequency of minicell formation in λ lysogens containing two *ftsZ* alleles. Two copies of *ftsZ* present in a λ 16-2 lysogen did not lead to detectable minicell formation (Fig. 3A). However, lysogens constructed with λBEF2 [*ftsZ2*(Rsa)] and λBEF3 [*ftsZ3*(Rsa)] produced an easily detectable level of minicells, indicating that these *ftsZ* alleles are resistant to MinCD and dominant to the wild type with respect to this phenotype (Fig. 3B; only lysogen with λBEF2 [*ftsZ2*(Rsa)] shown). Quantitative immunoblotting demonstrated that the level of FtsZ was identical in all three lysogens (data not shown), confirming that this phenotype was due to an alteration of the FtsZ protein by these mutations and not due to altered levels of FtsZ.

DISCUSSION

In this report we have examined the effect of increased FtsZ and mutant *ftsZ* alleles on the inhibition of cell division

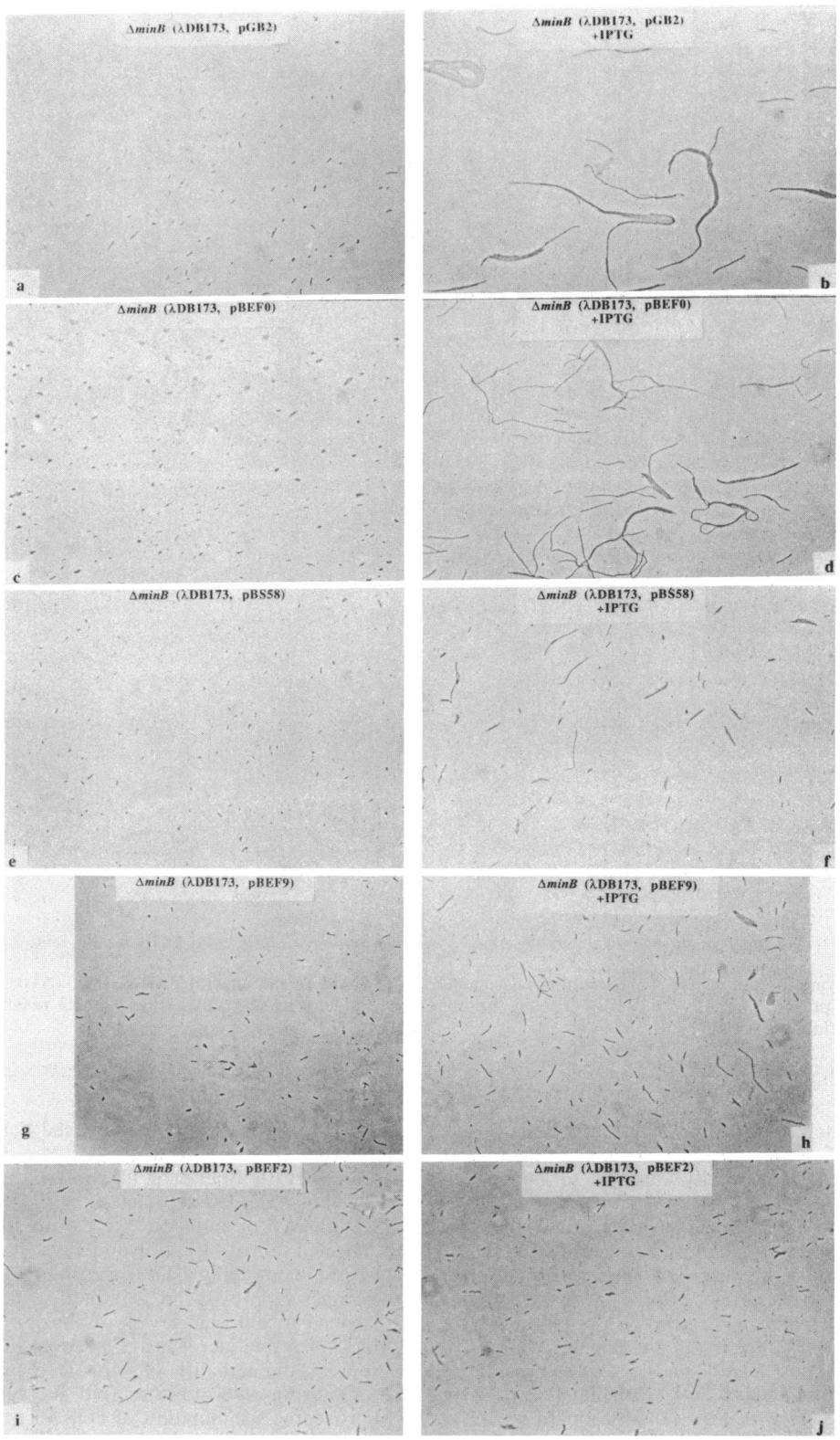

FIG. 2. Effect of alleles of *ftsZ* and FtsZ levels on MinCD induction. Exponential-phase cultures of PB114(λDB173) containing the indicated plasmids were incubated in the absence or presence of 0.5 mM IPTG for 4 h before being examined by phase-contrast microscopy. The plasmids were pGB2 (a and b), pBEF0 (c and d), pBS58 (e and f), pBEF9 (g and h), and pBEF2 (i and j). Magnification, ×200.

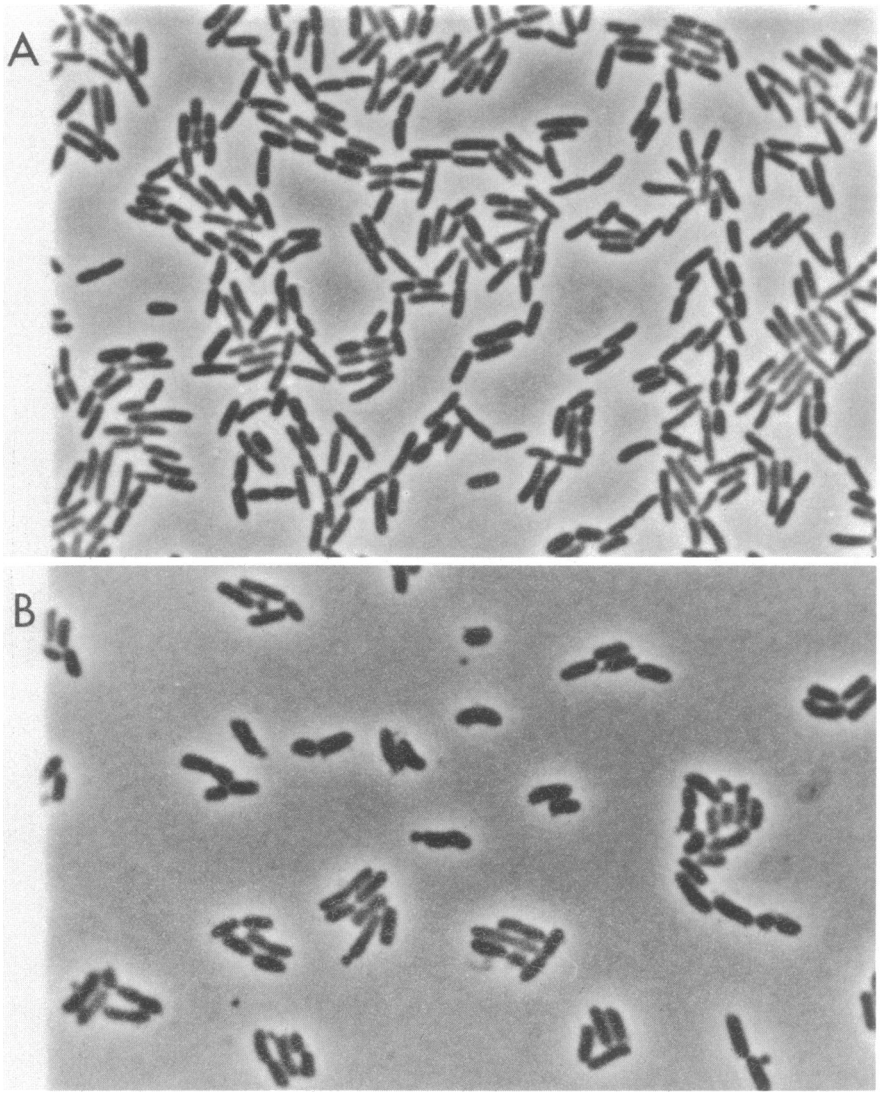

FIG. 3. Minicell formation due to *ftsZ2*. Exponential-phase cultures of TKF12 containing either λ16-2 (*ftsZ*) (A) or λBEF2 [*ftsZ2*(Rsa)] (b) were examined. The presence of λ16-2 did not result in the appearance of any minicells, whereas λBEF2 resulted in a clear minicell phenotype. Magnification, ×625.

brought about by increased levels of the inhibitor MinCD. The results of this study suggest that overproduction of MinCD may block FtsZ activity directly to inhibit cell division.

The formation of minicells occurs as the result of the polar placement of the septum and can be induced by deletion of the *min* locus or overproduction of FtsZ. Normally this eccentric location of the septum is prevented by the action of the *min* locus, which masks polar septation sites through the action of the MinCD inhibitor in the presence of MinE. This action of the *min* locus results in the division potential, which is dictated by the level of FtsZ (2), being utilized at the nascent division site (Fig. 4). Since overproduction of FtsZ results in minicell formation, this suggested that an increased level of FtsZ could overcome the MinCD inhibitor. The results of this study indicate that this is indeed the case. Since mutants altered in segregation also have a minicell phenotype, this raises the possibility that such mutants have increased FtsZ levels or decreased activity of the MinCD inhibitor.

Recently, de Boer et al. (7) showed that the plasmid pZAQ as well as a derivative deleted for *ftsQ* and *ftsA* suppressed the lethality of induced expression of *minCD*. We have confirmed this observation and have shown that a derivative of pZAQ containing a Tn*5* insertion within the *ftsZ* gene can no longer suppress MinCD lethality. Using various plasmids that lead to different levels of FtsZ, we determined that a four- to fivefold increase in FtsZ was sufficient to completely suppress the lethality of MinCD expressed from the *lac* promoter; a two- to threefold increase was insufficient. Microscopic examination of cells in the presence of IPTG revealed that although the lethality was completely suppressed by increased FtsZ, inhibition of cell division was not completely suppressed; cells containing a four- to fivefold increase in FtsZ were heterogeneous in length in the presence of induced MinCD.

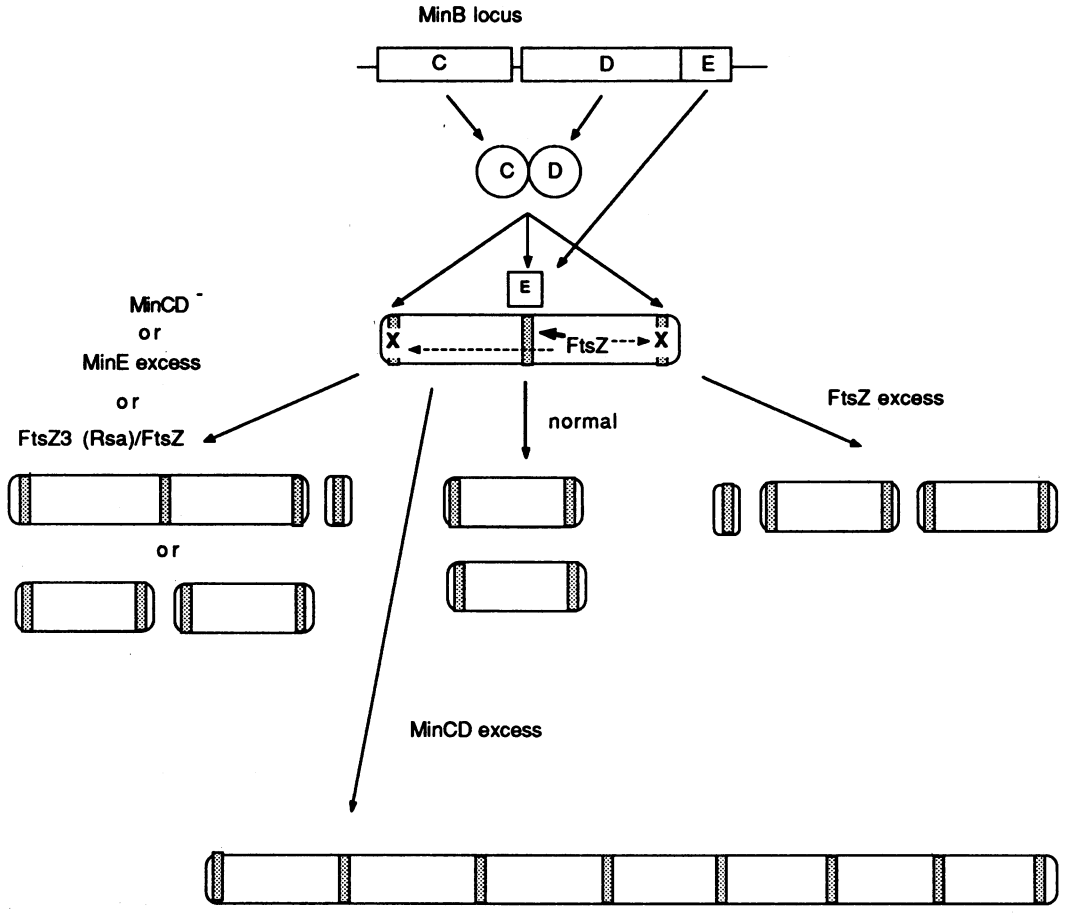

FIG. 4. Model for septation. Depicted in the center of the diagram is a cell that is ready to divide. The cell has three potential division sites; which and how many sites will be used depends on the levels of FtsZ and MinCDE. Under normal physiological conditions, division occurs at the cell center. This division is localized through the action of the *minB* locus, which specifies an inhibitor, MinCD, and an additional gene product, MinE, that causes this inhibitor to act at the cell poles. Division occurs when a critical FtsZ concentration is reached and the nascent site is ready (2, 22). Overproduction of MinCD results in inhibition of cell division at all sites, resulting in filamentation. Loss of MinCD through mutation or an excess of MinE leads to activation of the poles and the minicell phenotype (6). Minicell production is also seen with alleles of *ftsZ*, such as *ftsZ3*(Rsa), that appear to be resistant to MinCD (see Fig. 3; note that the *ftsZ3* allele requires *ftsZ* to be present). In such cases division occurs at any one of the three sites. Overproduction of FtsZ can overcome MinCDE inhibition at the poles, and this results in a minicell phenotype (22). This minicell phenotype is distinct in that more than one division event can occur per mass doubling. As shown in this study, overproduction of FtsZ can suppress the filamentation caused by overproduction of MinCD.

Our results demonstrate that MinCD does not alter the level of FtsZ, ruling out one possible mechanism for MinCD inhibition. To further explore the MinCD-FtsZ interplay, we examined *ftsZ*(Rsa) alleles that had been selected for their resistance to the SOS-inducible inhibitor SulA and for resistance to MinCD. Various *ftsZ*(Rsa) alleles present on a low-copy plasmid vector were compared with wild-type *ftsZ* on the same vector for their ability to suppress MinCD. Although the level of FtsZ was increased two- to threefold by these plasmids, that alone was not sufficient to suppress MinCD lethality. Each of the *ftsZ*(Rsa) alleles, however, was able to completely suppress MinCD lethality under these conditions. Since the level of FtsZ was identical for each of the plasmids, the suppression was due to the *ftsZ*(Rsa) mutations.

Morphological examination revealed that the *ftsZ*(Rsa) alleles could be divided into two classes, partially resistant and completely resistant. The partially resistant class was larger and included the classical *sulB* and *sfiB* alleles. The fully resistant class consisted of two recently isolated *ftsZ*(Rsa) alleles, *ftsZ2*(Rsa) and *ftsZ3*(Rsa). These two alleles also appear to be unique in that they resulted in an elongated cell length, were somewhat unstable on plasmids, suggesting a strong growth disadvantage, and did not appear to support cell growth when present in single copy, since we have been unable to construct such strains.

The complete resistance of *ftsZ2*(Rsa) and *ftsZ3*(Rsa) to MinCD is indicated by the failure of MinCD induction to increase cell length (in strains containing low-copy plasmids with these alleles, Fig. 2j) and the minicell production observed in strains that contained a second copy of these alleles on a λ transducing phage (Fig. 3B). Cells containing two copies of *ftsZ*, one allele on a λ transducing phage, did not produce detectable levels of minicells; however, if one of the copies was *ftsZ2*(Rsa) or *ftsZ3*(Rsa), but not any of the other *ftsZ*(Rsa) alleles, readily detectable levels of minicells were produced. Since the level of FtsZ is not altered among the different lysogens, the appearance of minicells must be due to the presence of the FtsZ2(Rsa) and FtsZ3(Rsa) proteins. This argues that these mutant proteins are resistant

to MinCD, allowing the division potential to be used at both polar and internal division sites. It should be noted that the phenotype observed with the *ftsZ3*(Rsa)/*ftsZ*$^+$ diploid was not the classic "*minB*" phenotype, with the increase in the average nucleated cell length. This may mean that a strain with two copies of *ftsZ* may have more division capacity than a single-copy strain. When both copies are wild type, it is not sufficient to override MinCD inhibition; however, if one copy is fully MinCD resistant, such as *ftsZ3*(Rsa), a minicell phenotype is induced without an accompanying increase in cell length.

Since *ftsZ*(Rsa) mutations, selected for their resistance to SulA, result in resistance to MinCD, it was possible that SulA might act through MinCD. We were able to show that this is not the case, since SulA is a potent inhibitor in a Δ*min* background. While this manuscript was in preparation, de Boer et al. (7) reported that SulA inhibition was independent of MinCD, and they had earlier shown that MinCD inhibition was independent of SulA. Thus, these two independent division inhibitors are both suppressed by increased FtsZ and by the same alterations within FtsZ.

The *ftsZ*(Rsa) mutations confer resistance to several inhibitors of cell division. Not only do they confer resistance to SulA and MinCD; they also confer resistance to a LacZ-FtsZ fusion protein, which is essentially an amino-terminal-truncated FtsZ (21). To explain this resistance of *ftsZ*(Rsa) mutations to multiple inhibitors, we have suggested that FtsZ may function as a multimer and that *ftsZ*(Rsa) mutations might lead to increased affinity for multimerization. The inhibitors SulA and MinCD may function to block this multimerization.

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