JOURNAL OF BACTERIOLOGY, Mar. 1993, p. 1553
0021-9193/93/051553-01$02.00/0
Copyright © 1993, American Society for Microbiology
Vol. 175, No. 5

Location of the Gene Coding for GTP Cyclohydrolase I on the Physical Map of *Escherichia coli*

HARALD RITZ, GISELA KELLER, GERALD RICHTER, GERD KATZENMEIER, AND ADELBERT BACHER*

Lehrstuhl für Organische Chemie und Biochemie, Technische Universität München, Lichtenbergstrasse 4, D-8046 Garching, Germany

GTP cyclohydrolase I (EC 3.5.4.16) catalyzes the formation of 7,8-dihydroneopterin triphosphate from GTP. In microorganisms and plants, the enzyme product serves as the first committed intermediate in the biosynthesis of tetrahydrofolate. In insects and vertebrates, it represents an intermediate in the biosynthesis of tetrahydrobiopterin.

We have cloned and sequenced the gene coding for GTP cyclohydrolase I from *Escherichia coli* (EMBL data library accession number X63910) (6, 7). The rat gene has also been cloned and sequenced (5) and shows a remarkably high degree of sequence homology with the bacterial gene (5–7). More recently, it was shown that the *mtrA* gene of *Bacillus subtilis* codes for GTP cyclohydrolase I (1).

Southern blots of genomic *E. coli* DNA with the 3.8-kb insert of plasmid pCYH (6) used as a probe suggested a location in the 45-min region of Kohara's physical map of the *E. coli* chromosome (8). This location was confirmed by Southern blot analysis of selected lambda phages from the Kohara library (Fig. 1). Moreover, these phage clones gave positive results in Western blots (immunoblots) with anti-GTP cyclohydrolase I antibodies (6).

Data derived from restriction analysis of the cloned 3.8-kb *Bam*HI fragment (6) and sequencing of the coding region (7) place the gene coding for GTP cyclohydrolase I at 2251 kb on the physical map of *E. coli*, corresponding to a genetic map position of 45.0 min. The gene is transcribed counterclockwise.

We propose tentatively that the gene coding for GTP cyclohydrolase I should be designated *folE*. The *folA* gene codes for dihydrofolate reductase (2), *folC* codes for dihydrofolate:folylpolyglutamate synthetase (3), and *folD* codes for 5,10-methylene-tetrahydrofolate dehydrogenase/5,10-methenyltetrahydrofolate cyclohydrolase (4). It should be noted that mutants deficient in GTP cyclohydrolase I have not been reported in the literature.

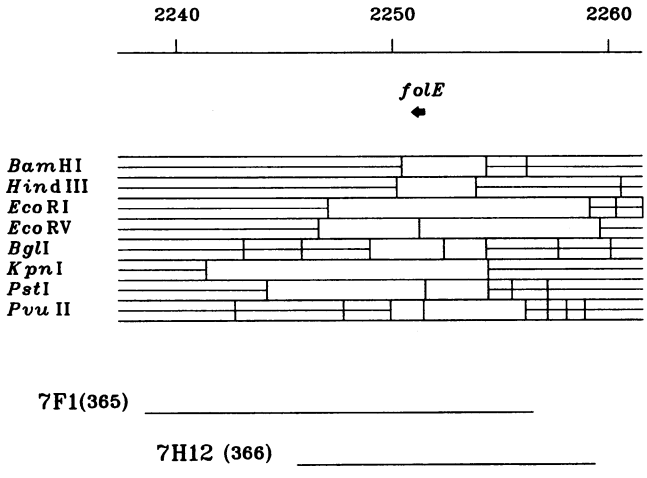

FIG. 1. Location of the *folE* gene on the physical map of *E. coli* (8). The map shown is according to the format of Kohara et al. (8), with positions (in kilobase pairs) given at the top. The open bars represent restriction fragments which have been mapped by Southern analysis using the cloned 3.8-kb *Bam*HI fragment as a hybridization probe. Below the map, the inserts of those Kohara lambda clones that were positive on test are indicated (numbers in parentheses refer to the miniset available from Y. Kohara). The position of *folE* and its transcriptional direction are indicated by the arrow above the map.

* Corresponding author.

We thank Y. Kohara, B. Ernsting, and R. Matthews for the supply of phages.

This work was supported by the Deutsche Forschungsgemeinschaft and the Fonds der Chemischen Industrie.

REFERENCES

1. **Babitzke, P., P. Gollnick, and C. Yanofsky.** 1992. The *mtrAB* operon of *Bacillus subtilis* encodes GTP cyclohydrolase I (MtrA), an enzyme involved in folic acid biosynthesis, and MtrB, a regulator of tryptophan biosynthesis. J. Bacteriol. **174**:2059–2064.
2. **Bachmann, B. J.** 1990. Linkage map of *Escherichia coli* K-12, edition 8. Microbiol. Rev. **54**:130–197.
3. **Bognar, A. L., C. Osborne, and B. Shane.** 1987. Primary structure of the *Escherichia coli folC* gene and its folylpolyglutamate synthetase-dihydrofolate synthetase product and regulation of expression by an upstream gene. J. Biol. Chem. **262**:12337–12343.
4. **Dimri, G. P., G. F.-L. Ames, L. D'Ari, and J. C. Rabinowitz.** 1991. Physical map location of the *Escherichia coli* gene encoding the bifunctional enzyme 5,10-methylene-tetrahydrofolate dehydrogenase/5,10-methenyl-tetrahydrofolate cyclohydrolase. J. Bacteriol. **173**:5251.
5. **Hatakeyama, K., Y. Inoue, T. Harada, and H. Kagamiyama.** 1991. Cloning and sequencing of cDNA encoding rat GTP cyclohydrolase I. The first enzyme of the tetrahydrobiopterin biosynthetic pathway. J. Biol. Chem. **266**:765–769.
6. **Katzenmeier, G., C. Schmid, and A. Bacher.** 1990. Cloning and expression of the putative gene coding for GTP cyclohydrolase I from *Escherichia coli*. FEMS Microbiol. Lett. **66**:231–234.
7. **Katzenmeier, G., C. Schmid, J. Kellermann, F. Lottspeich, and A. Bacher.** 1991. Sequence of GTP cyclohydrolase I from *Escherichia coli*. Biol. Chem. Hoppe-Seyler **372**:991–997.
8. **Kohara, Y., K. Akiyama, and K. Isono.** 1987. The physical map of the whole *E. coli* chromosome: application of a new strategy for rapid analysis and sorting of a large genomic library. Cell **50**:495–508.