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# Functional Homology of Chemotaxis Genes in *Escherichia coli* and *Salmonella typhimurium*

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Generally nonchemotactic mutants of *Escherichia coli* and *Salmonella typhimurium* were analyzed by interspecies complementation tests to determine the functional correspondence between the *che* genes of these two organisms. The *E. coli che* region was introduced into *Salmonella* recipients by means of a series of F-prime elements. Wild-type *che* genes of *E. coli* F'420 complemented all *che* mutants of *Salmonella* except *cheS*, *cheV*, and a subclass of *cheU*. A series of tester episomes carrying *E. coli che* mutations were then used to determine which *E. coli che* function was responsible for the complementation of each *Salmonella che* defect. By this method, the following correspondences were determined: $cheA_E$ and $cheP_S$, $cheW_E$ and $cheW_S$, $cheX_E$ and $cheR_S$, $cheY_E$ and $cheQ_S$, $cheC_E$ and $cheU_S$, $cheB_E$ and $cheX_S$, and $cheZ_E$ and $cheT_S$. (The subscripts E and S refer to *E. coli* and *S. typhimurium* genes, respectively.) In some tests, especially those involving the last two pairs of genes, poor complementation was observed between noncorresponding genes. A model explaining these observations in terms of subunit interactions is proposed.

Bacterial chemotaxis has attracted interest as a simple behavioral system which exhibits many of the properties of neuronal and hormonal systems in eucaryotes (1, 9, 10, 14, 18). For example, *Escherichia coli* and *Salmonella typhimurium*, the best-studied organisms, detect chemical stimuli by means of specific receptors that in turn transmit sensory information to the flagella to elicit motor responses. The information-processing machinery in these bacteria is capable of integrating receptor signals and of undergoing both adaptation and potentiation (16).

One of the major advantages of bacterial chemotaxis as a model sensory system is its amenability to genetic analysis. Mutants defective in chemoreception, signalling, and flagellar responses have served to dissect the path of information flow during chemotaxis, as summarized in Fig. 1. Receptor signals are funnelled through a series of signalling elements to a central processing machinery which integrates and analyzes all inputs from the sensory network and then initiates an appropriate flagellar response. Mutants defective in the central machinery are motile, but generally nonchemotactic, and have been the subject of considerable investigation in both *E. coli* and *S. typhimurium*.

In *E. coli* eight genes and in *Salmonella* nine genes that can mutate to a generally nonchemotactic phenotype have been identified (Fig. 1). In *E. coli* they are as follows: *cheA*, *cheB*, and *cheC*, first defined by Armstrong and Adler (2); *cheD*, first defined by Parkinson (12); and *cheW*, *cheX*, *cheY*, and *cheZ*, which were recently described by Silverman and Simon (18), who showed that the original *cheA* and *cheB* "genes" were actually complex loci. Work by Aswad and Koshland (3), Collins and Stocker (5), and Warrick et al. (22) with *S. typhimurium* established that there are at least nine *che* genes in that organism. The genes were designated *cheP*, *cheQ*, *cheR*, *cheS*, *cheT*, *cheU*, *cheV*, *cheW*, and *cheX* (Fig. 1).

Because *S. typhimurium* and *E. coli* each offer certain advantages in chemotaxis studies, and because their genetic similarity is of general interest, it seemed worthwhile to investigate the relationship between *che* functions in the two organisms. We therefore carried out complementation tests to establish the correspondences between *che* genes and compared these genetic data with the known biochemical and physiological properties of *che* mutants in the two organisms. In general, *che* functions in *E. coli* and *S. typhimurium* appeared to be interchangeable. However, several interesting anomalies were noted, and these are also discussed.

## MATERIALS AND METHODS

**Bacterial strains.** *S. typhimurium* and *E. coli*

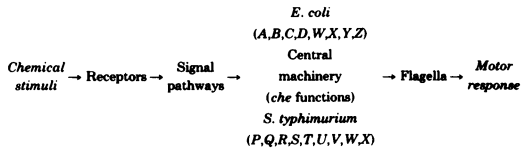


FIG. 1. *General scheme for bacterial chemotaxis in E. coli and S. typhimurium. This paper is concerned with those genes required for chemotaxis to all chemical stimuli, referred to here as the central machinery of chemotaxis. The che genes that have been identified to date are listed.*

strains and F-prime elements used in this work are listed in Table 1.

**Media.** Tryptone swarm plates contained 1.0% tryptone, 0.5% NaCl, and 0.3% agar (Difco). Vogel-Bonner citrate medium (21) was supplemented with 1% glycerol (VBC-glycerol) or 0.4% glucose (VBC-glucose). M9 glucose minimal medium (11) was used for growth of *E. coli* F′ *che* strains. Minimal media were supplemented with required amino acids (0.1 mM) and required vitamins (1 μg/ml).

**Complementation tests.** Complementation between *E. coli* and *S. typhimurium* chemotaxis mutants was determined by transferring F′ *che* episomes containing the region of the *E. coli* chromosome around 42 min (Fig. 2) into *S. typhimurium* recipients. Both donors and recipients were grown to early stationary phase at 37°C in minimal medium and spotted together on appropriately supplemented VBC-glucose plates to select for *his*$^+$ recombinants which had received F-prime elements from *E. coli*. Partial diploids formed in this way displayed a mucoid morphology, as previously reported for *E. coli* (13). After single-colony purification, these F-ductants were tested for chemotaxis on tryptone swarm plates. When negative or weak complementation was observed, the partial diploids were further analyzed by observation in a dark-field microscope after growth in VBC-glycerol at 37°C.

The F′ *che* episomes were checked after transfer into *Salmonella*, in some cases, by transferring the episomes to various *E. coli che* mutants. In all such cases the complementation behavior was exactly as expected, indicating that the F′ element had not been altered during transfer to *S. typhimurium*.

**Construction of ST335.** The transfer of F-prime elements into *Salmonella* strains required that the recipients be *his*. One strain, SL2516 (*cheV*), was *his*$^+$. The *cheV107* mutation was transduced by P22 into ST23 by cotransduction with a Tn*10* (tetracycline transposon) insertion that maps near *cheV*. This Tn*10* insertion, present in strain ST322, was isolated by M. Snyder (M. Snyder and D. E. Koshland, Jr., unpublished data). Tetracycline-resistant transductants were tested for their ability to respond to chemotactic stimuli on tryptone swarm plates. One *che* transductant, ST335, was used in these experiments.

**Nomenclature.** The nomenclature of the *che* genes in *Salmonella* and *E. coli* evolved independently, and any correspondence between genes designated by the same letter in the two species is totally coincidental. For clarity we therefore use a subscript E to indicate *E. coli* genes and a subscript S for *S. typhimurium* genes. Some further suggestions with regard to nomenclature are made below.

## RESULTS

**Correspondence of *E. coli* and *S. typhimurium che* genes.** With the exception of *cheD*, which maps at 99 min, all of the *E. coli che* genes are located between 41 and 43 min, near the *his* locus (Fig. 2). Most of the *che* genes in *S. typhimurium* also map near the *his* locus (22). Various F-prime elements carrying the major chemotaxis region of *E. coli* were transferred to recipient *che* mutants of *S. typhimurium* to establish the functional relationship between the genes for chemotaxis in the two organisms. F′420, which carries wild-type chemotaxis genes

TABLE 1. *Bacterial strains*

| Strain | Genotype | Reference |
|---|---|---|
| *S. typhimurium* | | |
| ST23 | *thyA1981 hisF8786* | 22 |
| ST36 | *cheR$_S$57 recA1 hisF8786* | 22 |
| ST56 | *cheW$_S$227 recA1 hisF8786* | 22 |
| ST171 | *cheT$_S$221 thyA1981 hisF8786* | 22 |
| ST172 | *cheP$_S$51 recA1 hisF8786* | 22 |
| ST176 | *cheQ$_S$62 recA1 hisF8786* | 22 |
| SL4041 | *cheX$_S$111 trpA8 hisC527* | 5 |
| ST108 | *cheS$_S$58 thyA1981 hisF8786* | 22 |
| ST120 | *cheU$_S$70 thyA1981 hisF8786* | 22 |
| ST134 | *cheU$_S$84 thyA1981 hisF8786* | 22 |
| ST203 | *cheU$_S$303 thyA1981 hisF8786* | 22 |
| ST213 | *cheU$_S$313 thyA1981 hisF8786* | 22 |
| SL2516 | *cheV$_S$107 (his$^+$)* | 5 |
| ST335 | *cheV$_S$107 thyA1981 hisF8786* | This paper |
| *E. coli* | | |
| RP120 | *recA aroD his pro* | 13 |
| F-prime elements (in RP120) | | |
| F′410 | See Fig. 2 | 13 |
| F′420 | See Fig. 2 | 13 |

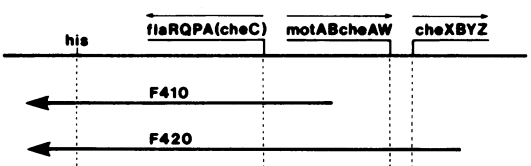


FIG. 2. *Genetic map of the major chemotaxis and flagellar region of E. coli (4), showing the location of che genes and the genetic content of the F-prime elements used in this work. Distances are shown approximately to scale.*

of *E. coli* (Fig. 2), complemented *S. typhimurium* mutants in seven different genes (*cheP*$_S$, *cheQ*$_S$, *cheR*$_S$, *cheT*$_S$, *cheU*$_S$, *cheW*$_S$, and *cheX*$_S$) (Tables 2 and 3). It did not complement *cheS*$_S$ or *cheV*$_S$ (Table 3). Since the *E. coli* wild-type *che* gene functions are able to correct most *S. typhimurium che* defects, the two systems appear to have considerable functional homology. However, unlike *E. coli* × *E. coli* crosses, we observed no formation of wild-type recombinants in these tests (data not shown), indicating insufficient base sequence homology for genetic exchanges in the *che* region. This fact enabled us to examine complementation between *E. coli* and *S. typhimurium che* mutants in an unambiguous manner since wild-type recombinants could not obscure the results.

A series of F'420 derivatives carrying various *che* alleles from *E. coli* were transferred to *S. typhimurium che* mutants, and the resulting merodiploids were tested for chemotaxis on tryptone swarm agar (Table 2). In most cases, clear complementation was observed, indicating that the functional defect of the F-prime element was different from that of the recipient. However, some mutant combinations failed to complement, which implies that the donor and recipient were both defective in the same chemotaxis function. Each of these combinations is discussed below.

***cheA*$_E$ × *cheP*$_S$ and *cheW*$_E$ × *cheW*$_S$.** The *cheP*$_S$ recipient was complemented by all F' testers except those bearing *cheA*$_E$ mutations; conversely, the F' *cheA*$_E$ testers complemented all but the *cheP*$_S$ recipient (Table 2). These results indicate that *cheA*$_E$ and *cheP*$_S$ mutants have the same functional defect. Several other observations are also consistent with this conclusion. First, both *cheA*$_E$ and *cheP*$_S$ strains have similar mutant phenotypes: they are unable to tumble and cannot respond to any type of chemotactic stimulus. Second, the *cheA*$_E$ locus has the largest mutational target size of any *che* gene in *E. coli* (15), and similarly, *cheP*$_S$ mutants are by far the most frequent class of *che* isolate in *S. typhimurium* (22). (Although the factors influencing mutational target size are not well understood, it is interesting that this property of these two homologous genes has been conserved.)

The data in Table 2 also indicate that the *cheW* functions of *E. coli* and *S. typhimurium* are homologous. Strains with these mutations, like those with *cheA*$_E$ and *cheP*$_S$, cannot tumble or respond to chemotactic stimuli.

***cheX*$_E$ and *cheY*$_E$ × *cheR*$_S$ and *cheQ*$_S$.** The data in Table 2 indicate that *cheX*$_E$ may correspond to *cheR*$_S$ and that *cheY*$_E$ may correspond to *cheQ*$_S$ since these mutant combinations never exhibited any complementation for chemotaxis. In *E. coli* certain pairs of *cheX*$_E$ and *cheY*$_E$ mutants complement rather poorly, even though the individual mutations are clearly in different genes and are recessive to wild type (14). Similar effects were observed in the interspecies tests (Table 2): *cheX*$_E$ and *cheQ*$_S$ complemented rather poorly, as did *cheY*$_E$ and *cheR*$_S$. This behavior may be due to interaction of the *cheX*$_E$ (*cheR*$_S$) and *cheY*$_E$ (*cheQ*$_S$) gene products, a possibility which is considered in more detail below. In any event, gene correspondences based on the complementation data alone must be

TABLE 3. *Complementation of cheU*$_S$, *cheV*$_S$, *and cheS*$_S$ *mutants with E. coli F' episomes*

| Recipient | Complementation with:[a] | | | |
|---|---|---|---|---|
| | F'420 | F'410 | F'410 *cheC497* | F'410 *flaA371* |
| *cheU*$_S$ (tumbly) | | | | |
| ST120 | + | + | + | − |
| ST134 | ND | + | ± | ± |
| *cheU*$_S$ (smooth swimming) | | | | |
| ST203 | ND | 0 | 0 | 0 |
| ST213 | ND | 0 | 0 | 0 |
| *cheV*$_S$ | | | | |
| ST335 | 0 | 0 | 0 | 0 |
| *cheS*$_S$ | | | | |
| ST108 | 0 | 0 | 0 | 0 |

[a] For explanation of symbols, see Table 2, footnote *a*. ND, Not done.

TABLE 2. *Complementation of Salmonella che mutants with E. coli F-prime elements*

| *S. typhimurium* recipient | | Complementation with *che* allele of *E. coli* F' tester:[a] | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Strain | *che* allele | *che*$^+$ | *A*$_E$*114* | *A*$_E$*115* | *W*$_E$*113* | *X*$_E$*202* | *X*$_E$*203* | *Y*$_E$*201* | *Y*$_E$*219* | *Y*$_E$*220* | *B*$_E$*274* | *B*$_E$*275* | *Z*$_E$*280* | *Z*$_E$*281* |
| ST172 | *P*$_S$*51* | + | 0 | 0 | + | + | + | + | + | + | + | + | + | + |
| ST56 | *W*$_S$*227* | + | + | + | 0 | + | + | + | + | + | + | + | + | + |
| ST36 | *R*$_S$*57* | + | + | + | + | 0 | 0 | ± | 0 | ± | + | + | + | + |
| ST176 | *Q*$_S$*62* | + | + | + | + | ∓ | ± | 0 | 0 | 0 | + | + | + | + |
| SL4041 | *X*$_S$*111* | + | + | + | + | + | + | + | + | + | ∓ | 0 | 0 | ± |
| ST171 | *T*$_S$*221* | + | + | + | + | + | + | + | + | + | 0 | ∓ | ∓ | 0 |

[a] Symbols: +, complementation; ±, weak complementation; ∓, very weak complementation; 0, no detectable complementation.

considered as tentative in this case, since mutants believed to be defective in different genes showed only partial complementation.

A number of the crosses were checked for complementation in another way. Since the ability to tumble and the ability to modulate tumbling frequency in response to stimuli are basic features of chemotactic behavior, it seemed reasonable to examine the swimming pattern of *cheR*$_S$/F′ *cheX*$_E$ and *cheR*$_S$/F′ *cheY*$_E$ merodiploids. No tumbling was seen in the former strains, whereas two of four F′ *cheY*$_E$/*cheR*$_S$ strains did exhibit spontaneous tumbling behavior while swimming, indicating that *cheY*$_E$ and *cheR*$_S$ mutants are not defective in the same chemotaxis function (data not shown).

Other lines of evidence indicate that these assignments are correct. For example, *cheY*$_E$ mutants are the second most frequent type of *che* isolate in *E. coli* (15), which is also true for *cheQ*$_S$ mutants of *S. typhimurium* (22). Thus, *cheY*$_E$ and *cheQ*$_S$ have similar mutational target sizes relative to other *che* genes in the two organisms. Moreover, both mutant types are unable to tumble or to respond to chemotactic stimuli. Mutants defective in *cheX*$_E$ or *cheR*$_S$ function also lack spontaneous tumbling behavior, but, unlike *cheY*$_E$ and *cheQ*$_S$, they can be induced to tumble by certain types of stimuli (22). Both *cheR*$_S$ and *cheX*$_E$ mutants have been found to be defective in a methyltransferase activity that somehow controls tumbling frequency (19).

***cheB*$_E$ and *cheZ*$_E$ × *cheX*$_S$ and *cheT*$_S$.** These four classes of mutants tumble constantly and generally complement well with all of the nontumbling mutants discussed above (Table 2). Although none of the tumbly mutants we studied were dominant, *cheB*$_E$ and *cheZ*$_E$ complemented *cheX*$_S$ and *cheT*$_S$ poorly in all combinations (Table 2). This result was also confirmed by examining the swimming patterns of the various merodiploids (Table 4). These complementation tests were also performed with three newly isolated *cheT*$_S$ mutants (obtained from B. Taylor, Loma Linda University) as recipients, with similarly equivocal results.

Since *cheX*$_S$ and *cheT*$_S$ mutants of *Salmonella* are complemented by the wild-type F-prime element from *E. coli* and by other F-prime elements that furnish wild-type alleles of both the *cheB*$_E$ and *cheZ*$_E$ genes, it seemed possible that the *cheB*$_E$ and *cheZ*$_E$ gene products were functioning as a complex and that this complex was compatible with the rest of the *Salmonella* chemotaxis machinery, whereas the individual subunits were interacting in a species-specific manner and were not readily interchangeable. This model suggests that formation of a functional hybrid complex containing subunits from both species might be facilitated by using a mutation that leads to complete loss of the polypeptide product as opposed to one that leads to production of an altered, nonfunctional subunit. To accomplish this, complementation tests were carried out with an *E. coli* F-prime element that carried a polar mutation in *cheY*$_E$. This mutation should prevent synthesis of any product of the *cheZ*$_E$ gene and should leave *cheB*$_E$ expression unaffected. We reasoned that in the complete absence of *cheZ*$_E$ product, the *cheB*$_E$ subunit might be able to interact with the appropriate *Salmonella* subunit and restore a measurable degree of chemotaxis. The results of this test are summarized in Table 5 and demonstrate that complementation occurred with *cheX*$_S$ recipients but not with *cheT*$_S$ recipients, suggesting that *cheB*$_E$ corresponds to *cheX*$_S$ and *cheZ*$_E$ corresponds to *cheT*$_S$.

These conclusions are consistent with the phenotypic properties of the mutants (Table 6). In these mutants, as in the wild type, tumbling can be transiently suppressed by large temporal increases in attractant concentration. The wild-type responses are longer, indicating that the tumbly strains are partially defective in their response to attractant stimuli. In general, *cheB*$_E$ mutants respond better to serine than to aspartate, whereas *cheZ*$_E$ mutants respond better to aspartate than to serine (Table 6). These re-

TABLE 4. *Swimming behavior of cheT*$_S$ *and cheX*$_S$ *mutants containing F′cheB*$_E$ *and F′cheZ*$_E$ *episomes*

| *che* allele on F-prime element | Behavior with the following *che* allele in recipient | |
|---|---|---|
| | *cheX*$_S$*111* | *cheT*$_S$*221* |
| *cheB*$_E$*274* | Similar to wild type | Tumbly, with occasional swimming |
| *cheB*$_E$*275* | Tumbly, with occasional swimming | Tumbly, with occasional swimming |
| *cheZ*$_E$*280* | Similar to wild type | Tumbly, with occasional swimming |
| *cheZ*$_E$*281* | Tumbly, with occasional swimming | Tumbly, with occasional swimming |

TABLE 5. *Complementation of E. coli and S. typhimurium che mutants with F′cheY*$_E$*200 (polar)*

| *E. coli* | | *S. typhimurium* | |
|---|---|---|---|
| Mutant | Complementation[a] | Mutant | Complementation |
| *cheB*$_E$ | + | *cheX*$_S$ | ± |
| *cheY*$_E$ | 0 | *cheQ*$_S$ | 0 |
| *cheZ*$_E$ | 0 | *cheT*$_S$ | 0 |

[a] For explanation of symbols, see Table 2, footnote *a*.

TABLE 6. *Phenotypes of tumbly mutants*

| Property | *Salmonella* | | *E. coli* | | Reference |
|---|---|---|---|---|---|
| | *cheX*$_S$ | *cheT*$_S$ | *cheB*$_E$ | *cheZ*$_E$ | |
| Swimming behavior | Tumbly | Tumbly | Tumbly | Tumbly | 13, 22 |
| Responses to aspartate and serine (relative to wild type) | Ser > Asp (1/1)[a] | Asp > Ser (4/4) | Ser > Asp (3/4) | Asp > Ser (5/6) | 13[b, c] |
| Response to multiple stimuli | Potentiation | Additivity | Potentiation | Additivity | 16[c] |
| Level of in vivo methylation | 49%[d] | 71% | 10% | 50% | 14, 19 |
| Methylesterase activity in vitro | 1%, 3%[d] | 1%, 47% | 8% | 92% | 20 |

[a] Numbers in parentheses indicate number of mutants that have this phenotype/total number of mutants examined.

[b] Information also obtained from R. D. Jaecks and B. L. Taylor (personal communication).

[c] Information also obtained from B. Rubik and D. E. Koshland, Jr. (unpublished observations).

[d] Percentage of wild-type level.

sponses have now been examined in the corresponding *S. typhimurium* mutants, with similar findings: *cheX*$_S$ behaves like *cheB*$_E$ and *cheT*$_S$ behaves like *cheZ*$_E$. Although there is only one *cheX*$_S$ mutant, four *cheT*$_S$ strains are available, and all four, like *cheZ*$_E$, are more defective in their response to serine than to aspartate (R. D. Jaecks and B. L. Taylor, personal communication). Rubik and Koshland (16) have also shown that *cheB*$_E$ and *cheX*$_S$ mutants undergo response potentiation. Potentiation is seen when two simultaneous stimuli produce a significantly longer response than is expected from the sum of the individual response times. Wild-type strains and *cheT*$_S$ and *cheZ*$_E$ mutants exhibit essentially additive response times to simultaneous stimuli.

***cheC*$_E$ and *cheD*$_E$ × *cheS*$_S$, *cheV*$_S$, and *cheU*$_S$.** Several *che* loci, *cheU*$_S$ and *cheV*$_S$ in *Salmonella* (5, 22) and *cheC*$_E$ in *E. coli* (17), appear to coincide with *fla* genes. This has been interpreted to mean that the products of these genes are essential components of the basal body structure of the flagellum. According to this model, loss or gross mutational alteration of these gene products prevents formation of flagella. However, some mutations in these genes alter the protein such that functional flagella can be formed, but chemotaxis is prevented. This would occur, for example, if the altered protein allowed flagellar rotation in only one direction or if the flagellar basal bodies in such mutants were defective in their ability to receive or respond to the chemotactic signals which determine the direction of rotation of the flagellum. The latter explanation appears to be most consistent with the properties of *cheU*$_S$ mutants of *Salmonella* (7, 14) and *cheC*$_E$ mutants of *E. coli* (12, 15a).

There is reason to believe that *cheC*$_E$ may be the *E. coli* gene that corresponds to *cheU*$_S$. The map positions of the *cheU*$_S$ (*flaQ*) gene (5, 22) and the *cheC*$_E$ (*flaA*) gene (17) are very similar (6). Furthermore, both can yield two sorts of nonchemotactic mutants characterized by very low or very high tumbling rates, respectively.

To test whether *cheU*$_S$ and *cheC*$_E$ are corresponding genes, various F′ episomes from *E. coli* were transferred into one *cheV*$_S$, one *cheS*$_S$, and four different *cheU*$_S$ mutants (Table 3). The *cheU*$_S$ mutants that have a tumbly phenotype were complemented by F′420 and F′410. The F′410*cheC* tester complemented these two mutants only partially, and the F′410*flaA* tester did not complement them at all (Table 3), indicating that *cheC*$_E$ (*flaA*) and *cheU*$_S$ mutants are most likely defective in homologous chemotaxis functions.

*cheV*$_S$, *cheS*$_S$, and *cheU*$_S$ mutants with low tumbling frequencies were not complemented by either F′420 or F′410 (Table 3). F′410 carries many of the same genes that F′420 carries, including *cheC*$_E$. It does not, however, carry the main cluster of *che* genes (near *motB*; Fig. 2). The lack of complementation may be due to dominance by the mutant alleles of *cheU*$_S$, *cheS*$_S$, and *cheV*$_S$, as seen previously in abortive transduction complementation (22; DeFranco and Koshland, unpublished data). Alternatively, the F-prime elements may not carry the corresponding *E. coli* gene(s), or these particular functions may not be interchangeable in the two species. Since the *cheS*$_S$ gene has not been mapped and could lie elsewhere in the genome,

this may explain the failure of F'410 and F'420 to complement *cheS*$_S$. The gene corresponding to *cheV*$_S$, on the other hand, is probably carried by F'410. *cheV*$_S$ maps in the *flaAII* gene (5), and it is known that this gene corresponds to *flaC* in *E. coli* (6), which maps near *cheC*$_E$. Thus, lack of complementation of *cheV*$_S$ by F'410 or F'420 is probably due to dominance by *cheV*$_S$.

The *cheD*$_E$ mutants appear to have defects in the *tsr* gene in *E. coli* (12), a locus involved in chemotactic responses to serine, alanine, and some repellents. These mutants are dominent in complementation tests and often revert to a Tsr$^-$ phenotype (Parkinson, manuscript in preparation). A number of revertants of *cheS*$_S$ were examined for the Tsr$^-$ phenotype but all were Tsr$^+$ (data not shown), suggesting that *cheD*$_E$ and *cheS*$_S$ mutants are different. Thus, it seems likely that neither mutants in *Salmonella* similar to *cheD*$_E$ nor mutants in *E. coli* similar to *cheV*$_S$ or *cheS*$_S$ have been isolated yet.

## DISCUSSION

The correspondences between *che* functions in *E. coli* and *S. typhimurium* have been established through interspecies complementation tests and comparisons of mutant phenotypes. Our findings are summarized in Fig. 3, which depicts the *E. coli che* genes in their correct map order with each *che* gene of *S. typhimurium* directly below the corresponding *E. coli* gene. In some cases, complementation tests provided strong evidence in favor of the conclusions presented here (for example, the correspondence of *cheP*$_S$ and *cheA*$_E$). In other cases, two different correspondences could not be ruled out entirely by the complementation data. For example, *cheR*$_S$ was clearly different from *cheA*$_E$, *cheW*$_E$, *cheB*$_E$, and *cheZ*$_E$ because it was complemented well by F-prime elements carrying mutations in those genes. But it was not complemented well by some alleles of both *cheX*$_E$ and *cheY*$_E$. Complementation studies with a number of different alleles showed that, although *cheR*$_S$ and *cheX*$_E$ never complemented each other, and neither did *cheQ*$_S$ and *cheY*$_E$, some combinations of *cheR*$_S$ and *cheY*$_E$ alleles did result in detectable complementation, as did some combinations of *cheQ*$_S$ and *cheX*$_E$. The most likely conclusion from these results is that *cheR*$_S$ is homologous to *cheX*$_E$ and *cheQ*$_S$ is homologous to *cheY*$_E$. One explanation for the lack of complementation between strains with mutations in nonhomologous genes is given below.

| *E. coli* | *Z* | *Y* | *B* | *X* | *W* | *A* | | *C* (*flaA*) | | *D* (*tsr*) |
|---|---|---|---|---|---|---|---|---|---|---|
| *Salmonella* | *T* | *Q* | *X* | *R* | *W* | *P* | *V* (*flaAII*) | *U* (*flaQ*) | *S* | |

FIG. 3. *Correspondence of the genes for chemotaxis in S. typhimurium and E. coli. The che genes are listed according to the map order in E. coli, with each Salmonella gene directly below the corresponding E. coli gene.*

The correspondence between the four genes that result in tumbly behavior was more difficult to determine. The main piece of genetic evidence in favor of the assignments indicated in Fig. 3 is that a polar mutation in *cheY*$_E$ complements *cheX*$_S$ and not *cheT*$_S$, a result that would be expected by the homologies indicated. A second indication that the postulated homologies are correct is obtained from analysis of the behavior of these mutants. Particularly striking are the differences in their responses to multiple stimuli; *cheB*$_E$ and *cheX*$_S$ mutants display response potentiation (extremely long responses to multiple stimuli), whereas *cheZ*$_E$ and *cheT*$_S$ mutants have essentially additive responses to two stimuli added at the same time. Thus, although the evidence clearly favors *cheB*$_E$ and *cheX*$_S$ as well as *cheZ*$_E$ and *cheT*$_S$ as being homologous, the alternative possibility for correspondence of these four genes is not entirely excluded.

**Nomenclature suggestions.** Studies of the genetic and biochemical properties of the *che* genes are proceeding in both *E. coli* and *S. typhimurium*. The functional homology of the *che* genes of these two organisms, as demonstrated in this paper, means that results obtained in one organism can be compared with results in the other. At present, the ability to compare results is hindered by the confusing nomenclature.

Because the true function of all of the *che* genes has not yet been elucidated, it seems unnecessarily complicated to rename all the genes with a common system at this point. It seems that a gradual approach to a more rational nomenclature is needed, and we suggest the following.

(i) Wherever ambiguity is to be avoided or emphasis is needed, the subscript E or S should be used to designate the origin of the gene.

(ii) For new genes in one species which are shown to correspond to existing genes in the other species, the letter already utilized should be kept. Thus, a gene in *E. coli* which corresponds to *cheS* in *Salmonella* should (when discovered) be called *cheS*.

**Effects of gene product interactions on complementation patterns.** In *E. coli*, poor complementation has been observed between certain combinations of *cheX*$_E$ and *cheY*$_E$ mutations and between some *cheB*$_E$ and *cheZ*$_E$ mu-

tations (14). Although these four genes are cotranscribed, polarity effects cannot be responsible for these phenomena because only specific combinations of mutant alleles fail to complement and, moreover, *cheX*$_E$ and *cheY*$_E$ always complement *cheB*$_E$ and *cheZ*$_E$. There are several ways in which apparently nonpolar, recessive mutations in different genes could fail to complement, providing that the products of the two genes interact in some fashion, presumably through direct protein-protein contacts. The data on *cheX*$_E$ × *cheY*$_E$ and *cheB*$_E$ × *cheZ*$_E$ are most consistent with a dominant complex model in which altered subunits synthesized by the two mutant genes associate to form an aberrant complex that inhibits or masks the activity of the wild-type product complexes, perhaps by competing for substrate or by blocking binding sites (Fig. 4a). This model correctly predicts that poor complementation should be allele specific since many combinations of mutant subunits would not be expected to interact in this way. Moreover, null defects in one of the mutant genes should not lead to poor complementation because no aberrant product would be made. This prediction has been confirmed by examining the complementation properties of polar mutations. For example, polar defects in *cheY*$_E$, which prevent *cheZ*$_E$ expression, complement fully with all *cheB*$_E$ mutants. Similarly, polar mutations in either *cheY*$_E$ or *cheB*$_E$, which abolish *cheY*$_E$ expression, fully complement all *cheX*$_E$ mutants (Parkinson, unpublished data).

It seems reasonable to suppose that similar interactions take place among the corresponding *che* gene products of *S. typhimurium*, and, in fact, Stock and Koshland (20) have obtained biochemical data in support of one such interaction. They were able to assay an enzyme that removes the methyl group from the "methyl-accepting chemotaxis protein" (8). This protein methylesterase activity was absent in *cheB*$_E$ strains but present in *cheZ*$_E$ strains (Table 5). This activity was also lacking in *cheX*$_S$ strains and in a *cheT*$_S$ point mutant. A *cheQ*$_S$-*cheT*$_S$ mutant (probably a polar mutant), however, had about one-half the wild-type level of this enzyme. From these data, the authors concluded that *cheB*$_E$ in *E. coli* and *cheX*$_S$ in *Salmonella* are probably the genes coding for the methylesterase and that the *cheZ*$_E$ and *cheT*$_S$ gene products may interact with the enzyme in some manner to regulate its activity.

Formation of product complexes could account for some of the anomalies we encountered in using *E. coli* F-prime elements to correct chemotaxis defects in *Salmonella*. For example, *E. coli* mutants defective in either *cheB*$_E$ or *cheZ*$_E$ function failed to complement both *cheX*$_S$ and *cheT*$_S$ mutants of *Salmonella*. Similarly, *cheX*$_E$ and *cheY*$_E$ mutants of *E. coli* did not complement *cheR*$_S$ and *cheQ*$_S$ strains of *Sal-*

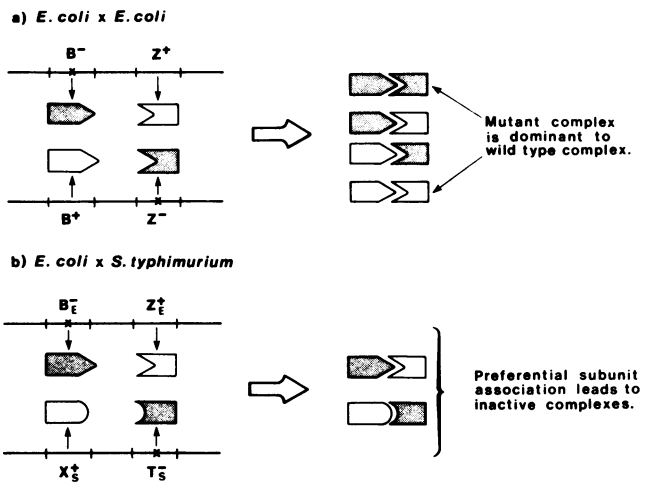


FIG. 4. *Subunit interaction models for explaining weak complementation of noncorresponding genes. It is proposed that the products of the cheB*$_E$ *(cheX*$_S$*) gene and the cheZ*$_E$ *(cheT*$_S$*) gene interact to form a functionally active protein. (a) Weak complementation in E. coli × E. coli heterozygotes is believed to result from dominance of a mutant complex. This only occurs with specific allele pairs. (b) In E. coli × Salmonella heterozygotes, weak complementation is more prevalent and could be due to species-specific association of subunits. Since it was possible to obtain functional interaction of E. coli and S. typhimurium subunits by using a polar cheY*$_E$ *mutation to eliminate cheZ*$_E$ *expression completely, poor complementation is evidently dependent on the presence of mutant (presumably missense) gene products.*

*monella.* These instances of poor complementation could be due to formation of dominant complexes comparable to those thought to occur in *E. coli* × *E. coli* tests (Fig. 4a). However, a somewhat different possibility is suggested by the fact that poor complementation in interspecies tests was not allele specific, but rather occurred with all combinations of mutant alleles. Full complementation was only observed when the members of an interacting gene pair originating from the same species (e.g., $cheB_E$-$cheZ_E$) were both wild type, implying that *E. coli* subunits may not interact properly with *Salmonella* subunits to form a functional product complex (Fig. 4b). If this analysis is proven to be correct, it must mean that individual chemotaxis gene products of *E. coli* are not necessarily interchangeable with those of *S. typhimurium.* At some level, however, product complexes must be functionally equivalent because *Salmonella che* defects can be fully corrected by furnishing an appropriate ensemble of *che* functions from *E. coli.* The level at which interchangeability can occur is not obvious because the F-prime elements used to perform these interspecies complementation tests probably carried genes specifying a major portion of the flagellar and chemotaxis machinery of *E. coli.* Further studies will be needed to assess the true extent of functional homology in these two species. It may be that some single products and perhaps even small product complexes are not readily interchangeable, but in any event, the initial studies reported here demonstrate considerable similarity in overall organization and operation of the chemotaxis systems in these two organisms.

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