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D-Fucose as a Gratuitous Inducer of the L-Arabinose Operon in Strains of *Escherichia coli* B/r Mutant in Gene *araC*[1]

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D-Fucose, a nonmetabolizable analogue of L-arabinose, prevents growth of *Escherichia coli* B/r on a mineral salts medium plus L-arabinose by inhibiting induction of the L-arabinose operon. Mutations giving rise to D-fucose resistance map in gene *araC* and result in constitutive expression of the L-arabinose operon. Most of these mutations also permit D-fucose to serve as a gratuitous inducer. It is concluded that D-fucose-resistant mutants produce an *araC* gene product with an altered inducer specificity. Addition of L-arabinose to cells induced with the gratuitous inducer, D-fucose, resulted in severe transient repression of operon expression followed by permanent catabolite repression. Transient repression but no permanent catabolite repression was obtained when cells unable to metabolize L-arabinose were employed. It is concluded that transport of L-arabinose alone is sufficient to achieve transient repression of its own operon, but that metabolism of L-arabinose must occur to achieve permanent catabolite repression of the L-arabinose operon. This general effect has been termed "self-catabolite repression."

Induction of the L-arabinose operon is assumed to be controlled by the interaction of several regulatory components (Fig. 1; see references 7, 8, 17). These include a repressor, the primary product of gene *araC*, whose proposed role is to interact with the operator region (*araO*) to prevent operon expression in the absence of inducer, and an activator, whose formation is proposed to occur as a consequence of an interaction between the inducer (L-arabinose) and the repressor. According to this model, operon induction occurs upon interaction of the activator with the initiator region (*araI*). The level of operon induction is also subject to catabolite repression by certain, as yet unspecified, cellular catabolites (10). It is presumed that catabolite repression of the L-arabinose operon occurs by a mechanism analogous to that of catabolite repression of other catabolic operons such as the *lac* and *gal* operons (13, 16, 21, 22).

In mutants (*araA*$^-$ or *araB*$^-$) in which the *inducer*, L-arabinose, cannot be metabolized, operon induction occurs at two to three times the rate usually observed in wild-type strains (hyperinduction; references 1, 2, 4, 5, 11, 12, 18). It has been proposed (10, 18) that, in such strains, L-arabinose cannot be metabolized to yield those cellular catabolites active in catabolite repression. The operon, thus relieved from "self catabolite repression," would then effectively undergo hyperinduction.

In this study, mutants will be described in which D-fucose, a nonmetabolizable analogue of L-arabinose (6), can serve as a gratuitous inducer to achieve hyperinducible levels of operon expression. Genetic analysis of these mutants supports that portion of the model that specifies a direct interaction between inducer and *araC* gene product (the repressor) to yield activator. In addition, these mutants permit one to study "self catabolite repression" (10) of the L-arabinose operon by L-arabinose under conditions of hyperinduction by a gratuitous inducer.

MATERIALS AND METHODS

Media. L-broth medium contained 1% tryptone (Difco), 0.5% yeast extract, 0.5% NaCl, and 0.1% glucose. Mineral base contained 0.7% K_2HPO_4, 0.3% KH_2PO_4, 0.1% $(NH_4)_2SO_4$, and 0.01% $MgSO_4 \cdot 7H_2O$. Mineral-L-arabinose medium (MA) contained mineral base plus 0.2% L-arabinose. Mineral-L-arabinose-D-fucose medium (MAF) contained mineral base plus 0.1% L-arabinose and 0.15% D-fucose. Amino acids (0.004% final concentration) and agar (1.5% final concentra-

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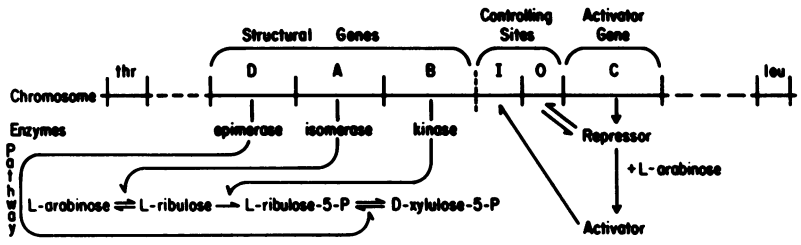

FIG. 1. *L-Arabinose operon in Escherichia coli* B/r.

tion) were added as needed. Casein hydrolysate (CH) medium contained mineral base plus 1.0% casein hydrolysate. L-Arabinose or D-fucose (or both) was added to CH medium at the concentration indicated in the tables and figures.

Bacterial strains. The following strain abbreviations are used: Δ, deletion mutation; *araCc*, D-fucose-resistant mutation; *araC-*, a mutation resulting in complete loss of both *araC* gene products (activator and repressor). Table 1 lists some of the strains employed in this study. All of the D-fucose-resistant mutants were isolated in strain UP1006 after diethyl sulfate mutagenesis and were assigned the following strain and mutation designations: CN5101 (*araCc201*), CN5102 (*araCc202*), CN5103 (*araCc203*), CN5104 (*araCc205*), CN5105 (*araCc206*, CN5106 (*araCc207*), CN5107 (*araCc209*), CN5108 (*araCc217*), CN5109 (*araCc218*), CN5110 (*araCc220*), CN5111 (*araCc228*), CN5112 (*araCc236*), CN5113 (*araCc237*), CN5114 (*araCc238*), CN5115 (*araCc239*), CN5116 (*araCc242*), and CN5117 (*araCc243*). Strain CN5119 (*araCc311*) was isolated in strain UP1006 in two steps. The first-stage mutant, CN5118 (*araCc300*), was temperature-sensitive, D-fucose-resistant. CN5119 was subsequently isolated from CN5118 as a temperature-resistant, D-fucose-resistant strain. Double mutants of the type *araA araCc* and *araΔB809 araCc* were prepared with the use of P1 transducing phage. The *araCc* mutation was transferred into strain CN5120 (*araA2 leuB1*), strain CN5121 (*araA54 leuB1*), or strain CN5122 (*araD139 araΔB809 leuB1*) by cotransduction with *leuB1*$^+$. Leucine-positive transductants were then progeny-tested to identify those transductants that carried both the L-arabinose-negative and D-fucose-resistant mutations.

Isolation of D-fucose-resistant mutants. Approximately 4×10^8 cells of strain UP1006 (*ara*$^+$) were plated onto each of a series of MAF agar plates. A drop of diethyl sulfate (Fisher) was then added to the agar surface of each plate. After incubation at 37 C for 48 to 72 hr, 100 to 200 "D-fucose-resistant" mutant colonies appeared in the area of the mutagen. One colony was picked from each plate and subjected to at least two successive single-colony isolations on MAF medium. Permanent stocks were maintained on nutrient agar (Difco) slants. This procedure is modified from one described by Englesberg et al. (6).

Mapping of D-fucose-resistant mutants. P1 transducing phage prepared upon seven independently isolated D-fucose-resistant mutants was used to transduce strains SB1074 (*araΔBIOC711*), SB1085 (*araΔC766*), and ME1166 (*araΔBIOC2201*) to the L-arabinose-positive phenotype. At least 270 L-arabinose-positive transductants from each cross were then tested for D-fucose resistance by replica plating to MAF medium. Appearance of at least three L-arabinose-positive, D-fucose-sensitive transductants in any cross was taken as evidence that the D-fucose-resistant mutation in question lies outside the region of the *araC* gene encompassed by the particular deletion mutation employed. Analysis of this type permitted the construction of the deletion map shown in Fig. 3.

Growth and sampling of cells for enzyme analysis. The rate of synthesis of L-arabinose isomerase (gene *araA*) was used to measure the level of induction of the L-arabinose operon in all experiments. In most cases, the steady-state level of L-arabinose isomerase (EC 5.3.1.4) specific activity was determined in a single sample taken after at least four generations of growth in 75 ml of M + CH medium to which L-arabinose or D-fucose (or both) had been added at the desired concentrations. All of these cultures were grown in duplicate in 500-ml flasks on a New Brunswick Gyratory shaker, model G25. In a few experiments, differential rates of L-arabinose isomerase were determined from a series of samples taken at successive intervals. Cultures were grown in 800 ml of M + CH medium in 2-liter flasks on a New Brunswick gyratory shaker, model G25. Samples (40 ml) were transferred (with an automatic syringe) directly into centrifuge tubes containing a final concentration of 400 μg of chloramphenicol per ml. L-Arabinose or D-fucose (or both) was added at a final concentration of 2.2×10^{-2}M at the times indicated in the figure legends. Growth was followed turbidometrically at 420 nm with a Klett-Summerson colorimeter. Units of L-arabinose isomerase per milliliter of

TABLE 1. *Bacterial strains*

Strain	Mating type	Genotype	Source
UP1006	F$^-$	*ara+*	(10)
CN5110	F$^-$	*araCc220*	From UP1006
CN5119	F$^-$	*araCc311*	From UP1006
CN7001	F$^-$	*araD139 araΔB809 araCc311*	This paper
ME1166	F$^-$	*araΔBIOC2201*	This paper
SB1074	F$^-$	*araD139 araΔBIOC711*	(17)
SB1085	F$^-$	*araΔC766*	This paper
SB3112	F'*ara*	*araB80/ araB80*	(16)
SB3114	F'*ara*	*araC3/ araC3*	(16)

culture were calculated in arbitrary units as: (units of L-arabinose isomerase)/(milligram of protein) × (culture turbidity).

Preparation of cell extracts and enzyme assays. Cell-free extracts were prepared as previously described (17). Isomerase and protein assays were performed as previously described (17), except that all isomerase assays were performed at 30 C.

Merodiploid construction and analysis. Construction of heterogenotes and the determination of the genotypes of all exo- and endogenotes were carried out as previously described (17).

RESULTS

Inhibition of operon induction by D-fucose. In Fig. 2, the inhibition of operon induction (as measured by the rate of isomerase production) by D-fucose in strain UP1006 (*ara*+) is presented as a double-reciprocal plot. It is clear that in this strain the degree of inhibition by D-fucose increases with an increase in D-fucose concentration. The kinetics of inhibition are essentially competitive. Growth inhibition of wild-type *Escherichia coli* B/r by D-fucose is therefore due to the inability of the cells to become induced for the enzymes necessary for the utilization of L-arabinose as a sole carbon and energy source.

Genetic location of mutations giving rise to D-fucose resistance. By using P1 transducing phage prepared upon selected strains containing D-fucose-resistant mutations, and recipient strains carrying mutations that delete various portions of gene *araC*, it was possible to identify three regions in which mutation to D-fucose resistance can occur (Fig. 3). One region, containing mutations *araCc205*, *araCc217*, and *araCc243*, lies within the region of overlap between deletion mutations *araΔBIOC711* and *araΔC766* and, therefore, can definitely be positioned within the *araC* gene. Mutation *araCc311* lies at the right end of gene *araC* or in an as yet undefined genetic region to the right of gene *araC*. Mutations *araCc203*, *araCc220*, and *araCc244* lie either to the extreme left end of gene *araC* or in a region to the left of gene *araC*. Mutations *araCc203* and *araCc220*, are clearly in gene *araC*, since they can control the expression of an *araA* gene in the *trans* position (*see* Table 2). Mutations in *araI* and *araO*, the regions immediately to the left of gene *araC*, are *trans* recessive (7, 8, 17, 18). From this analysis, we conclude that mutations giving rise to D-fucose resistance arise in gene *araC* and presumably result in the production of an altered *araC* gene product. These results are consistent with the previous mapping of D-fucose-resistant mutations in gene *araC* by Englesberg et al. (6).

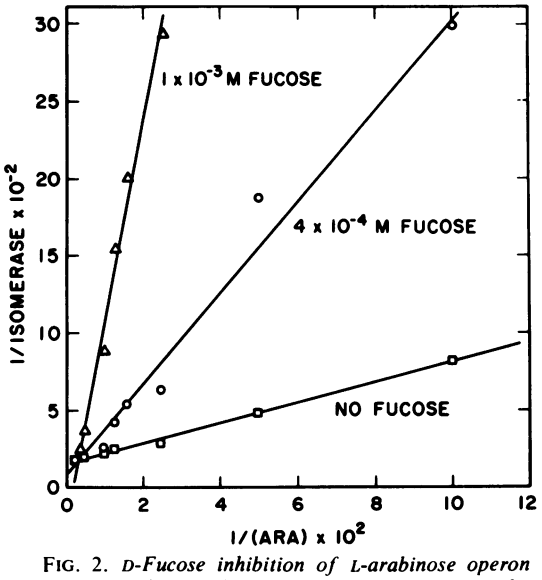

FIG. 2. *D-Fucose inhibition of L-arabinose operon induction. Cultures of UP1006 (ara+) were grown for at least four cell generations after addition of D-fucose and L-arabinose at the desired concentrations before harvesting. Each point represents the average L-arabinose isomerase specific activity value obtained from duplicate cultures. Symbols: no addition (□), 4 × 10⁻⁴ M D-fucose (○), 10⁻³ M D-fucose (△).*

Inducibility of D-fucose-resistant mutants by D-fucose. In Fig. 4, the level of operon expression in the presence and absence of 2.2×10^{-2} M D-fucose is compared for 18 independently isolated D-fucose-resistant mutants. These mutants are similar to those described by Englesberg et al. (6) in that the constitutive level of L-arabinose isomerase ranges from 2 to 58 specific activity units. When grown in the presence of 2.2×10^{-2} M D-fucose, 15 of the 18 mutants exhibited L-arabinose isomerase specific activity levels ranging from 1.2- to 150-fold higher than their constitutive levels. Clearly, D-fucose is functioning as a gratuitous inducer in the majority of these D-fucose-resistant mutants. Five of the mutants were of particular interest in that they

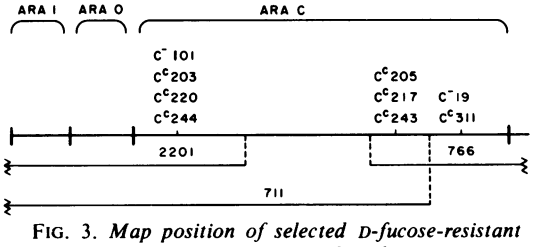

FIG. 3. *Map position of selected D-fucose-resistant mutations in gene araC. Cc is used to designate mutations giving rise to D-fucose resistance. The positions of araC101 and araC19, two mutations that prevent the formation of any functional araC gene product, are shown for reference.*

TABLE 2. *Merodiploid analysis of D-fucose-resistant mutants (araCc)*[a]

Strain	Genotype	Isomerase (*araA*) specific activity (inducer)		
		None	Arabinose	D-Fucose
CN5104	*A+ B+* Cc205	26.0	26.4	51.7
CN9012	F *A+ B+ C3/A2 B+ Cc203*	47.7	39.2	123.7
CN9013	F *A+ B+ C3/A2 B+ Cc206*	66.6	50.0	139.3
CN9014	F *A+ B+ C3/A54 B+ Cc220*	15.8	39.1	38.0
CN9015	F *A+ B+ C3/A2 B+ Cc242*	38.4	52.0	122.5
CN9016	F *A+ B80 C+/A2 B+ Cc205*	<0.3	13.8	<0.3
CN9017	F *A+ B80 C+/A2 B+ Cc203*	0.6	19.0	1.6
CN9018	F *A+ B80 C+/A2 B+ Cc206*	0.5	10.4	1.6
CN9019	F *A+ B80 C+/A54 B+ Cc220*	0.5	15.3	0.6
CN9020	F *A+ B80 C+/A2 B+ Cc242*	<0.3	14.7	1.0

[a] Merodiploids were prepared and were then assayed for L-isomerase specific activity, and progeny were tested to establish the presence of the mutations carried by the exo- and endogenotes. Each value represents the average determination obtained from duplicate cultures. All merodiploids included had segregation rates of less than 20%.

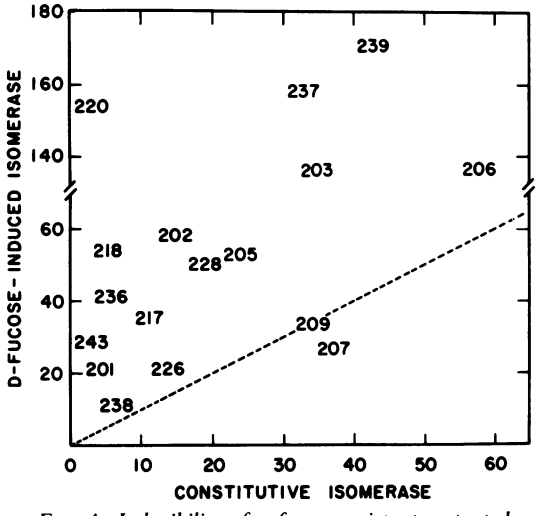

FIG. 4. *Inducibility of D-fucose-resistant mutants by D-fucose. The constitutive versus the D-fucose-induced levels of operon induction are plotted coordinately for each of 18 D-fucose-resistant mutants. Each mutant is identified by its mutation number. The dotted line indicates the theoretical position expected for all of the points if D-fucose has no effect upon the level of operon expression. Each strain was grown for at least four generations in the absence of inducer or in the presence of* 2.2×10^{-2} *M D-fucose before harvesting. Each point represents the average L-arabinose isomerase specific activity value obtained from duplicate cultures.*

exhibited levels of operon induction with D-fucose two- to threefold higher (Table 3) than when L-arabinose was employed as inducer in strain UP1006 (*ara+*).

Concentration dependence of D-fucose and L-arabinose for induction. Figure 5 illustrates the dependence upon D-fucose or L-arabinose for induction of strain CN5110 (*araCc220*), a D-fucose-resistant mutant exhibiting a low constitutive rate of operon expression. A maximum induction of approximately 30 specific activity units of L-arabinose isomerase occurs at an L-arabinose concentration of 2×10^{-2}M. With a D-fucose concentration of 8×10^{-3}M, a maximum rate of induction of approximately 100 specific activity units of L-arabinose isomerase is obtained. Clearly this mutant responds to both L-arabinose and D-fucose as inducers over a wide range of concentrations.

Dominance relationships of mutations conferring resistance to D-fucose (araCc). It had been previously demonstrated that the constitutive expression of the L-arabinose operon, as determined by the *araCc* allele, was dominant to the *araC−* allele but recessive to the *araC+* allele (6, 17). These results were interpreted to mean that (i) the *araCc* allele resulted in the production of an altered *araC* gene product that did not require inducer to achieve activator function, (ii) the *araC−* allele failed to produce any functional *araC* gene product, and (iii) in the absence of inducer, the *araC+* allele produced a product (a repressor) that prevented the *araCc* gene product from causing the constitutive expression of the operon. With the observation that D-fucose interacts with the *araCc* gene product to increase the rate of induction, it became possible to determine whether the repressor function of the *araC+* gene product could be eliminated upon interaction with D-fucose. In merodiploids of the type F A+ B+ C3/A− B+ Cc, the *araCc* allele is dominant over the *araC−* allele in the presence and absence of D-fucose (Table 2). Strain CN9014 is a possible exception in that it exhibits a higher constitutive level and a lower D-fucose-induced level of L-isomerase activity than re-

TABLE 3. *Hyperinducibility in the absence of inducer metabolism*[a]

Strain	Genotype	D-Fucose	L-Arabinose	Isomerase specific activity
CN7001	*BΔ809 Cc311*		2×10^{-2}M	92.6
CN7001	*BΔ809 Cc311*	2×10^{-2}M		98.2
CN5119	*B+ Cc311*			4.5
CN5119	*B+ Cc311*		2×10^{-2}M	33.6
CN5119	*B+ Cc311*	2×10^{-2}M		112.0
UP1006	*B+ C+*		2×10^{-2}M	39.2

[a] Level of operon induction was determined by measuring L-arabinose isomerase specific activity after growth for at least four generations in the presence of the specified inducer. Each value represents the average determination obtained from duplicate cultures.

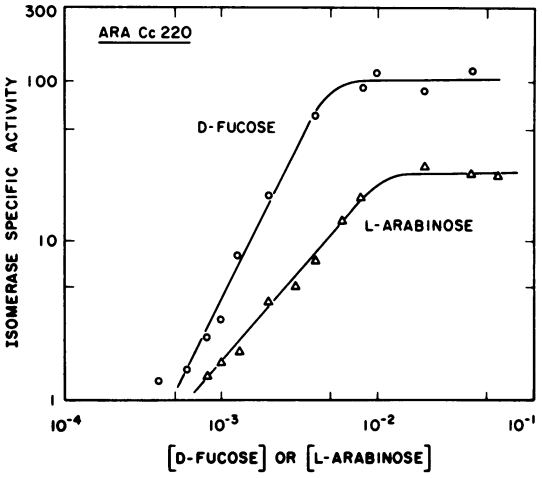

FIG. 5. *Dependence upon D-fucose or L-arabinose for induction of a D-fucose-resistant mutant. Cultures of CN5110 (araCc220) were grown for at least four generations in M + CH medium to which D-fucose or L-arabinose had been added at the desired concentration. Samples were taken at the end of the exponential phase of growth and assayed for L-arabinose isomerase specific activity. Each point represents the average value obtained from duplicate cultures.*

ported for the haploid strain in Fig. 4. At the moment, we have no explanation for this discrepancy, other than the possibility of some complication arising during the construction of the double mutant or the merodiploid. In merodiploids of the type F A+ B80 C+/A− B+ Cc, on the other hand, the *araCc* allele is recessive to the *araC+* allele both in the presence and in the absence of D-fucose. Thus, D-fucose does not prevent the product of the *araC+* allele from blocking the action of the *araCc* gene product. The reduction in inducibility by L-arabinose in merodiploids of the type F A+ B80 C+/A− B+ Cc is due to the polar nature of the *araB80* mutation (2).

Role of L-arabinose as a self-catabolite repressor. At least two different mechanisms could be invoked to explain the threefold higher rate of operon expression in strain CN5110 (*araCc220*) when D-fucose rather than L-arabinose was employed as inducer (*see* Fig. 5). (i) The interaction of D-fucose with the *araCc220* gene product might produce a much more efficient activator than does a similar interaction with L-arabinose. (ii) Since L-arabinose is a metabolizable inducer, whereas D-fucose is gratuitous, some product of L-arabinose metabolism might serve to partially repress the expression of the operon. To discriminate between these two models, it was necessary to construct a double mutant such that neither D-fucose nor L-arabinose could be metabolized. For unknown technical reasons, it was not possible to construct the appropriate double mutant by using mutation *araCc220*. Thus strain CN5119 (*araCc311*), which exhibited a similar response with D-fucose and L-arabinose, was employed for subsequent analysis. Upon introduction of mutation *araCc311* into a strain containing a deletion mutation in gene *araB*, D-fucose and L-arabinose are equally effective in causing hyperinduction of the operon (Table 3). Thus, the hyperinducible effect is determined by inability to metabolize the inducer and is not a direct consequence of a mutation in gene *araC*.

If L-arabinose gives rise to catabolites that partially repress the L-arabinose operon, addition of L-arabinose to a D-fucose-induced culture of CN5119 (*araB+ araCc311*) should result in partial repression of the operon. Table 4 demonstrates that such repression does occur and is dependent upon the concentration of L-arabinose added. Presumably competition between L-arabinose and D-fucose for entry into the cell (14) prevents complete repression of the hyperinducible effect at the L-arabinose concentrations employed.

To compare self-catabolite repression by L-arabinose to the more general mechanism of ca-

TABLE 4. *Repression by* L-*arabinose of* D-*fucose-mediated hyperinducibility in strain CN5119 (araB+ araCc311)*[a]

D-Fucose	L-Arabinose	Isomerase specific activity
8×10^{-3}M		120.5
8×10^{-3}M	8×10^{-4}M	128.5
8×10^{-3}M	1×10^{-3}M	102.0
8×10^{-3}M	2×10^{-3}M	73.3
8×10^{-3}M	4×10^{-3}M	69.3
8×10^{-3}M	8×10^{-3}M	42.5
8×10^{-3}M	4×10^{-2}M	45.0
	2×10^{-2}M	37.5

[a] L-Arabinose isomerase specific activity was used to determine the level of operon induction after growth for at least four generations in the presence of $8 + 10^{-3}$M D-fucose and a range of comparisons of L-arabinose. Each value represents the average determination obtained from duplicate cultures.

tabolite repression, the kinetics of operon inhibition by L-arabinose were examined. When L-arabinose (2.2×10^{-2}M) is added to an exponentially growing culture of CN5119 (*araB+ araCc311*) in which D-fucose had been serving as the sole inducer, a severe transient repression occurs, followed, after approximately one-half a cell generation, by a permanent catabolite repression. The kinetics follow the same general pattern observed upon catabolite repression of other operons such as the *lac* operon (13, 16). When a similar experiment is performed with CN7001 (*araΔB809 araCc311*), a severe transient repression occurs, but permanent catabolite repression does not occur. In fact, after the period of transient repression, the addition of L-arabinose dramatically increases the rate of operon expression. At the moment, we are not certain as to the cause of this stimulatory effect.

DISCUSSION

The striking feature of the D-fucose-resistant mutants is their ability to respond to the L-arabinose analogue, D-fucose, as a gratuitous inducer to achieve levels of induction significantly above their constitutive levels. Since mutations giving rise to D-fucose resistance used in this study, as well as in previous studies (6), map in gene *araC*, the most plausible interpretation is that the altered *araC* gene product produced by D-fucose-resistant mutants now has a modified inducer specificity such that D-fucose can serve as an inducer. If this interpretation is correct, these mutants provide strong evidence for a direct interaction between the inducer and the *araC* gene product in wild-type cells.

When merodiploids of the type F A+ B+ C3/A− B+ Cc were constructed by using five different D-fucose-resistant mutations (*araCc*), operon induction occurred constitutively, as expected from previous studies (6). Although only two of the merodiploids were further induced upon addition of L-arabinose to the growth medium, all five underwent further induction upon addition of D-fucose. Thus, constitutivity as well

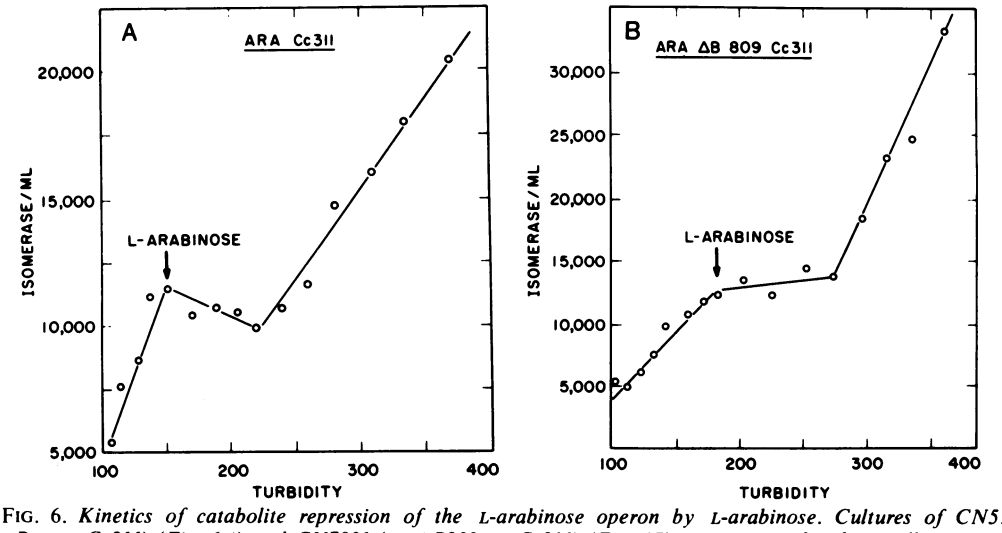

FIG. 6. *Kinetics of catabolite repression of the* L-*arabinose operon by* L-*arabinose. Cultures of CN5119 (araB+ araCc311) (Fig. 6A) and CN7001 (araΔB809 araCc311) (Fig. 6B) were grown for three cell generations with* 2.2×10^{-2}M D-*fucose as inducer before addition of* 2.2×10^{-2}M L-*arabinose. Turbidity measurements were used to convert isomerase specific activity measurements to enzyme per milliliter.*

as D-fucose inducibility are dominant over an *araC* gene containing nonsense mutation *araC3* (9). From this we conclude that the product of an *araC* gene containing a D-fucose-resistant mutation can interact with D-fucose and then act *trans* to achieve operon induction. In merodiploids of the type F A+ B80 C+/A B+ Cc, the constitutive expression of the operon is repressed by the presence of the *araC*+ allele. Addition of L arabinose to the growth medium relieves the repression, presumably by converting the repressor produced by the *araC*+ allele to activator. Addition of D-fucose, on the other hand, fails to significantly relieve the repression caused by the *araC*+ repressor. This suggests that, either D-fucose does not interact at all with the *araC*+ repressor (and thus inhibition of operon induction by D-fucose in wild-type strains is strictly a function of reduced inducer uptake), or an interaction does occur between D-fucose and the *araC*+ repressor that does not significantly alter repressor function and may or may not block the L-arabinose-mediated conversion of repressor to activator.

This observation provides further support for the dominant epistatic role of the repressor form of the *araC* gene product over the activator form.

Previously, hyperinducible levels (two- to threefold above wild type) of operon induction were achieved only in strains containing nonpolar mutational defects in genes *araA* (L-arabinose isomerase) and *araB* (L-ribulose kinase; see references 1, 2, 4, 5, 11, 12, 18). In such strains, L-arabinose cannot be used as a carbon and energy source. Katz and Englesberg (10) have proposed that, in wild-type strains, hyperinduction does not occur because L-arabinose gives rise to various catabolites that partially repress the expression of the operon. Presumably this repression occurs by a mechanism similar to that of glucose-mediated catabolite repression in the *lac* and *gal* operons (13, 16, 21). In *araA* and *araB* mutants, on the other hand, the catabolites involved in repression could not be derived from L-arabinose. Under such circumstances, hyperinduction would occur since the system would be released from "self-catabolite repression".

With the observation that D-fucose could also cause hyperinduction in certain D-fucose-resistant mutants, it became possible to test directly the notion that catabolites derived from L-arabinose cause repression of the L-arabinose operon. The following observations, reported in this study, support the proposal that hyperinducibility occurs as a consequence of release from self-catabolite repression. (i) Strain CN5119 (*araB*+ *araCc311*) is hyperinducible when D-fucose is used as inducer but yields wild-type levels of induction when L-arabinose is used as inducer. By contrast, in the double mutant CN7001 (*araΔB809 Cc311*), hyperinduction occurs when either D-fucose or L-arabinose is employed as inducer. This suggests that the inability to metabolize the inducer is a critical factor in determining hyperinducibility. (ii) Addition of both D-fucose and L-arabinose to strain CN5119 (*araB*+ *araCc311*) results in a repression of the hyperinducible level expected when only D-fucose is present as inducer. Furthermore, the degree of repression increases with an increase in the concentration of L-arabinose provided. (iii) Kinetic analysis of L-arabinose-mediated catabolite repression in D-fucose-induced cells has many similarities to catabolite repression in the *lac* and *gal* operons (13, 16, 21). For example, transient repression occurs upon addition of L-arabinose to both strain CN5119 (*araB*+ *araCc311*) and strain CN7001 (*araΔB809 araCc311*) even though L-arabinose cannot be degraded in the latter strain. This is consistent with the observation that transient repression is dependent only upon transport of the added carbohydrate and not on its subsequent metabolism (23). Permanent catabolite repression, however, occurs only in strain CN5119 (*araB*+ *araCc311*) in which L-arabinose can be metabolized. Additional support for the similarity between self-catabolite repression and classical catabolite repression comes from the observation by Katz and Englesberg (10) that addition of cyclic 3,5-adenosine monophosphate, a compound known to reverse catabolite repression in the *lac* and *gal* operons, partially reverses L-arabinose-mediated catabolite repression (3, 15, 16, 21).

Mutational alterations of the *lac* promoter region have been shown to result in an altered sensitivity to catabolite repression for that operon (15, 19, 20). From this it has been inferred that the *lac* promoter plays a direct role in catabolite repression. Certain strains containing mutations in the *araI* region and the *araC* gene are now being screened for altered sensitivity to catabolite repression. Such an analysis may permit the identification of those regulatory element(s) directly involved in catabolite repression of the L-arabinose operon.

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