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This Week's Citation Classic

Rickenberg H V, Cohen G N, Buttin G & Monod J. La galactoside-perméase d' *Escherichia coli. Ann. Inst. Pasteur* **91**:829-57, 1956. [Institut Pasteur, Service de Biochimie Cellulaire. Paris, France]

The experiments described in this paper demonstrated the existence in the bacterium *E. coli* of a 'system,' which mediated the stereospecific, concentrative uptake of ß-galactosides. The use of mutants and of inhibitors of protein synthesis permitted the conclusion that the stereospecific component was a protein. [The *SCI*® indicates that this paper has been cited over 230 times since 1961.]

H.V. Rickenberg
Department of Molecular
and Cellular Biology
National Jewish Hospital
and Research Center
Denver, CO 80206

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"In 1954 little was known about the mechanism by which the substrates of certain bacterial enzymes stimulated the synthesis of these enzymes. When I joined Monod's group at the Institut Pasteur as a postdoctoral fellow, he suggested to me and his colleagues, Georges Cohen and Gérard Buttin, that we attempt to trace the intracellular fate of ^{35}S-labeled thiomethylgalactoside, an analog of lactose and an effective inducer of ß-galactosidase in *Escherichia coli.* ß-Galactosidase was the most intensively studied inducible enzyme at the time. We found to our surprise that bacteria previously exposed to a /3-galactoside concentrated the labeled galactoside several hundredfold, whereas bacteria which had not been pre-exposed to a ß-galactoside did not concentrate the sugar. Bacteria which formed ß-galactosiclase constitutively also concentrated galactosides without prior exposure. Certain unusual mutants isolated earlier by Gabriel Lester and myself[1] (when graduate students at Yale) on the basis of their inability to grow on lactose and yet endowed with ß-galactosidase activity, we now found, did not concentrate galactosides These and related observations led us to postulate an inducible, stereospecific transport system composed, at least in part, of protein. At about the same time, Georges Cohen and I found similar systems, specific for the transport of individual amino acids in *E. coli.*[2]

"Monod, in a fit of semantic exuberance, proposed the term 'permease.' Cohen, Buttin, and I were somewhat less enthusiastic about the term since, in addition to a certain lack of euphony, the suffix 'ase' carried the connotation of enzymic activity which we did not mean to imply in any strict sense. However, not feeling strongly about the matter, we let Monod have his way When we submitted the paper to *Biochimica et Biophysica Acta,* the response was prompt and unequivocal: '...an exciting paper, but the term permease is inadmissible .' (I paraphrase). By this time Monod had become enamored of 'permease' and insisted on its use; and thus the paper was published (in French instead of the original English version) in the more compliant *Annales de L'Institut Pasteur.* Nine years later, Fox and Kennedy isolated a membranal protein with the ability to bind ß-galactosides and other properties postulated by us earlier [3]

"The relevance of our observation and the reason for the high citation of this paper are two-fold The finding of the galactoside permease was at the origin of a trail of research that led, albeit often tortuously, to an ever more profound understanding of not only membranal transport in bacteria but, more importantly, of the role of the membrane in energy transduction in general Sec - ondly, the discovery of the permease and the finding that its synthesis was controlled coordinately with that of the ß-galactosidase (and of the thiogalactoside transacetylase) gave rise to the concept of the operon."

1. **Rickenberg H V.** *ß-galactosidase in Escherichia coli. Aspects of its formation and activity.* Unpublished thesis. New Haven. CT: Yale University, l954. 114 p.
2. **Cohen G N & Rickenberg H V**. Concentration spécifique réversible des amino acides chez *Escherichia coli. Ann. Inst. Pasteur* **91**:693-720,1956.
3. **Fox C F & Kennedy E P.** Specific labeling and partial purification of the M protein, a component of the *ß*-gulactoside transport system of *Escherichia coli. Proc. Nat. Acad. Sci. US* 54:891-9.1965.