

**Pardee A B, Jacob F & Monod J.** The genetic control and cytoplasmic expression of "inducibility" in the synthesis of  $\beta$ -galactosidase by *E. coli*.  
*J. Mol. Biol.* 1:165-78, 1959.  
[Inst. Pasteur, Paris, France and Univ. California, Berkeley, CA]

The Pajama (Pardee, Jacob, Monod) experiment provided a breakthrough in our understanding of the molecular mechanisms by which gene expression is regulated. From this experiment emerged entities such as repressors, regulatory genes, the operon as a group of jointly controlled genes, the allosteric control mechanism, and messenger RNA. Today, 25 years later, it provides a paradigm for thinking about complex problems of gene expression, embodied in growth regulation and differentiation. [The SCI® indicates that this paper has been cited in over 735 publications since 1959.]

Arthur B. Pardee  
Department of Pharmacology  
Harvard Medical School  
and  
Division of Cell Growth and Regulation  
Dana-Farber Cancer Institute  
Boston, MA 02115

January 21, 1985

Since the turn of the century, bacteria were known to produce certain enzymes only when their substrates were present. This property was regarded as benefiting the organism, and so these enzymes were called "adaptive"—for example,  $\beta$ -galactosidase can increase 10,000-fold in activity upon addition of lactose. Around 1950, emphasis turned to inquiring into the mechanism connecting formation of these enzymes with their low-molecular-weight inducers and with the bacterial genetic and biochemical machinery. Jacques Monod was a leader in these studies. My interests were on mechanisms used by cells to control their growth and metabolism, such as feedback control of enzyme activity and the control of enzyme formation by induction and derepression. I arranged to spend a sabbatical year to investigate enzyme induction, and the Pajama experiment was carried out in the fall and

winter of 1957 with Monod and François Jacob in Paris.

The Pajama experiment developed from a synthesis of bacterial physiology, genetics, and enzymology. Its main conclusion was that gene regulation depends upon a hitherto unsuspected regulatory molecule, the repressor, that links external agents with genetic expression. The repressor interacts with inducer and also with a specific regulatory gene, allowing the inducer to modulate repression of the gene product. The repressor (for  $\beta$ -galactosidase) was subsequently shown to be a protein by Walter Gilbert and Benno Müller-Hill, who isolated and characterized it.<sup>1</sup>

The Pajama experiment opened up molecular studies of gene regulation. From it evolved the concepts of operator and promoter regulatory genes and of the organization of genes into co-regulated sets named operons.<sup>2</sup> The repressor has the Janus-like property of looking simultaneously in two biochemical directions. Feedback-regulated enzymes also have separate molecular domains for function and for control.<sup>3</sup> This similarity generated the allosteric mechanism for regulation of numerous diverse phenomena.

The concept of an unstable intermediate (shown later to be mRNA) arose in large part from the immediate, full-rate turn-on of enzyme synthesis and its cessation upon destruction of DNA or removal of inducer,<sup>4</sup> both seen with great clarity in the Pajama experiment.

The Pajama experiment turned out to be pivotal in the evolution of ideas regarding molecular mechanisms of biological and metabolic regulation. The concepts that emerged from it still shape our thinking in exploring the molecular nature of all biological regulatory processes. The Pajama experiment today provides a paradigm for study of complex biological-biochemical-genetic problems such as growth and development.

This experiment was a principal one that, along with their other contributions, led to Nobel Prizes in 1965 to Monod and Jacob and to my receiving the 3M Award in 1980 from the Federation of American Societies for Experimental Biology.

1. Gilbert W & Müller-Hill B. Isolation of the lac repressor. *Proc. Nat. Acad. Sci. US* 56:1891-8, 1966. (Cited 365 times.)
2. Jacob F & Monod J. Genetic regulatory mechanisms in the synthesis of proteins. *J. Mol. Biol.* 3:138-56, 1961. (Cited 2,750 times.)
3. Pardee A B. Molecular basis of biological regulation: origins from feedback inhibition and allostery. *BioEssays* 2:37-40, 1985.
4. Pardee A B. Molecular basis of gene expression: origins from the Pajama experiment. *BioEssays* 2, 1985. (In press.)