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Michael A. Savageau* (savageau@umich.edu). *Relating Genotype to Phenotype Through Analysis of Gene Circuitry.*

The relationship between two different hierarchical levels of organization – genotype and phenotype – has traditionally been approached from the bottom-up perspective. Study of gene systems have revealed an enormous diversity of molecular elements and circuits. The relationship between genotype and phenotype can now be approached from the top-down perspective as well. The new technologies from the Human Genome Project allow global measurements of the organism's phenotype. However, there are theoretical limits to the knowledge of the underlying mechanisms that can be determined solely by systemic measurements. Success in relating genotype to phenotype will require a combination of both approaches and an appropriate systems theory to relate the information at these different levels of organization, or our understanding will be descriptive and lack predictive value. I will describe recent work on a quantitative theory that relates molecular mechanisms of gene control to the organism's physiological behavior in its natural environment. When applied to the lactose operon of *Escherichia coli* in the human intestine, the theory predicts selection for the correct mode of gene control. It also makes surprising predictions concerning the organisms phenotype and habitat. (Received October 03, 2000)