2001 and all that: a tale of a third science

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Abstract

The paper describes the change from molecular genetics to postgenomic biology. It focuses on phenomena in the regulation of gene expression that provide a break with the central dogma, according to which sequence specificity for a gene product must be template derived. In its place we find what is called here ‘ constitutive molecular epigenesis ’ . Its three classes of phenomena, which I call sequence ‘ activation ’ , ‘ selection ’ and ‘ creation ’ , are exemplified by processes such as transcriptional activation, alternative cis- and trans-splicing, and RNA editing. These phenomena support the following main theses of the paper: 1. Other molecular resources share the causal role of ‘ genes ’ : the ‘ causal specificity ’ for the linear sequence of any gene product is distributed between the coding sequence, cis-acting sequences, trans-acting factors, environmental signals, and the contingent history of the cell (the cellular code) (thesis of distributed causal specificity). 2. These multiple and overlapping processing and targeting mechanisms amplify the repertoire of RNA and protein products specified through the eukaryotic genome, expanding the possibilities specified by the literal code of DNA (thesis of genetic underdeterminism). 3. These mechanisms of gene expression change the focus of postgenomic research from single molecules and their molecular, biochemical and intrinsic function to their cellular, constituent, component or contextual function due to their recruitment and organization in complex cellular networks. In other words, all agents involved in the regulation of gene expression, including DNA, must interact with other agents to achieve full specificity, which is imposed by regulated recruitment and combinatorial control (theses of regulated recruitment and of system analysis). I conclude from these three main theses that the complexity of higher organisms lies not in its number of genes but in the flexibility, versatility and reactivity of its whole genome.

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