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Canalization

Scott F. Gilbert
Swarthmore College, sgilber1@swarthmore.edu

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The supposition that the earliest metazoans will be found by existing and agreed to take two specialists, to collect, respectively, planktonic larvae and meiofauna. This is on the supposition that the earliest metazoans will be found either floating in the oceans or slithering around sediment grains. The director was, however, correct. Metazoans are found, but they have no significant similarity to either living larvae or meiofauna. Minute but multicellular, these early animals are convergent on the group of protists known as the ciliates, which 800 million years ago are their main competitors. A further surprise is that a good part of the molecular architecture characteristic of more advanced metazoans is already present, but the circuitry of the gene networks is considerably less complex.

Now we advance to 560 million years ago. Microbial life is still abundant, but the seafloor is littered with large Ediacaran animals. Comparative anatomy and histology reveal the Ediacaran animals to represent the stem groups of all the principal divisions of metazoan life. A last stop, at 500 million years ago. The hatch opens, and cheers echo across the deserted landscape. The continents are still deserts, but life teems in the seas and oceans. Among the metazoans most of the principal body plans are now well established. The Cambrian explosion is over, but the director points to some hardy arthropods scuttling across the tidal flats. She reminds us that the story of evolution is by no means finished.

[See also Body Plans; Metazoans; Molluscs.]

BIBLIOGRAPHY


— Simon Conway Morris

CANALIZATION

Canalization is the property of developmental pathways to produce standard phenotypes despite mild environmental or genetic perturbations. The term was proposed by Conrad Hal Waddington (1940; 1942, p. 563) to describe the phenomenon that "developmental pathways ... are adjusted so as to bring about one definite end-result regardless of minor variations in conditions during the course of the reaction." Developmental biologists and evolutionary biologists emphasize slightly different aspects of canalization in their definitions. The first sentence reflects the definition of Hall (1992) and points to the role of canalization as a developmental genetic mechanism to explain the constancy of phenotype. Similarly, Wilkins (1997, p. 257) emphasizes its devel-
opmental aspect when he defines canalization as "the stabilization of developmental pathways by multiple genetic factors within the genome, a form of genetic buffering." Gibson and Wagner (2000, p. 372) emphasize the evolutionary outcome of canalization as a reduction in variability, and they define canalization as "genetic buffering that has evolved under natural selection in order to stabilize the phenotype," although canalization may have components other than genetic.

Canalization allows mutations to accrue in the genotype without being expressed in the phenotype (and therefore without being immediately accessible to natural selection). Thus, in the short term, canalization limits the variability of the phenotype by promoting cryptic genetic variation. However, in the long term, canalization can act as a capacitor for phenotypic change because it allows mutant alleles to accumulate in a genome without their individual expression. Such genetic variability can be made manifest by changing the environmental conditions and can then be selected. The notion of canalization has been proposed several times under different names, including stabilizing selection (Schmalhausen, 1949), genetic homeostasis (Lerner, 1954) and universal pleiotropy (Wright, 1968).

Waddington (1942, p. 564) noted that canalization would limit variations in development such that "if wild animals of almost any species are collected, they will usually be found 'as like as peas in a pod.'" Indeed, canalization has been seen across the animal and plant kingdoms and has been invoked where the phenotypes of the wild-type organism have much less variance than phenotypes of mutants (see Eshel and Matessi, 1998; Rendel, 1967; Scharloo, 1991). The ability of developmental pathways to resist perturbations also has been demonstrated by computer models of phenotype production. Nijhout and Paulsen (1997) have shown that the phenotypic effect of variation at a single locus depends critically on the allelic values of other genes in the same pathway and on the frequency of those genes in the population. Moreover, they found that genetic background—the other genes in the genome—buffers pathways so that only a small fraction of the genes that affect the development of a particular trait can be identified in a single sampling. Von Dassow and colleagues (2000) have shown that highly evolved developmental pathways are robust entities that can regulate to produce the same phenotype even if the genotype varies within certain limits.

**Hsp90 As an Agent of Canalization.** The genetic mechanisms of canalization have recently become amenable to study. Two, in particular, have received attention in recent years: Hsp90 and functional redundancy. In 1999, Rutherford and Lindquist showed that a major agent responsible for buffering the phenotype was the "heat shock protein" Hsp90. Hsp90 is a protein that binds to a set of signal transduction molecules that are inherently unstable. Binding stabilizes their tertiary structure so that they can respond to the upstream signaling molecules. However, heat shock causes other proteins in the cell to become unstable, and Hsp90 is diverted from its normal function (of stabilizing the signal transduction proteins) to the more general function of stabilizing any of the cell's partially denatured peptides. Because Hsp90 is involved with stabilizing the structure of unstable proteins, Hsp90 might be involved in buffering developmental pathways against environmental contingencies that would destabilize proteins and against genetic mutations that might produce unstable proteins.

Evidence for the role of Hsp90 as a developmental buffer first came from mutations of Hsp83, the gene for Hsp90. Homozygous mutations of Hsp83 are lethal in Drosophila. In their heterozygous state, these mutations increase the proportion of developmental abnormalities in the population into which they are introduced. In populations of Drosophila heterozygous for Hsp83, deformed eyes, bristle duplications, and abnormalities of legs and wings appeared. When different mutant alleles of Hsp83 were brought together in the same flies, the incidence and severity of the abnormalities increased. The same abnormalities could be seen when a specific inhibitor of Hsp90 (geldanamycin) was added to the food of wild-type flies, whereas the types of defects differed between different stocks of flies.

The abnormalities did not show simple Mendelian inheritance, but were the outcome of interactions between several gene products. Selective breeding of flies with the abnormalities led, over a few generations, to populations where 80–90 percent of the progeny had the mutant phenotype. Moreover, these mutants did not keep the Hsp83 mutation. In other words, once the mutation in Hsp83 allowed the cryptic mutants to become expressed, selective matings could retain the abnormal phenotype even in the absence of abnormal Hsp90. Thus, Hsp90 is probably a major component of the buffering system that enables the canalization of development. Hsp90 might also be responsible for allowing mutations to accumulate but keeping them from being expressed until the environment changes. In other words, transient decreases in Hsp90 (resulting from its aiding stress-damaged proteins) would uncover preexisting genetic interactions that would produce morphological variations. Most of these morphological variations would probably be deleterious, but some might be selected for in the new environment. Canalization might thus be responsible for the long periods of stasis in the paleontological record of certain species, and the releasing of hidden morphological variation may be re-
sponsible for periods of radiation and morphological change.

Genetic Redundancy As an Agent of Canalization. One of the major discoveries of recent developmental biology has been the stability of phenotype even after the deletion of major developmentally important genes (Wilkins, 1997). In many instances, the loss of function of a particular gene is compensated for by the activation of another gene, sometimes from a different family than the one deleted. In other instances, there is already another protein in the cell whose activities are partially redundant to those of the protein encoded by the lost gene (Erickson, 1993; Wilkins, 1997). Nowak and colleagues (1997) have provided mathematical models to explain how redundancy can be selected for by natural selection and how redundancy can be made evolutionarily stable.

Canalization As a Link for Genetics, Evolution, and Development. Waddington's use of the term canalization to describe this limiting of phenotypic variability may have its origins in his interpretation of Alfred North Whitehead's Process and Reality (1929), a book used by several British embryologists seeking a philosophy of organization in which to ground their data (see Gilbert, 1991). Within his own theories of development and evolution, canalization had a central role. Canalization caused the formation of predictable trajectories of cell development, or chreodes; we would now call these developmental pathways. Such developmental pathways were organized into the “epigenetic landscape,” wherein canalization increased as the pathways became more completely separated from each other. Genetic assimilation could occur when the canalized pathway of development was originally initiated by an external inducer. If, by mutation or by the chance assortment of different alleles, the same pathway could be initiated by an internal inducer, the same phenotype would be produced genetically as had been induced externally (Waddington, 1942, 1953). The Hsp90 studies mentioned earlier provide a mechanism for genetic assimilation as well as for canalization. Canalization thus provides an important link unifying genetics, development, and evolution.

[See also Phenotypic Plasticity; Phenotypic Stability.]

BIBLIOGRAPHY


— SCOTT F. GILBERT

CANCER

Only a small portion of human cancer cases are caused by familial cancer syndromes, but there is strong evidence that most cancers are influenced by genetic factors. The identification of genetic variants that increase or decrease an individual's risk would provide valuable information that could lead to strategies to avoid or prevent cancer, detect it earlier, or treat it more effectively. However, this availability of genetic profiles for cancer susceptibility raises important privacy and ethical issues that have implications for individuals and their families.

Familial Cancers. In some families, cancer is inherited as a genetic disease. The prototype example of this is the eye tumor retinoblastoma. In 1971, Dr. Alfred Knudson, then of the University of Texas, proposed that these individuals inherited a defective copy of a gene present in all of the cells in their body. If a mutation occurred in the other copy of the gene, in any of the individual's retinoblasts (precursor cells to the retina), then that cell could develop into a tumor. Because there are millions of retinoblasts, there is a high probability that at least one will develop a defect and become cancerous. Knudson correctly hypothesized that those individuals that did not have the familial form of retino-