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PERSPECTIVE

The Sea Urchin Genome: Where Will It Lead Us?

Eric H. Davidson

The sea urchin genome reveals large domains of biology heretofore unexplored at the genome level, as this is the first nonchordate deuterostome sequence. The sequence will accelerate progress toward complete understanding of the genomic regulatory system that controls developmental specification and morphogenetic function, thus illuminating basic developmental process in all animals.

On 1 December 1997, a large male sea urchin of the species *Strongylocentrotus purpuratus*, probably at least 20 years old, donated several milliliters of his sperm in order for a bacterial artificial chromosome (BAC) library to be made of his genome. Immortalized and arrayed in many thousands of small wells, this library contained all the genes and all the hard-wired regulatory instructions required for construction of this sea urchin's body and for his physiological performance in confronting the natural environment (and our laboratory environment), as well as the millions of sequence differences distinguishing his maternal and paternal genomes. This particular library has played an unusually rich role in current bioscience. It provided the sequence base for the first large-scale developmental gene regulatory network to be solved for embryogenesis, the initial version of which was published in these pages in 2002 (1), and it was the DNA of this same male and of this same BAC library that have now been sequenced as presented in this issue of *Science* (2). The white paper on the basis of which it was decided to proceed with the sequencing effort was written in 2002. This was exactly a century after Boveri concluded from a famous experiment that all chromosomes (i.e., the complete genome) must be present in every cell of a sea urchin embryo for embryonic development to occur normally (3).

We now have in digital form the first genome of a nonchordate deuterostome. This is of particular interest because the deuterostomes are the large group of animal species to which both we and sea urchins belong. Sea urchins are hence more closely related to us in evolution than are flies or worms. This is also the first genome of a nonchordate marine animal of any kind to be sequenced. Among the important insights from the genome sequence was the definition of the "deuterostome toolkit," the set of genes particular to this group of animals and not shared with others kinds of animal (4). This in turn affords a definition of what genes are truly vertebrate inventions; many genes previously thought to be vertebrate-specific were found in the sea urchin genome.

Because of the sea urchin's evolutionary relation to ourselves, its genome provides what evolutionists consider an extremely useful outgroup for the understanding of our own genomes—an intellectual version of Archimedes' idea that with a leverage point removed from Earth he could move the globe. Beyond digesting all this, what will be the more global and far-reaching importance of the sea urchin genome?

We have learned that in the fundamental domain of the genomic control of life, in the genomic organization of development, in genomic explanations of evolutionary process, every animal is in some measure a model for every other animal. The sea urchin embryo has become one of the great model systems in several areas that lie within the domain of genome control. One such area is discovery of the rule set for cis-regulatory design in developmental gene regulatory modules (5). These are the discrete genomic units of regulatory function, which determine whether, when, and how much all genes are to be expressed at any given time in any given cell. Cis-regulatory modules usually consist of several hundred base pairs of



Fig. 1. A sea star, *Pisaster ochraceus*, on a bed of *Strongylocentrotus purpuratus*, the sea urchin species whose genome has now been sequenced. The body plans of these echinoderms are obviously different. But although their genomes no doubt contain a few distinct genes, the root of their different developmental processes lies in their diverse gene regulatory apparatus, which is also encoded in the genomic DNA. The sequence of the sea urchin genome opens the way to experimental analysis of the regulatory code. [Photograph: Robert Potts, California Academy of Sciences]

genomic sequence, in which are clustered multiple specifically recognized target sites for regulatory proteins (transcription factors). Someday we will be able to read the sequence of regulatory modules on which we cannot do experiments, such as our own, and understand on sight the logic functions they execute in response to the sets of transcription factors in given cells at given times. But to do that, we need to know their design principles—which can only be deduced from a deep base of structure-function data obtained by experimentally mutating the module sequence and introducing it back into the egg to see how it works in development. Gene transfer into sea urchin eggs is an uncommonly easy and efficient procedure. For the past several years, most information of this kind has come from the sea urchin and *Drosophila* model systems, and this will continue to be true, although similar experiments in mouse, *Xenopus*, *Caenorhabditis elegans*, chick, and *Ciona* show that there is a universal animal regulatory code remaining to be reduced to principles.

The sea urchin genome will directly contribute to solving the principles of design of gene regulatory networks for embryonic development. These are interacting systems of all the regulatory genes participating in each aspect of development. Such principles can only be obtained by comparing network architecture in different animals developing in similar or different ways. The sea urchin embryo is likely to be the first embryo for which a global network analysis will become available, in which every input into every regulatory gene in the network comes from some other gene in the network—or, put another way, to which the criterion of completeness can be applied everywhere. We will, in the future, be able to account for the course, and hence the outcome, of development—the body plan of each species.

The genome will not only provide the "code" for development but will also contribute to linkage between gene regulatory networks and the actual realization of developmental events. For example, the genomics of gastrulation, epithelium-mesenchyme transitions, and species-specific patterning functions are now accessible. It remains to connect the genes that execute these functions to the control circuitry that specifies their occurrence.

Many other questions will also be approachable if new genome sequences continue to emerge. Just as one example, what is speciation? The large polymorphism of sea urchins invites a direct test of the idea that most genes diverge continuously within and among species, whereas sharper changes

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in a minor fraction of genes account for the adaptive differences that separate diverging species. If we had the sequence of several additional closely related sea urchin genomes, this model could be directly assessed. Another opportunity would arise if the genome sequences of two other widely used sea urchin species, *Lytechinus variegatus* and *Paracentrotus lividus*, were available: Comparison with the genome of *S. purpuratus* would yield a global map of conserved regulatory modules around every gene. Finally and most essentially, comparative regulatory genomics provides the key to unlock the basic processes of evolution. It has been possible to compare on a small scale the embryonic networks of two animals that have evolved independently for half a billion years, the sea urchin and the sea star (6). The comparison revealed both a shocking degree of architectural conservation in certain subcircuits and a shocking level of change of

others. This cuts close to the bone of the evolutionary processes by which body plans have diverged in evolution (7). Large-scale comparisons of regulatory gene networks between multiple species of different degrees of relatedness will provide a new dimension to our understanding of evolutionary mechanism and of network architecture and system design.

The sea urchin genome sequence did not open the door to a new pathway to knowledge; it opened the door to a nexus of such pathways. They lead in diverse directions, but their central and unifying reference is the genome sequence. Indeed, its central foundation in genomics will characterize a large area of bioscience, a reorganization that is already upon us, the coalescence of what might be called “informational bioscience.” This will consist of a scientific continuum over what used to be the distinct disciplines of regulation molecular bi-

ology, evolution, developmental biology, and genomics, together with their mathematical and computational support and more traditional descriptive knowledge. The sea urchin research community is now experiencing this intellectual revolution.

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PERSPECTIVE

Ecological Role of Purple Sea Urchins

John S. Pearse

Sea urchins are major components of marine communities. Their grazing limits algal biomass, and they are preyed upon by many predators. Purple sea urchins (*Strongylocentrotus purpuratus*) are among the best studied species. They live in environments that alternate between two stable states: luxuriant, species-rich kelp forests and sea urchin-dominated “barrens.” The transition from one state to the other can be initiated by several factors, including the abundance of algal food, predators, storm intensities, and incidence of disease. Purple sea urchins compete with other grazers, some of which are important fishery resources (such as abalones and red sea urchins), and they are harvested for scientific research. Revelations from their genome will lead to a better understanding of how they maintain their ecological importance, and may in turn enhance their economic potential.

Sea urchins are major grazers in shallow seas worldwide (1). Purple sea urchins (*S. purpuratus*) and other stronglycentrotid sea urchins of the Northern Hemisphere are particularly important and are the most intensively studied (2). A delicate balance between sea urchin grazing and kelp forest productivity leads to stable states that alternate between luxuriant kelp forests and relatively species-depauperate sea urchin “barrens” (3). Curiously, the densities of sea urchins are often similar within kelp forests and sea urchin barrens. Within kelp forests, sea urchins are nearly stationary, feeding on captured pieces of kelp litter (“drift kelp”) that are produced and shed in high quantities from the kelp plants. However, when the kelps are removed by storms or El Niño events, the remaining sea urchins actively forage on young kelp recruits and on drift kelp brought

in from elsewhere, preventing the reestablishment of the kelp forest. The sea urchins can be decimated by storms (4) or diseases (5), allowing the kelp forest to return to the area.

In addition to the alternation of kelp forests and sea urchin barrens, temporal and spatial variation in recruitment of sea urchins can greatly influence their abundance, and therefore their ecological role, within kelp forests. Infrequent peaks in recruitment can lead to spurts in sea urchin densities (6), sometimes triggering intense grazing that removes the kelp, transforming a kelp forest into a sea urchin barren (7) (Fig. 1). Recruitment intensity is determined mainly by the supply of sea urchin larvae, which in turn depends on the oceanographic conditions that bring the larvae to suitable areas to settle (8).

Predators almost certainly limited the abundance of sea urchins in the past, and the presence of sea urchin barrens around the world is due at least in part to decimation of predators by humans (9). In southern California, where

sea urchin-dominated barrens are common, major predators such as spiny lobsters, sheep-head fish, and sea otters have been greatly reduced during the past century (10). Sea otters, in particular, are effective in keeping sea urchin densities low throughout their range (11), which often tips the balance toward kelp forests and enhances kelp forest productivity and biodiversity (12). Other factors also can favor kelp forests or barrens, even in the absence of major sea urchin predators (13). For example, sea urchins compete with other grazers. Purple sea urchins compete in particular with abalones and red sea urchins (14). However, because both abalones and red sea urchins have experienced intensive fishing pressure for the past several decades, competitive interactions among these species have probably decreased, perhaps relieving purple sea urchins from adverse competition. On the other hand, juvenile purple sea urchins and abalones often are sheltered from predators under the spines of red sea urchins (15), and both may be negatively affected by heavy fishing of red sea urchins. The strengths of these interactions remain poorly known and are complicated by variation in fishing pressures. Red sea urchins have been the basis of a major fishery in the eastern Pacific for the past several decades. However, the U.S. sea urchin fishery has been in decline, mainly because of a decline in demand by the Japanese market (\$110 million worth of sea urchins were exported from the United States to Japan in 1993 compared with about \$36 million in 2003) (16). The smaller, less valuable, purple sea urchins have been a minor component of the fishery but continue to play an extensive role in scientific research (2).

Sea urchins are central in structuring marine benthic communities, both as grazers and prey, and are economically valuable in fisheries.

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