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System Level Genomic Regulatory Logic: Gene Network for Sea Urchin Development

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Light Refreshments served at 2:45 p.m.

If the premise of system biology is correct then causal explanations of biological phenomena should emerge from system level analyses if they approach completeness in respect to the functional linkages among the parts of the model. The developmental GRN controlling development of the skeletogenic micromere lineage of the sea urchin embryo now includes experimentally established, causal transcriptional links to every regulatory gene expressed specifically in this lineage. It provides the opportunity to challenge directly this argument. We show that at its current level of maturity GRN structure provides an explanation, in terms of the topology of its genomically encoded subcircuits, of why all of the functions this lineage executes occur. These functions are: transformation of the initial maternal cues localized in the micromeres into an initial transcriptional regulatory state; activation of downstream genes through a double negative transcriptional gate; presentation of inductive signals to adjacent cells; dynamic lockdown of the definitive transcriptional regulatory state; specific activation of skeletogenic differentiation gene batteries; exclusion of alternative regulatory states. This progression of developmental functions can be considered as a series of logic operations and the dynamics of the system also fall, out from GRN structure. Additional GRN circuitry controls a dynamic concentric wave of gene expression beginning in the skeletogenic micromere lineage and sweeping outward across the mesodermal and endodermal domains. The GRN provides a new way to understand evolution as well as development. For example, the skeletogenic function of the micromere lineage is a derived feature of modern echinoderms that probably arose in the Triassic <250 mya. By mapping onto the topology of the GRN the genes expressed and not expressed in adult skeletogenic centers, we can discern the regulatory linkages that had to be formulated in order to co-opt skeletogenic genetic function to the micromere embryological address. This idea is subject to experimental test.

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