Embryos and ancestors: Reconstructing gene regulatory networks and embryonic development in ancestral echinoids

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“Embryos undergo development; ancestors have undergone development, but in their day they also were the products of development.”

p. 1 (1940)
Embryos and ancestors

Archaeocidaris brownwoodensis

Eucidaris tribuloides adult

Eucidaris tribuloides larva
Motivating questions

• What can we say about the embryos and developmental programs of *Archaeocidaris spp.*?

• What kinds of data are at our disposal?

• Can we simultaneously investigate fundamental processes of development and evolution along the way?
Phylogeny of echinoids

Archaeocidaris sp.

Eucidaris tribuloides

Strongylocentrotidae
- Echinometridae
- Toxopneustidae
- Parechinidae
- Arbaclidae
- Diadematidae
- Echinothuridae
- Histocidaridae
- Cidaridae

Cidaroida

Euechinoidea

Cidaridea

Time Scale:
- Triassic: 250 - 200 Mya
- Jurassic: 200 - 160 Mya
- Cretaceous: 160 - 65 Mya
- Cenozoic: 65 Mya - Present

Million Years Ago
What kinds of data can we collect to make inferences about ancestral embryos?

- **Developmental modes**
  - larval life strategies, e.g. direct v. indirect development

- **Cell lineages**
  - clade-specific novelties, e.g. larval skeleton, larval pigment, etc.

- **Gene families**
  - Gene loss, sub- and neo-functionalization of duplicated genes, etc.

- **Gene regulation**
  - Gene regulatory networks (linkages, circuits), regulatory states (spatial localization of gene products), etc.

→ Common to all of these datasets is the importance of sampling numerous taxa
What is a gene regulatory network (GRN)?

**Gene Regulation**
Protein products of genes (e.g., transcription factors, signaling cascades) regulate the production (transcription) of other genes.

**Gene Regulatory Network**
A wiring diagram representing the intricate, recursive regulatory circuitry of gene/protein interactions in the cell (or the embryo).
What is a regulatory state (RS)?

**Regulatory State**
-- The spatial output of gene regulatory networks in the embryo

-- The total set of regulatory genes present in a given cell
Strongylocentrotus purpuratus Global GRN, 18-30 hpf (hours post fertilization)
Comparative analyses in echinoderms

Embryonic development of echinoid outgroups, e.g. asteroids, ophiuroids, holothuroids, afford polarity of developmental programs and modes
Accurate dating of echinoderm fossils combined with developmental studies of modern descendants reveals the tempo and mode of developmental evolution.

Expression of mesoderm-specific regulatory gene *tbrain* in echinoderms
Dating deep-time developmental programs

Divergence estimates based on fossil data allow us to make evolutionary statements about echinoderm developmental programs.

1: 480 mya (Jell, 2014) Tbrain is deployed in endomesoderm of eleutherozoa

2: 268.8 mya (Thompson et al., 2015): Tbrain is deployed in mesoderm of echinoids

3: ~250-170 mya: Tbrain is deployed in skeletogenic mesoderm of euechinoids
A highly conserved mesodermal regulatory state in echinoderms

**erg-hex-tgif subcircuit in euechinoids**

**erg-hex-tgif subcircuit in asteroids**

**erg-hex-tgif subcircuit in cidaroids**

Erkenbrack et al. (2016) Dev Gen Evo
Table 4 Ancestral state reconstruction for embryos of ancestors of extant echinoderm clades by comparative analysis of spatial gene expression data from three or more taxa.

At least 481 mya: in ancestral embryos prior to the asterozoan–echinozoan divergence
1. erg was a mesodermal driver at blastula stage and gastrula stage
2. hex was a mesodermal driver at blastula stage
3. tgf was a mesodermal driver at blastula stage and gastrula stage
4. tgf was an endodermal driver at mid-gastrula
5. erg–hex–tgf kernel operated in mesoderm
6. Prediction: hex is likely to be expressed in mesoderm of holothurians, but endodermal expression after blastula stage is unclear

At least 482 mya: in ancestral embryos prior to the holothurian–echinoid divergence
7. erg and tgf were initiated in the mesoderm and tgf came to be expressed in the endoderm at a later time in development; whereas erg remained restricted to the mesoderm throughout early embryonic development to fulfill its ancestral function; tgf was expressed first in the mesoderm and then in the mesoderm and the endoderm
8. tgf mesoderm expression at mid-gastrula stage was either lost in asteroids or gained in the lineage leading to the last common ancestor of echinoids
9. erg was expressed in the skeletogenic lineage at least as late in development as mid-gastrula stage
10. hex endodermal expression is acquired early in asteroid embryogenesis or lost in last common ancestor of extant echinoids

At least 268 mya: in ancestral embryos at the cidaroid–euechinoid divergence, e.g., in Archaeocidarids embryos
11. erg, hex, and tgf were initiated in a few cells at the center of the vegetal pole; later in the lineage leading to camarodont euechinoids following the cidaroid–euechinoid divergence, these three genes are restricted PMCs prior to PMC ingress
12. tgf remains expressed in mesodermal cells that ingressed into the blastocoel (tgf is not expressed in mesodermal cells that have ingressed in holothurians)
Going forward

**Conceptual Toolkit**
Integrating paleontological data and embryonic developmental data informs assumptions regarding the genomic and morphological alterations that must have occurred in lineages leading to modern taxa.

**Evolution of developmental programs**
Interdisciplinary studies reveal the tempo and mode of evolution of genomically encoded developmental programs.

**More taxa, fewer problems**
Comparative analyses of embryonic development and omics data of numerous taxa afford triangulation of evolutionary inferences and ancestral state reconstruction.
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WARNING

Interdisciplinary Advertisement

I encourage paleontologists in the audience to reach out to developmental biologists!
Evolutionary inferences of the appearance of GRN circuitry

Comparative analyses of gene expression and knowledge of the fossil record revealed probability metrics for the appearance of this developmental program.

Thompson, Erkenbrack, et al. (In review) PNAS