NEWS

# A Close Look at Urbisexuality

## A developmental biologist takes aim at understanding the evolutionary origins of eggs and sperm in our 600-million-year-old ancestor

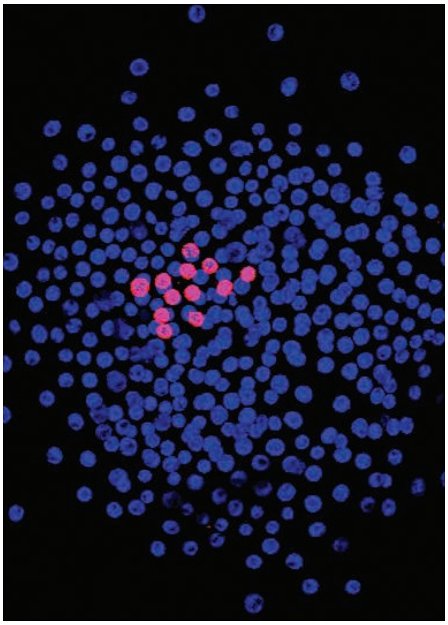
For a creature no one has ever seen and never will see alive, Urbilateria generates a lot of passion. Scientists have vigorously debated whether it sported legs or antennae, whether it had a true heart, and whether its body was segmented. Such arguments may never be settled, however. Urbilateria is a hypothetical organism that lived 550 million to 800 million years ago and was the last common ancestor of a menagerie that includes mollusks, worms, flies, mice, and people.

Discussions of this mythical creature are more than just pub-fueled speculations at the end of a long day in the laboratory, say practitioners of evo-devo, a field that uses developmental biology to study evolution and vice versa. Although some animals have no anatomical symmetry (sponges) or display radial symmetry (corals and jellyfish), most animal phyla have bilateral symmetry, and Urbilateria would have been their forerunner. As such, Urbilateria offers a framework for thinking about how the current diversity of bilaterians emerged from the twists and turns of evolution.

In 2002, Cassandra Extavour, a postdoc in Michael Akam's laboratory at the University of Cambridge in the U.K., realized something was missing from all the musings on Urbilateria. "So much of evo-devo over the last 20 years centered on what Urbilateria looked like," says Extavour. "But no one [was] talking about how this animal reproduced."

So, in talks at the Society for Integrative and Comparative Biology annual meeting in January, and in book chapters in press, this developmental biologist has begun to discuss what she cleverly calls "urbisexuality." Her approach makes sense, says Adam Wilkins, editor of *Bioessays* and a geneticist who studies sex determination. "We'd like to know what the earliest bilateral animals looked like and acted like, and that includes their reproductive history."

The sex lives of these ancient creatures has eluded Extavour, but she has made progress understanding one of the more fundamental aspects of Urbilaterian reproduction: the origins of their sperm and egg. Her work "is original," says paleobiologist Douglas Erwin of the National Museum of Natural History in Washington, D.C., who has written considerably on the nature of Urbilateria. "It never dawned on me to consider these sorts of issues." Wilkins agrees: "As far as I know, this is the first serious attempt to look at their reproduction." Moreover, Extavour's contemplation of urbisexuality has led her to rethink the evolutionary connections between primordial germ cells, which ultimately make sperm and eggs, and the stem cells that give rise to other tissues.



**Future sperm or eggs.** Antibodies to a protein called Vasa (pink) reveal the relatively few cells in this crustacean embryo destined to become germ cells.

### Humble beginnings

The sexiest questions about urbisexuality obviously concern Urbilateria's sex life. Was the ancient animal hermaphroditic? Or were the sexes of Urbilateria separate, and if so, did reproduction rely on external or internal fertilization? If the latter were the case, then Urbilateria's gonads would have been quite sophisticated.

Extavour considers the answers to such questions largely unknowable. Typically, evolutionary biologists piece together the lifestyle of a long-gone organism by scanning the modern tips of evolutionary trees for physical traits or developmental genetic networks shared by most of its descendents. Traits in common to a broad spectrum are likely ancestral. But so many reproductive strategies are strewn across every bilaterian phyla that the identification of an ancestral state is probably impossible. Both egg laying and vivipary, in which an embryo develops inside a parent, are seen across all clades, for example, so it's hard for researchers to tell which strategy evolved first.

Picking a more tractable question about urbisexuality, Extavour has concentrated on what got her thinking about Urbilateria in the first place: primordial germ cells. She notes that these germ-cell precursors compete with one another during development within arthropods. The primordial germ cells often arise in one portion of the embryo and migrate relatively long distances to what becomes a gonad; there they develop into sperm or eggs. But studies had shown that only some of the primordial germ cells win this race to the gonad; the latecomers vanish from the embryo's so-called germ line, its eggs or sperm. This example of survival of the fittest—or fastest—led Extavour to take a broader Darwinian look at primordial germ cells. "I started to think about the role of germ cells in evolution and began wondering how different animals make germ lines," she says.

Much has been written about when and why animals first evolved a germ line. Some researchers have even argued that the emergence of specialized reproductive cells distinct from other tissue—the soma—was a prerequisite for multicellular organisms. Extavour agrees with that thinking. So, assuming that a germ line predated Urbilateria, she asked how certain cells in an Urbilateria embryo ended up as the animal's germ cells, not a heart or a nerve cell.

Modern organisms typically use one of two methods to give germ cells their unique identity. By one route, preformation, part of an unfertilized egg's cytoplasm contains a distinctive mix of proteins, chemicals, and genetic instructions. This material is the so-called germplasm. As the egg divides and redivides, bits of germplasm wind up in some cells but not others. Inside those cells, it sets off a genetic cascade. Genes such as

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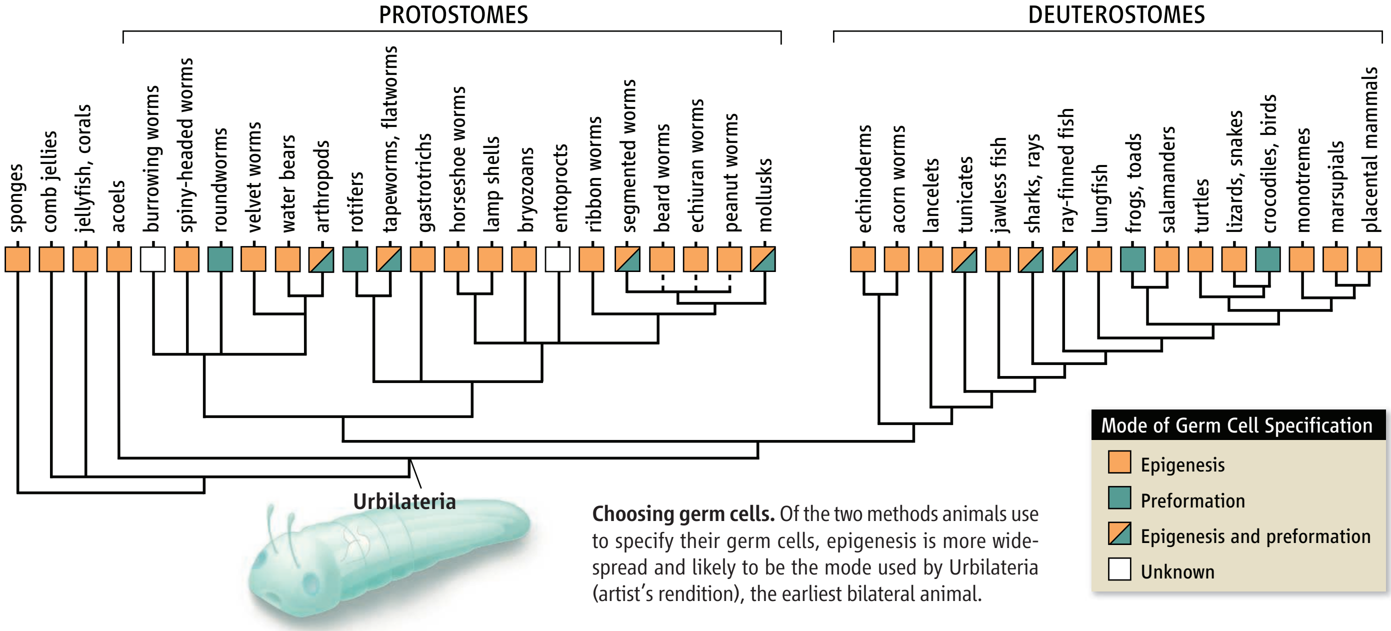


**Choosing germ cells.** Of the two methods animals use to specify their germ cells, epigenesis is more widespread and likely to be the mode used by Urbilateria (artist's rendition), the earliest bilateral animal.

*vasa* and *nanos* become active, for example, and help prepare those cells for a future as eggs or sperm. In animals relying on preformation, that germplasm is retained or restocked within new oocytes; thus, it is inherited from generation to generation.

Where there is no germplasm, epigenesis comes into play. All the cells in the embryo start out apparently equal. But as the embryo grows, certain cells release chemicals that force their neighbors to become the germ line. The question for Urbilateria: Do the cells that decide to become its primordial germ cells "inherit something or get an instruction?" asks Extavour.

The mouse relies on epigenesis: Certain embryonic cells release bone-morphogenic proteins that tell other cells to become germ cells. But the more primitive animals commonly studied in the lab—zebrafish, fruit flies, nematodes, frogs—all depend on germplasm to specify their germ cells, so biologists had assumed that preformation was the ancestral state. In a 2003 review of existing data on 28 animal phyla, however, Extavour and Akam found little cytological, cell lineage, or experimental data to indicate preformation in most species. They concluded that epigenesis was very widespread and that it probably arose first.

## From stem cells to germ cells?

Extavour has continued to amass data supporting that surprise and has also developed a model of how preformation could have arisen in some of Urbilateria's descendents. In epigenesis, many of the molecules inside primordial germ cells that drive the cells' differentiation into sperm or eggs vanish once that job is done. Extavour thinks that at some point post-Urbilateria, a mutation occurred that allowed those factors to persist in an oocyte—voilà, preformation. It could have been a simple matter of keeping genes such as *vasa* and *nanos* turned on in oocytes instead of turning them off—so simple, in fact, that Extavour suspects this happened multiple times on different evolutionary branches. If that's true, she speculates, there are modern animals able to employ both modes of germ cell specification. Even so, their embryos likely rely on only one.

"Of all the evo-devo stories, Extavour's work is among the most interesting," says Helen White-Cooper of the University of Oxford, U.K., who studies germ-cell development in fruit flies. To strengthen her case, Extavour should try to confirm whether an animal known to rely upon preformation "might be able to use another mechanism if forced," White-Cooper suggests. Indeed, Extavour and collaborators are now doing just that.

Next, Extavour wants to understand evolutionary links between primordial germ cells and the somatic stem cells that give rise to all the nongermline tissues in an organism. The two cell types share many morphological features, and certain genes that guide somatic stem cell growth appear related to genes active in primordial germ cells. Also, at the most basic level, both classes of cells are close to immortal: They survive and divide for a long time without specializing.

Moreover, researchers have shown that the primordial germ cells of some species, including humans, can act as somatic stem cells, giving rise to more than just reproductive cells. And others are coaxing nongermline stem cells from early embryos to develop into sperm and eggs (*Science*, 23 September 2005, p. 1982).

Cell biologists have considered somatic stem cells to be developmental spinoffs of germ cells because of their similarities in gene expression and differentiation. Twisting that idea a bit, Extavour hypothesizes that germ cells arose as a subset of stem cells. She notes that primitive nonbilateral animals such as sponges and jellyfish maintain stem cells that can give rise to either new somatic cells or gametes. Because the stem cells of sponges and jellyfish are dispersed throughout their bodies, she suggests that Urbilateria's germ cells were similarly scattered. As scientists identify more genes that are active in both primordial germ cells and somatic stem cells and trace their history, Extavour hopes to confirm this evolutionary scenario.

Wilkins, who plans to collaborate with Extavour, calls her unconventional revision of the history of germ cells and stem cells a "big idea." And he thinks Extavour's investigations of urbisexuality will draw others to probe the evolution of germ cells and reproductive systems. The topic, Wilkins laughs, "will become, I can't resist saying, sexier to study."

–JOHN TRAVIS

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