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Knowing your head from your tail

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Abstract

Information for establishing the anterior-posterior axis of a mammalian embryo is contained in the fertilized egg.

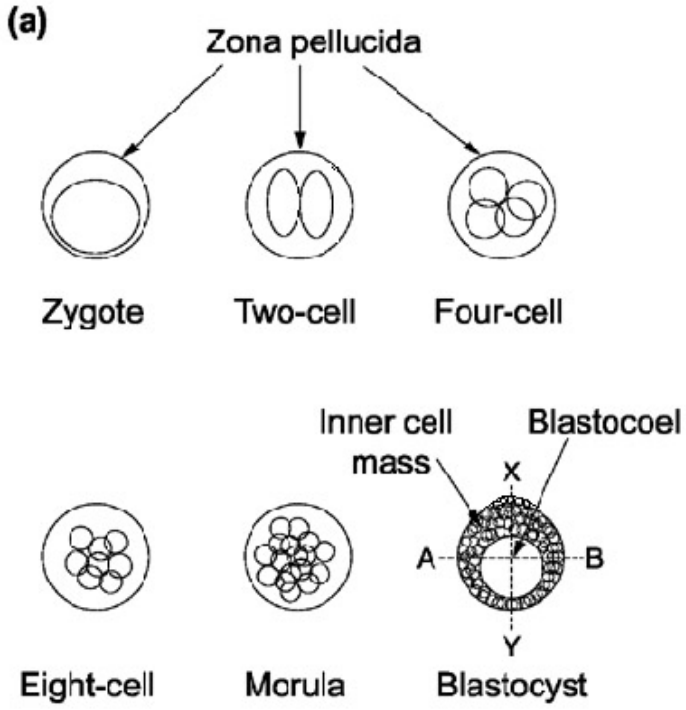
Significance and context

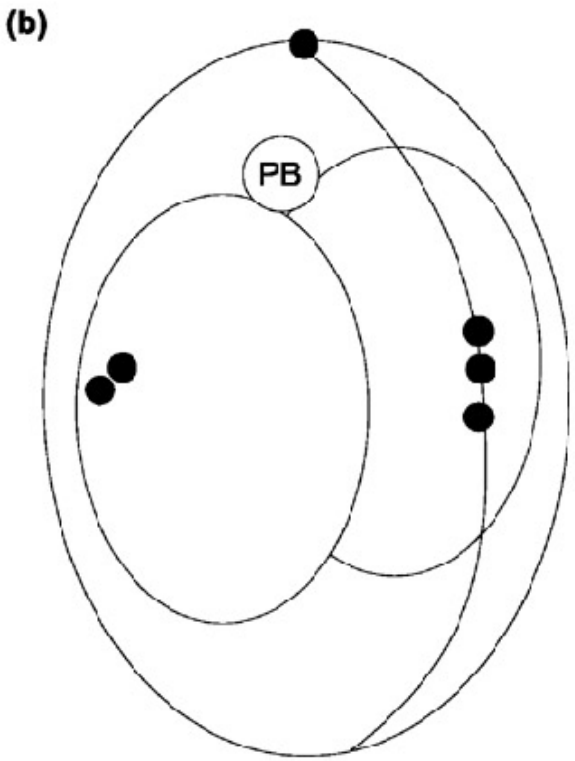
How does a single cell develop into a complete multicellular animal with a head and a tail and a front and a back? The fertilized mouse egg, or zygote, cleaves into two cells, then four, eight and sixteen cells, and again to form a morula and finally the blastocyst (Figure 1a); these are the preimplantation stages of mammalian development. The blastocyst then hatches from the zona pellucida and implants in the uterus wall. The mouse embryo proper subsequently develops from the inner cell mass of the blastocyst.

In many vertebrates, the establishment of anterior-posterior (head-tail) and dorsal-ventral (back-belly) axes starts in the fertilized egg. But until recently, studies had suggested that, in mammals, axis specification did not occur until much later in embryonic development, after the blastocyst stage. Gardner has previously challenged this view, and here he presents more evidence for a very early specification of the anterior-posterior axis in the mouse. He bases his argument on his earlier finding that the early blastocyst is already bilaterally rather than radially symmetrical (Figure 1a), and that this bilateral axis (the future anterior-posterior axis) is aligned with the animal-vegetal axis of the zygote, as determined from the consistent position of the surviving second polar body (the other product of the final meiotic division that yields the oocyte). It has recently been demonstrated that in the mouse, the point of entry of the sperm into the egg predicts the plane of the first cleavage, suggesting that spatial patterning is established at fertilization.

In the present paper, Gardner provides further evidence in support of this by investigating the two-cell stage of preimplantation development. He had previously observed that the zona pellucida surrounding the cells is elliptical; it has a smaller diameter at the plane of first cleavage. This prompted Gardner to investigate whether there was any relationship between the topography of the two-cell embryo and the blastocyst. If there is, it would clearly argue that specification of embryonic pattern in mammals begins much earlier in development than previously thought.

Figure 1 **(a)** Stages of preimplantation mouse embryo development. Axes of polarity are marked on the blastocyst. XY is known as the embryonic-abembryonic axis, as it starts in the inner cell mass, from which the embryo derives, and finishes at the floor of the blastocoel, from which extra-embryonic tissues originate. AB is the 'axis of bilateral symmetry', and corresponds to the anterior-posterior axis of the later embryo. The second polar body (not shown) lies at one end of this axis, showing that it is aligned with the so-called animal-vegetal axis of the zygote.
(b) Oil-drop mark points in the zona pellucida of the two-cell stage.

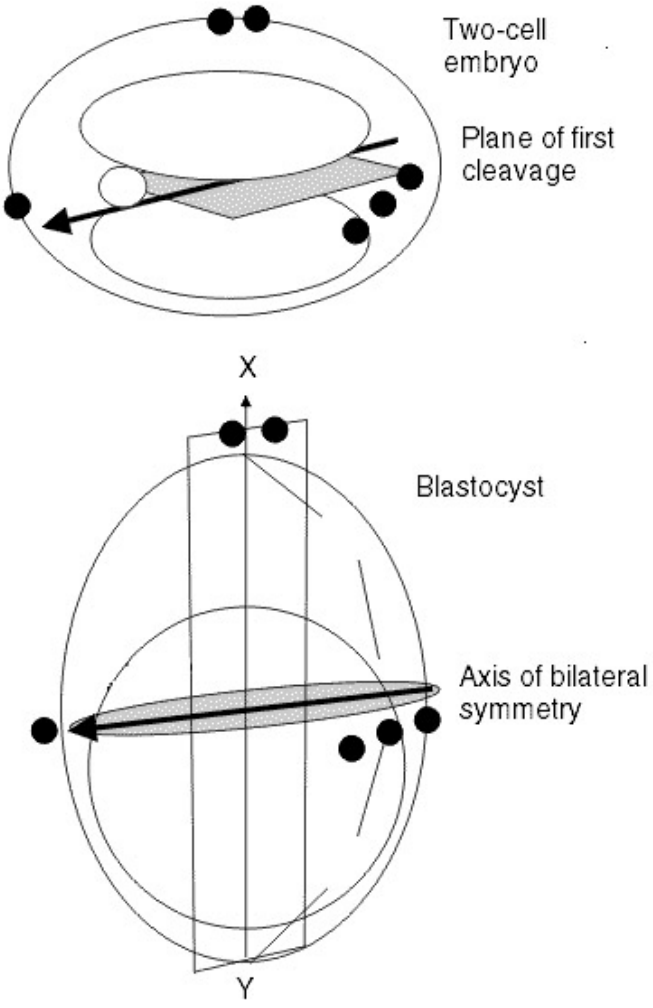




Key results

Gardner found a definite topographical relationship between the blastocyst and the two-cell stage, as demonstrated by the position of oil droplets (see Methodological innovations) in the zona pellucida at these two stages. He found that the one- and three-drop marks, which marked the plane of first cleavage (see Figure 1b), typically lay over the equatorial region of the blastocyst in a distribution he describes as 'impressively non-random'. The one-drop mark, indicating the position of the second polar body, was typically aligned with the line of greatest diameter of the blastocyst and the axis of bilateral symmetry, and the three-drop mark with the line of least diameter. Thus Gardner showed that the embryonic-abembryonic axis and its plane of symmetry in the early blastocyst always appeared at right angles to the plane of first cleavage in the two-cell stage, and to the axis of bilateral symmetry and its plane of symmetry in the blastocyst (Figure 2).

Figure 2 Relationships between two-cell embryo and blastocyst topography and axes



Methodological innovations

Gardner devised a non-invasive method of marking the zona pellucida in order to uncover the relationship between flattening of cleavage-stage embryos and the early blastocyst. He had previously noted that the cells of the cleavage-stage embryo do not rotate inside the zona pellucida, so he injected tiny drops of oil, visible in the optical microscope, into the zona pellucida. One drop was placed directly in front of the polar body, and two drops at right angles to this in the same plane. The embryo was then rotated, so that one was looking down on the polar body and its oil drop, and three drops were placed to mark the space between the two cells, the plane of first cleavage (see Figure 1b). In this way, the one-drop and three-drop marks lay on the plane of first cleavage, and the two-drop mark lay at right angles to it. Gardner then observed the distribution of these oil drops following cleavage *in vitro* up to the early blastocyst stage.

Conclusions

The novel non-invasive marking technique demonstrates how patterning is initiated during normal development. As both the embryonic-abembryonic and bilateral axes of the blastocyst are established before the second cleavage occurs, both must depend on information already present in the zygote. Signals provided by the animal-vegetal axis of the zygote could provide cues for the axis of bilateral symmetry, but the embryonic-abembryonic axis must require patterning information that is at right angles to this.

Reporter's comments

The work presented by Gardner and his insights into developmental processes have been instrumental in questioning previously held beliefs about mammalian spatial patterning.

Table of links

Development

References

1. Gardner RL: Specification of embryonic axes begins before cleavage in normal mouse development. Development. 2001, 128: 839-847. 0950-1991