epiblast, which alone is destined to form the entire mouse (Fig. 1a). The future posterior end of the embryo is defined by formation of the primitive streak, an avenue through which epiblast cells can move to form a new tissue layer, the mesoderm. The anterior end of the streak corresponds to the organizer which, in the mouse, has many of the inductive and gene-expression properties of its frog counterpart. It gives rise to the axial mesendoderm, which populates the midline of the embryo. The middle of the streak produces more lateral embryonic mesoderm, whereas extra-embryonic mesoderm emerges from its posterior end. Traditional thinking is that axial mesendoderm from the organizer should induce anterior character in the embryo.

Using targeted mutagenesis, Ding *et al.*[2] studied the function of *Cripto*. This gene belongs to a newly discovered family that encodes secreted proteins with cysteine-rich and epidermal-growth-factor-like motifs. *Cripto* is initially expressed exclusively and uniformly in the epiblast. Then, gradually, its transcripts become restricted to the proximal rim of the epiblast, which is fated to form the primitive streak (Fig. 1a). The authors found that embryos lacking *Cripto* have neither a streak nor an embryonic mesoderm, although extra-embryonic mesoderm is present. Markers of the streak are transiently expressed throughout proximal epiblast, but they never become localized — as they should if a streak formed. Likewise, the organizer and axial mesendoderm are absent. Yet in spite of this, the epiblast differentiates into neural tissue that shows only anterior (forebrain and midbrain) character (Fig. 1b). How can this anterior identity arise without an organizer?

It transpires that antero-posterior asymmetry in the mouse embryo not only precedes formation of the streak — and hence the organizer — but that it first appears extra-embryonically in the visceral endoderm. Immediately after the embryo has implanted, expression of a homeobox gene, *Hex*, delineates a small cluster of visceral endoderm cells at the distal end of the embryo (Fig. 1a). Expression of *Hex* then shifts to one side of the embryo because, remarkably, these distal visceral endoderm cells give rise only to anterior progeny[3]. Thus, almost a day before the primitive streak is formed, there is asymmetrical cell deployment in the visceral endoderm, converting a proximo-distal difference in gene expression to an antero-posterior one. Cell movements in the proximal epiblast rapidly mirror this, so that cells expressing genes associated with formation of the primitive streak congregate posteriorly. Although Ding *et al.* found that antero-posterior patterning occurs in *Cripto* null embryos, it is not in the correct orientation (Fig. 1b) — the anterior tissue remains in a distal location, whereas the most posterior epiblast derivative, extra-embryonic mesoderm, emerges proximally. Hence, the Cripto protein, secreted by epiblast, is necessary for the complementary cell movements in the visceral endoderm and epiblast that orientate the antero-posterior axis.

Other studies have revealed that extra-embryonic tissues are not simply nutritive — they also directly influence embryonic patterning. Removal of the anterior visceral endoderm inhibits differentiation of anterior neural tissue[4]. Expression of genes such as *nodal*[5] (a member of the transforming growth factor-β (TGF-β) superfamily) and *Otx2* (ref. 6; a transcription factor) is required in the visceral endoderm, rather than the epiblast, for initiation of embryonic anterior pattern. Anterior development also needs Smad2 (a component of the TGF-β signal-transduction pathway) extra-embryonically[7,8]. This all points to a mechanism for defining the anterior terminus that does not rely on signals from the classical embryonic organizer, but depends instead on interaction with the enveloping extra-embryonic tissues.

We do not yet know the details of this interaction, nor how the initial proximo-distal asymmetries arise. Likewise, the functions of Cripto and its relatives are not clear. We also need to know whether this extra-embryonic source of anterior patterning is a peculiarity of development in the uterus, or whether it has evolved from specialized cells with similar patterning functions in other vertebrate embryos. Where would such antecedents reside in lower vertebrates? In frogs, yolky cells in the deepest reaches of the organizer express *cerberus*, a gene that is instrumental in head formation[9]. Because a *cerberus* homologue is first expressed in the anterior visceral endoderm of mouse embryos[10], the yolky cells may be the frog equivalent of extra-embryonic endoderm. In which case, do the same cues that induce the frog organizer induce these *cerberus*-expressing cells? Or, as in the mouse, does the tissue responsible for imparting anterior identity have a separate origin? □

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1. Harland, R. & Gerhart, J. *Annu. Rev. Cell Dev. Biol.* **13,** 611–667 (1997).
2. Ding, J. *et al. Nature* **395,** 702–707 (1998).
3. Thomas, P., Brown, A. & Beddington, R. S. P. *Development* **125,** 85–94 (1998).
4. Thomas, P. & Beddington, R. S. P. *Curr. Biol.* **6,** 1487–1496 (1996).
5. Varlet, I., Collignon, J. & Robertson, E. J. *Development* **124,** 1033–1044 (1997).
6. Rhinn, M., Dierich, A., LeMeur, M. & Ang, S. L. *Development* **125,** 845–856 (1998).
7. Waldrip, W. R. *et al. Cell* **92,** 797–808 (1998).
8. Nomura, M. & Li, E. *Nature* **393,** 786–790 (1998).
9. Bouwmeester, T. *et al. Nature* **382,** 595–601 (1996).
10. Belo, J. A. *et al. Mech. Dev.* **68,** 45–57 (1997).

Daedalus

New smells for old

Body odour is a worry for thousands of people. Chemical products alleged to abolish or modify it enjoy enormous sales. Daedalus now has a new approach.

He points out that our body odour depends on our 'personal ecology' of skin bacteria, which make a living by fermenting our sweat. Some unfortunates are home to bacteria that ferment their sweat to highly offensive compounds. No amount of washing or deodorizing can abolish this problem. The skin bacteria form a stable equilibrium ecology, suited to the local conditions. They can never be completely eliminated, and the few survivors will recolonize their territory and establish the equilibrium anew.

But, says Daedalus, it is most unlikely that skin can sustain just one equilibrium ecology. He points out that our gut also harbours a complex stable consortium of organisms. Yet a few newcomers can sometimes precipitate an eruption of 'episodic gastroenteritis' that expels the old consortium and establishes a new one.

So DREADCO bacteriologists and cosmeticians are doing the same with the skin. They are sampling the skin flora of volunteers, and identifying the metabolic role of each organism in the consortium. For each volunteer, they will then devise a different mixture of organisms, calculated to exploit his sweat a little more efficiently, or be more at home in his surface microclimate. When spotted onto his skin, the new consortium will spread rapidly — possibly with a moving line of itching and reddening as the microscopic battle rages. When it has died down, his new occupiers will ferment his sweat differently. So he will smell different.

Discovering which consortia are most stable on what type of skin, and what smell they produce, will be a complex and demanding piece of research. But DREADCO's 'bioactive anti-odour treatment' should then be wildly popular. Victims of body odour will run (or be pushed) to the DREADCO clinic for the treatment. Criminals on the run may join the queue, hoping to change their smell and baffle the bloodhounds. And the Brussels bureaucracy, always keen to impose yet another intrusive European harmonization, may ask Daedalus to devise a super-dominant skin consortium, to be spotted onto every EU citizen. A uniform European smell, eliminating all xenophobic remarks about smelly foreigners, could bring a new instinctive unity to the emerging superstate.

David Jones