Daedalus

Problems with niches

Why are there so many species? One answer is that each species has its own 'niche'. If two species occupy exactly the same niche, says the doctrine, one will drive the other extinct. Accordingly, the natural world is a mass of subtly different niches, each exploited by a specialized species. Hence, for example, a forest is a mass of different trees. Each has its own shape of leaf with its own chemical composition, discouraging the insects and other forest creatures that live in that niche from eating it. A 'standard leaf', optimizing the uptake of solar energy and common to many plants, has not evolved.

Sadly, a niche is left undefined. Yet the central claim is often made that just one species of a given type can inhabit one. To resolve the matter, Daedalus will try out 'artificial life'. He will allow a mix of programmed species to evolve in a computer. He recalls Robert Axelrod's famous work on how cooperation evolved. Many programs playing 'Iterated Prisoner's Dilemma' competed together, and the ensemble tested the way cooperation or competition survived or grew under 'darwinian' conditions. Similarly, if we could recognize a niche in practice, we could discover if niche theory made real sense.

So DREADCO information technologists are setting up a large number of closely related species in a big computer, and are setting them all to mutate and evolve simultaneously. There are two possible outcomes. The most successful species may drive all the others extinct, leaving it in sole command of the computer. Alternatively, the programs may diversify into a whole batch of different species, each fairly secure in some niche of program space. To make this work, a niche must be properly defined in computer terms.

Daedalus also recalls how the Soviet Union tried to identify, for example, the 'best' sewing machine. It could then be made in a huge factory for the whole Union. This idea came unstuck. By contrast, Western competition lets many small manufacturers compete, and each somehow survives in its own economic niche. Indeed, some analogy must relate an economic niche to a biological one. If Daedalus can spot it in practice, he will be able to find the ideal economic number of manufacturers, and compare it with the number found in free-market economics. With luck, the free market will turn out to be as closely ideal as freely evolved darwinian ecology is in the natural world.

David Jones

Chromosome segregation is then triggered by the anaphase-promoting complex (APC), which mediates the degradation of cyclin B2 and, hence, inactivation of MPF.

Entry into the second meiotic division occurs as MPF is reactivated, when newly synthesized cyclin B2 associates with Cdc2. But now the degradation of cyclin B2 is blocked so eggs arrest division before they separate their replicated chromosomes, at a stage called metaphase II. This arrest may be a safeguard against parthenogenesis — embryonic development without fertilization — as its release is triggered by fertilization.

Our first insight into how oocytes arrest in metaphase II came from Masui and Markert¹, who showed that cytoplasm from a metaphase-II-arrested oocyte could induce a similar arrest when injected into a mitotically dividing embryonic cell (blastomere). They concluded that this arrest could be attributed to a specific activity, dubbed CSF, in the cytoplasm of the arrested oocyte. They found that CSF arose in the cytoplasm following the appearance of MPF, roughly when the first meiotic division began; and that CSF levels increased between the first and second meiotic divisions and declined after fertilization, shortly after the inactivation of MPF¹.

But attempts to biochemically purify CSF were frustrated by its instability, and the study of the molecular properties of CSF languished for almost 20 years, until Sagata *et al.*³ showed that the Mos protein has many characteristics in common with CSF. Mos was synthesized prior to entry into the first meiotic division and degraded after fertilization; injection of Mos into a mitotic blastomere caused metaphase-II-like arrest; and extracts of metaphase-II-arrested eggs that had been depleted of Mos lacked CSF activity³. Thus, Mos is a component of CSF.

Mos is a protein kinase that activates the mitogen-activated protein kinase (MAPK) pathway. Like Mos, each component of this pathway, including MAPK and p90^{rk}, behaves like CSF when injected into blastomeres^{4–6}. Most recently⁷, p90^{rk} has been shown to phosphorylate and activate the APC inhibitor Bub1. Thus, synthesis of Mos and activation of the MAPK pathway might culminate in activation of Bub1 and inhibition of APC activity, which consequently cannot trigger cyclin B2 degradation and release from metaphase II arrest.

However, although the Mos pathway is a necessary component of CSF, by itself it is insufficient to maintain metaphase II arrest; after fertilization, cyclin B2 is degraded before inactivation of the Mos pathway. Indeed, it does not even appear to be necessary to maintain metaphase II arrest, as Reimann and Jackson² now show that blocking this pathway with a MAPK inhibitor does not cause cyclin B2 degradation in CSF-containing extracts. These authors instead propose that the Emi1 protein, identified

previously as an APC inhibitor, is needed to maintain metaphase II arrest.

Reimann and Jackson found that adding extra Emi1 to the CSF-containing extracts prevented the destruction of cyclin B2 that is triggered by the addition of calcium — a process that mimics fertilization. By contrast, depletion of Emi1 led to cyclin B2 degradation. Furthermore, as shown previously⁸, adding Emi1 to mitotic blastomeres arrests their division. Their results suggest that Emi1 arrests the second meiotic division by preventing the destruction of cyclin B2, in a MAPK-independent way, and that fertilization would lead to the inhibition of Emi1 and activation of the APC, releasing the egg from metaphase II arrest.

What, then, is the role of the Mos pathway in CSF activity? The observation that mouse oocytes lacking the *mos* gene fail to arrest at metaphase II and spontaneously complete the second meiotic division^{9,10} indicates that Mos is both necessary and sufficient for entry into metaphase II arrest, especially given that naturally occurring (endogenous) Emi1 fails to cause this arrest in the absence of Mos. Thus it would seem that endogenous Emi1 is not sufficient to activate the CSF activity and that the activity of, or responsiveness to, endogenous Emi1 is regulated in a Mos-dependent fashion.

Given the involvement of Mos in the formation of the meiotic spindle^{11–14}, we propose that Mos-mediated modification of this spindle, perhaps at the kinetochores (where chromosomes attach), is required for Emi1 activity. If so, then blastomeres injected with Mos would arrest their division because Mos-induced changes in spindle structure increase its sensitivity to the effects of endogenous Emi1. By contrast, exogenous Emi1 might induce blastomere arrest because it compensates for the usual lack of sensitivity of the mitotic spindle to endogenous Emi1. This remains to be seen. But for now, it is satisfying to see that another piece in a 30-year-old puzzle is in place. ■

Nicholas S. Duesbery is in the Laboratory of Developmental Cell Biology, and George F. Vande Woude is in the Laboratory of Molecular Oncology, Van Andel Research Institute, 333 Bostwick NE, Grand Rapids, Michigan 49503, USA. e-mail: george.vandewoude@vai.org

- Masui, Y. & Markert, C. L. *J. Exp. Zool.* 177, 129–145 (1971).
- Reimann, J. D. R. & Jackson, P. K. *Nature* 416, 850–854 (2002).
- Sagata, N., Watanabe, N., Vande Woude, G. F. & Ikawa, Y. *Nature* 342, 512–518 (1989).
- Haccard, O. *et al.* *Science* 262, 1262–1265 (1993).
- Gross, S. D., Schwab, M. S., Lewellyn, A. L. & Maller, J. L. *Science* 286, 1365–1367 (1999).
- Bhatt, R. R. & Ferrell, J. E. Jr *Science* 286, 1362–1365 (1999).
- Schwab, M. S. *et al.* *Curr. Biol.* 11, 141–150 (2001).
- Reimann, J. D. *et al.* *Cell* 105, 645–655 (2001).
- Colledge, W. H., Carlton, M. B., Udy, G. B. & Evans, M. J. *Nature* 370, 65–68 (1994).
- Hashimoto, N. *et al.* *Nature* 370, 68–71 (1994).
- Choi, T. *et al.* *Proc. Natl Acad. Sci. USA* 93, 7032–7035 (1996).
- Verlhaac, M.-H. *et al.* *Development* 122, 815–822 (1996).
- Gross, S. D. *et al.* *Curr. Biol.* 10, 430–438 (2000).
- Bodart, J. F. *et al.* *Dev. Biol.* (in the press).