HIGHLIGHTS

IN THE NEWS

Update on GM

On 4 February 2002, the Royal Society released a report entitled 'Genetically modified plants for food use and human health — an update'. Prepared by a group of experts, led by Jim Smith from the Wellcome/CRC in Cambridge, UK, it focused on **"the effects that GM foods might have on human health"** (*The Royal Society report*). It states that **"the dangers of eating GM food were negligible"** (*Financial Times*), and that **"GM products licensed for sale in Britain are safe"** (*The Independent*). The report questions **"whether commonly used safety tests for modified food are adequate"** (*The Independent*) and calls for more rigorous tests. At present, GM safety assessment relies on a principle of "substantial equivalence", **"whereby a new GM crop is deemed safe if it is essentially the same as the unmodified equivalent"** (*Financial Times*). But the experts found this method insufficient, and warned that genetic modification **"could lead to unpredicted harmful changes in the nutritional state of foods"** (*The Guardian*). There was special concern about the potential effects of GM food on those with restricted nutritional intake, such as babies, and **"... the poor of Central America, who have maize as 50% of their food ... [and] might be affected by poorer nutritional standards in the new crops"** (*The Guardian*). The experts also called **"for more work to rule out possible links between GM crops and the development of allergic reactions"** (*The Independent*). The report coincides with a finding that **"super weeds ... in field margins or some distance from GM crops"** acquired **"genes from modified crops and ... became resistant to a series of herbicides"** (*The Guardian*).

Magdalena Skipper

DEVELOPMENTAL BIOLOGY

The making of an organ

Events that underlie organ specification continue to elude developmental biologists, largely because most organs are complex structures that form late in embryogenesis, as a result of multistep processes. The *Caenorhabditis elegans* pharynx, however, is a rather simple model, and so researchers have turned to it for clues about organogenesis. This organ has proved particularly useful for Gaudet and Mango, who have found that pharyngeal identity in *C. elegans* is specified directly by a master transcription factor, PHA-4, which turns on different genes at different times depending on the affinity with which it interacts with its targets. The finding raises the possibility that direct transcriptional regulation of gene networks is a general theme in organogenesis.

PHA-4, which is closely related to FoxA, a transcription factor of the forkhead box A family, has been implicated in gut development in *Drosophila* and mammals. Although this molecule has a fundamental role in pharynx specification in worms — *pha-4* loss-of-function mutants have no pharynx — few of its downstream targets had been described. To address this problem, the authors probed *C. elegans* microarrays with cDNAs from mutant worms that either had an excess of pharyngeal cells or lacked them completely. The validity of their approach was confirmed when genes already known to be regulated by PHA-4 were found among the 240 initially identified targets. Some of the new PHA-4 targets were expressed early in embryogenesis and some late, so, to show that PHA-4 regulates its targets throughout pharynx development, the authors made temperature-sensitive (*ts*) *pha-4* mutants. Shifting *pha-4* (*ts*) worms to the restrictive temperature at any time during embryogenesis resulted in an abnormal pharynx and lethality.

The authors searched the regulatory regions of the newly identified targets for the known PHA-4 consensus binding site. Not only were they able to find multiple PHA-4 binding sites, but also, using deletion analysis, they showed that pharyngeal expression of these targets absolutely depended on the presence of these consensus sites. *In vitro* analysis showed that the affinity of PHA-4 for its consensus binding site depends on the core sequence. Satisfyingly, early pharynx genes have a high affinity for PHA-4 — necessary when PHA-4 levels are low — but low-affinity PHA-4 binding sites are sufficient for late expression, when PHA-4 levels have had time to build up. By altering the binding site sequence, the authors were able to turn early genes into late ones and vice versa. On their observations, Gaudet and Mango propose a model of pharynx development in which PHA-4 directly regulates pharyngeal genes through differential affinity for its binding sites.

Direct transcriptional regulation might be a general feature of organ specification; for example, *Pax6/eyeless* is crucial for eye specification in *Drosophila* and is required to activate early and late targets. And there is evidence that FoxA proteins are required early and late in development in mammals and *Drosophila*. The authors point out that this master-regulator model has interesting evolutionary implications — gene networks, such as the one regulated by PHA-4 could evolve by sequential recruitment of new genes, leading to increased organ complexity. Although this model needs to be substantiated in other systems, it might represent an important step towards understanding how organs are specified and how they evolve.

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References and links

ORIGINAL RESEARCH PAPER Gaudet, J. & Mango, S. E. Regulation of organogenesis by the *Caenorhabditis elegans* FoxA protein PHA-4. *Science* **295**, 821–825 (2002)

WEB SITE

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