must be isolated from the clusters of cells that release them into the environment.

This is typically done by picking a single suspect cell from the mixture of microbes in a water sample from an estuary or ocean during a harmful event, and allowing it to multiply in the laboratory. Chemical constituents are then extracted from several litres of the cells, and toxic components are identified using a bioassay, a test that assesses whether a particular fraction is poisonous, usually to a fish or mouse. For almost a decade, researchers have tried unsuccessfully to identify, from many litres of isolated *Pfiesteria* cells, a toxin that could explain the mass mortalities observed in the wild[6].

Vogelbein *et al.*[3] and — in a related study, with some authors in common — Berry *et al.*[7] have taken a different approach to the quest for a toxin released by *Pfiesteria*. First, they grew *Pfiesteria* in the lab and determined that the cultures could kill fish through direct contact. Then they separated the cells from the rest of the material using several methods, including filtration, centrifugation and dialysis (Fig. 1). They theorized that, if *Pfiesteria* cells release a toxin into sea water, this should be present in the cell-free fractions. But the experiments showed that the cell-free fractions do not cause fish death, and that *Pfiesteria* is lethal only when cells are in direct contact with the fish. The researchers therefore concluded that a toxin is not released into the surrounding sea water.

If they are not killed by a toxin, how do fish exposed to *Pfiesteria* die? It has been known for many years that *Pfiesteria* cells extend a suction-cup-like appendage called a peduncle to digest fish tissue[2]. Vogelbein *et al.* go a step further and propose that fish die because *Pfiesteria* literally sucks the life out of them. It attaches to fish skin using the peduncle, extending finger-like protrusions called filopodia, then ingests cell matter from the fish. This parasitic feeding behaviour by *Pfiesteria* is detailed in high-magnification microscope images in Vogelbein *et al.*[3], and in a video clip available in their Supplementary Information.

The new work promises to bring us closer to unveiling the true nature of this phantom of the ocean. Many loose ends remain, however, and it is possible nonetheless that a toxin is involved. Humans have suffered from memory impairment thought to stem from exposure to *Pfiesteria*[8]. Are these memory problems caused by a toxin, in aerosol form, produced by another organism that often coexists with *Pfiesteria*, as Berry *et al.*[7] suggest? Do the rod-shaped granules that Vogelbein and colleagues identified in *Pfiesteria* (see Fig. 4 on page 969) contain toxins that are released only after the peduncle becomes attached? Do only certain *Pfiesteria* isolates produce toxins, as Burkholder *et al.*[9] have proposed, indicating that the *Pfiesteria* studied by Vogelbein, Berry and their colleagues were simply non-toxic strains? Can contamination by a fungus or other microbe explain why *Pfiesteria* cultures routinely grown in the presence of fish do indeed appear to produce a toxin[10]?

Assembling these pieces of the complex puzzle posed by *Pfiesteria* will require exceptional cooperation among researchers of differing expertise. The opportunity to discuss the outstanding questions and to establish new collaborations will engage scientists at the Tenth International Conference on Harmful Algal Blooms, to be held in St Petersburg, Florida, this October. ■

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Apoptosis

Sculpture of a fly's head

Jun R. Huh and Bruce A. Hay

Hox proteins are needed during development to produce body segments with different shapes and functions. In fruitflies, one Hox protein sculpts certain segments of the head by activating a cell-death-inducing gene.

Cell death occurs throughout the development of every animal, enabling excess cells to be eliminated, tissues to be sculpted, and cells or tissues that have outlived their usefulness to be removed[1]. Much of this death occurs by an active 'suicide' process known as apoptosis. Quite a lot is known about the molecular signals and machinery that bring about apoptosis[2], but much less is understood about how the regulators of development access this machinery to determine where and when cells should die. Writing last week in *Cell*, Lohmann and colleagues[3] revealed one way in which this happens.

In developing fruitflies (*Drosophila melanogaster*), almost all normal cell death requires some combination of three death activators, namely the proteins encoded by the *reaper* (*rpr*), *head involution defective* (*hid*) and *grim* genes[4]. These proteins, and their mammalian counterparts, promote apoptosis at least in part by de-inhibiting the cellular executioners — protein-cleaving enzymes known as caspases[5]. Of the fruitfly cell-death activators, *rpr* is particularly fascinating because its expression (transcription) is increased in every cell that is committed to die. So the control regions of the *rpr* gene constitute a site at which many different developmental and environmental cell-death signals are integrated (Fig. 1), and analysis of those regions should provide insight into how the signals promote death. This approach has, for example, been successful in helping us understand the cell death that occurs during insect metamorphosis, which is dependent on the hormone ecdysone[6], and cell death induced by DNA damage[7].

One important class of developmental regulators consists of the Hox genes. Found in a wide range of species, these genes encode transcription factors that have major roles in creating specific segment identities along the head-to-tail (anterior–posterior) body axis during development, rendering each segment unique in its shape and function[8]. In fruitflies, for example, Hox genes determine which segments will produce legs, wings or antennae, and so on. They do this by activating and repressing the activity of particular target genes in specific spatial and temporal domains. Their importance is illustrated by what happens when they are mutated: one segment becomes transformed into another, resulting in one segment-specific body structure being replaced by another (a leg for an antenna, for example).

The central question about Hox gene function is how a single transcription factor can generate the many characteristics of a particular segment, which are the result of a variety of developmental processes such as cell division, apoptosis and tissue invagination. It has long been accepted that Hox genes must regulate the activity of many different target genes. But the identification of these targets, and an understanding of how changes in their activity lead to specific developmental outcomes, has been slow in coming.

Lohmann *et al.*[3] have now tied the fields

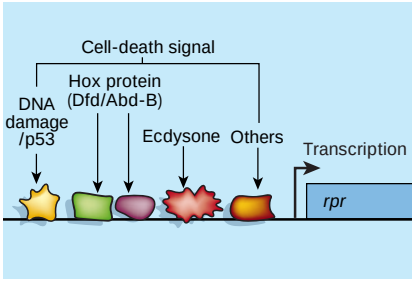

Figure 1 **Focal point for the control of cell death: the *reaper* (*rpr*) gene is activated in all fruitfly cells fated to die. Activation requires particular gene-transcription factors (coloured shapes) to bind to specific sequences upstream of the *rpr* promoter (a control region). These factors and their associated binding sites have been identified for several different cell-death activators, including the insect steroid hormone ecdysone[6], which triggers the destruction of tissues during metamorphosis, and DNA damage[7], removing cells with potentially damaged genomes. Lohmann *et al.*[3] have found that the Hox protein Dfd, and perhaps Abd-B, uses transcriptional activation of *rpr* to sculpt segment boundaries during development. It is likely that many other regulators of *rpr* transcription remain to be identified.**

of development and apoptosis together, giving an insight into how Hox genes harness cell death to sculpt tissues in fruitflies. They show that the protein encoded by the Hox gene *Deformed* (*Dfd*) directly activates the expression of *rpr*, and that this is both necessary and sufficient to account for *Dfd*'s ability to maintain a segment boundary in the fruitfly head.

Lohmann *et al.* took a beguilingly straightforward approach to finding out which genes are targets for *Dfd*. They sought out gene mutations that result in embryonic defects similar to those caused by *Dfd* mutations, the idea being that the mutated genes might encode important *Dfd* targets. *Dfd* mutants have several prominent defects in the jaw region: they have too many cells in the ventral maxillary segment, and they lack the boundary between the maxillary and mandibular segments. Similar defects had been seen previously[9] in fruitfly embryos lacking a chunk of DNA sequence in a chromosomal interval designated Df(3)H99. This interval contains the *rpr*, *hid* and *grim* genes, and embryos lacking the interval entirely show almost no normal cell deaths[10]. These findings, together with earlier observations that both cell death and *rpr* expression are prominent in the head[9,10], pointed to the idea that *Dfd* might carve out the boundary between the maxillary and mandibular segments by promoting *rpr*-dependent cell death.

Lohmann and colleagues have several results that support this hypothesis. First they find that embryos with mutant *Dfd* show decreased apoptosis in the head, consistent with the idea that *Dfd* normally functions to promote cell death, whether directly or indirectly. Second, forced expression of DIAP1 — an inhibitor of *rpr*-, *hid*- and *grim*-dependent cell death — in the head region of wild-type embryos gives rise to defects similar to those seen in *Dfd* mutants. This observation is critical because it shows that reduced apoptosis alone can account for the head defects seen in the *Dfd* and Df(3)H99 mutant embryos.

Is the *rpr* gene a direct target of the Dfd protein? The authors argue that it is. For instance, the expression of *rpr* at the boundary between maxillary and mandibular segments requires the presence of Dfd, but the expression of *hid* and *grim* in the maxillary segment does not. Moreover, forced expression of Dfd can induce *rpr* expression and cell death. Finally, DNA sequences upstream of the *rpr* gene contain sites that bind Dfd; DNA fragments containing these sites are enough to drive the expression of a test gene at the maxillary–mandibular boundary in wild-type embryos. This requires a functional Dfd protein, as well as intact Dfd-binding sites.

So *rpr* is a direct transcriptional target of Dfd. But is the expression of *rpr* actually required to sculpt the fruitfly head? Lohmann *et al.* show that in one sense it is, because if *rpr* alone — and not *hid* and *grim* — is deleted, segment-boundary defects characteristic of *Dfd* mutants are seen during mid-embryo development. But in another sense (that of ultimate outcomes) *rpr* is not required, because *rpr* mutants hatch with normal head structures. The likely explanation is that *rpr* normally works together with other apoptosis inducers such as *hid*, which is also expressed in maxillary cells at several stages and is required for head development. So the loss of *rpr* delays, but does not eliminate, the crucial cell deaths.

Could this Hox-gene-dependent induction of cell death be a more general phenomenon? Several observations suggest that it might be. Lohmann *et al.* found that mutants showing abnormal expression of a second Hox gene, *Abd-B*, have a partial fusion of the abdominal segments in which *Abd-B* would normally be expressed. These mutants also show a decrease in *rpr* expression in cells at the posterior segment border, which would usually express *Abd-B*. So *Abd-B*-dependent expression of *rpr* could be important for generating or maintaining these segment boundaries, too. Moreover, several mouse Hox gene mutants have been described in which segment boundaries are not maintained[11], or in which normal apoptotic tissue sculpting fails to occur[12]. Direct links between these Hox genes and components of the apoptotic machinery have not been documented. But the results of Lohmann *et al.*

100 YEARS AGO

While working on the reflective power of cyanin mirrors I have noticed some very interesting effects of light on that substance. Freshly fused cyanin is of a deep metallic bronze colour, but exposure to light turns it plum colour and finally a steely blue-black. In the moderate light of a cloudy day the change is perceptible in half an hour, in direct sunlight in less than a minute… By an exposure of thirty hours I have obtained on cyanin easily recognisable photographs of small, well-illuminated objects. A cyanin mirror, or better yet a piece of ground glass washed over with fused cyanin, exposed for ten hours to the spectrum of a Nernst lamp shows the effect to be very strong in the yellow, just perceptible in the adjacent red and green, and imperceptible in the blue and ultra-violet… At the same time, the exposure to light greatly decreases the absorbing power where it was originally large, as may be easily seen on looking at a sodium flame or a spectrum through an exposed coating of cyanin. It is as though the absorption were due to molecular resonance and the light produced a fatigue or destruction of this resonating power.
From *Nature* 28 August 1902.

50 YEARS AGO

A brief survey of housing development in the U.S.S.R. from 1917 until the present day… shows that the material difficulties with which the Government has had to deal have been formidable. The housing resources taken over by the Soviet authorities after the Revolution were both quantitatively inadequate and in appallingly poor condition. Very little new construction took place until the late 1920's… so that the pre-revolutionary level of housing was restored less quickly than that of the other branches of the economy… In the present stringent housing situation, the Government has controlled the distribution of available housing resources, taking into consideration the priority claims of ex-servicemen, the dependants of war casualties and invalids, the partisans and their families. The relationship between work (type, quantity and quality) and the allocation of limited housing resources, already recognized before the War, has now been further strengthened… Housing is thus regarded as one of the instruments for increasing the productivity of labour and building up permanent staffs in industry.
From *Nature* 30 August 1952.

suggest that it would be well worth looking for such connections. ■

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Renewable fuels

Harnessing hydrogen

Esteban Chornet and Stefan Czernik

Biomass can produce clean fuels and could be a vital, renewable energy source for the future. The demonstration of hydrogen production from biomass-derived molecules marks progress towards this goal.

Fossil-fuel stocks are a limited resource and, as the world's governments struggle to agree on a strategy to combat pollution and greenhouse-gas emissions, the search for clean, renewable energy sources has never been more intense. On page 964 of this issue, Cortright *et al.*[1] provide experimental evidence that simple biomass-derived molecules, such as glucose and glycerol, can be treated to produce hydrogen with reasonable efficiency. The authors suggest that, with some additional effort, their technique could also be technologically and commercially viable.

Cortright *et al.* demonstrate that glucose (the sugar used as an energy source in both plants and animals) and glycerol (derived from fats) can be reformed in the aqueous phase in the presence of a platinum-based catalyst to produce H_2. The conversion takes place at moderate temperatures, around 225–265 °C, and at pressures of 27–54 bar — conditions that prevent steam formation and ensure that the reaction sequence takes place in the aqueous phase.

The authors propose that the mechanism of hydrogen production involves the rupture and rearrangement of the biomolecules' C–C and C–O bonds on the platinum catalyst, leading to the formation of intermediates. These can then produce H_2 by reacting with the abundant water present — glucose was used at a water–carbon molar ratio of 165, but the authors indicate that ratios as low as 15 are possible. Simple hydrocarbons and carbon dioxide are also formed. The amount of gaseous H_2 produced as a proportion of the reaction products ranges from 36–50% for glucose to 51–75% for glycerol; and carbon conversion to gaseous products is 50–84% for glucose and 83–99% for glycerol. A yield of up to 80 g of H_2 per kilogram of catalyst per hour is possible.

Cortright *et al.* claim that their approach represents a significant departure from traditional high-temperature, steam-reforming technologies. Even though these can be carried out at atmospheric pressure, they require temperatures of around 800 °C to be effective with steam–carbon molar ratios typically of 5 and even lower[2]. Alcohols offer a lower-temperature option; vapour-phase steam reforming of those can be effectively carried out at temperatures of around 300 °C (ref. 3).

But does the proof of concept reported by Cortright *et al.*[1] hold the promise of an aqueous-phase technology for producing H_2 fuel from renewable biomass? To answer that question requires an interlinking of science, engineering and the economics of H_2 production.

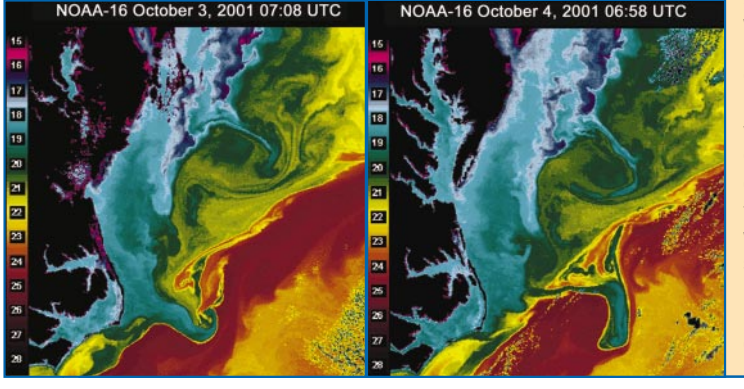
Today's benchmark in H_2 production is provided by catalytic steam-reforming technology that uses simple hydrocarbons (such as methane and liquid petroleum gases) as feedstocks, and catalysts that are variations of well established nickel-based preparations and whose robustness guarantees operation over thousands of hours. The

Oceanography

Crossing the highway

The powerful current of the Gulf Stream is like a highway, carrying warm tropical waters from the Caribbean to Europe. The current is known to meander and to shed rotating rings of water on both sides. However, its interaction with the surrounding water tends to be limited to the outer edges of the current, especially along the well defined northern wall of the Gulf Stream.

But satellite images presented by Xiaofeng Li and his colleagues in *Geophysical Research Letters* show a parcel of cold water from a region known as the Middle Atlantic Bight breaching the northern boundary of the Gulf Stream, and traversing the full width of the current (*Geophys. Res. Lett.* **29,** 10.1029/2002GL015378; 2002).



The left panel of the picture, taken at 7:08 a.m. on 3 October 2001, shows the penetration of cold water as a green tongue that extends into the main current just east of Cape Hatteras, where the Gulf Stream leaves the American East Coast and veers off into the North Atlantic Ocean. The right panel shows the fate of the intrusion about 24 hours later: the cold tongue has been swept along with the current while extending southeastwards.

In early October 2001, strong and persistent winds from northerly directions blowing along the shore north of Cape Hatteras piled up cold water from the Middle Atlantic Bight in the corner formed by the coastline and the Gulf Stream's north wall. Under less extraordinary wind conditions, long streaks of the relatively cold shelf water are slowly mixed into the Gulf Stream along its northwestern edge. But after three days of wind speeds exceeding 12.8 m s^{-1} — conditions unique for early autumn in the 11-year period from 1991 to 2001 — the cold coastal water broke into the main Gulf Stream and eventually crossed it.

Li and colleagues say they are not aware of any other reports of such a breaching event. After all, crossing a busy highway is rarely attempted and is even less often successful. **Heike Langenberg**

NOAA/NESDIS COAST WATCH PROGRAM