tinue to fire to an image they have to keep in working memory even after it has disappeared. As Schall says, "V1 is a lot smarter than it used to be."

To test V1's role in memory, Supèr and Amsterdam colleagues Henk Spekreijse and Victor Lamme taught monkeys to watch a computer screen filled with flickering black and white pixels and wait for directions. While the animals kept their eyes focused on a central red dot, a small, rectangular patch of pixels somewhere in the monkey's peripheral vision would occasionally jerk to one side and then quickly vanish into the background flicker. Then, when the central dot disappeared—which could happen up to 2 seconds after the patch came and went—the monkey had to move its eyes to where the patch had been. If successful, the animal earned a treat.

The team monitored V1 neurons, which are location specific, that were tuned to respond to a spot where the patch sometimes appeared. When the animals had learned that the patch (and not some other object on the screen) was tied to a reward, these neurons fired more robustly, as earlier studies have shown. The heightened firing then continued while the animal was waiting to move its eyes—presumably keeping the location in mind.

What's more, the continued firing appeared to help the animals remember correctly. The monkeys sometimes failed to move their eyes to the right spot. When the researchers compared neuronal firing patterns in the incorrect trials to patterns in the correct ones, they found that the V1 neurons' firing had dwindled to baseline levels shortly before the monkey made a mistake.

The team suggests that V1 neurons are communicating with other, higher level areas of the brain that are responsible for understanding the task and formulating a plan to respond. The V1 neurons contribute by keeping in mind the exact location that has to be remembered. So even if V1 isn't the ringleader of the memory gang, the new work shows that it plays an important role as a lookout.

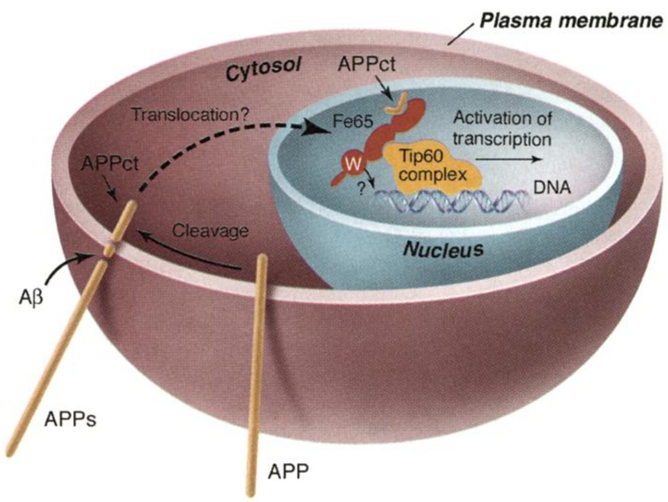
–LAURA HELMUTH

NEUROSCIENCE

Elusive Protein Auditions For Several New Roles

Few proteins are as hot as the amyloid precursor protein (APP), at least among neurobiologists. Highly expressed in brain neurons, APP is the source of amyloid-β (Aβ), the small protein whose abnormal deposition in the brain is thought to cause Alzheimer's disease. But APP's normal role has remained elusive, despite years of study. Now, on page 115, neurobiologists Xinwei Cao and Thomas Südhof of the University of Texas Southwestern Medical Center in Dallas provide an intriguing clue about one possible function.

APP appears to be located in the cell membrane, with part extending outside the cell and part—the so-called cytoplasmic tail—projecting inside. Cao and Südhof now have evidence that the cytoplasmic tail, when released from APP, can activate gene expression in the nucleus, possibly acting directly as a transcription factor, a protein that binds to regulatory regions and turns genes on and off. This is the first time anyone has linked APP to control of gene expression, and Alzheimer's researcher Sam Sisodia of the University of Chicago School of Medicine predicts that the finding "will capture the attention of many folk in the cell biology and Alzheimer's worlds." He cautions, however, that more work will be needed to confirm this "tantalizing" result.



Gene regulator? When released from APP, the protein's cytoplasmic tail (APPct) may activate gene expression with the help of Fe65 and the Tip60 complex.

This is new territory for Südhof, whose research has dealt mainly with understanding the synapse, the specialized structure through which neurons communicate with one another. But he's been thinking about the protein for a long time. "It's hard not to be interested in APP, given the importance of Alzheimer's," he notes.

A couple of findings prompted him to focus on a possible physiological function for the cytoplasmic tail. It associates with a variety of cell proteins. In addition, one of the two enzymes that cuts Aβ from the APP molecule also releases the cytoplasmic tail. Together these findings suggested to Südhof that APP might behave like another membrane protein called Notch, which plays an important role in embryonic development. When appropriately stimulated, Notch releases its cytoplasmic segment, which migrates to the nucleus, where it interacts with other proteins to turn on various genes.

To find out whether APP might play a similar role in gene transcription, Cao and Südhof introduced the gene for luciferase, an easily detectable enzyme, into various mammalian cells. Then, the researchers introduced the *APP* gene, modified so that at least theoretically its product could bind to and activate the luciferase gene. But the APP constructs alone had little effect on luciferase production, leading the researchers to conclude that APP might need help from another protein or proteins to stimulate gene transcription. They searched for such partners by looking for proteins that bind to the cytoplasmic tail of APP in yeast. They came up with a protein of unknown function called Fe65, which was already known to bind APP.

When Cao and Südhof then added the *Fe65* gene along with the *APP* genes to the luciferase gene–bearing cells, luciferase production shot up—more than 2000-fold in some cells. But when the APP tail is mutated so that it can't interact with Fe65, transcription remains low, confirming that the two are partners. The researchers also showed that the APP tail and Fe65 bind a protein, called Tip60, which is part of a large complex of proteins involved in gene transcription.

Südhof proposes that when the tail is cleaved from APP, it moves to the nucleus, where it binds Fe65 and the Tip60 complex, thus activating gene transcription. If APP is involved in such a signaling pathway, he says, "the results imply there's some degree a regulation of [APP] cleavage." That could be important for understanding Alzheimer's if, for example, that regulation goes awry and fosters Aβ production or other neuronal abnormalities. But the case is not yet airtight, says Südhof, because the results were obtained in altered cells; the researchers still need to show that the cell's own proteins act the same way.

And the APP-Fe65 partners may have other functions to boot. In the 25 June issue of the *Journal of Cell Biology*, a team led by Paul Greengard of Rockefeller University and Joseph Buxbaum of Mount Sinai School of Medicine, both in New York City, report that the two proteins foster the cell movements needed in wound healing. Fur-

ILLUSTRATION: C. CAIN

thermore, that paper cites unpublished work by the group suggesting that the proteins may also be involved in the movements of the growing tips of neurons and might thus contribute to axonal migration during development and synapse formation. If all this is borne out by future work, APP may turn out to have more talents than anyone suspected.

—JEAN MARX

MARINE BIOLOGY

Interest Blooms in Growing Jellyfish Boom

SAN FRANCISCO, CALIFORNIA—A jellyfish invasion might sound like the plot of a bad movie on late-night TV. But the pulsing, tentacled predators were a star attraction at a marine science meeting* here last week.

Populations of some jellyfish appear to be exploding in several parts of the world, U.S. and Russian scientists reported, raising fears that they are taking over ecosystems that nurture key commercial fish stocks. The Gulf of Mexico and the Bering and Black seas have been particularly hard hit. In some cases, however, researchers don't know whether the blooms are unusual or just natural population fluctuations, says Claudia Mills, a jellyfish expert at the University of Washington's marine laboratory in Friday Harbor.

In the Bering Sea off Alaska, the population of *Chrysaora melanaster* has jumped at least 10-fold over the past decade, reaching record numbers last year, reported biologist Richard Brodeur of the National Marine Fisheries Service in Newport, Oregon. Brodeur suspects that long-term climate shifts, which have affected ice cover and water temperatures, may explain the increase. But whatever the cause, the huge summer blooms could deliver a two-fisted punch to the Bering's fish stocks, which account for 5% of the world's catch.

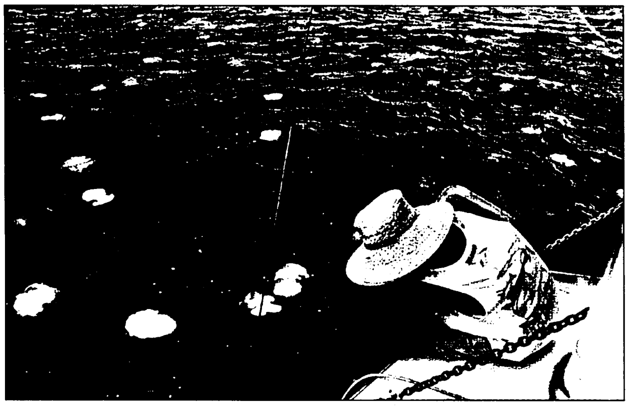
The problem is that the 2-meter-long jellyfish not only compete for food with young pollock—one of the Bering's most valuable fish—but also feed on them. In a 1999 study conducted off the Pribilof Islands, Brodeur reported, the jellyfish consumed about 5% of the annual crop of zooplankton and about 3% of newborn pollock. Some fishing boat captains now avoid one area, dubbed "Slime Bank," because countless jellyfish foul their nets.

In the northern Gulf of Mexico, a foreign jellyfish produced a huge bloom last summer, reported Monty Graham of Alabama's Dauphin Island Sea Lab. Native to the tropical Pacific Ocean, *Phyllorhiza punctata* apparently drifted in from the Caribbean. Now, Graham and colleagues are waiting to see whether it and several native species continue to thrive, perhaps encouraged by declining coastal water quality and a growing thicket of offshore oil-drilling platforms. The platforms' steel legs, Graham speculates, may be one source of the hard substrate that jellyfish polyps—a bottom-dwelling life stage—need to thrive.

Russian scientists, meanwhile, are keeping a close eye on booming Black Sea jellyfish, which have contributed to falling anchovy catches in the past several decades. Tamara Shiganova of the Shirshov Institute of Oceanology in Gelendzhik, Russia, noted that two species—one apparently native and the other introduced from the western Atlantic Ocean—now appear in often alternating blooms, vacuuming up the plankton that feed young fish. The Atlantic invader, *Mnemiopsis leidyi*, may soon get its comeuppance, however, because yet another exotic jellyfish has arrived—one that feasts on *M. leidyi*. Meanwhile, *Mnemiopsis* has invaded the nearby Caspian Sea, prompting fears that it could endanger a threatened seal species by reducing fish populations.

On the flip side, notes Mills, some jellyfish have disappeared—along with other marine species—with little notice from polluted coastal waters, such as the Adriatic Sea and Puget Sound. Determining how such departures and arrivals influence complicated marine food webs will be difficult work, she says, involving laborious field surveys and careful counts of the contents of jellyfish's stomachs. Handling their gelatinous, watery bodies and stinging tentacles can be a chore, she adds: "Jellyfish can be really unpleasant."

—DAVID MALAKOFF



Gelatinous onslaught. Jellyfish blooms, like this one in the Gulf of Mexico, present a puzzle.

* Second Symposium on Marine Conservation Biology, 22–25 June.

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Going with the flow. Harbor seals use their whiskers to follow trails of turbulence.

MARINE MAMMALS

By a Whisker, Harbor Seals Catch Their Prey

When mammals began to colonize the ocean some 50 million years ago, they immediately faced a huge challenge: hunting under water. The sharp vision their ancestors had evolved on land to take advantage of the transparency of air was of little use in the ocean's murky darkness.

Some species of dolphins and whales adapted to the new environment by evolving echolocation, which allows them to "see" with their ears. How other marine mammals manage to hunt without echolocation has long been a mystery, though. On page 102, German researchers report that part of the answer has been hiding in plain view: They use their whiskers.

Earlier studies by several researchers had shown that seal whiskers are remarkably sensitive to even the slightest bending. "They can use whiskers like we can use our hands for object identification," explains Guido Dehnhardt of Ruhr University Bochum in Germany. "They can measure the height of objects, they can discriminate different shapes, and they can very accurately determine an object's surface." In 1998 Dehnhardt, then at the University of Bonn, and his colleagues showed that whiskers are not just sensitive to objects but even to tiny movements of water generated by passing fish.

Given this exquisite sensitivity, seals might use their whiskers at close quarters to detect moving prey and then identify them