help from a small number of other proteins; Raf-1 activates the rest of the MAP kinase cascade, finally culminating in the phosphorylation of transcription factors and other cellular proteins that bring about the cell's responses. As Weinberg puts it, "It's a simple linear progression. It has many steps, but many of those steps are occupied by well-known friends"—among them the oncogene products that he and other researchers have been studying for years.

Still, while the general outline of the pathway may be relatively straightforward, there are sure to be complications. As Wigler says, the path is not just a "bucket brigade," in which one component simply passes the signal to the next. For one thing, there are already indications of branch points and alternate routes. One such example comes from Moodie and Wolfman, who could still get activation of MEK in cells from which they had depleted the Raf protein, indicating that cells contain another enzyme that can do the job. The most likely candidate: an enzyme called MEK kinase, recently described by Gary Johnson of the National Jewish Center for Immunology and Respiratory Medicine in Denver and his colleagues (*Science*, 16 April, p. 315).

What's more, the GRB2-Sos complex does not always have to interact directly with a tyrosine kinase growth factor receptor, as it does in the case of the EGF receptor. Papers from Joseph Schlessinger's group at New York University Medical Center and that of Michael Czech of the University of Massachusetts Medical Center in Worcester, which are in press in *Science*, show that the insulin receptor transmits its signals to the complex with the aid of two additional proteins. Still another complication may come from the fact that many of the participants in the growth control pathway, including Ras, Raf and MEK, are members of large protein families. "Which ones really see each other [in the cell] is going to be hard to sort out," says Wigler. Downward agrees that the pathway will have its complications. "It would be a mistake to think we know how it all works," he says. Still, the way the work is going makes him optimistic that it can be done. "We have a good model with the EGF receptor, and that's a good place to start," he concludes.

It's still too early to tell whether the information will pay off in a practical way with new cancer drugs. Meanwhile, Wigler says, the discoveries point to a fundamental cell biology lesson. The pathway was very highly conserved during evolution, he notes, since it's found in species as diverse as yeast, the fruit fly, and the roundworm *Caenorhabditis elegans*. The Ras pathway and kinase cascade weren't just "jury-rigged" during the course of mammalian evolution, Wigler points out, "but were a stable solution to a problem"—how to relay signals, whether for growth or development, to the cell interior.

–Jean Marx

NEUROSCIENCE

Magnetism Triggers a Brain Response

From before birth until death, the human brain is bathed in magnetic fields. Earth itself generates a pervasive field, and human technology adds electromagnetic fields from devices ranging from high-tension power lines to hair dryers. Does the brain respond to these subtle fields? The notion that humans can perceive magnetic fields, as homing pigeons seem to do, has remained more than a little controversial (*Science*, 15 May 1992, p. 967). Also controversial is the possibility, posed by a few epidemiological studies, that electromagnetic fields might cause cancer, in the brain and other tissues. But now a pair of geophysicists, taking a break from studying magnetism in rocks, may have cast some light into this confusion.

Working with neurosurgeon Hans Wieser at University Hospital in Zurich, Michael Fuller of the University of California, Santa Barbara, and Jon Paul Dobson of the Swiss Federal Institute of Technology have measured what seems to be a distinct physiological response in human brains exposed to weak magnetic fields. The study says nothing about the alleged dangers of such fields, and it has its share of caveats—from a small sample size to the not entirely normal brains involved. Furthermore, the study hasn't been vetted by the full community of researchers who study the subject, since details have not spread beyond last month's meeting of the American Geophysical Union. Still, some researchers in human magnetoreception are intrigued. Says Andrew Marino of the Louisiana State University Medical Center in Shreveport: "It [sounds like] a very interesting observation and merits following up."

The Zurich researchers aren't the first to look for brain responses to magnetic fields. But in earlier studies, researchers listened in on subjects' brain activity through scalp electrodes, and the results were inconclusive. During a chance meeting, however, Fuller learned of a more promising possibility. Fuller, who has had a long and prominent career studying the record of Earth's changing magnetic field, was on a sabbatical at the Zurich institute and, with Dobson, was interested in looking into human magnetoreception. Over coffee an institute colleague suggested they contact Wieser, a specialist in the treatment of epilepsy. Wieser, the colleague said, would have just the technical setup they needed.

What Wieser had were patients with electrodes inserted into their brains as a first step in treating epileptic symptoms that had not responded to drug treatment. The only recourse for these patients is surgical removal of small portions of the brain (usually in the hippocampus) that generate the storms of brain activity responsible for their seizures. The electrodes are crucial to precisely locating the regions requiring excision. Coincidentally, Fuller and Dobson realized, they could serve as particularly sensitive monitors of any physiological activity elicited by a magnetic field.

Working with Wieser, Fuller and Dobson enclosed each patient's head in a pair of direct-current coils that generated a magnetic field of 1 to 2 milliteslas. Such fields are 100 times stronger than Earth's, approaching the strength of fields induced by household appliances, says Fuller. To their surprise, all three patients tested so far showed an apparent response to the induced magnetic field.

The first patient had a total of 25 bursts of epileptiform—epilepsy-like—activity during the 10-second periods after the field came on, compared with only three during the preceding 10-second periods. The second patient's counts were none before and 15 after. The third patient had had no bursts of activity during 2 full days of monitoring, but activity began within seconds of applying the field.

These preliminary results "do seem to indicate that we have induced some epileptiform activity," says Dobson. However, "the physiological mechanism is something we don't understand yet." The researchers speculate that the magnetic field could be triggering activity directly, by changing the flow of ions through nerve cell membranes, or indirectly, perhaps by way of the microscopic bits of the mineral magnetite recently found in human brains (*Science*, 15 May 1992, p. 967). Both mechanisms, however, fail to explain the roughly 5-second delay seen between the onset of the field and the first bursts of activity.

Still, says Fuller, "I don't think this is an artifact." He adds that "even if it is, it's a beneficial one." Neurosurgeons now have to monitor epilepsy patients for days or even weeks, waiting for the problem area in the brain to reveal itself, but by triggering activity with a magnetic field, doctors might be able to track down the key area in a few minutes. And if the effect does hold up, it could offer insights into how our brains, like those of navigating birds, might "feel" the unseen magnetic fields that surround us from birth to death.

–Richard A. Kerr