Cellular gene role in puzzling disease

Despite the onslaught of molecular biology, the agent behind a set of slowly devastating nervous system diseases still guards its identity. A joint attempt by three teams of scientists to resolve controversies has produced a surprising result — one that raises more new questions than it answers.

Despite years of intensive research, no virus or other microorganism has been associated with scrapie, a disease of sheep and goats, or with the human diseases kuru and Creutzfeldt-Jakob disease. In laboratory experiments, scrapie can be transmitted by moving brain tissue from a diseased animal into a healthy one. Some scientists suggest that a small, reasonably conventional — although still undetected — virus carries the disease. But Stanley B. Prusiner of the University of California at San Francisco supports a more radical hypothesis — that scrapie and the related diseases are transmitted by a protein, rather than by a nucleic acid as in all other infectious agents (SN: 2/27/82, p. 135).

When Prusiner and his colleagues attempted to isolate the infectious agent from scrapie-infected hamster brains, they found predominantly a single protein. They report that infectivity resists treatments that destroy nucleic acids but not procedures that destroy protein. However, the most highly purified sample of protein is not itself infectious. They call the evasive infectious agent a prion.

In a *tour de force* of molecular biology, Prusiner's group, along with researchers led by Charles Weissmann at the University of Zurich, and by Leroy Hood at Caltech in Pasadena, located the gene that encodes the major prion protein. Surprisingly, the gene was found to be present and active in healthy cells of several species, as well as in scrapie-infected tissues, they report in the April CELL. The scientists don't yet know whether, as in some oncogenes, there are minor differences between the genes in the normal and infected cells. Preliminary evidence using antibodies to the prion protein suggests that a related protein is produced in normal cells.

The presence of this gene triggers many questions. What does the protein do in normal cells? How does it cause disease in infected cells? Can the properties of scrapie be attributed solely to a cell-encoded protein? Cautions Paul W. Brown of the National Institutes of Health, "It may just be a host-determined response to the infectious agent."

But Prusiner favors the hypothesis that the prion protein is the major component of the infectious particle. He suggests that during infection the prion alters a natural protein in the body, creating exact copies of itself. — *J.A. Miller*

Fractals, fractures and faults

Since they were first introduced in 1977, fractals have made the description of many of the twisted and tangled patterns found in nature much more manageable. Fractal analysis — the geometric technique for measuring the complexity and self-similarity of patterns when viewed on different scales — has been applied to everything from the shapes of clouds to the distribution of galaxies (SN: 1/24/84, p. 42). So it's no surprise that fractals would also find a home in the geosciences. A number of researchers are now using fractals to understand the surface traces of faults created when earthquakes tear through the upper crust. The hope is that by using fractals to quantify the jaggedness of a fault, seismologists may one day be able to predict the destructiveness of earthquakes that reactivate the fault.

Cathleen Aviles and Chris Scholz at Lamont-Doherty Geological Observatory in Palisades, N.Y., have recently used fractals to study four sections of the San Andreas fault in California and the Pleasant Valley trace in Nevada. Aviles, who plans to present their conclusions at the American Geophysical Union meeting in Baltimore later this month, says they have found that the fractal nature of each of the segments reflects some of the seismic behavior along that region of the fault.

The researchers characterize the roughness or jaggedness of a fault by calculating its fractal dimension, or the degree to which the trace fills the space and adds complexity to a straight line. In one method they estimate the fractal dimension by looking at maps and measuring the length of the fault segment with rulers of various sizes. Using a very large ruler, says Aviles, is like viewing the fault from an airplane — the trace would look like a straight, uncomplicated line. With a smaller ruler, a person on the ground would see much more of the detailed zigzagging of the fault. As a result, the total measured length of the trace would be greater as measured by the smaller ruler than by the large one. By plotting the measured length as a function of the ruler size, the researchers obtain a graph for each fault segment. And the slope of the curve on this graph is related to the fractal dimension.

"The first thing I see is that with each different section, there's a different character, a different slope or fractal dimension," says Aviles. The most pronounced difference is between three segments of the San Andreas and a fourth that runs between San Juan Bautista and Parkfield. The fractal dimension of the latter is about the same regardless of ruler length, whereas the fractal dimensions of the three San Andreas segments change abruptly as the ruler length approaches about 12 kilometers from either longer or shorter ruler sizes.

This means that the two types of regions are governed by different physical processes, says Aviles. Indeed, the San Juan Bautista section is moving by creep, in which very small earthquakes are produced as blocks on either side of the fault slide smoothly by one another. In contrast, the other three sections create large earthquakes when they suddenly slip and jerk after being locked in place.

The 12-kilometer-long dividing line is physically significant because earthquakes in California cannot rupture the ductile crust lying below 12 km deep. While small earthquakes can be as long as they are deep, this 12-km depth limit forces large quakes to grow only along the length of the fault. And this differing distribution of seismic energy in large and small earthquakes is reflected in the fractal profiles of the sections.

The important lesson of the fractal studies, says Aviles, is that big earthquakes cannot be duplicated simply by magnifying the features of a small earthquake; the earthquakes that create features longer than 12 km on the fault are not just large-scale mock-ups of those that make smaller features.

In addition to comparing sections along the San Andreas, Aviles and Scholz compared the San Andreas section that tore through San Francisco in 1906 with the Pleasant Valley fault that ruptured in 1915. Aviles concludes that on a smaller scale, the Pleasant Valley trace is much more jagged and rough than the San Francisco segment. These small-scale bends and twists in the Nevada fault, she adds, correspond to high-frequency ground shaking that can be the most damaging aspect of an earthquake. "So Pleasant Valley should release more high-frequency energy," she says, "and that's just what is observed."

Eventually, after the fractal techniques are calibrated to faults like San Andreas that are fairly well understood, Aviles and others would like to use them to predict seismic hazards on less familiar faults. China would be a good candidate, she says, because the sheer number of traces there precludes monitoring of every fault.

Paul Okubo at Massachusetts Institute of Technology and Ketti Aki at the University of Southern California at Los Angeles, who were the first to apply fractals to the San Andreas, have obtained results similar to those of Aviles and Scholz using slightly different fractal methods and concentrating more on southern California. Their findings have been submitted to the JOURNAL OF GEOPHYSICAL RESEARCH. — *S. Weisburd*