three very faint absorption features lying just to one side of the emission peak. Given a redshift of 72%, these features correspond quite well to known lines of cyanogen molecules, ionized calcium, and iron. Given a redshift of 37%, however, they do not correspond to anything.

Meanwhile, the gravitational lens model also provides a natural explanation for the strikingly blue color of the arcs. (Their emissions peak in the blue and ultraviolet.) They have the color of hot young stars because they are the images of hot young stars—swarms of them residing in the far-distant lensed galaxies. Indeed, the model even explains why the width of the Abell 370 arc varies with wavelength. It is about 1 arc second wide in red light and about 3 arc seconds wide in the ultraviolet. "This is exactly what you would expect if you were imaging a disk galaxy in which the older, redder stars are concentrated in the central bulge," says Lynds, "while the newer, hotter stars are mostly out in the disk."

Finally, the gravitational lens model gives a good explanation for the shape of the arcs. "We've tried to model the process on a computer," says Petrosian. "If you assume a spherical mass distribution for the lensing object, and if the source is directly behind it, then you expect the image to be a perfect ring. Then if you displace the source to one side slightly, you find that the ring breaks up into two arcs." So the semicircular shape arises naturally.

Next, says Petrosian, consider a more realistic cluster that has a nonspherical mass distribution and several lensing masses orbiting close together. "Then you find that one of the arcs can shrink and get lost in the background," says Petrosian. "It seems to happen very naturally when you have two scattering centers." Indeed, he thinks it is significant that both Abell 370 and Cluster 2242–02 contain a pair of massive elliptical galaxies in close proximity, whereas most other clusters have only one such elliptical galaxy or none at all.

Strictly speaking, Lynds and Petrosian's results only apply to the arc in Abell 370. They are not yet ready to say anything conclusive about their spectra of the second arc, which is located in a cluster known as 2242–02; the object is fainter, it contains nothing as dramatic as the Abell 370 oxygen emission, and the researchers are still analyzing their data. Nonetheless, they feel confident that this arc, too, is a gravitational image.

If true, then one is left with some intriguing implications. First, since the arcs represent the first gravitational images of normal galaxies as opposed to quasars, and since the images are magnified and brightened by a factor of about 25, they offer a unique probe of star formation at early times. (At a redshift of 72% we are seeing the universe at 15% of its present age.) The source of the arc in Abell 370 seems to be a heftier than average spiral galaxy. "And yet from the strong ultraviolet signal," says Lynds, "you know that it has lots of stars that are very, very hot, which is consistent with the early stages of star formation."

Second, Lynds and Petrosian have found from their computer simulations that a cluster can only form the kind of images they see if it contains about ten times as much mass as accounted for in the visible stars. This discrepancy is presumably the famous "dark matter." It is also the kind of increase that is called for in currently fashionable cosmological models, which postulate a great deal of extra mass to make the universe geometrically flat.

And finally, the computer simulations suggest that clusters can produce highly fragmented images as well as arcs. "I wouldn't be surprised if we hadn't seen a lot of artifacts already and interpreted them as galaxies," says Lynds. "That means we have to start being more cautious about interpreting the odd little things we see in clusters." ■ **M. MITCHELL WALDROP**

Role of Alzheimer's Protein Is Tangled

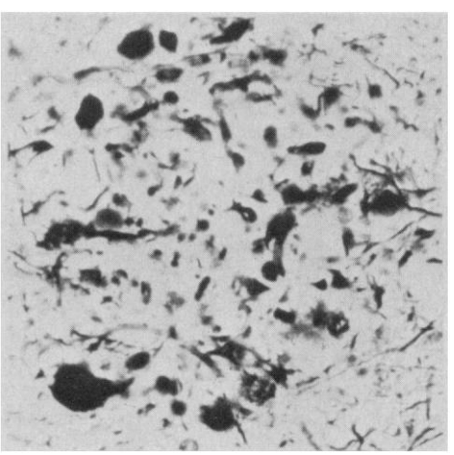
Duplication of the gene for the amyloid β protein does not cause Alzheimer's disease, but a role for the protein has not been completely ruled out

Early this year hopes were high that the genetic defect that causes the hereditary form of Alzheimer's disease might soon be identified. The finger of suspicion pointed to the gene encoding a protein, called amyloid β, that is a prominent component of the plaques that are a pathological feature of the brains of Alzheimer's patients. The idea then was that duplicaton of the amyloid gene might result in an overproduction of the protein, thereby causing the neurological disease.

That possibility has now been ruled out, as results presented at the annual meeting of the Society for Neuroscience* and in recent issues of *Science* and *Nature* have made clear. Nevertheless, some intriguing observations about the expression of the amyloid gene have kept it in contention as a contributor to Alzheimer's development, if not as the primary cause.

The original reasons for thinking that amyloid gene duplication might be implicated in the etiology of Alzheimer's disease included its position on chromosome 21, very close to, and perhaps at, the site where James Gusella and Peter St George-Hyslop of Harvard's Massachusetts General Hospital and their colleagues had located the gene that causes the hereditary form of Alzheimer's disease. The observations were especially interesting in view of the connection between chromosome 21 and Down syndrome.

Down syndrome occurs in individuals who inherit an extra copy of the chromosome. People with the condition not only suffer mental retardation, but the brains of those who live into their thirties and forties,



Laboratory of Neuroscience, NIA

Plaques in an Alzheimer's brain. *Amyloid-containing plaques, stained dark in this view, occur in high numbers in deteriorating areas of Alzheimer's brains.*

*The 17th Annual Meeting of the Society for Neuroscience was held in New Orleans on 16 to 21 November.

show changes, such as plaque formation, similar to the pathological features of Alzheimer's disease. This suggests that Down syndrome and Alzheimer's disease might have common etiologies.

Although Alzheimer's patients do not have an extra copy of chromosome 21, they might have more subtle abnormalities of the chromosome, such as a duplication of a small region. When Jean-Maurice Delabar of the Hopital Necker in Paris, and Dmitry Goldgaber and G. Carleton Gajdusek of the National Institute of Neurological and Communicative Disorders and Stroke (NINCDS), and their colleagues found that three Alzheimer's patients have an extra copy of the amyloid gene, the stage seemed to be set for finding that duplication of the gene is the genetic event underlying the development of both Alzheimer's disease and Down syndrome.

However, three groups have now reported that they can find no duplication of the amyloid gene in a total of about 100 Alzheimer's patients. The groups are those of Gusella and St George-Hyslop; Rudolph Tanzi and Rachael Neve of Harvard Medical School; and Dennis Selkoe, also of Harvard Medical School. Delabar and his colleagues have also failed to find the gene duplication in an additional three patients. "My conclusion," Goldgaber says, "is that duplication of the gene is not a key event in Alzheimer's disease."

Moreover, Tanzi, Neve, and Gusella have performed a classical genetic analysis of four families with hereditary Alzheimer's disease to see how closely linked the amyloid and Alzheimer's genes are. They found, Tanzi says, that "The amyloid gene can be no closer to the familial Alzheimer's disease gene than 8 centimorgans, or 8 million bases." "It's not the Alzheimer's gene," Neve concurs, "but it still could be the Down syndrome gene." A large group of European researchers has also performed a genetic analysis of Alzheimer's families and found that the amyloid and Alzheimer's genes are distinct.

Although these results would seem to knock the amyloid gene out of the Alzheimer's picture, a role may still be possible, even though it may not be a primary one. At the neuroscience meeting, Tanzi and Neve reported an intriguing, although currently unexplained, observation. "Just when it looked like the amyloid gene was down and out in Alzheimer's disease," Tanzi explains, "we looked for alternative forms of amyloid gene expression."

They found it. At least two forms of amyloid messenger RNA are made, with one of the messengers being longer than the other because it contains an 168 base pair insert. The insert may be an intron that is spliced out of one messenger, but not the other. The protein sequence encoded by the insert resembles that of a segment of the Kunitz protease inhibitor.

Tanzi and Neve find that the large quantities of the longer messenger RNA are made throughout the brain, including in the hippocampus, an area that is severely affected in Alzheimer's disease and contains numerous plaques. Whether the synthesis of the alternate amyloid form there contributes to the deterioration remains to be established, but the investigators note that the synthesis of the longer message is also high in the brains of Down syndrome and Alzheimer's patients.

"My conclusion is that duplication of the [amyloid] gene is not a key event in Alzheimer's disease."

Tanzi and Neve were not the only researchers who pointed to a possible involvement of a protease inhibitor in plaque formation. Carmella Abraham, who works with Selkoe and Huntington Potter of Harvard Medical School, reported at the neuroscience meeting that Alzheimer's plaques contain the protease inhibitor α-1-antichymotrypsin. The structure of the protease inhibitor domain that is encoded by the insert in the alternate amyloid messenger RNA is unrelated to that of this protease inhibitor.

The role, if any, of α-1-antichymotrypsin in Alzheimer's disease also remains to be established. One possibility is that protease inhibitors block the action of enzymes that would otherwise remove debris and prevent plaque formation.

Other indications of a posssible role for the amyloid gene in Alzheimer's disease come from Mark Cohen, Linda Younkin, Steven Younkin and their colleagues at Case Western Reserve University in Cleveland. They found increased expression of the gene in the nucleus basalis of Meynert, another area of the brain that degenerates to a great degree in Alzheimer's patients.

In addition, Gerald Higgins and John Morrison of the Research Institute of Scripps Clinic in La Jolla, in collaboration with the NINCDS group, found high expression of the gene in the hippocampus. The Scripps workers note, however, that high expression of the gene is not limited only to those brain areas that are prone to the damage of Alzheimer's disease. It is found in resistant areas as well. Nevertheless, the discovery of alternate forms of amyloid gene expression complicates the interpretation of these results, because it is now necessary to distinguish which messenger form is being made and where to track a correlation with Alzheimer's disease degeneration.

Another question still to be resolved concerns the normal role of the amyloid protein. The amyloid β that is found in the plaques consists of only about 40 amino acids and is a small fragment of the complete protein, which contains 695 amino acids. At the neuroscience meeting, Brenda Shivers, who works with Peter Seeburg at the University of Heidelberg, Germany, reported that the sequence of the amyloid protein from the rat is 97% identical to the sequence of the human protein, which was determined by Konrad Beyreuther and his colleagues at the University of Cologne, Germany.

That is an extremely high degree of sequence conservation, especially for a protein as big as amyloid. "The phylogenetic conservation implies an important function," Shivers notes.

The sequence of the amyloid protein suggests that it is embedded in the cell membrane, much as a receptor is. According to Shivers, the protein is widely distributed on rat brain neurons, where it has a patchy distribution, a result indicating that it may be needed to form or maintain cell-to-cell contacts, such as those needed for memory formation.

All in all, it is reasonable to assume that amyloid will continue to receive a great deal of research attention, even though the gene has now been ruled out as the site of the primary genetic defect of familial Alzheimer's disease. As Neve sums it up, "There are a lot of questions, but no answers yet." ■ **JEAN L. MARX**

ADDITIONAL READING

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