

ins into pieces with proteases, biochemists have discovered that one region is important for transport into a target cell and another domain is responsible for the toxin's destructive actions.

A similar approach has been used to study tryptophan synthetase, a complicated protein complex with about six binding sites. Removing pieces of the protein and determining which activities are lost gives clues to the overall organization, says Michel Goldberg of the Institut Pasteur. Protease experiments also can provide information about how proteins are folded into complexes. Edith Miles of NIH finds that in tryptophan synthetase, protease-sensitive sites available on the four subunits are unavailable within the folded structure.

An intriguing focus on proteases is their natural role in cells. Why would a cell harbor an enzyme capable of chewing up valuable material? At least three different answers to that puzzle were proposed during the meeting. The first is that cleavage by proteases can generate building blocks for growth. For example, proteins are stored in the spores of the bacterium *Bacillus megaterium*. Peter Setlow of the University of Connecticut Health Center described breakdown of those proteins to provide amino acids during germination.

Trimming proteins during production appears another use of proteases. For example, the research of Günter Blobel of Rockefeller University shows many secretory proteins are manufactured with an attached extension that is cut off before the protein is excreted (SN: 7/30/77, p. 73). Another fine honing of a cell product is reported by Michael K. Showe of the University of Basel in Switzerland. In making the virus T4, four proteins are assembled into an unstable "prehead." Cuts by a protease convert the prehead into the stable head structure. That T4 protease is far more specific than most; it acts only on the proteins when they are assembled into the prehead. Those protease molecules also nibble at each other, achieving both auto-activation and autodestruction.

Regulation of metabolism is the third natural function proposed for proteases. Many enzymes are turned off by binding inhibitory molecules. But in some cases an activity may be better halted by actually destroying the relevant enzyme. Frank H. Gaertner of Oak Ridge National Laboratory suggests proteolysis may be an override on other types of metabolic control. He reports a large number of proteases in the red bread mold *Neurospora crassa* help control cell metabolism.

And finally nipping at proteins may even affect the genes. Jeffrey W. Roberts of Cornell University reports that the gene product of the bacterial gene *rec A* is a proteolytic enzyme (or activates a proteolytic enzyme). He proposes that the protease removes a specific protein from DNA and thus allows strands of genes to recombine. □

Enkephalins: Pleasures and seizures

In 1974 two tiny brain proteins were discovered that act on nerve sites in the brain where morphine also acts. They were christened "enkephalins," for the Greek word for brain. In 1976 enkephalins extracted from the brain and injected into test animals were found to relieve pain. Thus they constitute the brain's own natural pain-relieving molecules.

But the enkephalin story is just beginning, it seems. For last year, when enkephalins were extracted from brain tissue and injected into rats, they were also able to improve learning (SN: 7/23/77, p. 59). And now injected enkephalins are showing three more talents—the ability to induce pleasure and the abilities to trigger epilepsy and to reduce memory loss.

A few months ago, Larry Stein and James D. Belluzzi of Wyeth Laboratories in Philadelphia hypothesized that the enkephalins probably help the brain mediate pleasure as well as relieve pain. After all, morphine, an artificial pain reliever, also produces pleasure, and both it and the enkephalins act on the same nerves in the brain.

The researchers implanted cannulas (small tubes) into the brains of rats. For the next 66 hours, the animals had access, by pressing a lever, to one of the two enkephalins, morphine or Ringer's solution (a solution of chlorides that served as a control substance for the experiment).

As Stein and Belluzzi report in *Opioid Peptides* (a book soon to be published by the Macmillan Press Ltd. of London), the rates of self-administration were much higher for the enkephalins and morphine than they were for Ringer's solution. This finding shows that the enkephalins must induce pleasure, as does morphine. Otherwise the rats wouldn't have shown any more interest in imbibing the enkephalins than they did in the Ringer's solution.

The enkephalins' ability to give pleasure, in fact, may be the key to their involvement in epilepsy. Extraordinary feelings of joy and satisfaction preceded the fits of the 19th century novelist Fyodor Dostoevsky. In 1972 an epileptic underwent electrical stimulation of that part of his brain which has since turned out to be rich in enkephalins — the amygdala. In response to the stimulation, the subject reported opiate-like pleasure that lasted from minutes to hours. So Hanan Frenk of Tel Aviv University and Bradford C. McCarty and John C. Liebskind of the University of California at Los Angeles asked: Might the enkephalins actually participate in epileptic seizures?

An enkephalin was injected into either the forebrain or the midbrain of rats. As the researchers report in the April 21 SCIENCE, the molecule induced pain-relief when put in the midbrain and seizures when placed in the forebrain, not vice

versa. So it looks as if enkephalin-induced pain relief and enkephalin-induced seizures are mediated by nerves in different areas of the brain. What's more, some drug might be found that inhibits the action of the enkephalins in the forebrain and thus provide a new, specific treatment for epilepsy.

The enkephalins themselves, in fact, might eventually be used to treat persons suffering amnesia. Several years ago, Henk Rigter of Organon International in Oss, the Netherlands, and his colleagues found that when a tiny stretch of the pituitary hormone ACTH was used as a drug, it had an anti-amnesic effect. This protein stretch is identical to that found in the pituitary hormone Beta-lipoprotein. The enkephalins' chemical compositions also correspond to part of that found in Beta-lipoprotein. So both the ACTH stretch and the enkephalins are cousins, so to speak, all apparently deriving from the same large parent molecule — Beta-lipoprotein. This kinship prompted Rigter to speculate: Might the enkephalins also have anti-amnesia activity if used as drugs?

He tested each of them on rats and, as he reports in the April 7 SCIENCE, both can reduce memory loss. Even more interesting, from a clinical standpoint, the enkephalins reduce memory loss when injected into the bloodstream in low doses, in contrast to their pain-relieving effects, which are seen only after their injection into the brain in large quantities. So, it's quite possible that the enkephalins, or some analogs thereof, might be used to treat persons who suffer amnesia from car accidents or other causes. □

Burbidge to Kitt Peak

Geoffrey Burbidge, now a professor in the Department of Physics at the University of California at San Diego, will be the new director of the Kitt Peak National Observatory at Tucson, Ariz. Last week, John M. Teem, president of the Association of Universities for Research in Astronomy, which operates the observatory for the National Science Foundation, announced Burbidge's acceptance.

Of English birth, Burbidge received his Ph.D. in theoretical physics from University College, London. He has been a professor at UCSD since 1962. His research interests include stellar evolution, nucleosynthesis, extragalactic astronomy — he has been prominent in the debate over the physics and cosmological meaning of quasars — and cosmic-ray physics. He is married to another prominent astronomer, E. Margaret Burbidge, who for some time was director of Britain's Royal Greenwich Observatory. He will take up the Kitt Peak post in the autumn. □