

way. Knowing that some natural peptides have acetyl groups at one end, the Guillemin team acetylated the six tripeptides (which Hoffman-La Roche had synthesized in record time) and tested each for biological activity. Roger Burgus recalls as the most exciting moment of his scientific life standing beside the radiation counter that was set to record results of assays with the six acetylated tripeptides and seeing that just one of the six had biological activity.

The active tripeptide was that with the sequence Glu-His-Pro. The Guillemin team on 15 April dispatched to *Science* a paper describing this first step of the last lap in their 7-year search for TRF. The paper was rejected, Guillemin has written,[†] "on the comments of a referee who said (or words to this effect) that '... these hypothalamic releasing factors were not much else than a lasting fancy of Guillemin's vivid imagination.'"[‡]

Several more steps remained before the structure was solved. The Guillemin team learned that it was not an acetyl group that blocked the end of their bio-

logically active TRF molecule but something else that just happened to occur during the acetylation process—the bending round of the glutamate unit to form an internal ring, known to chemists as pyroglutamate. The other end of TRF was also blocked, perhaps by an amide group. In a paper submitted on 30 June 1969, the Guillemin team discussed for the first time the substance known as pyroGlu-His-Pro-amide, only to conclude on the basis of infrared spectroscopy that the real TRF was something slightly different.

The team comprising Schally, Folkers, and Cyril Bowers of the Tulane Medical School, joined the race scarcely a month later. In a paper dated 8 August they suggested that they had synthesized TRF. Although they didn't know what the structure was, one of the substances in their reaction mixture was pyroGlu-His-

[†]Memoir contributed to *Pioneers in Neuroendocrinology*, vol. 2, edited by Joseph Meites, to be published by Plenum Press, New York, in press.

[‡]A search of *Science's* archives indicates that the manuscript was rejected, but the referee's report to which he is evidently referring makes no mention of Guillemin's vivid imagination.

Pro-amide. On 22 September they submitted a second paper stating for the first time that this was indeed the structure of pig TRF.

By this time the Guillemin team was realizing that they had been over fussy in the interpretation of their infrared data. In a paper submitted on 29 October they announced on the basis of mass spectroscopy that sheep TRF was indeed pyroGlu-His-Pro-amide. Guillemin and Burgus argue that the Schally-Folkers-Bowers paper of 22 September is not definitive because of the ambiguous nature of the method of identification, which depended on the behavior of natural and synthetic TRF in chromatographic systems. "Our evidence was the ultimate proof," says Guillemin. Folkers states that the chromatographic identification was conclusive, and Bowers adds that their data on biological activity helped clinch the case.

The patent on TRF is held neither by Schally nor Guillemin but by Folkers and a colleague, Franz Enzmann.

To the narrow question of who was first with the structure of TRF, the an-

Briefing

Mottur Resigns from OTA Job

Ellis Mottur, the long-term aide to Senator Edward M. Kennedy (D-Mass.) who was influential in helping to establish Congress' Office of Technology Assessment (OTA), has resigned from his OTA job and is no longer part of the Kennedy staff. The move came at the end of a series of events in which Mottur's considerable power was reduced.

Kennedy helped to get legislation passed that capped some 10 years of debate on Congress' need for more technical advice. As a result, Kennedy became chairman of the OTA's governing Congressional Board of Directors in alternating sessions of Congress. Hence, Mottur, as Kennedy's most senior staff aide at OTA, had considerable influence, a fact that was widely noted and sometimes resented around OTA. In fact, last year, when a Republican board member resigned, protesting that Kennedy was trying to use the supposedly nonpartisan office for his own political gain, the charges were widely taken to be aimed partly at Mottur. After this incident, Kennedy appointed another staffer as his offi-

cial liaison, and his board of directors went out of its way to pick a prominent Republican, Russell T. Peterson, who was head of the Council of Environmental Quality and formerly governor of Delaware, as the office's new director.

After taking office, however, Peterson made two moves which substantially reduced Mottur's influence. The first was a one-line change in the rules, giving authority to the director instead of the board, to hire and fire all OTA employees. This small change thus ended the practice of having staffers answerable to their Congressional sponsors instead of to the office itself. The change was described by staffers as part of Peterson's move to "depoliticize" OTA.

A second move was a reorganization of the office announced in early April, which would have programs such as the one Mottur runs there, which is on the health and impact of national R & D, reporting through a layer of division directors instead of to Peterson himself. There will be three division directors, Peterson announced; another OTA staffer was promoted to one of the slots, and the other two will be filled from the outside. Mottur handed in his resignation on the day the change was announced.

Mottur could not be reached for com-

ment despite several attempts to reach him before press time. His letter of resignation to Peterson gave "personal renewal and career progression" as the reason he was moving on. Associates say he is enthusiastic about a new job he will undertake, but he could not be reached for information on what it will be.

Security Agency's Role in DES Confirmed

The Senate Intelligence Committee has released a report of its investigation of charges that the National Security Agency (NSA) tried to influence development of a public encryption system for its own secret purposes and that it harassed university researchers working at the forefront of cryptography and their government sponsors.

The unclassified summary of the committee's classified report leaves unanswered many of the original questions about NSA's role (*Science* 29 July 1977). But the report also calls for clarification of "vague and ambiguous" federal regulations that apply to the general field of

swer is the Schally-Folkers-Bowers team, by a margin of 5 weeks in a 7-year race. In a wider sense, perhaps the Guillemin team scores more points. Schally's team came tantalizingly close to the structure in 1966 but was clearly on the wrong track until the Guillemin team brought them back again in January 1969. Without the powerful last minute help of Folkers and his laboratory, Schally's team would probably not have done as well as they did. The Guillemin team, relying principally on their own resources, kept the initiative from January onward in fitting together the successive pieces of the chemical puzzle. Their 30 June paper, though wrong, was within a hairsbreadth of stealing victory before Schally, Folkers, and Bowers had even started. Yet Schally by a whisker turned his impending defeat into a technical victory. The result of the 7-year race was in substantial measure a draw, but one so complexly attained that each team could interpret it as a win.

Discovery of the structure of TRF was a milestone in all sorts of ways. It proved to a world that still needed convincing

that the postulated hypothalamic hormones (or factors) really existed. It laid a firm basis for a whole new branch of endocrinology. It assured continued funding for work which the National Institutes of Health would otherwise almost certainly have suspended. And it vindicated not only Geoffrey Harris's theory but Roger Guillemin and Andrew Schally and the long years they had spent in the wilderness. After the discovery of TRF, "No one could laugh at Guillemin and Schally any more," says a fellow physiologist.

The Two Team Error with LRF

With TRF solved, both teams turned with new energy to the next lap of the race, the isolation of LRF. Situated at the apex of the body's hierarchy of reproductive hormones, luteinizing hormone-releasing factor is a substance of considerably greater medical interest than TRF, and its isolation would be a proportionately greater coup. Proof of LRF's existence was first found in 1960 by S. M. McCann in America and Geoffrey Harris in England, the two teams

working independently of each other. Guillemin, then based in Paris, started the search for LRF shortly thereafter. After 4 years' work he abandoned it because the best available physiological test for LRF was in his view too erratic to serve as the basis for an isolation program.

By 1969, however, more reliable tests had been developed. It took comparatively little time for both teams to get hot on the trail of LRF. By the end of 1970 each team had reported that LRF is a nonapeptide, a chain of nine amino acid units. The conclusion was not only wrong but put them in jeopardy of being scooped by a rival team. Cy Bowers and Karl Folkers, Schally's collaborators on TRF, had not been invited by him to join the search for LRF, so decided to set out on their own. After processing some 500,000 hypothalamic fragments they had not got as far as Guillemin and Schally but one thing they did know was that LRF contained the amino acid tryptophan. When peptides are broken down by acid, the conventional first stage in analysis, tryptophan is de-

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cryptology. It has received a mixed reception among scientists.

The most unsettling part of the report is that which confirms that NSA had a hand in developing the new data encryption standard, or DES, a public encryption system developed by the IBM corporation and approved by the National Bureau of Standards for commercial use in the United States and for export. Some scientists believe that the DES could have been made more secure at little extra cost by a number of methods, among them making longer the 56-bit key which defines the code. They suspected that the NSA wanted DES to be less than fully secure so that it could break into the encrypted traffic once the standard was in widespread commercial use.

The report confirms what had previously only been alleged: that NSA had a hand in IBM's development of the DES, and among other things, that "NSA convinced IBM that a reduced key size was sufficient." It also says that NSA "indirectly assisted in the development of S-box structures"—a feature of the scheme which scientists had said looked suspiciously vulnerable to someone who wanted to break onto the code. However, the report gives no reason why NSA

played this role, or what its motives were.

The report says that the "overwhelming majority of scientists" and the NSA find the DES "adequate for at least a 5-10 year time span for the unclassified data for which it will be used." But Martin Hellman, one of the most prominent critics of the DES, objects that the government is doing a disservice to commercial customers by not proposing a code system that will be secure for any longer period.

Hellman adds that the report does not answer the key issue, which is, he says, whether NSA can crack the DES scheme.

On the question of harassment of academic scientists, including Hellman, who have developed new approaches to encryption that could lead to codes more secure than the DES, the report exonerates the NSA from any wrongdoing. "There has been no direct or indirect government harassment of scientists working in the field of computer security" it says. It claims that a letter, written by J. A. Meyer to the Institute for Electrical and Electronics Engineers (IEEE) which was interpreted by scientists as a form of harassment, was written by Meyer as an individual and "was not prompted by any NSA official." Press reports had

identified Meyer as an NSA employee, but the Senate Report declined to confirm this.

The committee also looked into press reports that NSA had pressured the National Science Foundation (NSF) to withhold funds for research in public cryptology. NSF supports Hellman and other researchers who, as a by-product of basic work in problems in mathematical complexity, stumbled on a new approach to cryptology which could have wide application in electronic banking, communications, and perhaps even in verification of the comprehensive test ban treaty. The report says NSA had not pressured NSF in this fashion, but suggests that the two agencies clarify the "ambiguity and uncertainty" in their relationship.

After the report's release, NSF Director Richard C. Atkinson was quite blunt about not wanting NSA to harass his agency on the cryptology issue.

Atkinson says that the new developments promised by this research—such as virtually complete communications security—are too valuable to forego. "If we don't do the research other countries will get farther along with it. The long term disadvantage of not doing this research on our own in this is monumental."

Deborah Shapley