H. Gobind Khorana: professor of Enzyme Institute. 1960/1976

[Madison, Wisconsin]: UW Communications, 1960/1976

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TEMPORARY NEWS SERVICE LOCATION:
115 Science Hall
550 North Park Street

From The University of Wisconsin-Madison / University News and Publications Service, Bascom Hall, Madison 53706 / Telephone: (608) 262-3571

Release: Immediately 3/5/76 ksg

SCIENTIST KHORANA, AUTHOR HAHN AMONG FIVE TO RECEIVE HONORARY DEGREES

MADISON--A brilliant scientist whose synthesis of gene fragments won him a Nobel prize while at the University of Wisconsin-Madison in 1968, and the school's first woman graduate in Engineering who became a distinguished author are among five persons selected to receive honorary degrees at the 1976 spring commencement May 29.

Prof. Har Gobind Khorana, now at Massachusetts Institute of Technology after 10 years at the Madison campus as a team leader in the Enzyme Institute, and Miss Emily Hahn, who wrote influential books on the China of the 1930s and was a regular contributor to the New Yorker magazine, were recommended by the faculty and the Committee on Honorary Degrees and approved by UW System regents Friday.

Degrees also will be presented to George R. Currie, former chief justice of the Wisconsin Supreme Court; Walter J. Burke, secretary treasurer of the United Steelworkers of America, Pittsburgh; and Guillermo Soberon, rector of the National University of Mexico, Mexico City.

Khorana, 54, who will receive a Doctor of Science degree, is a native of India where he studied at Punjab University, graduating in 1943. After studying at the University of Liverpool, the Federal Technical Institute in Zurich, the University of Cambridge, England, he was named professor at the University of British Columbia in 1952. He came to UW-Madison in 1960. After synthesizing gene fragments at UW-Madison he succeeded in the far more exacting and imaginative task of discovering the synthesis of an entire gene. He has been at MIT as research professor since 1970.

- more -

Add one--honorary degrees

Hahn will receive the Doctor of Humane Letters. After graduating from the UW School of Engineering in 1926, she traveled to China, returning to the U.S. following Pearl Harbor. While primarily an author, Miss Hahn has also worked as a mining engineer, a geology instructor, an English instructor in Shanghai, a Red Cross worker in the Belgian Congo, and taught creative writing at Yale and in the UW-Madison English department in 1964. She has been a pioneer in establishing the right of women to have their own careers.

She is the author of 27 books, many of which have appeared in excerpt form in the New Yorker. Her most recent are: "Once Upon a Pedestal," 1974, a history of the leaders of the feminist movement in the U.S.; and "Lorenzo: D.H. Lawrence and the Women Who Love Him," which appeared last year. She has been married to Prof. Charles Boxer, University of London, since 1945 and they have two daughters. She was born in 1905 in St. Louis, Mo.

Justice Currie, 76, was born at Princeton, Wis. He graduated from the UW Law School in 1925, and practiced law in Sheboygan until named to the Wisconsin Supreme Court in 1951. He was reelected to the Supreme Court through 1967, the last four years serving as chief justice. After leaving the Court, he taught at the UW Law School for several years. He is recognized as being a strong enforcer of individual liberty, and environmental and consumer protection laws.

Soberon is recognized throughout Latin America as a leader in the development of higher education systems and in their science and technology. Born in Mexico, Soberon received a Ph.D. in physiological chemistry at UW-Madison in 1958. He has continued his contacts with the Madison campus appearing here last fall to give several lectures. Soberon, 51, will receive the Doctor of Science degree.

Burke, 64, is a pioneer in the establishment of CIO and industrial unionism in Wisconsin. From 1937 to 1948 he was a staff representative of the United Steelworkers of America assigned to Wisconsin. From 1948 to 1965 he was director of the Wisconsin District of the USWA with headquarters in Milwaukee. Burke served on the Wisconsin Coordinating Committee on Higher Education, and former Governor Gaylord Nelson's Blue Ribbon Tax Study Committee. He has served as secretary treasurer of the United Steelworkers of America since 1965.

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TEMPORARY NEWS SERVICE LOCATION:
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From The University of Wisconsin-Madison / University News and Publications Service, Bascom Hall, Madison 53706 / Telephone: (608) 262-3571

Release: Immediately 10/16/75

(WITH NOBEL PRIZE)

The Nobel Prize awarded to Dr. Howard Temin is the third received by a member of the University of Wisconsin-Madison faculty.

Dr. Har Gobind Khorana was co-winner of the 1968 Nobel Prize for Medicine and Physiology for his pioneering work in the complex field of nucleic acid chemistry. He is currently at the Massachusetts Institute of Technology (MIT).

A decade earlier, Dr. Joshua Lederberg, an eminent biologist, received the Nobel Prize for Medicine for his studies on organization of the genetic material in bacteria. In 1967, Dr. Lederberg presented to the University Board of Regents the gold medal awarded him in 1958. He is currently chairman of the Department of Genetics and professor of Biological Sciences at Stanford University, Palo Alto, Calif.

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From The University of Wisconsin News and Publications Service, Bascom Hall, Madison 53706 • Telephone: (608) 262-3571

Release: Immediately 6/15/70 rt

MADISON, Wis.--How much does it cost to synthesize a gene, and who pays for it?

University of Wisconsin Pres. Fred Harvey Harrington made an effort to tie down such costs last weekend in a report to UW Regents on Dr. Har Gobind Khorana's recent announcement of the first complete laboratory synthesis of a gene.

Pres. Harrington called Dr. Khorana's accomplishment "the most significant event of the year for the University of Wisconsin," and said he could answer questions about its cost only in terms of the total support of Dr. Khorana's work since he came to Wisconsin a decade ago.

"In the 10 years Dr. Khorana has been with us he has directed projects totalling $2.7-million," Dr. Harrington reported. "In this total were $226-thousand of State appropriations. Thus for every dollar the State of Wisconsin put into the studies by him and his group over the period, Dr. Khorana's group attracted $10 from the outside. In addition to the State appropriation, the University invested a similar amount ($230-thousand) from the Wisconsin Alumni Research Foundation--which included Dr. Khorana's full salary as Elvehjem Professor since 1964.

- more -

Add one--Khorana's funding

"The major support of the Khorana group's work came from federal agencies, just over $2-million. Of this, $1.5 million came from the National Institutes of Health, $.5 million from the National Science Foundation, and $1,000 from the Atomic Energy Commission for a fellowship for one of the members of Dr. Khorana's group.

"Private agencies which supported their work include the Life Insurance Medical Research Fund, the Upjohn Pharmaceutical Co., and the American Cancer Society. Together these totalled $159-thousand."

In addition to the $2.2 million provided by federal and private sources to support the Khorana projects, the president reported, these agencies also paid indirect costs to the University totalling $337-thousand, which went into the State treasury to offset State appropriations to the University.

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Release: PLEASE OBSERVE OUR RELEASE DATE 6/1/70
Release 3:00 p.m. June 2 CDT

Slides, Newsclips & Pix on request

UIR Science Writing Program (262-5984)

By NANCY THORN AND JAMES A. LARSEN

MADISON, Wis.--The first total synthesis of a gene--the basic hereditary unit--has been accomplished by University of Wisconsin Nobelist H. Gobind Khorana and his colleagues at Wisconsin's Institute for Enzyme Research.

The achievement--long awaited by molecular biologists--will now make it possible for organic chemists to synthesize the basic genetic material from simple organic chemicals.

This is the first time that chemists have shown it is possible to synthesize a gene by putting the building blocks known as nucleotides into the sequence in which they occur in natural genes.

Scientists previously learned how to take small bits of genetic material out of living cells. They could make copies of natural genetic material in the test tube. Khorana is the first to show, however, that genes can be synthesized from atoms or the simple chemical building blocks, nucleotides. No natural gene is required as a model in the reaction mixture.

Khorana is the first to produce a gene completely by synthetic methods, using as his model the gene for alanine transfer RNA from yeast. The structure of the yeast alanine transfer RNA molecule was elucidated by Nobelist Robert Holley, now of the Salk Institute, some years ago. From the order of the nucleotides the structure of the gene coding for this molecule can be deduced.

- more -

The gene is a molecule of deoxyribonucleic acid (DNA), made up of two strands. Each strand is composed of four basic building blocks or nucleotides--these consist of four bases adenine, thymine, guanine, and cytosine. These bases, represented by the letters A, T, G, C, are linked to a sugar and a phosphoric acid molecule. The two strands of the gene are wound in a helix and are complementary in that the A's of one strand are always opposite the T's in the other. The same is true for the G's and C's.

These four coding units are arranged in various combinations to code genetic information used in producing molecules of transfer RNA, which are then employed in synthesizing the proteins of cells along with many other components.

Khorana started with the four nucleotides which can be synthesized easily from atoms. He joined the four basic building blocks into a number of shorter single-stranded segments with the nucleotides in proper sequence, then later joined these fragments into the complete double-stranded 77 nucleotide gene.

The single-stranded fragments were designed by Khorana so that they spontaneously line up in proper sequence to form the double-strands exactly as happens in natural DNA. The ends of the fragments are then joined by the enzyme DNA ligase, which is purified from living cells.

Khorana's group showed that the gene they had synthesized is exactly the same as the one they set out to make. They checked the sequence in each of the segments and demonstrated that they joined together in the correct manner.

One ultimate test would be to check the gene for biological activity in a living cell, by introducing the artificial gene into a cell lacking the gene, showing that by this introduction the cell was transformed into a normal cell. Other more immediate experiments for biological activity can also be carried on and these are now under way. These experiments include learning how to copy the artificial gene in a test tube using an enzyme called DNA polymerase discovered

several years ago by Nobelist Arthur Kornberg. The next job is to copy the gene into the transfer RNA.

After learning how to copy the artificial gene, Khorana wants to find out what turns a gene off and on in a living cell--or what its starting and terminating "signals" are. The ultimate challenge would be to introduce the artificial gene into a living cell.

The work on the yeast transfer RNA gene was started in 1965 and Khorana is now at work on the synthesis of a second gene, called tyrosine-supressor transfer RNA, found in a species of bacteria known as E. coli. Synthesis of the fragments of this gene is now nearly complete, but the work of joining the segments has only been begun. The work on this second gene is expected to be completed within a few months. Mutants lacking the gene are already known and will be available for testing the biological activity of the artificial gene when synthesis is complete.

Khorana began the synthesis of this second gene because it will be easier to test for biological activity in living cells; its function in the protein synthesizing system is well known.

Now that he has determined the rules for chemically synthesizing genes, theoretically any desired gene could be manufactured in the test tube. Thus, some scientists foresee the time when genetic diseases, such as diabetes and some mental illnesses, might be cured by providing the tissues of affected individuals with a supply of normal genes.

Other characteristics--not necessarily pathological ones--could even be altered in the same manner.

Scientists caution, however, that this is many years in the future and a problem can be foreseen in developing techniques for introducing the genes into the proper target areas. Methods now contemplated would involve using purified genetic material or viruses as carriers to introduce genes into affected cells.

Add three--Khorana

Khorana shared the 1968 Nobel Prize in medicine with Robert Holley and Marshall Nirenberg. It was awarded to Khorana for his work in elucidating the genetic code by synthesizing double stranded DNA polymers of various sequences and then determining which proteins were synthesized from information encoded in the various DNA sequences.

Khorana would also like to know how the transfer RNA molecules act the way they do in protein synthesis. To understand their function better, he plans to modify chemically specific parts of the molecule and to see what the effects are.

Khorana made his momentous announcement Tuesday to a small colloquium of biochemists and molecular biologists at the University of Wisconsin. He pointed out that he made the announcement in this way rather than at a large scientific meeting, in recognition of the support and encouragement provided him during the past decade by the University of Wisconsin.

An article describing the achievement will be submitted to a scientific journal shortly. The work will also be presented at an international symposium at Riga, Russia, under the auspices of the U.S.S.R. Academy of Sciences late in June.

A native of India, Khorana joined the Wisconsin faculty as a co-director of the University's Institute for Enzyme Research, in 1960. He received his early education under a tree in India, meeting informally with other students and a government teacher, and was the only member of his family to obtain a higher education. His first major scientific accomplishment was the synthesis of adenosine triphosphate and co-enzyme A.

He has been assisted through the years by a large and international group of young, hard-working chemists who come to the laboratory at Wisconsin specifically to work with such a distinguished individual.

Those who helped in the synthesis of the yeast gene were Vittorio Sgaramella, Italy; Hans van de Sande, Netherlands; Kjell Kleppe, Norway; Marv Caruthers, U.S.; Ashok Kumar and Naba Gupta, India; E. Ohtsuka, Japan; and Hans Weber and Henri Buchi, Switzerland.

The present group will accompany Khorana when he leaves Wisconsin to move to the Massachusetts Institute of Technology this fall.

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From the Office of Public Relations
Massachusetts Institute of Technology
Cambridge, Massachusetts 02139
Telephone: 864-6900, Ext. 2701

9/26/69

FOR IMMEDIATE RELEASE

9/26/69

Professor H. G. Khorana, a molecular biologist who shared the 1968 Nobel Prize in Medicine or Physiology, will join the Faculty of the Massachusetts Institute of Technology as Sloan Professor of Biology and Chemistry, Provost Jerome B. Wiesner announced.

Professor Khorana is currently a professor in the Enzyme Institute at the University of Wisconsin, a post he has held since 1960. The author of some 200 research papers, he is best known professionally for developing novel methods for the synthesis of nucleotides--the building blocks of DNA and other nucleic acids. Specifically, he devised laboratory methods for synthesizing specific chains of nucleotides of known sequence. Since the sequence of nucleotides specifies the functions of genes, his work represents the first attempt to make genes in the test tube.

This and other research by Khorana played a major part in the deciphering of the genetic code and in uncovering how genetic messages inscribed in the genes are translated into the structure of enzymes and other proteins.

It was largely for the work in genetic coding that Professor Khorana shared the 1968 Nobel Prize with Robert W. Holley of the Salk Institute and Marshall W. Nirenberg, National Institutes of Health.

Professor Khorana was born January 9, 1922, in Raipur, India, and received his bachelor's and master's degrees in chemistry from the University of Punjab. In 1948, he took a doctoral degree, also in chemistry, at the University of Liverpool in Great Britain.

From 1948 to 1949, he served as a post-doctoral fellow for the Indian government at the Federal Institute of Technology in Zurich, Switzerland. He married a Swiss citizen there, and they now have two teen-age daughters and an 11-year-old son.

He was selected a Nuffield Fellow and, as such, worked at Cambridge University from 1950 to 1952. For the next eight years, he was head of the organic chemistry division of the University of British Columbia in Vancouver, Canada. Also during this period (1958-60), he was visiting professor at the Rockefeller Institute in New York.

His professional honors include membership in the National Academy of Sciences; receipt of the Merck Award from the Chemical Institute of Canada in 1958 for outstanding contributions in organic chemistry and biochemistry, and of the 1960 Gold Medal of the Professional Institute of the Public Service of Canada.

# # # #

September 24, 1969

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From The University of Wisconsin News and Publications Service, Bascom Hall, Madison 53706 • Telephone: (608) 262-3571

Release: Advance for use P.M.'s Tuesday, April 15 4/14/69

UIR Science Writing Division (262-5984)

By DENNIS MEREDITH

ATLANTIC CITY, N.J.--(For use pm's of Tuesday, April 15)--Har Gobind Khorana, 1968 co-recipient of the Nobel Prize in Medicine and Physiology, and his associates Vittorio Sgaramella and Naba K. Gupta have announced significant progress in their synthesis of a gene--the basic blueprint for all life.

In a paper given before the annual meeting of the Federation of American Societies for Experimental Biology, the three scientists revealed preliminary evidence that they have synthesized approximately two-thirds of a small gene found in yeast cells.

Their approach to synthesis involved chemically producing small segments of the 80 unit DNA chain of the gene and then using an enzyme to join the segments in the precise order of the naturally-occurring gene.

The small individual segments of the gene were produced by chemically adding the individual units of the DNA chain one at a time. Special care was required to assure that the units were added in the correct order and that no unwanted reactions occurred.

The enzyme, called DNA ligase, is thought to be one of the enzymes which rejoins broken DNA molecules in the cell.

The biochemists hope, by chemically producing small segments of the gene and carefully joining them with the enzyme, to build the entire gene.

They hope to test their synthetic gene by inducing it to function in a test tube and then comparing the product of the gene, a type of amino acid carrier called transfer-RNA, with the one found in living yeast cells.

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From The University of Wisconsin News and Publications Service, Bascom Hall, Madison 53706 • Telephone: (608) 262-3571

Release: Immediately 10/16/68 jb

WITH NOBEL PRIZE

MADISON, Wis.--The University of Wisconsin's Dr. H. Gobind Khorana, who shares the 1968 Nobel Prize for Medicine, is widely recognized as one of the world's leading researchers in molecular biology.

The native of Raipur, India, came to Wisconsin in 1960 as professor of biochemistry and co-director of the Institute for Enzyme Research. He has held the Conrad A. Elvehjem Professorship in the Life Sciences since 1964.

His work has been directed toward synthesizing a simple gene--the basic hereditary "blueprint"--to learn how genes work, the nature of embryonic development, how major diseases are genetically determined, and the mechanisms that underlie the malignant transformation of cells.

Dr. Khorana and Dr. Marshall Warren Nirenberg of the National Institutes of Health will receive the Louisa Gross Horwitz Prize for outstanding research in biochemistry in New York Thursday. The $25,000 award, given by Columbia University, cites the researchers efforts, "for brilliantly and successfully elucidating the detailed nature of the genetic code."

In September Dr. Khorana won the $1,000 American Chemical Society Award for creative work in synthetic organic chemistry.

He received the B. Sc. in 1943 and the M. Sc. in 1945 from Punjab University, India, with honors, and the Ph.D. in 1948 at the University of Liverpool, England. He was a postdoctoral fellow of the government of India at the Federal Institute of Technology, Zurich, Switzerland, and a Nuffield Fellow at the University of Cambridge, England.

- more -

Add one--Khorana

Dr. Khorana was head of the organic chemistry group of the British Commonwealth Research Council from 1952 to 1960, the last two years of which he spent as a visiting professor at the Rockefeller Institute, New York.

The researcher has synthesized all 64 of the possible trainucleotides and confirmed that the genetic code is read in a linear and consecutive manner and that it is a non-overlapping triplet code.

His other awards have included the Merck Award from the Chemical Institute of Canada and the gold medal of the Professional Institute of the Public Service of Canada.

Dr. Khorana has written and published more than 200 scientific articles on his studies, was elected to the National Academy of Sciences and American Association for the Advancement of Science in 1966, and the American Academy of Arts and Sciences in 1967. He has received an honorary doctorate from the University of Chicago; the Dannie-Heinneman Preiz in Gottingen, Germany; and the Remsen Award from Johns Hopkins University. He has been elected Overseas Fellow of Churchill College in Cambridge, England, and to membership in Deutsche Akademie der Naturforscher Leopoldina, Halle/Saale, Germany.

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Release: Immediately 10/16/68

UIR Science Writing Division (262-5984)

Photographs available

Wife's name Esther or maiden Fitzgerald

By MARLETTE SWENSON

MADISON, Wis.--A University of Wisconsin scientist who shuns publicity for himself and spends most of his time alone, "to think," is co-winner of the 1968 Nobel Prize for Medicine and Physiology.

When announcement of the Nobel Prize winners flashed on the radio in the early morning hours of Wednesday (October 16), Dr. Har Gobind Khorana was busy preparing a lecture he will give in conjunction with another award he is to receive later in the week. Dr. Khorana spent the morning in his "hideaway" outside Madison so he could finish his lecture before receiving the accolades of his colleagues and the public.

Dr. Khorana, quiet and reserved, explains he is "happy to spend all my time in serious things." His devotion to his research for the past quarter of a century has made him a pioneer in the complex field of nucleic acid chemistry, and today he is one of the world's most advanced researchers in the field.

Indeed, Dr. Khorana and the field of nucleic acid chemistry have grown together, "hand in hand," so to speak, for the young researcher from India has directed research on the nucleic acids ever since the field of molecular biology developed in the early 1950's.

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"If you're doing research in both chemistry and biology you're involved in a lot of excitement," Dr. Khorana explains, smiling, "and that does not leave one with much time for anything else.

"In fact," he continues, more seriously now, "I would not choose any other interest that would take up this time."

He is deeply interested in music, for a researcher can think about his work, or relax for a few moments, while listening.

Dr. Khorana was born in Raipur, India, on January 9, 1922. He did not pick up his interest in science from his parents, for they were not scientists, but picked it up later in his schooling. He received his undergraduate and graduate education at Punjab University in India, a B.Sc. with honors in 1943 and a M.Sc. also with honors in 1945.

That year he received a Government of India Studentship to continue his graduate education in organic chemistry at the University of Liverpool in England, and he received the Ph.D. there in 1948.

Next he worked at the Federal Institute of Technology in Zurich, Switzerland, for a year as a post-doctoral Fellow of the Government of India, and at the University of Cambridge, England, for two years as Nuffield Fellow.

In 1952 Dr. Khorana went to Canada to become head of the organic chemistry section of the British Columbia Research Council and the University of British Columbia in Vancouver.

It was while he was working in British Columbia that Dr. Khorana achieved international recognition for synthesizing coenzyme A, in conjunction with Dr. John G. Moffatt. Synthesis of coenzyme A is a noteworthy achievement in itself, but it only stimulated Dr. Khorana to further research in molecular biology.

"We did not know necessarily where we were headed in our research," he explains, thinking back of those early years, "but we desired to elucidate the nucleic acids.

"Then molecular biology developed in the early 1950's, and we were involved in the excitement of both fields--chemistry and biology."

In 1958 Dr. Khorana received the coveted Merck Award from the Chemical Institute of Canada for his outstanding contributions to the fields of organic chemistry and biochemistry. Two years later he was awarded the Gold Medal in the field of pure and applied science from the Professional Institute of the Public Service of Canada.

On September 1, 1960, Dr. Khorana joined the University of Wisconsin as co-director of the Institute for Enzyme Research and Professor of Biochemistry. In 1964 he was named to the Conrad A. Elvehjem Professorship in the Life Sciences, a distinguished honor, for Prof. Elvehjem was a renowned biochemist himself and later president of the University, and his name is given to the leading professorship at the University of Wisconsin.

At the University of Wisconsin Dr. Khorana holds a unique position in that he has no class responsibilities. He spends all his time continuing his far-flung research efforts in the areas of the genetic code, nucleic acids, the mechanics of genetic factors and the control of these factors by artificial means.

It was at Wisconsin that Dr. Khorana recently synthesized all 64 of the possible trinucleotides and confirmed that the genetic code is read in a linear and consecutive manner and that it is a non-overlapping triplet code.

Dr. Khorana's distinguished research group now has taken a giant step toward the first laboratory creation of a gene, the chemical unit of heredity. The research group expects to complete the synthesis of the first man-made gene within three to six months. This phase of their research began in 1965.

This expected achievement will be a key advance in learning about--and eventually controlling--heredity.

Dr. Khorana is quick to give credit to his colleagues in his research group for all his achievements, and he prefers to call his research a "team effort."

His researchers at the Enzyme Institute are all "very senior researchers," he calls them, for they are all at the post-doctoral level. And Dr. Khorana is very proud of the fact that these researchers have come from 27 countries around the world, and that they have brought experiences in many backgrounds--such as pure chemistry, enzymology, and molecular biology as well as biochemistry--to contribute to the team effort.

Although the research is a team effort, Dr. Khorana is the guiding force who determines the direction of the research. Dr. Khorana tries to spend a few months alone each summer to "feel out" new problems for forthcoming research.

"For 12 years I never took any vacation or time off from my work," Dr. Khorana explains, "but now I think vacations are important. I enjoy hiking in the out-of-doors and being completely physically occupied to exercise my body as well as my mind."

He spends much of every working day walking on the Wisconsin campus, between the Enzyme Institute and the Union, and along the lake shore to the willows.

"Many of my colleagues don't realize how much time I spend walking on campus," he admits, with a twinkle in his eye, "but many ideas come to me at these times, while I am walking."

Dr. Khorana constantly carries colored index cards and a pen with him on these walks, and when he returns to his laboratory the colored cards are filled with notes--new ideas for research in progress, perhaps, or new ideas for future research.

"I can think most effectively when I'm left alone and not rushing from one place to the next," Dr. Khorana explains.

Dr. Khorana, who has written and published more than 200 scientific articles on his research, was elected to the National Academy of Sciences in 1966 and was elected to fellowship in both the American Association for the Advancement of Science, in 1966, and the American Academy of Arts and Sciences, in 1967. He

has received an honorary doctorate degree from the University of Chicago; the Dannie-Heinneman Preiz in Gottingen, Germany; and the Remsen Award from Johns Hopkins University. He has been elected Overseas Fellow of Churchill College in Cambridge, England, and to membership in Deutsche Akademie der Naturforscher Leopoldina, Halle/Saale, Germany.

Dr. Khorana has been a special lecturer at scientific symposia and meetings around the world, including Poland, Canada, Switzerland, Japan, and England.

Dr. Khorana's latest award, and the one for which he was writing the lecture in his "hideaway" when news of the Nobel Prize flashed on the air, is the Louisa Gross Horwitz Prize from Columbia University. Dr. Khorana shared the $25,000 award with Dr. Marshall Warren Nirenberg of the National Institutes of Health.

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University of Wisconsin News Service, 10 Bascom Hall, Madison, Wis. 53706

June 1D

KHORANA'S SYNTHESIS OF A GENE (about 1:30)
FILM (about 1:05) shows Dr. Khorana and research colleagues in laboratory scenes; script is not keyed to specific film scenes.

AT THE UNIVERSITY OF WISCONSIN INSTITUTE FOR ENZYME RESEARCH, NOBEL PRIZE WINNER H. GOBIND KHORANA (Ko-RONN'-AH) ANNOUNCED THE FIRST TOTAL SYNTHESIS OF A GENE--THE BASIC HEREDITARY UNIT OF LIFE.

THE SYNTHESIS OF THIS GENE, FROM THE COMMON HOUSEHOLD YEAST, IS A BREAKTHROUGH IN DETERMINING THE RULES FOR CHEMICALLY BUILDING GENES FROM ATOMS OR SIMPLE MOLECULES.

THE ACHIEVEMENT, LONG AWAITED BY MOLECULAR BIOLOGISTS, PROVES THAT IT IS POSSIBLE FOR CHEMISTS TO PUT THESE SIMPLE MOLECULES, KNOWN AS NUCLEOTIDES, INTO THE SAME SEQUENCE IN WHICH THEY OCCUR IN NATURAL GENES. AND YET, NO NATURAL GENE NEED BE PRESENT IN THE TEST TUBE AS A MODEL.

IN 1968 ,DR. KHORANA OF THE WISCONSIN INSTITUTE FOR ENZYME RESEARCH, SHARED THE NOBEL PRIZE WITH TWO OTHER SCIENTISTS. KHORANA'S AWARD WAS THE RESULT OF HIS WORK IN CLARIFYING THE GENETIC CODE. THE CODE IS THE MECHANISM BY WHICH INFORMATION FOR ALL INHERITED TRAITS IS PASSED ON FROM ONE GENERATION OF LIVING ORGANISMS TO THE NEXT.

- more -

FILM 1:05

LS, ENZYME LAB :03

MS, LAB SIGN :02

MS, KHORANA OFFICE :05

CU, KHORANA :03

CU, HAND CUTAWAY :02

CU, KHORANA :03

MS, RESEARCHER (KATSUMARO MINAMOTO) IN LAB :07

CU, BOILING SOLUTION :02

MS, MINAMOTO :03

MS, RESEARCHER (KEN AGARWA) and EVAPORATOR :03

CU, AGARWA :02

MS, RESEARCHER (VICTORIO SGARAMELLA) IN LAB :05

CU, HANDS :02

CU, LAB TABLE :03

MS, RESEARCHER (KJELL KLEPPE) AND NUCLEOTIDE ANALYZER :04

CU, KLEPPE :02

CU, ANALYZER DIAL :02

CU, KLEPPE :02

MS, RESEARCHERS (MARVIN CARUTHERS AND HANS VANDE SANDE) WITH SCINTILLATION COUNTER :05

CU, PRINTOUT :02

CU, LIGHTED READOUT :02

CU, PRINTOUT :03

NOW HE IS THE FIRST TO PRODUCE A GENE COMPLETELY BY SYNTHETIC METHODS. THE WORK ON THIS GENE (THE YEAST ALANINE TRANSFER RNA GENE) REQUIRED FIVE YEARS TO COMPLETE. HOWEVER, THE SYNTHESIS OF A SECOND GENE, THIS TIME FROM A BACTERIUM, IS EXPECTED TO TAKE ONLY A FEW MONTHS.

THEORETICALLY NOW, ANY DESIRED GENE CAN BE MANUFACTURED IN A TEST TUBE. MANY SCIENTISTS FORESEE THE TIME WHEN GENETIC DISEASE--SUCH AS DIABETES AND SOME FORMS OF MENTAL ILLNESS--MIGHT BE CURED BY PROVIDING THE TISSUES OF AFFECTED PERSONS WITH A SUPPLY OF NORMAL GENES.

DOCTOR KHORANA AND HIS FELLOW RESEARCHERS CAUTION, HOWEVER, THAT THIS APPLICATION OF THEIR WORK WILL NOT COME FOR A NUMBER OF YEARS. AMONG OTHER THINGS, EXPERIMENTAL TECHNIQUES FOR INTRODUCING NORMAL GENES INTO THE DISEASED TISSUES WILL HAVE TO BE DEVELOPED.

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uw news

From The University of Wisconsin News and Publications Service, Bascom Hall, Madison 53706 • Telephone: (608) 262-3571

Release: Immediately 9/10/68 ns

MADISON--Dr. H. Gobind Khorana of the University of Wisconsin in Madison has won the $1,000 American Chemical Society Award for creative work in synthetic organic chemistry.

Announcement of the award, sponsored by the Synthetic Organic Chemical Manufacturers Association, was made Tuesday at the general assembly of the society's 156th national meeting in Atlantic City, N. J.

Dr. Khorana, widely recognized as one of the leading researchers in molecular biology, has developed chemical methods for the synthesis of certain phosphate-containing natural compounds that are of prime importance in the maintenance and transmission of the life process. His extensive and thorough work in this field has helped to make possible the dramatic developments of the past few years. He has published more than 200 scientific papers on his research.

Born in Raipur, India, Dr. Khorana received the B.Sc. Hons. in 1943 and the M.Sc. Hons. in 1945 from Punjab University, India, and the Ph.D. in 1948 at the University of Liverpool, England. He was a post-doctoral fellow of the government of India at the Federal Institute of Technology, Zurich, Switzerland, and the following year was a Nuffield Fellow at the University of Cambridge, England.

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Add one--Khorana

Dr. Khorana was head of the organic chemistry group of the British Commonwealth Research Council from 1952 through 1960, the last two years of which he spent as a visiting professor at the Rockefeller Institute, N.Y.

In September 1960 he came to the University of Wisconsin as professor and co-director of the Institute for Enzyme Research. He was made a professor in the department of biochemistry in 1962 and was given the Conrad A. Elvehjem Professorship in the Life Sciences in 1964.

The ACS award was established in 1955. It will be presented to Dr. Khorana at the 157th national ACS meeting in Minneapolis in April.

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THE AMERICAN CHEMICAL SOCIETY

NEWS SERVICE
1155 SIXTEENTH ST., N.W.
WASHINGTON, D.C. 20036
TEL. 202 RE 7-3337

CONFIDENTIAL

NOT TO BE RELEASED BEFORE
TUESDAY, SEPTEMBER 10, 1968

ATLANTIC CITY, September 9.--Dr. H. Gobind Khorana of the University of Wisconsin has won the $1,000 American Chemical Society Award for Creative Work in Synthetic Organic Chemistry sponsored by the Synthetic Organic Chemical Manufacturers Association. The announcement was made here tonight at a general assembly of the Society's 156th national meeting.

Dr. Khorana, widely recognized as one of the leading researchers in molecular biology, has developed chemical methods for the synthesis of certain phosphate-containing natural compounds that are of prime importance in the maintenance and transmission of the life process. His extensive and thorough work in this field has helped to make possible the dramatic developments of the past few years. He has published more than 200 scientific papers on his research.

Born in Raipur, India, Dr. Khorana received the B.Sc. Hons. in 1943 and the M.Sc. Hons. in 1945 from Punjab University, India, and the Ph.D. in 1948 at the University of Liverpool, England. He was a post-doctoral fellow of the government of India at the Federal Institute of Technology, Zurich, Switzerland, and the following year was a Nuffield Fellow at the University of Cambridge, England.

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Dr. Khorana, internationally renowned scientist and lecturer, was a fellow of the Chemical Institute of Canada in 1959 and received the Gold Medal for 1960 from the Professional Institute of the Public Service of Canada. He received the Dannie-Heinneman Preiz, Göttingen, Germany, in 1967 and was elected to the Deutsche Akademie der Naturforscher Leopoldina, Halle/Saale, Germany, this year. He is a fellow of the American Association for the Advancement of Science, and the American Academy of Arts and Sciences, an overseas fellow of Churchill College, Cambridge, England, and a member of the National Academy of Sciences.

The ACS Award for Creative Work in Synthetic Organic Chemistry was established in 1955. The award will be presented to Dr. Khorana at the 157th national ACS meeting in Minneapolis, Minn., in April 1969.

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uw news

From The University of Wisconsin News and Publications Service, Bascom Hall, Madison 53706 • Telephone: (608) 262-3571

Release: After 3 p.m. Saturday, Aug. 19 8/17/67 jw

UIR Science Writing Division (262-5984)

TOKYO--(For use after 3 p.m. Saturday, Aug. 19)--Work toward synthesizing a simple gene--the basic hereditary "blueprint"--was discussed Sunday by University of Wisconsin scientist H. Gobind Khorana, who opened the 7th International Congress of Biochemistry in Tokyo.

Khorana and his co-workers at Wisconsin's Institute for Enzyme Research are working on ways to join four chains, each with 20 molecular links, into an 80-unit gene.

Such a gene would direct the formation of a substance known as transfer-RNA. In living organisms, it is transfer-RNA which brings about production of proteins needed for growth and development.

Enzymes are the substances which Khorana hopes can be used to make the shorter chains join together properly to form a gene. He stressed that "this enzymatic part of the total work is still at a theoretical level."

He noted that the task of biochemistry in the coming decade will be to synthesize genes. Only after this is accomplished, Khorana feels, can molecular biologists learn how genes work.

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uw news

From The University of Wisconsin News and Publications Service, Bascom Hall, Madison 53706 • Telephone: (608) 262-3571

Release: **Immediately** 5/15/67 jb

BOSTON, Mass.--Three distinguished members of the University of Wisconsin faculty in Madison have been elected to fellowships in the American Academy of Arts and Sciences.

Selected at the academy's 187th annual meeting here this week were:

Drs. Har Gobind Khorana, co-director of the Wisconsin Enzyme Institute and professor of biochemistry; John Barkley Rosser, director of the Mathematics Research Center and professor of mathematics and computer sciences; and Jack L. Strominger, professor of pharmacology.

Among the 91 Americans elected to fellowship were leaders in a wide range of fields, including law, economics, science, medicine, architecture, and the arts.

A native of India, Dr. Khorana is recognized internationally as an authority on the genetic code, in the field of nucleic acids, on the mechanics of genetic factors, and on the control of these factors by artificial means.

Dr. Rosser, former president of the Society for Industrial and Applied Mathematics, was instrumental in development of the Polaris missile. His work has been commended by the Secretary of the Navy, and he received the Presidential Certificate of Merit for his discoveries in the field of rocketry.

Chairman of his department at the UW Medical School, Dr. Strominger has done research on penicillin for 15 years. He hopes to develop a penicillin of such potency it eventually will replace all other antibacterial agents. He won the U.S. Public Health Service Career Award in 1962.

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uw
news

From The University of Wisconsin News and Publications Service, Bascom Hall, Madison 53706 • Telephone: (608) 262-3571

Release: **Immediately** **4/26/67 db**

UIR Science Writing Division (262-5984)

By DENNIS BLAKESLEE

MADISON--Through use of a carefully planned series of synthetic DNA molecules with known repeating base sequences, essentially all of the genetic code can now be considered established with certainty.

The synthetic work and subsequent biological experiments that led up to this point were carried out by a research group at the University of Wisconsin Institute for Enzyme Research, headed by H. Ghobind Khorana.

Many codon assignments--correlation of a sequence of three bases with a certain amino acid--made earlier by a different experimental approach have been fully confirmed, while some previously uncertain codons have been definitely linked for the first time to specific amino acids.

Basic outlines of the long research trail leading to elucidation of the mechanisms of the genetic code are described in a series of articles prepared for publication in the Journal of the American Chemical Society. They appear in the issue of the Journal published April 26.

In the past few years, biochemists have used two main experimental approaches in their attempts to solve the genetic code.

One, called the binding technique, makes use of the fact that very short (as few as three bases) RNA molecules can cause amino acids, the building blocks of proteins, to be bound to ribosomes. These ribosomes are the tiny particles that

- more -

"read out" the genetic messeage contained in the base sequence of messenger RNA (mRNA), which in turn is a copy of DNA, the stuff of which genes are made.

Each different sequence of bases on these short RNA's, prepared by either enzymatic or by purely chemical means, causes the binding of certain amino acids to ribosomes--the particular amino acid that corresponds to that sequence of bases.

The genetic alphabet is composed of only four "letters," or bases: A, T, G and C in DNA; A, U, G and C in RNA. This means that there are but 64 possible combinations of three bases, called triplets or codons--the genetic code words.

Soon after the discovery of the binding technique (announced in 1964 by M. Nirenberg and P. Leder of the National Institutes of Health) all 64 triplets were made in different laboratories and each was tested to see what amino acid it would bind to ribosomes.

Many codon-amino acid assignments were made quickly using this method. The technique showed conclusively that many amino acids, of which there are 20 commonly used by living organisms to make proteins, were coded by more than one triplet.

For example, the short piece of RNA composed of the three bases CAU caused the amino acid histidine to be bound. However, CAC also directed the binding of the same amino acid.

Hence, the genetic code was discovered to be degenerate--with more than one codon specifying an amino acid. In fact, three amino acids can be coded by any of six (though usually similar) triplets, while several are coded for by four.

Though the binding technique afforded an excellent and relatively rapid tool with which to attack the code, it had limitations.

In some cases, the amount of amino acids bound to ribosomes by given triplets was too little to be measured with confidence, if at all. At other times, a triplet appeared to cause the "ambiguous" binding of more than one amino acid.

Fortunately, these difficulties were largely surmountable by the use of another more direct, though more difficult, appro-ch.

In 1961, Nirenberg announced the first codon assignment: the base sequence UUU coded for the amino acid phenylalanine, though it was not known for certain at the time that the code was in triplets. He reported only that some number of U's coded for the amino acid.

The technique used was the actual synthesis of a string of amino acids directed by an artificial messenger RNA molecule a great many bases in length.

In his first experiment, a long, synthetic messenger containing only the base U was made enzymatically. This in turn was placed in a protein-synthesizing system, a cell-free soup prepared by breaking the cells in a culture of bacteria. After removal of cell walls, DNA, RNA and other unwanted material, a solution remains containing all components necessary to make protein except for the coded, genetic message to direct its manufacture.

When the synthetic messenger poly-T, was added, a protein-like chain composed entirely of the amino acid phenylalanine was synthesized.

Though simple in design, the technique was not at first as useful as the binding technique in making definite codon assignments since it was not possible to make mRNA molecules with completely known base sequences, other than those molecules composed of only one base.

Soon after, however, Khorana and co-workers at Wisconsin were able to announce the development of purely chemical methods for the manufacture of short DNA molecules systematically built with an exactly defined sequence of bases.

Furthermore, these small molecules, usually no more than a dozen bases long, could be treated with a certain enzyme to make very long double-stranded DNA-like molecules, with the same known base sequence but now repeated over and over.

The long compound could, in turn, be acted upon by another enzyme to make equally long RNA molecules with the same, though complementary, repeating sequence.

By this means, artificial, totally defined genetic messengers were obtained that could be placed in the cell-free system.

A repeating sequence of two bases, repeated again and again, produced in the system a protein-like chain composed of only two amino acids in strictly alternating sequence.

For instance, the synthetic messenger poly-UC (i.e. UCUCUCUCUCUC...) made a chain of the alternating amino acids serine (UCU) and leucine (CUC). Since the same assignments had been made earlier on the basis of binding experiments, these two codons were considered to be definitely established. In all, it was possible to make four such messengers with alternating sequences of two bases, resulting in eight codon assignments.

In addition, this type of experiment offered direct proof that the genetic code was a non-overlapping one read three bases at a time, in triplets.

A synthetic messenger with a sequence of three repeating bases, for example poly-AAG, was found, as expected, to direct the synthesis of three different protein-like chains, each composed of a single amino acid. For, depending on where the "reading" begins, the messenger contains either the sequence AAG, GAA or AGA repeated over and over.

Finally, a sequence of four bases (i.e., poly-UAUC) directs the synthesis of a single type of protein chain composed of four amino acids in repeating order.

Recently, the Wisconsin group prepared a total of seven synthetic messengers with three-base sequences (in addition to poly-AAG which was made earlier) and four (including poly-UAUC) with four-base orders. All have been tested in the cell-free protein-synthesizing system.

Add four--genetic code

Altogether, the two, three and four base alternating sequences have allowed the assignment of 28 codons, most of them agreeing with assignments made by binding experiments, the rest comprising codons whose identity previously had been uncertain.

As a result, almost half of the 64 codons have been assigned by two independent means. Of the rest, all have been given assignments on the basis of strong binding experimental data. Many of these will later be confirmed in the cell-free protein-synthesizing system when the proper artifical messengers are made.

Though most of the binding and cell-free experiments have been carried out using the same strain of bacteria, one commonly used in much scientific work, sufficient evidence has accumulated to make it virtually certain that the code is universal--the same in all organisms.

But for minor details, then, the genetic code--the message of life--has been cracked.

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U.W. NEWS

From The University of Wisconsin News and Publications Service, Bascom Hall, Madison 53706
Telephone (Area Code 608) 262-3571

Release:
Immediately

4/26/66 jb

MADISON, Wis.--Two members of the University of Wisconsin faculty in Madison, Profs. Donald E. Osterbrock, astronomy, and H. Gobind Khorana, biochemistry, were elected to the National Academy of Sciences Monday.

As a result of the election, Wisconsin now counts 27 faculty members on the rolls of the distinguished body. Approximately 700 U.S. scientists and 70 foreign associates are members.

One of the nation's foremost astronomers, Dr. Osterbrock holds four degrees from the University of Chicago. In 1948 he received both the Ph.B. and B.S. degrees, in 1949 the M.S., and in 1952 the Ph.D. in astronomy and astrophysics.

He joined the Wisconsin staff in 1958 to participate in an expanded program in astronomy just starting on the Madison campus. Only a few days before his arrival Wisconsin dedicated a new $200,000 research observatory--the Pine Bluff country station.

His special areas of investigation are comets, extra-galactic nebula, and gaseous nebula. A native of Cincinnati, he taught at the California Institute of Technology before coming to Madison.

Dr. Osterbrock held a Guggenheim Fellowship in 1960-61, working at the Institute for Advance Studies, Princeton, N.J., in the field of magneto-hydrodynamics as applied to astrophysics.

Dr. Khorana is recognized internationally as an authority in the field of nucleic acids, on the genetic code, on the mechanics of genetic factors, and on the control of these factors by artificial means.

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Add one--national academy

In 1958 he received the Merck Award from the Chemical Institute of Canada for outstanding contributions in organic chemistry and biochemistry.

Chairman of the University's Institute for Enzyme Research, Section III, Dr. Khorana was born in India and was awarded the B.S. and M.S. by Punjab University. In 1946 he received his Ph.D. at the University of Liverpool, England.

Before coming to Madison in 1960, he served the Federal Institute of Technology, Zurich, Switzerland; the University of Cambridge, England, as a Nuffield Fellow; and the British Columbia Research Council as head of its organic chemistry group.

In 1964 he was appointed a Conrad A. Elvehjem Professor in the Life Sciences.

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U.W. NEWS

From The University of Wisconsin News and Publications Service, Bascom Hall, Madison 53706
Telephone (Area Code 608) 262-3571 Release: Immediately
4/6/66 jb

Prof. John F. C. Harrison, University of Wisconsin department of history, Madison, will be a discussant at the First Annual Conference on Explorations in Social and Comparative History at the State University of New York-Buffalo April 7 and 8.

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History Prof. Philip Curtin, University of Wisconsin, Madison, has been elected by the American Historical Association Council to serve as a director of the Social Science Research Council for a two-year term, beginning in 1967.

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An appointment from the American Historical Association to serve on its committee on university and college teaching has been received by Dr.William R. Taylor, professor of history, University of Wisconsin at Madison.

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Prof. William G. Hunter of the University of Wisconsin will present a short course in Response Surface Methodology at the 20th Annual Conference of the American Society of Quality Control in New York City June 1-3.

Prof. Hunter, a member of the statistics department and the Engineering Experiment Station staff on the Madison campus, will be assisted by William J. Hill, a research fellow.

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Add one--Fillers

Dr. Alfred Kadushin of the University of Wisconsin School of Social Work, Madison, will head a panel on "Handling Stress in Red Cross Relationships" in Chicago May 28. The session will be held during an institute for Red Cross staff members in connection with the annual forum of the National Conference on Social Welfare.

Dr. Kadushin has been a member of the service to military families committee of the Dane County chapter, Red Cross, since 1955.

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Dr. H. Gobind Khorana of the University of Wisconsin Institute for Enzyme Research is lecturing at the meeting of the Federation of European Biochemical Societies in Warsaw, Poland this week.

##

DRAFT (T) 6-22-65

Fite

Dear Dr. Carter:

Answering your invitation of April 15, the University of Wisconsin nominates Dr. Har Gobind Khorana, who holds the Conrad A. Elvehjem professorship in the Life Sciences at this University for the National Medal of Science.

He is co-director of our Institute for Enzyme Research, where he and his team recently accomplished one of the outstanding biological and biochemical feats of the decade---the first complete synthesis of polynucleotides---links in the DNA molecules that carry coded hereditary messages from generation to generation.

Not only has Dr. Khorana accomplished a notable dramatic advance in his field, but in so doing has settled, without doubt, many questions which scientists have had regarding the nature of the genetic code. His work, in effect, closed the ring of intense investigation by hundreds of scientists throughout the world which began when the Watson-Crick model for DNA was postulated in 1953. This accomplishment by Dr. Khorana was reported to the annual meeting of the Federation of American Societies for Experimental Biology, April 9, 1965.

A brief biography of the candidate is attached as Exhibit A. A statement of his achievements, including the names of three scientists or engineers who are well acquainted with his work, and a selected list of his publications is attached as Exhibit B. A complete list of his contributions to the literature of science and engineering is attached as Exhibit C.

The selection of Dr. Khorana was made by a committee of our most distinguished faculty members. I will be happy to supply any additional information you desire.

Cordially,

FHH
Pres.

File

U.W. NEWS

From The University of Wisconsin News and Publications Service, Observatory Hill Office, Madison 53706
Telephone (Area Code 608) 262-3571 Release:
4/9/65 jl PMS, April 12, 1965

By JAMES A. LARSEN

ATLANTIC CITY, N.J.-- Complete duplication in the test tube of the mechanism by which the genetic material--DNA--carries out its main function was reported today by University of Wisconsin scientists.

The work, in effect, closes the ring of intense investigation by hundreds of scientists throughout the world which began when the Watson-Crick model for DNA was postulated in 1953.

A team of scientists led by H. Gobind Khorana of the University of Wisconsin Institute for Enzyme Research reported the result of more than a decade of work today to the annual meeting of the Federation of American Societies for Experimental Biology.

Their report settles without doubt many questions which scientists have had regarding the nature of the genetic code carried in the key life molecule.

In scientific terminology, they have demonstrated that the genetic template is carried in a triplet, non-overlapping, unpunctuated code of nucleotides in the DNA molecule.

The work by Khorana and his team at Wisconsin essentially solves problems that only a year ago were first in the minds of chemists working to determine the nature of the genetic code.

The questions to be answered were these: Are the DNA code "words" spelled out by nucleotide pairs or triplets or by something else entirely? Does the code

-more-

overlap, in the sense that the second letter of the first word becomes the first letter of the second word, and so on? Are there breaks--chemical commas--between words?

The work at Wisconsin has answered these questions. The code is a triplet, non-overlapping, unpunctuated code.

To demonstrate the nature of the code, the Wisconsin scientists achieved a major advance in understanding of the chemistry of life. They are the first to have accomplished synthesis of polypeptide units of proteins, using synthetic DNA.

Last year, Khorana and his associates announced the first synthesis of short chain units of DNA. At the meeting today, they announced the first synthesis of polypeptides from the synthetic DNA.

In the recent work, relatively longer chains of synthetic DNA were employed. The DNA code was transcribed into polyribonucleotides, and the latter were, in turn, translated into polypeptides of the expected sequence. This was done with cell-free enzyme preparations in test tubes.

In the synthesis of polypeptides, each code "word" was accurately read and the designated amino acid placed in its proper position in the polypeptide chain.

This demonstrates that DNA not only can be synthesized, but that from the synthetic DNA it is possible to synthesize proteins of known composition.

The report of the Wisconsin scientists demonstrates that each amino acid is specified by a tri-nucleotide "word" and that, in instances, more than one word is used to specify a given amino acid. This is reasonable, since there are 64 possible different code words and 20 amino acids.

The methods developed by Khorana should now make it possible to determine relatively soon what code words specify each of the amino acids. This has already been accomplished for a number of the triplet code words by scientists working in a number of laboratories throughout the world.

The Wisconsin group has deciphered some additional code words that specify the amino acids, and they have also shown that more than one word is often used to specify a given amino acid.

It was known, for example, that AAA specified lysine. The Wisconsin group has now shown that AAG also specifies lysine. Another example of this kind is that both GUU and GUG specify valine.

The letters--A,G,U, and T--are used by chemists to designate the mucleotides adenine, guanine, uracil, and thymine, and it is the sequence in which these are placed in the DNA chain that spells out the genetic code. Thus a sequence AAAGUGAAGGUU would specify synthesis of a polypeptide chain of lysine-valine-lysine-valine in that order.

How the code is translated into protein in the living and growing cell is one of the great wonders of biology. Its accurate chemical description ranks scientifically with the major accomplishments of all time. Tremendous effort has gone into the problem by scientists working cooperatively throughout the world.

Before the Watson-Crick model was postulated, biologists could only marvel at what the living cell could accomplish. Now, little more than a decade later, the outlines of the method for genetic transfer of the templates used by living cells are known in some detail.

Since the initial postulation of the Watson-Crick model, molecular biologists have raced for the goal of final proof that the model is correct, and for knowledge of precisely how the coded nucleotides specify the right sequence of amino acid links in protein.

It is now known with certainty that when the protein-manufacturing apparatus of the living cell is extracted amd given synthetic DNA, it will go about using this DNA in the same manner as natural DNA. Thus, Khorana's synthetic DNA is biologically active, in scientific terminology.

Khorana elucidated the nature of the DNA code in two types of experiments. In both types, synthetic DNA molecules were used, of known repeating nucleotide sequence.

In one kind of experiment, an enzyme extracted from living cells and known as RNA polymerase was used to manufacture long ribopolynucleotides of repeating dinucleotide sequences from DNA with known repeating dinucleotide sequences.

In other experiments, the Wisconsin group used short synthetic DNA with repeating trinucleotide sequences in RNA polymerase reactions and obtained long ribopolynucleotides of known repeating trinucleotide sequence.

The ribopolynucleotides thus prepared were used as messengers in a cell-free protein synthesizing system and were found to yield polypeptides of sequences which provide direct proof for the validity of the biological code, and for its three-letter, non-overlapping, unpunctuated character.

One can now only speculate as to the implications the work will have eventually. Not only does it hold out great promise for advances in medicine and agriculture, but it opens entire new vistas for scientists in their exploration of the nature--perhaps even the meaning--of life.

It has been the greatest contemporary hope of biologists and chemists that the genetic code could be proved out by synthetic means.

This goal has now been accomplished.

The chemical techniques developed by the Wisconsin group in recent work leading to protein synthesis was described at the Atlantic City meetings today in a paper presented by Susuma Nishimura of the University of Wisconsin Institute for Enzyme Research. Co-authors of the paper presented were David S. Jones, T.M. Jacob, R.D. Wells, and Khorana.

add four--Khorana

At a symposium later in the week, Khorana will describe in more detail the work of his group, much of which has been reported at scientific meetings within the past two years. He will discuss the implications of the discovery to biology, and possible avenues for future research.

Khorana is careful to credit all of those with whom he has worked on the problems of DNA coding and the polypeptide synthesis: among these are many scientists at laboratories throughout the world. At Wisconsin, his colleagues are:

Polypeptide synthesis--Nishimura, Jones, Wells, Jacob, mentioned above; chemical synthesis of the encoded DNA chains--Rolf Lohmann, Dieter Soell, Eiko Ohtsuka, Hikoya Hayatsu.

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uw news

From The University of Wisconsin News and Publications Service, Bascom Hall, Madison 53706 • Telephone: (608) 262-3571

DOUBLE

Release: After 10:30 a.m. Thursday, April 20 db

UIR Science Writing Division (262-5984)

By DENNIS BLAKESLEE

CHICAGO--(Advance for release after 10:30 a.m. April 20)--Under the influence of a certain antibiotic, DNA can act as its own template for the synthesis of protein, bypassing the need for--but coding precisely like--messenger RNA.

Synthetic, single-stranded DNA molecules with known, repeating base sequences manufacture protein chains with the same order of amino acids as do the corresponding messenger RNAs when placed in a cell-free amino acid incorporating system with the antibiotic Neomycin B.

This result was reported today at the Federation of American Societies for Experimental Biology annual meeting by Drs. A.R. Morgan, R.D. Wells and H.G. Khorana of the University of Wisconsin Institute for Enzyme Research.

Without Neomycin B, DNA will not direct the incorporation of amino acids into a chain. In such a case, RNA is required.

Neomycin B is the only antibiotic thus far discovered that makes an efficient template for direct protein synthesis out of synthetic DNAs.

Previous work by these and other workers at Wisconsin has shown that synthetic messenger RNA molecules with a repeated, alternating sequence of two bases--for example poly-CA--directs the construction of a protein (or polypeptide) chain composed of only two amino acids in strictly alternating order, in this example threonine and histidine.

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Long, single-stranded DNA chains with the same alternating base sequence, plus the presence of the antibiotic, direct the placement of the same two amino acids in the same manner. In other tests, RNA and DNA plus Neomycin B behaved identically, the Wisconsin authors reported.

The base thymidine, T, which is found only in DNA, was read by the protein-synthesizing machinery of the cell-free system as uracil, U, the base that is found in RNA in place of T.

Some misreading of the code was encountered with the DNA template but the degree of this miscopying was not significantly different--a bit less, in fact--than that found using RNA as the template in the presence of the antibiotic.

No known organism, including some viruses that contain it, uses single-stranded DNA in nature directly for protein synthesis. All employ instead the messenger RNA intermediate.

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uw news

From The University of Wisconsin News and Publications Service, Bascom Hall, Madison 53706 • Telephone: (608) 262-3571

Release: After 2:15 p.m. Thursday, April 18 db

UIR SCIENCE WRITING DIVISION (262-5984)

By DENNIS BLAKESLEE

CHICAGO--(Advance for release 2:15 p.m. April 18)--The synthesis of a biologically active protein by a living organism is dependent on the correct translation of the genetic message. This can be achieved only when the genetic message is read at the proper initiator codon, University of Wisconsin researchers reported today.

Bacteria, and possibly higher organisms as well, may have as many as three separate starting signals for the rapid production of proteins.

Experiments using synthetic genetic messengers with predetermined base sequences have revealed that, under certain conditions, the base triplets (or codons) AUG, GUG and GUA all act as initiators of protein synthesis in vitro.

These findings were reported today at the annual meeting of the Federation of American Societies for Experimental Biology by Drs. H.P. Ghosh, D. Söll, and H. G. Khorana of the University of Wisconsin Institute for Enzyme Research.

For some time it has been believed that AUG was an initiating codon. It was shown that this triplet was recognized by two distinct types of transfer RNA, the relatively small RNA molecules that match specific amino acids with certain codons.

One type, called met-t RNA_M, places the amino acid methionine into its proper place in a growing protein chain in the usual manner. The other, called

- more -

met-t RNA_F, recognizes the same codon, AUG, but only when it occurs as the first triplet of a messenger RNA; when it does, it positions a slightly modified form of methionine, formylmethionine, as the first amino acid in the protein chain.

Placing this altered amino acid in the number one position stimulates the cellular protein-synthesizing mechanism, thus initiating rapid protein production.

In experiments where met-t RNA_F was carefully excluded from a mixture of protein-making components, initiation of synthesis was very slow if it occurred at all, again under certain conditions, in this case a low concentration of magnesium ion.

The Wisconsin group designed experiments to show if there were other codons that could recognize met-t RNA_F and to see if they too could stimulate protein production in the cell-free amino acid incorporating system, a major experimental technique used to study the genetic code and its control of protein manufacture.

By a different method, the researchers determined the number of likely candidates--codons that might be initiators--and tested them by synthesizing several different artificial messenger RNAs with each of these codons both in the first position and then repeated throughout the messenger chain.

They found that two other codons, in addition to AUG, could be recognized by met-t RNA_F. Both, GUG and GUA, were able to place formylmethionine in the first position of a protein chain, stimulating the synthesis of the rest of the protein chain as coded for by the artifical messenger.

Where these two codons occurred internally in the messenger, both coded for the amino acid valine.

These three initiator codons stimulate protein synthesis to differing degrees. The Wisconsin authors speculate that this may be of great importance in the reading of long messengers that contain the coding information for more than one protein.

Proteins coded for on such long messengers might be needed by the organisms in different amounts. The initiator codons at the start of each individual protein code could cause each protein to be made at different rates, the researchers pointed out.

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uw
news

From The University of Wisconsin News and Publications Service, Bascom Hall, Madison 53706 • Telephone: (608) 262-3571

Release: After 2 p.m. Monday, April 17 db

UIR Science Writing Division (262-5984)

By DENNIS BLAKESLEE

CHICAGO--(Advance for release after 2 p.m. April 17)--Long, man-made messenger RNA molecules with repeating sequences of the same arrangement of four bases direct the production of polypeptides, or chains of amino acids, with a sequence of amino acids repeated over and over.

Drs. H. Kossel and H.G. Khorana of the University of Wisconsin Institute for Enzyme Research today reported the results of several experiments employing different four-base sequences at the annual meeting of the Federation of American Societies for Experimental Biology.

Previously, four DNA preparations with repeating sequences of four bases had been made in their laboratory. The authors, with the aid of an enzyme, were able to produce from them four types of messenger RNA with the corresponding and complementary sequence of four bases.

These messengers were then used to direct polypeptide synthesis in a cell-free amino acid incorporating system derived from bacteria.

As an example, the RNA sequence poly-UAUC (i.e. UAUCUAUCUAUC.....) was expected, and found, to make a polypeptide chain of the amino acids tyrosine-leucine-serine-isoleucine repeated again and again.

The expectation was based on previous codon-amino acid assignments obtained by other means, where UAU codes for tyrosine; CUA for leucine; UCU for serine; and AUC for isoleucine.

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These experiments provide additional and direct support for the correctness of the particular codon assignments.

Of particular interest were two such messengers, each of which contained among its four codons either the sequence UAG or UAA.

Both of these are designated as nonsense codons that stop polypeptide synthesis whenever they occur. As expected, no long polypeptides were obtained when messenger RNA containing these codons was used.

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NEWS FROM THE UNIVERSITY OF WISCONSIN

Serving the state through campuses at Madison and Milwaukee, nine University Centers, and a statewide extension system.

11/13/64 jb

Immediate Release

MADISON, Wis.--A University of Wisconsin scientist whose work has been termed "one of the outstanding biological and biochemical feats of the decade" was named to the Conrad A. Elvehjem Professorship in the Life Sciences by University Regents Friday.

Dr. Har Gobind Khorana, a member of the University's Institute for Enzyme Research since 1960, is the first appointment to the new post established with Wisconsin Alumni Research Foundation funds in memory of the late president of the University.

Prof. Khorana and his co-workers in the Enzyme Institute achieved the first complete synthesis of polynucleotides--links in the DNA molecules that carry coded hereditary messages from generation to generation.

By using these chains--some 15 to 20 links in length--as templates, it is now possible to obtain much longer chains of known polynucleotide sequence. An enzyme preparation from living cells, known as the Kornberg system after the scientist who first isolated it, is used to manufacture long DNA molecules from the shorter synthetic templates. These long DNA strands are chemically similar in every respect to the natural DNA in living cells.

The arrangement in sequence of polynucleotides in the DNA molecules constitute a "code" for instructions passed from one generation to another for manufacture of chemicals needed by living cells to carry on life processes.

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The DNA strands of coded instructions are, in turn, used by the cell in manufacturing proteins. By analyzing the kind of protein turned out by known polynucleotide sequences, biochemists eventually should be able to decipher the recipe for life's basic chemicals.

Prof. Khorana has been described as "one of a new breed of scientists--chemical biologists who are as close to the meaning of life in these terms as anyone in the world has ever been."

Dr. Khorana was born Jan. 9, 1922, in Raipur, India. He obtained his bachelor's and master's degrees at Punjab University in Lahore. When he was 26, he won his Ph.D. degree in organic chemistry under Prof. Alexander Robertson at the University of Liverpool, England.

The next year he studied in Switzerland as a post-doctoral fellow, then returned to England for two years as a Nuffield Research Fellow under Cambridge's famous Alexander R. Todd. For the next eight years he headed the organic chemistry section of the British Columbia Research Council in Canada, coming to Wisconsin from that post.

The Regents Friday made four other major appointments and approved three changes in University assignments.

Chester L. Brisley, former consultant in management services for a New York accounting firm, was named professor of engineering in the University Extension Division at Milwaukee.

Archibald O. Haller, now professor of sociology at Michigan State University, was appointed professor of rural sociology, Madison, effective next July 1.

Clagett G. Smith, for several years study director of the Survey Research Center, Institute for Social Research, University of Michigan, was named associate professor of social psychology and organization science in the Center for Advanced Study in Organization Science, UW Extension Division, Milwaukee.

Add two--personnel actions

Prof. Jack C. Ferver, former coordinator of continuing education in Michigan, was named director of field services for the University's Extension Division.

Dr. James W. Cleary, UW professor of speech, was named assistant provost of the Madison campus to work with Provost Robben W. Fleming.

Thomas L. Moffatt, supervisor of the industrial relations programs of the UW Extension Division Management Institute, was appointed assistant to the dean for public services, Le Roy E. Luberg.

The title of Prof. George W. Sledge was changed from assistant to the dean of the College of Agriculture to assistant dean of resident instruction in the college. He has been a member of the faculty for 10 years, and is well known for his research on opportunities for rural youths to become established in farming.

The Regents accepted the resignation of Harry J. Solberg, associate professor in the University's School of Commerce, who has become an officer of the Fireman's Fund Insurance Co., San Francisco.

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NEWS FROM THE UNIVERSITY OF WISCONSIN

Serving the state through campuses at Madison and Milwaukee, nine University Centers, and a statewide extension system.

11/13/64 jl

Immediate Release

MADISON, Wis.--A biochemist noted for synthesis of links in the molecular chain that transmits hereditary traits in living organisms has been named to the Conrad A. Elvehjem Professorship in the Life Sciences at the University of Wisconsin.

The chemist, Har Gobind Khorana, a member of the University of Wisconsin Institute for Enzyme Research since 1960, is the first appointed to the new post established with Wisconsin Alumni Research Foundation funds in memory of the late president of the University of Wisconsin.

The appointment was approved by the University Board of Regents Friday.

Prof. Khorana is widely recognized in the scientific world for accomplishing what has been termed "one of the outstanding biological and biochemical feats of the decade."

He and his co-workers in the Enzyme Institute have achieved the first complete synthesis of polynucleotides--links in the DNA molecules that carry coded hereditary messages from generation to generation.

By using these chains--some 15 to 20 links in length--as templates, it is now possible to obtain much longer chains of known polynucleotide sequence. An enzyme preparation from living cells, known as the Kornberg system after the scientist who first isolated it, is used to manufacture long DNA molecules from the shorter synthetic templates. These long DNA strands are chemically similar in every respect to the natural DNA in living cells.

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The arrangment in sequence of polynucleotides in the DNA molecules constitute a "code" for instructions passed from one generation to another for manufacture of chemicals needed by living cells to carry on life processes.

The DNA strands of coded instructions are, in turn, used by the cell in manufacturing proteins. By analyzing the kind of protein turned out by known polynucleotide sequences, biochemists eventually should be able to decipher the recipe for life's basic chemicals.

This goal which now is in sight has been one of the great puzzles inspiring biochemical research since around the turn of the century when it was first shown that proteins are constructed of amino acid building blocks. Now it is known that DNA carries the coded plans for protein manufacture. Khorana has synthesized DNA--making it possible to unravel the code by determining the kind of protein synthesized by DNA of known structure.

Prof. Khorana has been described as "one of a new breed of scientists--chemical biologists who are as close to the meaning of life in these terms as anyone in the world has ever been."

Dr. Khorana was born Jan. 9, 1922, in Raipur, India. He obtained his bachelor's and master's degrees at Punjab University in Lahore. When he was 26, he won his Ph.D. degree in organic chemistry under Prof. Alexander Robertson at the University of Liverpool, England.

The next year he studied in Switzerland as a post-doctoral fellow, then returned to England for two years as a Nuffield Research Fellow under Cambridge's famous Alexander R. Todd. For the next eight years he headed the organic chemistry section of the British Columbia Research Council in Canada, coming to Wisconsin from that post.

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He additionally has been a visiting professor at the Rockefeller Institute, New York, and has received the Merck Award from the Chemical Institute of Canada, and the Gold Medal for 1960 from the Professional Institute of the Public Service of Canada.

The Elvehjem Professorship to which Prof. Khorana has been appointed is one of a number of similar academic posts at Wisconsin, named for distinguished faculty members of the past and supported by the Wisconsin Alumni Research Foundation.

Elvehjem was himself a distinguished biochemist, noted among other accomplishments for his discovery that deficiencies of the vitamin niacin was responsible for pellagra, the once-widespread nutritional disease. Elvehjem served as University of Wisconsin president from 1958 until his death in 1962.

The Wisconsin Alumni Research Foundation provides $35,000 annually in support of the Elvehjem Professorship, the largest portion of which is used for the salary of the individual holding the post and the remainder for assistants, laboratory employes, books, travel, and other expenses involved in maintaining research investigations.

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U.W. NEWS

FROM THE UNIVERSITY OF WISCONSIN NEWS SERVICE, MADISON, WISCONSIN 53706

8/3/64 db

RELEASE: Immediately

MADISON, Wis.--A $104,348 grant has been awarded to Dr. H. G. Khorana, co-director of the Institute for Enzyme Research at the University of Wisconsin, by the National Institutes of Health (NIH).

The grant, entitled "Chemical and Enzymic Studies of Polynucleotides," is a renewal of a continuing grant to Dr. Khorana to support his work, together with that of his colleagues, in molecular biology.

Recently, Dr. Khorana and his co-workers were able to announced the successful synthesis, through purely chemical means, of DNA, the genetic material.

The award will support further investigations of this synthesis of small bits of DNA, technically called polynucleotides, and the action of enzymes upon these materials. The work is a major step in the decoding of the genetic information carried in every living organism through the genes.

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MADISON NEWS

FROM THE UNIVERSITY OF WISCONSIN NEWS SERVICE, MADISON 6, WISCONSIN

10/11/63 db

RELEASE: Immediately

MADISON--Prof. H. Gobind Khorana of the University of Wisconsin Enzyme Institute will talk on "Polynucleotide Synthesis--Recent Work and Future Prospects" before the American Chemical Society's Wisconsin Section, Oct. 23.

The lecture will be given in Room 100, Chemistry Building, University Avenue and Charter Street, at 4:30 p.m. The public is invited.

Dr. Khorana is chairman of Section III of the Enzyme Institute and a professor of biochemistry.

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FEATURE STORY

FROM THE UNIVERSITY OF WISCONSIN NEWS SERVICE, MADISON 6, WISCONSIN

12/14/60 ml

RELEASE in PM's of Wednesday, Dec. 21

(ED. NOTE: This is the second of three articles on the University of Wisconsin's Institute for Enzyme Research and the secrets of life being explored there.)

By MACK LAING

MADISON, Wis.--(Advance for PM's of Wednesday, Dec. 21)--If you stop thinking about life in terms of rent, taxes, and babies for a moment and concentrate on the very minimum requirements for quite simple forms of cell life, sooner or later you reach the quite legitimate scientific idea that life in these terms is a series of chemical processes.

Since enzymes are chemicals that speed up the cell's vital processes, the University of Wisconsin Institute for Enzyme Research would seem a good place to get close to the chemical meaning of life.

Dr. H. Gobind Khorana is one of a new breed of scientists--chemical biologists who are closer to the meaning of life in these terms as anyone in the world has ever been. A few weeks ago he took over as leader of a third major research team in the expanded institute laboratories on University Avenue here.

Dr. Khorana started his own life 38 years ago in India. He got his bachelor's and master's degrees at Punjab University in Lahore. When he was 26, he won his Ph.D. degree in organic chemistry under the ~~noted Sir Robert Robinson~~ Professor Alexander Robertson at England's University of Liverpool.

The next year he studied in Switzerland as a post-doctoral fellow, then returned to England for two years as a Nuffield Research Fellow under Cambridge's famous Sir (now Lord, then Professor) Alexander R. Todd. For the last eight years, Dr. Khorana has headed the Organic Chemistry Section of the British Columbia Research Council in Canada.

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Members of the committee that picked Dr. Khorana for the Wisconsin post say he is probably one of the world's most advanced researchers in the organic chemistry of the nucleic acid molecule.

The target that researchers like Dr. Khorana are aiming for is an understanding of the nucleic acids. These are the cornerstones of heredity.

The differences among trees, fish, chipmunks, people--and all life--can be explained in terms of differences in the nucleic acids in the cell. All living things are made up of these life-units called cells. You have about 10 million million (cq) cells in your body. Each cell has a central part called the nucleus and within the nucleus, and named after it, are the puzzling nucleic acids.

They are extremely complicated. So far, Dr. Khorana's studies have concerned smaller and simpler compounds which result when a nucleic acid is "split" by an enzyme. These are the nucleotides, "model" compounds which are the building units of the nucleic acids.

Dr. Khorana has succeeded in chemically "stringing together" some of these nucleotides and manufacturing a number of polynucleotides in the laboratory. Years of work along this kind of research trail brings a chemist toward an understanding of the molecule, the smallest part of any substance that will combine with another substance to make a third substance.

The target is still the structure of the nucleic acid molecule. Theoretically, there are four to five million possible orders of arrangement of the chemicals involved that could result in nucleic acid formation. The problem is to find the code that nature has used to build the molecule.

This decoding puzzle is one of biochemistry's greatest problems. Scientists like Dr. Khorana who are working toward it keep clear of any thoughts of the applied, practical use of their work. Like all basic researchers, they concern themselves only with the challenge and the answer.

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However, this does not mean such research leads nowhere. Long before Dr. Khorana came to UW's Institute for Enzyme Research, his experimental results were known and applied here. Some of his methods are used in cancer research here in the development of new compounds. Other cancer researchers were able to use, check and support Dr. Khorana's research--a common balance in scientific investigation--when they found, at UW's McArdle Memorial Laboratory, that some substances Dr. Khorana was able to make experimentally in the lab, did occur naturally in animal tissue.

The final article in this series will outline some of the exciting questions nature is being asked at the enzyme institute. We will also have a look at a small factory which is thought to hold a world production record.

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CUT LINES

FROM THE UNIVERSITY OF WISCONSIN NEWS SERVICE, MADISON 6, WISCONSIN

12/14/60 ml

RELEASE:
in PM's of Wednesday, Dec. 21

MADISON, Wis.--(Advance for PM's of Wednesday, Dec. 21)--The University of Wisconsin Institute for Enzyme Research doubled its research space this fall, set up a third major research team, and brought in this internationally-known team leader. Dr. H. Gobind Khorana's work leads him toward the chemical basis of life itself--the puzzle of the nucleic acids inside the cell. They are the body's cornerstones of heredity. Here, Dr. Khorana uses a cellulose ion exchange column for separating nucleotides, model compounds that are the building units of the much more complex nucleic acids. Researchers all over the world are probing the mysteries of the structure of these life-chemicals. Because Wisconsin specializes in the field, has generous research support and researchers willing to spend years getting a handful of scientific clues, the UW institute is able to ask nature more numerous and more difficult questions than most laboratories. These factors put the Wisconsin institute among the top few in the world in this area of science.

--Gary Schulz Photo

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See Pix filed
Enzyme Institute

U. W. NEWS

FROM THE UNIVERSITY OF WISCONSIN NEWS SERVICE, MADISON 6, WISCONSIN

6/7/60 gb

RELEASE: Tuesday, June 7

MADISON, Wis.--The University of Wisconsin Board of Regents Tuesday approved 58 new faculty appointments for 1960-61.

The appointments include seven professors, nine associate professors, an assistant to the vice-president for academic affairs, 33 assistant professors, three visiting professors, two lecturers, a visiting lecturer, new track coach and assistant track coach.

New professors include:

Richard N. Current, professor of history, Wisconsin Ph.D., who since 1955 has been professor and head of the department of history and political science, Woman's College, University of North Carolina, and who has served as lecturer in Japan, India, and Germany;

Hellen M. Linksweiler, professor of home economics (food and nutrition), Wisconsin Ph.D., currently professor of home economics at the University of Nebraska;

H. Gobind Khorana, who will become professor and third co-director and research team chief at the Institute for Enzyme Research, from the University of British Columbia;

Chu-Kia Wang, civil engineering-structures professor, from the University of Illinois, well-known teacher of architectural engineering and structures who also has taught at University of Colorado and St. John's University, Shanghai, China and served as an engineer with Curtiss-Wright Corp. and as a consulting engineer;

-more-

Dr. Har Gobind Khorana
Institute for Enzyme Research
University of Wisconsin
Madison, Wisconsin

News and Publications Service
University of Wisconsin
Madison, Wisconsin

One of the world's most advanced researchers in the organic chemistry of nucleic acids, a pioneer in this field, Dr. Har Gobind Khorana serves the University of Wisconsin as co-director of its Institute for Enzyme Research.

Born in Raipur, India, in 1922, Dr. Khorana received his undergraduate and graduate education at Punjab University, Lahore, India: B.S. 1943 and M.S. 1945, with honors, and his Ph.D. at the University of Liverpool, England, in 1948.

In 1948, he went for a year as a government of India post-doctural fellow to Eiddenossische Technische Hochschule in Zurich, Switzerland, and from 1949 to 1952, to the University of Cambridge, England, as a Nuffield Research Fellow.

In 1952 he became head of the organic chemistry section of the British Columbia Research Council and the University of British Columbia in Vancouver. While there, Dr. Khorana gained international recognition for the synthesis of coenzyme A in conjunction with Dr. John G. Moffatt.

He recieved the coveted Merck Award fron the Chemical Institute of Canada in 1958 for outstanding contributions to the fields of organic and bio-chemistry. Two years later the scientist was awarded the Gold Medal in the field of pure and applied science from the Professional Institute of the Public Service of Canada.

In 1960 he joined the Wisconsin faculty and continued his far-flung research efforts in the areas of the genetic code, nucleic acids, the mechanics of genetic factors and on control of these factors by artificial means.

Dr. Khorana, who has written and published over 100 articles on his work, was named to the Conrad A. Elvehjem Professorship in the Life Sciences in 1964. In 1966 he was elected to the National Academy of Sciences, and in 1967 he was elected to fellowship in the American Academy of Arts and Sciences.

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U.W. NEWS

From The University of Wisconsin News and Publications Service, Observatory Hill Office, Madison 53706
Telephone (Area Code 608) 262-3571 Release: At Will

BACKGROUND INFORMATION

(The following material has been prepared in conjunction with Dr. H. Gobind Khorana of the Institute for Enzyme Research at the University of Wisconsin. It is an attempt to assist journalists in gaining as wide as possible a view of the scientific facts and theories surrounding the announcement of the synthesis of DNA molecules by Dr. Khorana and his immediate collaborators and their recent synthesis of polypeptides from these synthetic DNA molecules. It is hoped that this material will be useful to science writers as general background as well as a source of ready information for news stories concerning this recent work.)

A vast amount of experimental and theoretical evidence now exists to support the concept that the overall picture of the existence and propagation of life can be represented as:

DNA (deoxyribonucleic acid)-----RNA (ribonucleic acid)-----Protein.

The templates or coded plans for the propagation of life lies in DNA, the long, spiraling chemical known to be the carrier of genetic information. This information is passed on to RNA, a similar chemical. In effect, this transfer is a way of getting the genetic plans into a usable form; the passing of the blueprints from the architect to the construction engineer. The final step is the production of protein under the direction of RNA. It is the vast array of proteins that compose the vital structural and functional chemicals that support -- and probably actually are -- life.

Proteins are made up of subunits called amino acids, some 20 of which are commonly found in nature. From the fact that there are apparently no chemical restrictions governing the order in which these units may be hooked together to form proteins, plus the fact that amino acid chains can grow to thousands of units in length, it can readily be seen that the number of possible proteins is tremendously large.

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The nucleic acids (DNA and RNA), on the other hand, are composed primarily of four subunits called nucleotides. A nucleotide is a unit made up of a base, a sugar molecule and a phosphate group. When the base is attached only to the sugar (deoxyribose in the case of DNA) and the phosphate group is absent, the unit is called a nucleoside.

In the case of DNA, the bases (called as such because of their chemical personality) are generally guanine, thymine, cytosine and adenine, usually abbreviated G, T, C and A.

In nature, DNA exists in the form of a long double helix composed of two chains of nucleotides with the sugar of one unit linked to the phosphate group of the next, the bases projecting off to the side. The bases in the adjacent strands bond together like rungs on a ladder. Because of their geometric structure the bases hook together in a certain way, T always bonding with A and C always with G. The linkage is accomplished by means of hydrogen bonding, which forms a weak yet sufficiently strong bond. Thus, if one of the strands had on it the bases ATTC, for example, the strand next to it would have the bases TAAG. This picture of DNA is known as the Watson-Crick model.

It is this arrangement of paired bases that make it possible for DNA to replicate itself. If the two strands separate, as they do at the time of cell division, the A-to-T and G-to-C bonding characteristics enable each nucleotide to attract a complementary nucleotide, thereby forming a double helix once again.

RNA was also found to have four bases, the same with the exception that T is replaced by another base called uracil, or U. The two are very similar, differing only in the absence of a small side group on U that is present on T. More than one type of RNA has been found to occur within living cells, the most important being messenger RNA, or mRNA. This molecule is, in effect, the template or gene copy that migrates from the nucleus of a cell, where DNA resides and where

mRNA is formed, into the surrounding material (cytoplasm) where it directs the production of protein. mRNA is the complement of the information-carrying bases on a DNA strand--if the DNA base sequence was ATTC, the corresponding bases on the RNA chain would be UAAG.

Because of a lack of any similarity in the number or in the character of amino acids and nucleotides, it became obvious that no one-to-one, direct transfer of directions could exist. Thus, it was apparent that the sequence of bases on the nucleic acids must form some sort of a code. The most reasonable idea was that a sequence of three bases, called a triplet, specified a certain amino acid.

The first major advance toward solving the code came some three years ago when it was announced that an enzymatically synthesized RNA chain composed entirely of U (consequently called poly-U) directed the formation, in the laboratory, of a protein composed entirely of a single amino acid, phenylalanine. This work opened the way for the first great assault on the amino acid code by hundreds of biologists around the world.

But there were strict limitations as to both the extent and the precision of this general method of decipherment. Most important was the fact that RNA chains consisting of more than one base could not be prepared in known sequence. This meant that exact information about the code could be found only up to a point. For example, if it is assumed for a moment that the amino acid, or genetic, code is in triplets, then it might be possible to show that a certain triplet--a code word--composed, say, of two U's and an A specifies a particular amino acid. However, it wouldn't be possible to establish with absolute certainty whether the actual triplet in this case was UUA, UAU or AUU.

In spite of these limitations, a great deal about the code had come to light by 1963. It appeared, for example, that the code is degenerate, that more than one triplet (or doublet or whatever) codes for a particular amino acid. It was suspected, however, that this apparent degeneracy might well result from knowing only the composition of code words and not the exact arrangement of code letters within them. Also, there had been as yet no way of determining if there were breaks, or commas, between the code words.

To advance knowledge of the code beyond that stage, one of two things had to be placed within the control of scientists. Either (1) a way of precisely determining the lineup of bases along a natural DNA or RNA chain had to be developed, making correlation with the amino acid sequence possible, or (2) methods of synthetically constructing, or hand-tailoring, DNA and RNA chains of predetermined sequence were needed.

The first approach has thus far proven infeasible. It is relatively easy, though time consuming, to elucidate the amino acid sequence of a protein. Working out the order of nucleotides on a naturally occurring piece of DNA or RNA, however, simply cannot be accomplished by existing methods though new methods are now being developed. A protein can be examined by breaking many molecules of it into fragments and then identifying these. Different of these molecules break up into different overlapping fragments, with the result that a picture of what must have been the original order of the amino acid is obtained. When this sort of technique is applied to nucleic acids, the nucleotides break mainly into non-overlapping fragments. Thus, while it is possible to find out what bases are present in a nucleic acid molecule and in what percentages, it is impossible to establish their order, at least on molecules longer than 20 nucleotides.

The second approach--synthesis--offers the investigator the advantage of having considerable control over his experiments. He would know with certainty the base sequence of the nucleic acids he was starting with and, after amino acids

are put together into short proteins, he would need determine only the sequence of amino acids to find out the details of the code. It is this approach that has led to the methods worked out in the Institute for Enzyme Research at Wisconsin.

In principle, the chemical methods that have been employed to compose DNA of known sequence are simple. Two general types of reactions were used, both known to and used by chemists for decades. One is the selective protection and coupling of certain reactive sites on individual nucleotides one at a time. The other is polymerization, coupling many at a time.

Both the stepwise addition of nucleotides and polymerization of nucleotides were dependent upon the discovery of proper coupling reagents. Several years of work have gone into the investigation of coupling reagents most suitable for each type of approach. The first to be found was an organic chemical synthesized for this purpose. This compound, dicyclohexylcarbodiimide, was the result of considerable labor. Later, another compound was discovered that would also act as the condensing agent in the preparation of synthetic polynucleotides. This one, mesitylene sulfonyl chloride, is a relatively simple organic compound and is easily obtained. One or the other of the coupling agents are used in each step of a synthesis.

With the proper condensing agents in hand, it was possible to form DNA chains by two approaches, both involving the selective protection of reactive sites on a nucleotide, chemically a relatively simple matter in this case, and the joining together of these protected nucleotides. Briefly, this protection is the reacting of a nucleotide with certain chemicals that will bind to, and therefore mask, various reactive points on the molecule. These protecting groups must have the properties of being undamaging and unhindering to reactive sites other than the ones, or one, it bonds to and of being easily removed at the will of the chemist. In many cases, the discovery of the right protective groups is difficult

and requires a bit of hit or miss experimentation. With the nucleic acids, however, protective groups are known and are relatively simple. Using this technique, complex molecules can be made to join together in certain, proper ways, so long as the right condensing agents, conditions, catalysts, etc., are present.

Building a chain one nucleotide at a time, a process called stepwise addition, can, in theory, be employed to synthesize single-stranded DNA molecules of any desired order of bases and of any desired length. In practice, however, stepwise addition is limited at present to probably 20 units or so. The difficulties here are mainly those of separation. Each addition of a nucleotide to the growing chain is another chemical reaction, and between each step the chain must be separated from the reaction mixture and purified. As chains get longer, these separations become increasingly difficult. Chemists, however, are always working on means of improving techniques and thus it is likely that it will eventually be possible to construct longer and longer chains.

Polymerization is the running together of preformed pairs of nucleotides joined by the means just described. This procedure is one of the most common in chemistry and has found particular importance in the chemical industry. Perhaps the best example of polymerization is the application of the process to ethylene, a very simple two-carbon organic molecule. Under the proper conditions of heat and pressure, ethylene polymerizes to form carbon chains thousands of atoms long, a molecule called polyethylene. Any long molecule, for instance rubber, plastics, various synthetics and indeed proteins and nucleic acids are called polymers. DNA chains put together by this method are also limited to only a few bases because of unfavorable solubility-factors. When nucleotide pairs undergoing polymerization grow to chains of about 12 to 16 units, they precipitate out of solution and react no further.

Employing stepwise addition, synthetic DNA molecules composed of the repeating triplets TTC and TTH have been prepared, 12 and nine-bases long, respectively. The base H, hypoxanthine, is one that does not occur in nature but that can be used in place of G. It requires less protection than does G and is therefore easier to handle.

By means of polymerization, DNA chains containing the repeating doublets TC, TG and AG have been synthesized, the chains being six pairs or 12 bases long in each case. The polymerization of preformed triplets is under study.

Not long ago, it appeared that these methods for the synthesis of known-sequence DNA chains would be of only limited use in the exploration of the genetic code; the chains were too short. Recently, however, work in conjunction with Dr. Arthur Kornberg at Stanford University has shown that use of the enzyme DNA polymerase (discovered by Dr. Kornberg) makes it possible to prepare long chains of DNA from the short ones. Another enzyme, RNA polymerase, acts upon synthetic DNA to form longer chains of RNA.

That the code is triplet and not doublet or any other combination of letters is easily deduced from the recent work of Khorana and his group. It is the result of analyses of polypeptides formed from DNA of known sequence; the polypeptides are composed of amino acids laid down in the order that could be obtained only if the code were triplet. Thus, from a repeating sequence of nucleotides such as ABCABCABCABCABCABC and so on (in which the letters stand for any given nucleotide), there are a number of possible code sequences--of which the individual "words" in both doublet and triplet code might be ABC, BCA, CAB, AB, BC, CA. When analysed, however, the polypeptide always contains amino acids in the sequence designated by the "word" ABC, and the code is read without punctuation and directly in the sequence ABC, ABC, ABC, so there is no overlapping of letters. A nucleotide sequence, such as ABABABABAB is "read out" as ABA,BAB, ABA, BAB, and so on, further

substantiating the concept that the code is triplet, non-overlapping, and unpunctuated. The amount of work now done by Khorana and his group with various combinations of the code and analyses of the resulting polypeptides shows that this is at least the general rule in translation and syntheses and that if exceptions do exist they are, indeed, exceptions.

The importance and implications of the chemical techniques reported here are obvious. It cannot be stated with absolute certainty, of course, that the artificial DNA will, via RNA, make proteins in every case. But the evidence does indeed point in that direction. These new chemical tools, then, are the best methods to date by which to attack the amino acid code. The methods, along with refinements bound to come as more workers take up investigations using synthetic DNA of known sequence, should result in the eventual, if not rapid, deciphering of the genetic code. Not only that. Much is yet unclear concerning the mechanism of replication of DNA, a mechanism absolutely vital to life. The ability to prepare model DNA chains may well lead to the answer to this problem.

Dr. H. Gobind Khorana

Born--Raipur, India, 1922. Dr. Khorana received his undergraduate and graduate education at Punjab University, Lahore, India: B.Sc. 1943, M.Sc. 1945 (both degrees with honors). He received his Ph.D. from the University of Liverpool, England, in 1948.

After his doctorate, Dr. Khorana went for a year as a government of India post-doctoral fellow to the Eidgenossiche Technische Hochschule in Zurich and then, from 1949 to 1952, to the University of Cambridge as a Nuffield Research Fellow.

In 1952, he became head of the organic chemistry section of the British Columbia Research Council and the University of British Columbia in Vancouver. While at that institution, he gained international recognition for the synthesis of coenzyme A in conjunction with Dr. John G. Moffat. In 1958, he was given the Merck Award from the Chemical Institute of Canada for outstanding contributions to the fields of organic chemistry and in biochemistry in Canada. Two years later he was awarded the Gold Medal for 1960 in the field of pure and applied science from the Professional Institute of the Public Service of Canada.

Later that year he was invited by the University of Wisconsin to serve as a co-director of the Institute for Enzyme Research and as chairman of Section III, one of the three research groups at the institute.

He is widely recognized as one of the world's most advanced researchers in the organic chemistry of the nucleic acids and is a pioneer in the field.

EXHIBIT A BIOGRAPHY: HAR GOBIND KHORANA

Born in Raipur, India, January 9, 1922, Har Gobind Khorana was awarded his Bachelor of Science with Honors in 1943 and Master of Science with Honors in 1945, both by Punjab University, India, and the Ph.D. in 1948 by the University of Liverpool in England.

He held a post-doctoral fellowship at the University of Zurich, 1948-49, and Cambridge University, 1950-52.

He was head of the Organic Chemistry Group, British Columbia Research Council, 1952-60; Visiting Professor at Rockefeller Institute since 1958.

Dr. Khorana became Professor of Biochemistry and Co-director of the Institute for Enzyme Research at the University of Wisconsin in 1960, and was named the University of Wisconsin's first Conrad A. Elvehjem Professor in the Life Sciences in 1964.

He received the Merck Award from the Chemical Institute of Canada for outstanding contributions to the fields of organic chemistry and biochemistry in 1958; the Gold Medal of the Professional Institute of the Public Service of Canada in 1960.

Curriculum Vitae:

Date of Birth: January 9, 1922 Place of Birth: Raipur, India

1943	B.Sc. Hons., 1st Class Punjab University, India
1945	M.Sc. Hons., 1st Class Punjab University, India
1946-48	Ph.D. University of Liverpool, England Government of India Studentship Working under Professor A. Robertson, F.R.S.
1948-49	Federal Institute of Technology, Zurich, Switzerland Post-doctoral Fellow of Government of India Working with Professor V. Prelog
1950-52	University of Cambridge, England Nuffield Fellow Working with Professor Sir Alexander Todd, F.R.S.
1952-	B. C. Research Council Head, Organic Chemistry group
1958	Received the Merck Award from the Chemical Institute of Canada for outstanding contributions to the fields of Organic Chemistry and Biochemistry in Canada
1958-on	Visiting Professor, Rockefeller Institute, New York

EXHIBIT A (continued)

1959	Fellow of the Chemical Institute of Canada
1960	Gold Medal for 1960, Professional Institute of the Public Service of Canada
Sept. 1, 1960-	Professor and Co-director, Institute for Enzyme Research, University of Wisconsin, Madison, Wisconsin.
Sept. 1962-	Professor, Department of Biochemistry, University of Wisconsin, Madison, Wisconsin
April, 1964	Visiting Professor, Stanford University, Palo Alto, Calif.
November, 1964-	Conrad A. Elvehjem Professorship in the Life Sciences, University of Wisconsin, Madison, Wisconsin

EXHIBIT B

THE ACHIEVEMENTS OF DR. HAR GOBIND KHORANA

Har Gobind Khorana's research career began with the synthesis of several bacterial pigments in the Laboratory of A. Robertson, FRS, at Liverpool and continued with studies of Erythrina alkaloids in collaboration with Prelog. At Cambridge he undertook independent work on methods for determining the sequence of amino acids in peptides and developed the classic synthetic method involving carbodiimides.

In Vancouver and Madison, Dr. Khorana devised improved reagents for synthesizing biologically important phosphate compunds---nucleoside mono, di and triphosphates, dinucleotides, nucleotide diphospho sugars, Coenzyme A, nucleoside cyclic phosphates, and both ribo- and deoxyribo-polynucleotides of known sequence linked through the 3' and 5' positions. His studies of the phosphodiesterase of snake venom demonstrated that this enzyme attacks the 3' ends of the nucleic acid chain and degrades the molecule sequentially thus providing a useful tool for studying the structure of nucleic acids.

His most recent work is a brilliant attack on the detailed mechanism of genetic replication, transcription and translation. He has accomplished the chemical synthesis of all 64 possible trinucleotides, and has combined many of these into longer oligonucleotides. Using these synthetic deoxy-oligonucleotides of known sequences as templates for both RNA and DNA syntheses, he has found by the nearest-neighbor technique that the DNA or RNA polymerases faithfully transcribe the sequence, read successive units of the synthetic deoxyoligonucleotides in register, and produce high molecular weight DNA or RNA respectively. The synthesized RNA was then used as a messenger in a protein-synthesizing system of E. coli and specific polypetide synthesis occurred. These experiments have confirmed that the genetic code is based on a consecutively read, non-overlapping triplet of nucleotide bases, all three of which contribute information, and have established the sequence of bases within the codons for different amino acids.

By more simple techniques, employed also in other laboratories, Dr. Khorana has ascertained codons for all 20 naturally occuring amino acids.

He is the author of coauthor of 147 research publications, all of which are distinguished by their imaginative approach to difficult problems, precision of experimental execution, and clarity of exposition. His work marks him as one of the outstanding biochemists of our day.

Three scientists well acquainted with Dr. Khorana's work are:

Dr. Arthur Kornberg
Chairman, Department of Biochemistry
Stanford University
Palo Alto, California

Dr. Francis Crick
Cambridge University
Cambridge, England

Dr. Henry Lardy
Enzyme Institute
University of Wisconsin
Madison, Wisconsin

EXHIBIT B (continued)

A selected list of his scientific publications follows:

Peptides. Part III. Selective degradation from the carboxyl end. The use of carbodi-imides. J. Chem. Soc., June 1952 (387) 2081-2088.

The chemistry of carbodiimides. Chem. Rev., 53, 145 (1953).

Carbodiimides Part III. (A) A new method for the preparation of mixed esters of phosphoric acid. (B) Some observations on the base-catalyzed addition of alcohols to carbodiimides. Can. J. Chem., 32, 227 (1954).

Nucleoside Polyphosphates. VI. An improved and general method for the synthesis of ribo- and deoxyribonucleoside 5'-triphosphates. (With M. Smith.) J. Am. Chem. Soc., 80, 1141 (1958).

Phosphorylated Sugars. VI. Synthesis of α-D-Ribofuranose 1,5-diphosphate and α-D-ribofuranose 1-pyrophosphate 5-phosphate. (With G. M. Tener.) J. Am. Chem. Soc., 80, 1999 (1958).

Studies on Polynucleotides. IV. Enzymic degradation. The stepwise action of venom phosphodiesterase on deoxyribo-oligonucleotides. (With W. E. Razzell.) J. Biol. Chem., 234, 2114 (1959).

Nucleoside Polyphosphates. XII. The total synthesis of Coenzyme A. (With J. G. Moffatt.) J. Am. Chem. Soc., 83, 663 (1961).

Cyclic Phosphates. IV. Ribonucleoside-3',5' Cyclic Phosphates. A general method of synthesis and some properties. (With M. Smith and G. I. Drummond.) J. Am. Chem. Soc., 83, 698 (1961).

Some Recent Developments in the Chemistry of Phosphate Esters of Biological Interest. John Wiley and Sons, Inc., New York, 1961.

Studies on Polynucleotides. XIII. Stepwise synthesis of deoxyribo-oligonucleotides. An alternative general approach and the synthesis of thymidine di-, tri- and tetranucleotides bearing 3'-phosphomonoester end groups. (With G. Weimann.) J. Am. Chem. Soc., 84, 419 (1962).

Studies on Polynucleotides. XXVII. The stepwise synthesis of specific deoxyribopolynucleotides (7). The synthesis of polynucleotides containing deoxycytidine and deoxyguanosine in specific sequences and of homologous deoxycytidine polynucleotides terminating in thymidine. (With H. Schaller.) J. Am. Chem. Soc., 85, 3841 (1963).

Chemically synthesized deoxypolynucleotides as templates for RNA polymerase. (With A. Falaschi and J. Adler.) J. Biol. Chem., 238, 3080 (1963).

Synthetic deoxyribopolynucleotides as templates for ribonucleic acid polymerase. The formation and characterization of a ribopolynucleotide with a repeating trinucleotide sequence. (With S. Nishimura and T. M. Jacob.) Proc. Natl. Acad. Sci. U.S., 52, 1494 (1964).

EXHIBIT B (continued)

Synthetic deoxyribo-oligonucleotides as templates for the DNA polymerase of *Escherichia coli*. New DNA-like polymers containing repeating nucleotide sequences. (With C. Byrd, E. Ohtsuka, and M. W. Moon.) *Proc. Natl. Acad. Sci. U.S.*, 53, 79 (1965).

Exhibit C

LIST OF SCIENTIFIC PUBLICATIONS BY H. G. KHORANA

FROM CAMBRIDGE:

1. The Stepwise Degradation of Peptides. H.G. Khorana, Chem. and Ind. London, 1951, 129.

2. Peptides. Part II. Selective Degradation by Removal of the Terminal Amino-acid bearing a Free Amino-group. The Use of Alkyl Alkoxydithioformates (Dialkyl Xanthates). G.W. Kenner and H.G. Khorana, J. Chem. Soc., June 1952, (386), 2076-2081.

3. Peptides. Part III. Selective Degradation from the Carboxyl End. The Use of Carbodi-imides. H.G. Khorana, J. Chem. Soc., June 1952, (387), 2081-2088.

4. Peptides. Part IV. Selective Removal of the C-Terminal Residue as a Thiohydantoin. The Use of Diphenyl Phosphorisothiocyanatidate. G.W. Kenner, H.G. Khorana and R.J. Stedman, J. Chem. Soc., February 1953, (136), 673-678.

5. Structural Investigation of Peptides and Proteins. H.G. Khorana, Quarterly Reviews, VI, No. 4, 340 (1952).

6. Studies on Phosphorylation. Part XI. The Reaction between Carbodiimides and Acid Esters of Phosphoric Acid. A New Method for the Preparation of Pyrophosphates. H.G. Khorana and A.R. Todd, J. Chem. Soc., August 1953, (465), 2257-2260.

FROM ZÜRICH:

7. Erythrina Alkaloids. Part I. V. Prelog, K. Wiesner, H.G. Khorana and G.W. Kenner, Helv. Chim. Acta, 32, (59), 453 (1949).

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FROM LIVERPOOL:

9. The Melanin Problem. A Synthesis of 5:6-Dihydroxyindole. R.J.S. Beer, K. Clarke, H.G. Khorana and A. Robertson, Nature, 161, 525 (1948).

10. The Chemistry of Bacteria. Part I. The Synthesis of Hydroxyindoles. R.J.S. Beer, K. Clarke, H.G. Khorana and A. Robertson, J. Chem. Soc., October 1948 (324), 1605-1609.

11. The Chemistry of the Melanins. Part I. The Synthesis of 5:6-Dihydroxyindole and Related Compounds. R.J.S. Beer, K. Clarke, H.G. Khorana and A. Robertson, J. Chem. Soc., December 1948 (452), 2223-2226.

12. The Chemistry of Bacteria. Part II. Some Degradation Products of Violacein. R.J.S. Beer, K. Clarke, H.G. Khorana and A. Robertson, J. Chem. Soc., April 1949 (186), 885-889.

FROM 1952 (British Columbia, Madison):

13. The Chemistry of Carbodiimides. H. G. Khorana, Chem. Rev., 53, 145 (1953).

14. Carbodiimides Part II. The Reaction of Sulphonic Acids with Carbodiimides. A New Method of Preparation of Sulphonic Anhydrides. H. G. Khorana, Can. J. Chem., 31, 585 (1953).

15. Carbodiimides Part III. (A) A New Method for the Preparation of Mixed Esters of Phosphoric Acid. (B) Some Observations on the Base-Catalyzed Addition of Alcohols to Carbodiimides. H. G. Khorana, Can. J. Chem., 32, 227 (1954).

16. Carbodiimides Part IV. The Fission of N,N'-di-p-tolyl-O-benzyl and -O-allyl Pseudourea Ethers in the Presence of Acids. H. G. Khorana, Can. J. Chem., 32, 261 (1954).

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23. Nucleoside Polyphosphates. V. Syntheses of Guanosine 5'-Di- and Triphosphates. R. W. Chambers and H. G. Khorana, J. Am. Chem. Soc., 79, 3752 (1957).

24. Nucleoside Polyphosphates. VI. An Improved and General Method for the Synthesis of Ribo- and Deoxyribonucleoside 5'-Triphosphates. Michael Smith and H. G. Khorana, J. Am. Chem. Soc., 80, 1141 (1958).

25. The Use of Phosphoramidic Acids in the Synthesis of Nucleoside Pyrophosphates. R. W. Chambers and H. G. Khorana, Chem. and Ind. London, 1956, pp. 1022-1023.

26. Nucleoside Polyphosphates. VII. The Use of Phosphoramidic Acids in the Synthesis of Nucleoside-5' Pyrophosphates. R. W. Chambers and H. G. Khorana, J. Am. Chem. Soc., 80, 3749 (1958).

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27. Nucleoside Polyphosphates. VIII. New and Improved Syntheses of Uridine Diphosphate Glucose and Flavin Adenine Dinucleotide, Using Nucleoside-5' Phosphoramidates. J. G. Moffatt and H. G. Khorana, J. Am. Chem. Soc., 80, 3756 (1958).

28. The Preparation of Nucleoside 5'-Phosphoramidates and the Specific Synthesis of Nucleotide Coenzymes. R. W. Chambers, J. G. Moffatt and H. G. Khorana, J. Am. Chem. Soc., 79, 4240 (1957).

29. Carbodiimides. VII. Tetra-p-nitrophenyl Pyrophosphate, a New Phosphorylating Agent. J. G. Moffatt and H. G. Khorana, J. Am. Chem. Soc., 79, 3741 (1957).

30. Cyclic Phosphates. II. Further Studies of Ribonucleoside 2':3'-Cyclic Phosphates. G. M. Tener and H. G. Khorana, J. Am. Chem. Soc., 77, 5349 (1955).

31. Cyclic Phosphates. III. Some General Observations on the Formation and Properties of Five-, Six- and Seven-membered Cyclic Phosphate Esters. H. G. Khorana, G. M. Tener, R. S. Wright and J. G. Moffatt, J. Am. Chem. Soc., 79, 430 (1957).

32. A Synthesis of β-D-Ribofuranose-1-Phosphate. R. S. Wright and H. G. Khorana, J. Am. Chem. Soc., 77, 3423 (1955).

33. Phosphorylated Sugars. I. A Synthesis of β-D-Ribofuranose 1-Phosphate. R. S. Wright and H. G. Khorana, J. Am. Chem. Soc., 78, 811 (1956).

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39. Phosphorylated Sugars. V. Syntheses of Arabinofuranose and Arabinopyranose 1-Phosphates. R.S. Wright and H.G. Khorana, J. Am. Chem. Soc., 80, 1994 (1958).

40. Pyrophosphorylation of Ribose 5-Phosphate in the Enzymatic Synthesis of 5-Phosphorylribose 1-Pyrophosphate. H.G. Khorana, J. Fernandes and A. Kornberg, J. Biol. Chem., 230, 941 (1958).

41. Observations on the Use of Dicyclohexylcarbodiimide in the Synthesis of Peptides. H.G. Khorana, Chem. and Ind. London, 1955, pp. 1087-1088.

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43. Phosphorylated Sugars. VI. Syntheses of α-D-Ribofuranose 1,5-Diphosphate and α-D-Ribofuranose 1-Pyrophosphate 5-Phosphate. G.M. Tener and H.G. Khorana, J. Am. Chem. Soc., 80, 1999 (1958).

44. Synthesis of 9-(α-D-Ribofuranosyl) Adenine. R.S. Wright, G.M. Tener and H.G. Khorana, Chem. and Ind. London, 1957, p. 954.

45. The Synthesis of 9-α-D-Ribofuranosyladenine. R.S. Wright, G.M. Tener and H.G. Khorana, J. Am. Chem. Soc., 80, 2004 (1958).

46. A New Approach to the Synthesis of Polynucleotides. H.G. Khorana, G.M. Tener, J.G. Moffatt and E.H. Pol, Chem. and Ind. London, 1956, p. 1523.

47. Syntheses of Dideoxyribonucleotides. H.G. Khorana, W.E. Razzell, P.T. Gilham, G.M. Tener and E.H. Pol, J. Am. Chem. Soc., 79, 1002 (1957).

48. Purification and Properties of a Pyrimidine Deoxyriboside Phosphorylase from Escherichia coli. W.E. Razzell and H.G. Khorana, Biochim. et Biophys. Acta., 28, 562 (1958).

49. Carbodiimides. VIII. Observations on the Reactions of Carbodiimides with Acids and Some New Applications in the Synthesis of Phosphoric Acid Esters. M. Smith, J.G. Moffatt and H.G. Khorana, J. Am. Chem. Soc., 80, 6204 (1958).

50. The Stepwise Degradation of Thymidine Oligonucleotides by Snake Venom and Spleen Phosphodiesterases. W.E. Razzell and H.G. Khorana, J. Am. Chem. Soc., 80, 1770 (1958).

51. Chemical Synthesis of Oligo-thymidine Nucleotides and Their Degradation by Venom Phosphodiesterase. H.G. Khorana, G.M. Tener, W.E. Razzell and R. Markham, Federation Proc., 17, 253 (1958).

52. Studies on Polynucleotides. . I. A New and General Method for the Chemical Synthesis of the $C_5'-C_3'$ Internucleotidic Linkage. Syntheses of Deoxyribo-dinucleotides. P.T. Gilham and H.G. Khorana, J. Am. Chem. Soc., 80, 6212 (1958).

53. Studies on Polynucleotides. II. The Synthesis and Characterization of Linear and Cyclic Thymidine Oligonucleotides. G.M. Tener, H.G. Khorana, R. Markham and E.H. Pol. J. Am. Chem. Soc., 80, 6223 (1958).

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55. The Mode of Action of Ryegrass Ribonuclease. Louis Shuster, H.G. Khorana and Leon A. Heppel, Biochim. et Biophys. Acta., 33, 452 (1959).

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58. Nucleoside Polyphosphates. IX. The Reversible Formation of Pyrophosphates from Monoesters of Phosphoric Acid by Reaction with Acetic Anhydride. H.G. Khorana and J.P. Vizsolyi, J. Am. Chem. Soc., 81, 4660 (1959).

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HAR GOBIND KHORANA

Born January 9, 1922, in Raipur, India. B. Sc. Hons. Punjab University 1943; M. Sc. 1945; Ph. D. University of Liverpool 1948. Post-doctoral Fellow, Univ. of Zurich 1948-49; Cambridge University, 1950-52. Head, Organic Chemistry group, British Columbia Research Council 1952-60; Visiting Professor, Rockefeller Institute, 1958- . Professor of Biochemistry and Co-director, Institute for Enzyme Research, Univ. of Wisconsin 1960- . Conrad A. Elvehjem Professor in the Life Sciences, University of Wisconsin, 1964- . Merck Award, Chem. Inst. of Canada, 1958; Gold Medal for 1960, Professorial Inst. of Public Service of Canada.

Gobind Khorana's research career began with the synthesis of several bacterial pigments in the Laboratory of A. Robertson, FRS, at Liverpool and continued with studies of Erythrina alkaloids in collaboration with Prelog. At Cambridge he undertook independent work on methods for determining the sequence of amino acids in peptides and here developed the classic synthetic method involving carbodiimides.

In Vancouver and Madison, Dr. Khorana devised improved reagents for synthesizing biologically important phosphate compounds—nucleoside mono, di and triphosphates, dinucleotides, nucleotide diphospho sugars, Coenzyme A, nucleoside cyclic phosphates, and both ribo- and deoxyribo-polynucleotides of known sequence linked through the 3' and 5' positions. His studies of the phosphodiesterase of snake venom demonstrated that this enzyme attacks the 3' ends of the nucleic acid chain and degrades the molecule sequentially thus providing a useful tool for studying the structure of nucleic acids. His most recent work is a brilliant attack on the detailed mechanism of

He has accomplished the chemical synthesis of all 64 possible TRINUCLEOTIDES, and has combined many of these into longer OLIGONUCLEOTIDES genetic replication, transcription and translation. Using these synthetic deoxyoligonucleotides of known sequences as templates for both RNA and DNA syntheses, he has found by the nearest-neighbor technique that the DNA or RNA polymerases faithfully transcribe the sequence, read successive units of the synthetic deoxyoligonucleotides in register, and produce high molecular weight DNA or RNA respectively. The synthesized RNA was then used as a messenger in a protein-synthesizing system of E. coli and specific polypeptide synthesis occurred. These experiments have confirmed that the genetic code is based on a consecutively read, non-overlapping triplet of nucleotide bases, all three of which contribute information, and have established the sequence of bases within the codons for 11 different amino acids. By more simple techniques, employed also in other laboratories, Khorana has ascertained CODONS for all 20 naturally occurring amino acids.

He is the author or coauthor of ~~some 150~~ 147 research publications, all of which are distinguished by their imaginative approach to difficult problems, precision of experimental execution, and clarity of exposition. His work marks him as one of the outstanding biochemists of our day.

C7

Dr.

A selected list of his scientific publications follows:

C/ Three scientists well acquainted with Dr. Khorana's work are:

REQUIREMENTS FOR EACH NEW NOMINATION:

1. A biography of the candidate ("A" attached)
2. A statement of his achievements ("B" attached)
   including the names of three scientists or engineers who are well acquainted with his work:

Dr. Arthur Kornberg
Chairman, Department of Biochemistry
Stanford University
Palo Alto, California

[redacted]

Dr. Francis Crick
Cambridge University
Cambridge, England

Dr. Henry Lardy
Enzyme Institute
University of Wisconsin
Madison, Wis.

3. A list of his contributions to the literature of science and engineering:
   Selected list ("C" attached)
   Latest complete list ("D" attached)

SELECTED SCIENTIFIC PUBLICATIONS BY H. G. KHORANA

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Synthetic deoxyribo-oligonucleotides as templates for the DNA polymerase of *Escherichia coli*. New DNA-like polymers containing repeating nucleotide sequences. (With C. Byrd, E. Ohtsuka, and M. W. Moon.) *Proc. Natl. Acad. Sci. U.S.*, 53, 79 (1965).

Dr. K Khorana has published a considerable number of papers in addition to the 98 listed here, but this gives a good cross section of his work. At the moment he is about to release one of the most significant findings of his career on the synthesis of polynucleotides. This will be the subject of his talk at the National Academy of Sciences meeting, Play Circle of the Union, 10 a.m. Tues. Oct. 13.

HAR GOBIND KHORANA, B.Sc., M.Sc., Ph.D.

Curriculum Vitae

Born: January 9, 1922 **Place of Birth: Raipur, India**

1943	B.Sc. Hons., 1st Class Punjab University, India
1945	M.Sc. Hons., 1st Class Punjab University, India
1946-48	Ph.D. University of Liverpool, England Government of India Studentship Working under Professor A. Robertson, F.R.S.
1948-49	Federal Institute of Technology, Zurich, Switzerland Post-doctoral Fellow of Government of India Working with Professor V. Prelog
1950-52	University of Cambridge, England Nuffield Fellow Working with Professor Sir ~~Alexander~~ Todd, F.R.S.
1952-	B.C. Research Council, Head, Organic Chemistry group
1958	Received the Merck Award from the Chemical Institute of Canada for outstanding contributions to the fields of Organic Chemistry and Biochemistry in Canada
1958- on	**Visiting Professor, Rockefeller Institute, New York.**
1959	**Fellow of the Chemical Institute of Canada.**
1960	**Gold Medal for 1960, Professional Institute of the Public Service of Canada.**
From [illegible] 1, 1960 on -	**Professor and Group Leader, Institute for Enzyme Research, University of Wisconsin, Madison, Wisconsin.**