FRANK W. PUTNAM

1917-2006

A Biographical Memoir by

KENNETH E. NEET

Any opinions expressed in this memoir are those of the author and do not necessarily reflect the views of the National Academy of Sciences.

NATIONAL ACADEMY OF SCIENCES

FRANK W. PUTNAM

August 3, 1917—November 29, 2006

BY KENNETH E. NEET

The term "Greatest Generation" was coined by journalist Tom Brokaw to describe the cohort of people who were born before the Great Depression, took the United States through World War II, and led the country into the subsequent rebuilding/growth years. Similar traits apply to the biomedical scientists of those times. This "Greatest Scientific Generation" was characterized by a youth spent in the Depression, an education initiated before the war, a career interrupted by (or maintained during) the war, and research accomplishments in the subsequent Cold War era largely supported by the burgeoning National Institutes of Health (NIH). Riding the subsequent wave of technology and information, this scientific

generation led the molecular biology and molecular medicine revolutions that produced the complete sequencing of the human genome and is likely to culminate in truly personalized medicine during the 21st century.

Frank W. Putnam was a member in good standing of the Greatest Scientific Generation. He obtained his Ph.D. in 1942 and worked on plasma substitutes, botulinum toxin, and serological assays for syphilis during and after the war. He was able to move from his original interest in the biophysical characterization of proteins, when even the general structure of proteins was still open to debate, to cutting-edge (for the day) protein sequencing. In his later years, he kept pace with technology, all the way to DNA sequencing, to study mutations in serum proteins. Putnam was a significant contributor, throughout his distinguished career, during an explosive time for science. One of Putnam's memoirs is titled "Growing up in the Golden Age of Protein Chemistry," indicating that he himself was aware of the significant biochemical advances during these decades.[1] In another memoir,[2] he cites the "Golden Age of Biochemistry" and the "Flowering of Immunology," referring to the timeframe of his career. Reading his own recollections,[1,2,3] one is struck by the other giants of the era that were part of his network. The names that Putnam recalled in his reflections, including Nobel laureates and other illustrious scientists, read like a Who's Who of Biochemistry and Molecular Biology (Table 1).

Putnam remarked[1] that he was fortunate to have participated in three intellectually stimulating collaborations: the Phage Group [1947–52], the Cambridge Protein Group at the time of the double-helix discovery [1952–53], and the Chain Gang (Piece Corps) [1965–1973]. The latter group was in the race to sequence the immunoglobulin proteins and fragments that brought Putnam his greatest recognition. He clearly belonged among these scientific giants and contributed as much to the discussions and advances as he obtained from them. The Golden Age - Indeed! The Greatest Scientific Generation - Indeed!

EARLY LIFE AND FAMILY

Frank was born August 3, 1917, in New Britain, Connecticut, to Franz and Henrietta (née Holzmann) Poglitsch, who had emigrated from Austria around 1913–14. In America, Franz was a grinder (sharpener of knives and scissors) and Henrietta worked as a maid-servant for a prosperous family. Both of Frank's parents contracted tuberculosis, the scourge disease of the early 20th century. Shortly before their deaths, they placed Frank, at the age of 3, in the New Britain Children's Home, and he was raised in this orphanage until his teenage years.

Table 1. **Associates of Frank W. Putnam during his early years (1947–1960)**[1,2,3]	
Education and training	
Albert Lehninger (classmate at Wesleyan)	Charles A. Hoover (advisor at Wesleyan)
John Edsall (at a meeting)	E. J. Cohn (at a meeting)
George Schwert (fellow student at Minn)	David Briggs (advisor at Minnesota)
Ross A. Gortner, Sr. (advisor at Minnesota)	Hans Neurath (advisor at Duke)
Phil Handler (colleague at Duke)	Elliot Volkin (colleague at Duke)
Joe Beard (collaborator at Duke)	Erwin Brand (at a meeting)
University of Chicago	
Earl Evans (department chair during Putnam's first faculty position)	
Al Lehninger	Konrad Bloch
Paul Talalay	Elwood Jensen
Leo Szilard, (Biophysical Institute)	Charlie Huggins (Bence-Jones proteins source)
James Franck, (Biophysical Institute)	Enrico Fermi, (Biophysical Institute)
Daniel Koshland, chemist	Frank Westheimer, chemist
Stanley Miller, chemist	Harold Urey, chemist
Morris Friedkin, graduate student	Eugene Kennedy, graduate student
Irwin Rose, graduate student	Charles Gilvarg, graduate student
Lloyd Kozloff, graduate student	Eric Conn, graduate student
Eugene Goldwasser, graduate student	Arthur Koch, graduate student
Colleagues met at meetings	
Otto Warburg	Robert Emerson
Hans Gaffron	

Phage Group (at a meeting at Vanderbilt 1950)*	
*As a neophyte, Putnam was asked by Delbruck to summarize the phage meeting	
Max Delbruck	Salvador Luria
Renato Dulbecco	Seymour Cohen
Al Hershey	Tom Anderson
Mark Adams	Gus Doerrman
Cambridge, England	
Aaron Novick	Sir James Watson
Herman Kalckar	H.J. Muller
A.C. Chibnall	Sir Fred Sanger (protein sequencing)
Sir Alexander Todd	Kenneth Bailey
Frank Young	Gobind Khorana
Sam Perry	Dick Synge
Max Perutz	George Trevelyan
Sir Francis Crick	Sir John Kendrew
Gordon Conference 1955, chaired by Putnam	
Rodney R. Porter	Fred Sanger
James Watson	Sir Francis Crick
Chris Anfinsen	Hargobind Khorana
Klaus Hofman	C. H. Li
George Gamov	
The Chain Gang in the immunoglobulin sequencing race ~1960–1972	
Rodney R. Porter	Gerald M. Edelman
Georges Kohler	Cesar Milstein
Norbert Hilschmann	

While at the Children's Home, Frank was befriended by a local bank president, L. Marsden Hubbard. Frank had been an excellent student in high school, winning numerous prizes in the spelling, math, history, and economics contests that were then common. Given the boy's abilities, the banker took an interest in Frank and provided a long-term father figure for him.

New Britain, a working-class town seven miles from Hartford, was largely populated by Polish and German immigrants. It was then known as Hardware City because of its manufacturing; New Britain was headquarters for what is now Stanley Black & Decker. A small town at the time, New Britain had two only orphanages, the aforementioned Children's Home, affiliated with the Elm Baptist Church, and the Catholic-run Our Lady of Rose Hill Orphanage. Such institutions were fairly common during the early 20th century, in lieu of home adoptions. Frank's first job at age 16 was as an office boy, running errands for the mailroom of Stanley Tool Works.

His challenging early life in an orphanage without an immediate family may have helped shape many of the personal characteristics that Frank developed by adulthood. While at the Children's Home, Frank was befriended by a local bank president, L. Marsden Hubbard. Frank had been an excellent student in high school, winning numerous prizes in the spelling, math, history, and economics contests that were then common. Given the boy's abilities, the banker took an interest in Frank and provided a long-term father figure for him. Hubbard, who came from a prominent Connecticut family active in legal and political affairs, advised Frank to change his surname from Poglitsch to Putnam at the time he went to college.

He attended Wesleyan University, in Middleton, Connecticut, and received a B.A. in chemistry summa cum laude in 1939 and his M.A. in chemistry in 1940. Wesleyan at the time was a small men's liberal-arts college. Putnam, who was the college bell ringer and chapel sexton, supported himself on scholarships and by winning academic prizes in a variety of disciplines. He would enter academic contests, regardless of the subject, that had cash prizes. He was fond of saying that he went to college with $50 and left with $50, plus a gold watch that he had won in an economics contest (although he had never taken a course in the subject). His secret to winning these kinds of contests was to read the classic textbook the night before.

From Wesleyan, Putnam moved to the University of Minnesota, where he worked with David Briggs and Ross A. Gartner and obtained his Ph.D. in 1942. An admirer of the Swedish biochemist Arne Tiselius and the eponymous apparatus that Tiselius had developed to allow electrophoresis of free proteins in solution, Putnam's thesis also dealt with protein electrophoresis. He subsequently took a research associate (postdoctoral) position in the Department of Biochemistry at Duke University with Hans Neurath, another renowned protein chemist, to study the biophysical properties of serum albumin. The goal was to reduce its antigenicity so that it might serve as a possible plasma substitute for the war effort. Putnam was one of the first to study the effects of the detergent SDS on protein—in this case,

albumin—structure. He was then recruited into a project to determine the antigenic basis of the false-positive reactions in serological tests for syphilis. Here, Frank was fascinated by the bizarre electrophoretic patterns of hyperglobulinemic sera that often produced false positive in syphilis tests.

These projects stimulated Putnam's interests in immunochemistry and in albumin, myeloma globulins, and the other plasma proteins—interests that would stay with him for some 50 years. Putnam had a brief detour to Camp (now Fort) Detrick, Maryland, where he served as a civilian with the U.S. Chemical Warfare Service to study the botulinum toxin, a potent poison and putative warfare agent. In 1947 he moved to the University of Chicago for his first full-time faculty appointment as assistant professor; he was also a Markle Scholar in Medical Sciences there from 1950 to '55. Putnam's task under chair Earl Evans was to study the physicochemical properties of bacteriophages. This introduction led to his involvement with the Phage Group and isotopic studies of phage metabolism. Under his Markle Scholarship and an appointment as Lasdon Research Fellow, Putnam spent 1952–53 working in Fred Sanger's laboratory at the University of Cambridge, England at a time when insulin had just been the first protein to be sequenced. Putnam brought his Bence-Jones Proteins (BJPs) there and learned how to manually sequence proteins, a technology he would adopt and further develop for the next 25 to 30 years (see SCIENCE section below). The first indication of variable sequences in BJPs came from his N-terminal analyses in Cambridge. Putnam's first NIH grant, to study myeloma proteins and BJPs, came after he returned to the University of Chicago.

While still in Minnesota, Frank met Dorothy Linder (who worked at a local radio station) on a blind date. They were married in 1942 in the campus chapel of Duke University, where Frank was a postdoctoral fellow. Later, when they were in Gainesville—in the late 1950s and early '60s, at the height of the civil-rights movement and when Florida was still segregated—Dorothy was a quiet civil-rights advocate. Frank and Dorothy thoroughly enjoyed music, including opera and madrigals. They were regulars at the University Opera in Bloomington, Indiana, and they listened at home to a large collection of opera recordings and to the Metropolian Opera broadcasts on Sunday afternoons.

Frank and Dorothy had a mutually adoring marriage for 55 years, until her death in 1997. They had two children: Frank W. Putnam, Jr., M.D., (born 1947 in Minneapolis) and Beverly (Putnam) Gordon, MHA (born 1950 in Chicago). Frank, Jr., followed a path parallel to that of his father by becoming a physician and enjoying a successful research and clinical career in pediatric psychiatry. Beverly was a lieutenant in the Navy, a consultant for a health care trust, and chief organizer of the Schadt String Competition in Allentown,

Pennsylvania. Frank, Sr., and Dorothy Putnam also had five grandchildren: Jason, Abby, and Ted Gordon and Philip and Will Putnam.

ADMINISTRATIVE LEADERSHIP

In 1955, Putnam was recruited to the University of Florida College of Medicine (Gainesville) by its dean, George T. Harrell. At the relatively young age of 38, Putnam thus became the founding chair of the Department of Biochemistry of a fledgling medical school, the first medical school in the state of Florida. He demonstrated his own recruiting ability by hiring a cadre of bright young faculty, including James A. Olson, Arthur L. Koch, Melvin Fried, and Walter B. Dempsey. The University of Florida College of Medicine has since become a leading institution in medical education and research— no doubt due in part to the excellent start it got with leaders like Putnam. During his tenure, the immunoglobulin-sequencing race heated up (see SCIENCE section below). Putnam ably maintained his academic leadership while running an active and competitive laboratory.

After 10 years in Florida, Putnam moved to Indiana University (IU) in Bloomington, where he quickly set up his laboratory to continue sequencing BJPs and assumed a new set of administrative duties. In 1965 he was appointed professor of biology and named director of IU's newly formed Division of Biological Sciences. Directing the Division from 1965 to 1969, he organized it into subdivisions so that it could develop into an integrated Department of Biology. The department's program in molecular biology, for example, was one of the first in the country in this "new" discipline.

Putnam was a professor of molecular biology and zoology from 1969 to 1974 and a professor of biochemistry in the IU School of Medicine beginning in 1971. In 1974, he was appointed Distinguished Professor of Molecular Biology and Biochemistry, in recognition of his scientific accomplishments, administrative service, and teaching at IU. All this time, Putnam had maintained his active research program but had shifted from an emphasis on BJP sequences to structure determinations of other plasma proteins. In 1988, he retired from an active position at IU but continued serving on certain boards, including the Board of Governors of the Argonne National Laboratory. In his later retirement years, the Putnams moved to Maple Knoll Village in Cincinnati to be near their son's family. Even in retirement, Frank remained active—e.g., he was the editor of the *The Villager*, a newsletter for the community, and he also was a frequent contributor of reflective and entertaining articles.

His viewpoint was very controversial at the time and he once remarked that his move to the chairmanship at Florida in 1955 allowed him to work on what he wanted without criticism—as long as he ran the department successfully.

SCIENCE

At an early stage, Putnam had the foresight to realize the importance of BJPs—small (22,000 dalton) proteins found in the blood and urine of multiple myeloma patients. In the current era, which encourages the utilization of patient materials in research, it is not unusual to investigate a unique protein that would be easily isolatable from a patient's urine. But in the 1950s it was an intellectual leap to assume that BJPs had potential value, much less to base an entire research program on such an assumption. Putnam found the needed model for antibody analogs: the homogeneous serum myeloma globulins and urinary BJPs that are related to antibodies in structure and biosynthesis but that lack antibody specificity. His viewpoint was very controversial at the time and he once remarked that his move to the chairmanship at Florida in 1955 allowed him to work on what he wanted without criticism—as long as he ran the department successfully. In support of his hypothesis, Putnam obtained BJPs and myeloma proteins from many clinician colleagues and stockpiled significant amounts of these promising proteins under stable storage conditions. In many cases, gram amounts of the purified BJP could be obtained, which came to be highly important when the protein sequencing methods of the 1960s (which were crude compared to current nano methods) were applied to them.

An early key experiment from Putnam's laboratory showed that a heavy isotope 13C-labeled glycine was excreted in the BJP in the urine of the patient within 15 minutes of intravenous injection. This experiment was subsequently repeated with 15N-labeled glycine and 14C-labeled glutamate. These experiments validated the idea that BJPs were metabolically active and not simply an inert degradation product.[4] Putnam later said that this was the"most exciting experiment of my life"[1] and "the most important experiment of my life."[3]

The sequencing and primary-structure determination of BJPs, myeloma globulins, and immunoglobulins became of great value in the understanding of antibody function. With research associates Shunsuke Migita, Rudy Ballieux, and George Bernier, Putnam established a classification of light and heavy chains of immunoglobulins using physicochemical, serological, and N-terminal analysis. It soon became apparent from N-terminal and C-terminal sequencing that the BJPs varied with different individuals and fell into two broad classes, now known as kappa and lambda. However, it would take 10 more years of dogged work before the comparison of complete protein sequences could be done.

The Chain Gang, consisting of the laboratories of Putnam, Edelman, Hilschmann, Porter, and others, was a "collegial yet intensely competitive group"[3] that met informally and frequently to compare results. At the Antibody Workshop in early 1965, Putnam and

his postdoctoral fellow Koiti Titani presented evidence for variable sequences in kappa BJPs, and Hilschmann followed with a similar presentation of findings. The latter flashed results without time for examination and, indeed, had only shown composition of amino acids within peptides arranged alphabetically, indicating that complete sequencing had not yet been done. Both labs rushed to publish, with Hilschmann's paper appearing in July in the *Proceedings of the National Academy of Sciences*[5] and Putnam's appearing in August in *Science.*[6]

Finally, Putnam's original proposal that BJPs and myeloma proteins were a true representation of immunologically active antibodies was fully accepted. In his words, "the great sequence race to determine immunoglobulin structure and the origin of antibody variability and specificity was on."[1] Complete sequences with disulfide bond placement appeared in the *Journal of Biological Chemistry* both for kappa BJP in 1969[7] and lambda BJP in 1970,[8] reflecting results from Putnam's laboratory. These papers were chosen as *Journal of Biological Chemistry* classic papers (2007) for the *Journal's* centennial. This work established the variable and constant amino-acid regions of immunoglobulins/antibodies and provided the basis for understanding the wide specificity of antibodies that has since been confirmed many times over with modern DNA rapid-sequencing techniques. As noted above, Putnam reminisced on these events in several of his published reflections.[1,2,3]

In the subsequent decade, Putnam carried this work to its logical conclusion by sequencing IgM myeloma proteins—the largest of the antibody classes of proteins, complete with carbohydrate sites and disulfide linkages. IgA1 and IgA2 followed, and finally, in 1983, the primary structure of the "last" of the immunoglobulin classes, IgD, was determined in Putnam's laboratory.[9]

In those days, protein sequencing involved proteolytic or chemical cleavage of the protein, separation of the resultant peptides on gels, paper, or columns, and determination of sequence of short peptides. Edman degradation or exopeptidase digestion was used to remove an amino acid from the N- or C-terminus. Determination of amino-acid composition of the resultant, shortened, purified peptide at each step was required to determine sequence. As a result, Putnam's laboratory would have three or more amino-acid analyzers (*not* modern sequencers) running nearly continuously, as well as multitudes of columns and other apparatus for protein and peptide separation/purification. This was a very labor-intensive operation. A key contributor to these initial studies on BJP sequences was Koiti Titani, a postdoctoral fellow newly arrived from Japan, who led the sequencing effort. An effective pipeline of Japanese collaborators/postdocs to Gainesville and Bloomington was then established that came to include Nobuhiro Takahashi, Tomotaka Shinoda,

Yasuharu Tsuzukida, Kunio Arai, and Akira Shimizu. Putnam also maintained his interest in biophysical properties of proteins by studying the unusual aggregation and solubility properties of the BJPs by means of analytical ultracentrifugation at elevated temperatures, approaching 100°C.[10]

The 1972 Nobel Prize in Physiology or Medicine was awarded to Porter and Edelman for their "discoveries concerning the chemical structure of antibodies." Many colleagues and observers felt that Putnam should have shared in the prize, given his early insights, ideas, sequencing, and other experimental contributions to solving the "antibody problem." Indeed, Porter himself sent Putnam a message at the time of the award: "You must have been more closely concerned with the chemical work on Bence-Jones and antibodies for longer than anyone else. … You could very well have been with us in Stockholm. I am sorry you are not."[11] According to his son, Putnam was a little bit down for a few days about not having received this ultimate prize, but within a week he was back to his usual quietly optimistic self. He considered taking a more administrative position at this time, but after consideration he decided to remain an active research scientist. Indeed, the more complex and difficult immunoglobulin sequences—IgM, IgA, and IgD—were determined by Putnam's lab within the decade following the Nobel award to Porter and Edelman.

After the sequencing race and his completion of the primary structure of the other major immunoglobulins, Putnam did not rest on his laurels but pursued his longstanding interest in the other plasma proteins. His laboratory sequenced human serum albumin, ceruloplasmin, factor XIIIa, hemopexin, and alpha 1B-glycoprotein. Having also become interested in polymorphisms of human albumin, he sequenced variants obtained from individuals from many different countries—including Brazil, Japan, Italy, Ireland, Sweden, and New Zealand—as well as from Amerindians (native Americans). More than 30 alloalbumins (polymorphisms) were sequenced in Putnam's laboratory, either at the amino acid or DNA level, or both, to document the type of mutation, frequency of occurrence, and population distribution. These samples included point mutations, chain-termination mutants, proalbumins that were not properly processed at the N-terminus, and the rare analbuminea with a virtual absence of albumin. The nonrandom distribution, together with the clustering of point substitutions in the protein structure, reflected hypermutability of the albumin gene or ease of accommodation to structural changes. The ethnic and geographic distribution of these alloalbumins indicated that each of the mutations occurred independently, several times in different populations. Putnam's laboratory also described human serum albumin mutations that

demonstrated incomplete glycosylation and new disulfide bridges. Of his more than 250 total publications, about 55 (with more than 25 on serum albumin) came after the last immunoglobulin was sequenced in 1982.

OTHER CONTRIBUTIONS AND SERVICE

The Plasma Proteins. In the late 1950s, Putnam realized that there was a dearth of collected information on the plasma proteins. At that time, there was no shortage of writings on proteins in general. They included: a series of volumes called "The Proteins," edited by Hans Neurath (one of Putnam's early mentors); another series, "The Enzymes," edited by Paul D. Boyer; a series of monographs, "Advances in Protein Chemistry," edited by John T. Edsall, Christian B. Anfinsen, and others; and a book on "Enzymes" by Malcolm Dixon and Edwin C. Webb. But Putnam recognized the need for a collection of expert-written chapters on plasma albumin, immunoglobulins, and other plasma proteins (such as the less well-known haptoglobins), which were being ignored in the more general protein publications. Thus in 1960 an initial edition of two volumes of *The Plasma Proteins* (18 chapters in all) was published, with Volume 1 focused on "Isolation, Characterization, and Function" and Volume 2 addressing "Biosynthesis, Metabolism, and Alterations in Disease."

The preface to the first edition included the following: "The purpose of this treatise is to present an authoritative, interpretative, and integrative account of the plasma proteins, both for the individual purified components and as a dynamic system. … In order to achieve the comprehensive scope of a treatise without unnecessary length or duplication, the work was organized on an interdependent basis by exchange of outlines and through cross-reference. … Each author submitted a chapter outline for circulation to all contributors."

In 1975, a second edition of the first two volumes came out, later followed by three more volumes on other aspects of "Structure, Function, and Genetic Control." The finale of this five-volume set was published in 1987, the year before Putnam formally retired from Indiana University.

The preface to the second edition included the following: "The purpose of this treatise is to describe the plasma proteins in a systematic integrated fashion. The intention is to present first the perspectives and a global look at plasma proteins, then a series of chapters on the well-characterized major proteins, followed by comprehensive chapters on integrated systems of plasma proteins. The emphasis is on structure, function, and genetic control rather than on metabolism and biosynthesis."

This unique series marked a significant contribution to the protein literature. The books allowed Putnam himself to write an extensive history of the sequencing of myeloma proteins (and of Bence-Jones proteins in particular) and to emphasize the importance of the other plasma proteins. He also, through his worldwide stature and connections, managed to convince other leading investigators to contribute chapters and to help edit the result so that the resulting compendium was consistent, integrated, and intelligible. The series filled a void for many years after publication and is still relevant today. It provides a historical perspective as well.

Travels for the Atoms for Peace Program. In the spring of 1956, the U.S. State Department invited Putnam to make a scientific tour of South America under the auspices of the Atoms for Peace program that President Eisenhower had started. Putnam's work at the University of Chicago and Argonne Cancer Research Hospital on the administration of radioactive and heavy-isotope-labeled amino acids to patients, together with his phage work, led to this invitation. He was able to travel at that time because in 1956 he was the first chair of biochemistry of a new medical school in Florida that was still under construction, and hence no laboratories were open. Thus in April and May, Putnam spent six weeks in South America giving at least three talks (some of them in Spanish) in each of the countries visited—including Venezuela, Peru, Chile, Argentina, Uruguay, and Brazil. He made contacts with scientists there but also saw political and social unrest. Remarkably, good science was being produced in this area in spite of these conditions, with some research projects enjoying government support and others being privately financed. Some of Putnam's South American contacts—such as Cesar Milstein—carried over into his later immunoglobulin studies.

Putnam's description of his flight over the Andes in a DC-6 propeller plane and of being escorted through customs on a diplomatic passport by his State Department attaché are enlightening as to the respect with which scientists were viewed and treated by the U.S. government at that time. Putnam called this trip the most exciting and memorable of his life, even though he was already an experienced world traveler—to areas that included Europe, Russia, and Japan, among others.

The ABCC and RERF. Some of Putnam's early studies involved administration of stable isotopes (15N) or radioactive isotopes (14C) to patients in order to study metabolic processes, with a focus on myeloma patients and plasma proteins.[4] Shortly after World War II there was great interest in using isotopes, which were widely available. These conditions applied in particular at the University of Chicago and its associated Argonne National Laboratories. While Putnam's isotopic work

provided useful results, especially with respect to rapidity of turnover of BJPs and myeloma proteins, these studies also prepared him for a later relationship with the U.S. government in exploring the biological consequences of radiation exposure as an aftermath of the atomic-bomb attacks on Japan.

The Atomic Bomb Casualty Commission (ABCC) was conceived by the Japanese and American governments shortly after World War II. The ABCC (which functioned from 1947 to 1975) was succeeded by the Radiation Effects Research Foundation (RERF) in 1975. Putnam was chairman (1977–1981) of the Assembly of Life Sciences—the section of the National Academy of Sciences (NAS) to which RERF reported and through which it was funded; and he was on the RERF board of directors from 1982 to 1987. In these capacities, he made 10 separate trips to Hiroshima and Nagasaki. This was one of Putnam's lesser-known services but perhaps an even bigger contribution to mankind than his other activities. For over 50 years, medical and scientific studies were done with the survivors of the atomic bombing of Hiroshima and Nagasaki and their offspring.

This dual-government commission/foundation sponsored the longest-running epidemiological and genetic investigation of its kind, providing much of what is currently known about high-level radiation exposure in humans and constituting the basis for current radiation-related health standards. The ABCC/RERF venture was jointly supported by the American and Japanese governments and run, on the U.S. side, by the NAS via its operating arm, the National Research Council. Putnam authored a report in 1994 on the long-running study and an article on it in the *Proceedings of the NAS* in 1998.[12] A collection of Putnam's papers, consisting mostly of RERF-related materials from his period of service, are housed at the John P. McGovern Historical Collections and Research Center in Houston, Texas.[13]

THE PERSON

Frank Putnam was an excellent teacher who explained concepts to his students in a clear and comprehensible manner. In individual scientific conversations, he was precise and logical in his facts. For lectures, he would always be dressed in a clean and starched white lab coat. His manner came across as "reserved" at times, but he was always gracious and polite, had a wry sense of humor both personally and in his writings, and was almost always in a "teaching mode." I recall once sitting down for breakfast with Frank in the small coffee shop at the J. Hillis Miller Health Science Center in Gainesville, Florida, and sprinkling a little salt into my tomato juice. He immediately told this young first-year graduate student about

the deleterious effects of NaCl (high blood pressure in particular) in a most friendly, sincere, and informative manner—not at all condescending or preachy.

Frank was always there to help his students and postdocs and subsequently followed their careers. After I completed my M.S. degree, he personally helped me get into the Medical Service Corps of the U.S. Navy and fulfill my military obligation in a research laboratory in Bethesda. After I got out of the service, he warmly accepted me back into the Ph.D. graduate program at the University of Florida and allowed me to work in his laboratory. Upon my graduation, he helped me obtain a good postdoctoral position with Daniel E. Koshland, Jr., through the "old boys network" that operated at that time. Koshland, as noted above, had been a colleague of his at the University of Chicago many years before. Frank treated all of his laboratory people with respect and fairness and, as a result, he was a role model for many of us to emulate in later years. When he visited me in the 1990s at the Chicago Medical School/University of Health Sciences (now Rosalind Franklin University of Medicine and Science), where I was department chair, he was clearly interested in how I was doing and commented with pleasure that my faculty respected me.

Not only was he a consummate scientist, Frank was also a dedicated family man—a loving husband, father, and grandfather. In 1962 he and Dorothy bought a "camp" on Meddybemps Lake in Maine that soon became a summer retreat for the whole family. The camp consisted of a small island (alternately known as Loon Island, Todd's Island, or, finally, Putnam's Island), with a cabin made of pecky cypress wood walls and a fireplace of Canadian granite. It had no phone lines or electricity until some years later, when these services finally became available in this rural location. Frank loved to water ski, bass fish, and bird watch (herons, egrets, raptors, loons) in the summers and taught these pleasures to his family. Their pact was that if the thermometer on the front porch of the cabin read 68° or higher at 8:00 am, then his children—Beverly and Frank, Jr.—had to get up and take Frank, Sr., water skiing. Frank water skied into his mid-70s.

He loved being a grandfather and had a strong influence on his grandchildren, even reading the dictionary with them to emphasize the importance of words. Frank was an avid amateur photographer who took numerous pictures in his travels and amassed a large collection of slides from his many trips abroad. Frank's son remembers being taught "laboratory technique" for pouring liquids and handling things when he was a child. His father would take him to his laboratory on Saturdays and set up a little chemistry station with

Fig. 1. Frank W. Putnam in his Jordan Hall office at Indiana University, ca. 1967, with a model of the immunoglobulin molecule constructed in his Bloomington living room.

suggested experiments. Together they built large models of proteins, often at home, using snap-together atoms that Frank, Sr., photographed and used in his lectures (See Fig. 1).

After Frank's death in 2006 the family found a small Post-It note on which Frank had written "Oh, how wonderful my life has been."

A wonderful life, indeed!

In writing this memoir I relied heavily on the very useful recollections and reflections that Frank Putnam himself had written (cited in text). I gladly thank Frank Putnam, Jr., and Beverly Putnam Gordon for their enthusiastic help in providing information, insights, and family papers about their father. I also obtained useful information from the Memorial Resolution given by Dr. Elizabeth Raff at Indiana University in 2007 and from a more recent conversation with her. I thank Kellie E. Neet and Herbert Tabor for reading a draft version of this memoir and providing helpful suggestions. Any errors or oversights, however, are the author's responsibility.

APPENDIX

Degrees

Wesleyan University, B.A. (Honors, high distinction in chemistry), 1939

Wesleyan University, M.A. (Chemistry), 1940

University of Minnesota, Ph.D. (Biochemistry), 1942

Cambridge University, M.A. (Honorary), 1973

Academic Appointments

Instructor and research associate, Department of Biochemistry, Duke University School of Medicine, 1942–46

Biochemist, U.S. Chemical Corps, Camp Detrick, 1946

Assistant professor, Department of Biochemistry, University of Chicago, 1947–53

Associate Professor, Department of Biochemistry, University of Chicago, and Argonne Cancer Research Hospital, 1953–55

Markle Scholar in Medical Sciences, University of Chicago, 1950–55

Markle Scholar in Medical Sciences, University of Florida, 1955–56

Professor and head of biochemistry, University of Florida, 1955–65

Professor of biology and director of the Division of Biological Sciences, Indiana University, 1965–69

Professor of biochemistry, Indiana University Medical School, 1971–1988

Professor of molecular biology and zoology, Indiana University, 1969–74

Distinguished Professor of Molecular Biology and Biochemistry, Indiana University, 1974–1988

Distinguished professor emeritus, 1988–2006

APPENDIX

Professional and scientific organizations

National Academy of Sciences (1976)

American Academy of Arts and Sciences (Midwest Council, 1975–81; 1983–85)

American Association for the Advancement of Science (fellow)

American Society of Biological Chemists (secretary, 1958–63)

American Association of Immunologists

American Chemical Society (chairman, Division of Biological Chemistry, 1966–67)

Pan–American Association of Biochemical Societies (secretary-general, 1975–77) Federation of American Societies for Experimental Biology (board member, 1961–64)

New York Academy of Sciences (fellow)

Editorial Boards

Archives of Biochemistry and Biophysics (1954–59)

Federation Proceedings (1958–63)

Immunochemistry (1972–75)

Science (1968–81)

Editor, *The Plasma Proteins*,
Vol. I, II, (1960); Second Ed., Vol. I, II (1975), Vol. III (1977),Vol. IV (1984), Vol. V (1987).

APPENDIX

Committees, Boards

Chairman, AAAS Gordon Conference on Proteins and Nucleic Acids, 1955

Chairman, Secretaries Committee, (Fed. Am. Soc. Exptl. Biol.), 1958–63

Chairman, Divisional Committee on Institutional Programs (National Science Foundation), 1964–66

Chairman, Advisory Committee for Institutional Relations (National Science Foundation), 1965–67

Consultant to National Science Board, 1967–69

Board of Visitors, Duke University Medical Center, 1970–75

Chairman, IUIS Committee, Nomenclature of Human Immunoglobulins, 1971–76

Chairman, Cancer Cause and Prevention Advisory Committee (National Cancer Institute, NIH), 1974–75

Chairman, Virus Cancer Program Advisory Committee (National Cancer Institute), 1975–77

Secretary-General, Pan-American Association of Biochemical Societies, 1975–77

Chairman, USA National Academy of Sciences Delegation to the Academy of Sciences of the German Democratic Republic (1978 and 1988)

Chairman, Assembly of Life Sciences (National Academy of Sciences/National Research Council, 1977–81

Board of Trustees, Argonne Universities Association, 1981–82

Board of Directors, Radiation Effects Research Foundation, Hiroshima, Japan, 1982–87

APPENDIX

Congress president, Symposium sur les Marqueurs de l'Inflammation, Lyon, France, 1981–83, 1983–85; Honorary president, 1985–87

Nominating Committee, American Academy of Arts and Sciences, 1985–87

University of Chicago Board of Governors, Argonne National Laboratory 1983–89

Chairman, Scientific and Technical Advisory Committee for Argonne National Laboratory, 1983–86; member, 1987–89

Honors and awards

Phi Beta Kappa, 1939

Shevlin Fellow, 1940–42

Rockefeller Fellow, 1941

Markle Scholar, 1950–56

Lasdon Research Fellow, 1952–53

Guggenheim Fellow, 1970

Overseas Fellow, Churchill College, 1972

American Academy of Arts and Sciences, 1974

National Academy of Sciences, 1976

Honorary Fellow of the National Academy of Clinical Biochemistry, 1983

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2. Putnam, F. W. 1995. Milestones in structural immunology. *FASEB J* 9:146–147.

3. Putnam, F. W. 1993. From antigen to antibody. *FASEB J* 7:383–384.

4. Putnam, F. W., and S. Hardy. 1955. Proteins in multiple myeloma. III. Origin of Bence-Jones protein. *J. Biol. Chem.* 212:361–369.

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9. Takahashi, Y., N. Takahashi, D. Tetaert, and F. W. Putnam. 1983. Complete covalent structure of a human immunoglobulin D: Sequence of the lambda light chain. *Proc. Natl. Acad. Sci. U. S. A.* 80:3686–3690.

10. Neet, K. E., and F. W. Putnam. 1966. Characterization of the thermal denaturation of Bence-Jones proteins by ultracentrifugation at elevated temperatures. *J. Biol. Chem.* 241:2320–2325.

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With D. S. Martin, J. O. Erickson, and H. Neurath. Native and regenerated bovine albumin: II. Immunological properties. *J. Gen. Physi*ol. 26:533–539.

1945

With H. Neurath, E. Volkin, J. O. Erickson, H. W. Craig, G. R. Cooper, D. G. Sharp, A. R. Taylor, and J. W. Beard. The serological diagnosis of syphilis. *Science* 101:68–69.

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1946

With H. Neurath. Chemical and enzymatic properties of crystalline carboxypeptidase. *J. Biol. Chem.* 166:603–619.

With C. Lamanna and D. G. Sharp. Molecular weight and homogeneity of crystalline botulinus A toxin. *J. Biol. Chem.* 165:735.

1948

With L. M. Kozloff. On the origin of virus phosphorus. *Science* 108:386–387.

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With L. M. Kozloff. Biochemical studies of virus reproduction; chemical composition of *Escherichia coli* bacteriophage T6 and its host. *J. Biol. Chem.* 181:207–220.

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With L. M. Kozloff, K. Knowlton, and E. A. Evans, Jr. Biochemical studies of virus reproduction. V. The origin of bacteriophage nitrogen. *J. Biol. Chem.* 188:101–116.

1952

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1955

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With S. Hardy. Proteins in multiple myeloma. IV. Interaction with metabolic nitrogen. *J. Biol. Chem.* 212:371–378.

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1958

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1972

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1973

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1976

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1977

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1978

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1979

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1980

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1981

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1982

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1983

With Y. Takahashi, N. Takahashi, and D. Tetaert. Complete covalent structure of a human immunoglobulin D: Sequence of the lambda light chain. *Proc. Natl. Acad. Sci. U. S. A.* 80:3686–3690.

From the first to the last of the immunoglobulins. Perspectives and prospects. *Clin. Physiol. Biochem.* 1:63–91.

1984

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1986

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1987

With N. Takahashi, Y. Takahashi, and B. S. Blumberg. Amino-acid substitutions in genetic variants of human serum albumin and in sequences inferred from molecular cloning. *Proc. Natl. Acad. Sci. U. S. A.* 84:4413–4417.

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With K. Huss, J. Madison, N. Ishioka, N. Takahashi, and K. Arai. The same substitution, glutamic acid---lysine at position 501, occurs in three alloalbumins of Asiatic origin: albumins Vancouver, Birmingham, and Adana. *Proc. Natl. Acad. Sci. U. S. A.* 85:6692–6696.

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Published since 1877, *Biographical Memoirs* are brief biographies of deceased National Academy of Sciences members, written by those who knew them or their work. These biographies provide personal and scholarly views of America's most distinguished researchers and a biographical history of U.S. science. *Biographical Memoirs* are freely available online at www.nasonline.org/memoirs.