Ralph T. Holman

1918–2012

BIOGRAPHICAL *Memoirs*

A Biographical Memoir by
Gary R. List
and Douglas M. Bibus

NATIONAL ACADEMY OF SCIENCES

RALPH THEODORE **HOLMAN**

March 4, 1918–August 15, 2012

Elected to the NAS, 1981

By Gary R. List
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Preface

Ralph Theodore Holman was inducted into the National Academy of Sciences in 1981. Holman was a truly unique individual blessed with a keen intellect, a love for God, his family, students, associates, and fellow man. He possessed a genuine sense of humor, the ability to laugh at himself and not take himself too seriously. He was a man of integrity, humility, and a quiet and gentle spirit. Moreover, his personal life reflected a lifelong devotion to Christianity. Holman took his marriage vows very seriously. He was married nearly 60 years to the only girl he ever dated, Karla Holman. When Karla became ill, her devoted husband cared for her as long as possible, but eventually she was placed in a nursing facility. Every day for three years, Holman spent afternoons at her bedside until she passed away. Holman's life story should be an inspiration to everyone as it is emblematic of the American dream. He was raised during the Depression era in a modest but hard-working family who supported his aspirations to become a world-class biochemist.

Introduction

Holman grew up in Minnesota, where his parents and grandparents (descendants of Swedish immigrants) settled in the mid-1880s. His father was employed as a streetcar conductor in Minneapolis; during the Great Depression of the 1930s, he was forced to take a cut in pay, which resulted in the foreclosure of the family's home. Ralph Holman was a small boy with limited athletic ability; however, his mother encouraged him at an early age to read. The Minnehaha Baptist Church, with its Sunday school and Bible study programs, nurtured his lifelong Christian faith.

By the time Holman was old enough to attend high school, he took a job at his church as a janitor with wages of $3/month in the summer and $5/month in the winter. With

his limited monetary resources, college seemed impossible. His pastor recognized his intellect and work ethic, however, and arranged for Holman to meet with the Dean of Bethel Junior College to work out a plan for him to attend there. Holman maintained that divine providence allowed him to pursue his collegiate studies after completing his courses at Bethel at the University of Minnesota, where Ross Gortner, a professor, encouraged him to apply for a teaching assistant position at Rutgers University. This lead resulted in Holman's path to earning a master's degree in biochemistry. His first publication, "The sulfur balance of the non-laying, molting, and laying hen," was based on research related to his thesis. At Rutgers, the shy Holman met Karla Calais on a blind date. The two were married in 1943, and their love for each other grew for over 60 years until her passing in 2003.

After obtaining his master's degree at Rutgers, Holman returned to the University of Minnesota to continue his graduate work under George Burr, professor and discoverer of essential fatty acids (1929). After two years of work involving the growth of plants using labeled carbon dioxide, Holman's research came to a halt when his supply of labeled carbon dioxide ran out. Consequently, he began his life's work as a lipid chemist, which he never regretted. He quickly began a new project, which led to four publications. After earning his Ph.D. in 1944, Holman became an instructor in Physiological Chemistry at the University of Minnesota. In 1946, he was awarded a National Research Fellowship in Stockholm, where he worked with Hugo Theorell, a professor at the Nobel Institute. Their collaborations proved to be fruitful, and Holman was able to crystallize the enzyme lipoxidase and determine its activity and amino acid composition. In 1947, he received a grant from the Scandinavian-American Foundation and accepted a fellowship under Arne Tiselius, the professor who pioneered a new technique known as displacement analysis. This association, too, was fruitful; upon his return to the U.S. in 1948, he became an Associate Professor position at Texas A&M University, and he began publishing a series of 10 articles on the displacement analysis of lipids. In 1951, Holman returned to the University of Minnesota and the Hormel Institute for a five-year collaboration. After a year, he took a position as a resident in the Biochemistry Department in Minneapolis. In 1959, he returned to Hormel Institute.

By the early 1960s, mass spectrometry was being applied in work with lipids, and Holman realized its potential. By 1962, he had received a grant from the National Institutes of Health (NIH), and he was able to spend time in the lab of Einar Stenhagen, a professor at the University of Gothenberg (Sweden). Although no publications were forthcoming, the visit was of value to Holman's research. Some years later, W. W.

Christie, a visiting scientist at the Hormel Institute, synthesized a complete series of methylene-interrupted cis, cis-octadecadienoic acids, and he developed a method to derivatize cyclopentenyl fatty acids and determine their structures with mass spectrometry. Other Hormel scientists published research regarding the mass spectroscopy of lipids, including studies about fatty aldehydes, triglycerides, wax esters, and orchid fragrances. From 1975 to 1985, Holman was the director of the Hormel Institute, and under his leadership, the Institute was granted considerable funding ($1.62–3.37 million) in spite of cuts for research by government agencies. Publications increased from 779 to over 1,100 during this period. By 1988, Holman had retired but held the title of Professor Emeritus of Biochemistry. During his long and productive career, he published over 425 papers, with significant contributions pertaining to the biochemistry of fatty acids and their roles in human nutrition. At the time, some believed the work applied only to rats. However, Holman's results were validated by others and, by 2000, 20 diseases had been linked to essential fatty acid deficiency in humans. Today, this list has grown to about 50. This is the story of the man from humble beginnings who had a profound impact on the field of biochemistry.

Holman's roots and early years

The Holmen families emigrated from Sweden to the U.S., and Ralph Holman's paternal grandfather Alfred Johannson took the name Holmen when he arrived in Minnesota in 1886. Ralph's father Ted Holmen was the first of the clan to be born in America (1889); he moved from Upsala to St. Paul in 1908 and took a job as a streetcar conductor. In St. Paul, he became a Holman. In 1915, he married; on March 4, 1918, Ted's and May's son Ralph was born in Minneapolis.

Holman's earliest memories of his mother were of being rocked to sleep while she sang lullabies to him. His favorite was the "Little Dog under the Wagon." A generation later, she sang to his son Teddy. This early introduction to song led to Holman's lifelong appreciation for music. His faith began to develop at the age of four when his parents began attending Minnehaha Baptist Chapel, which at the time was a mission arm of Bethel Baptist Church (an outgrowth of the First Swedish Baptist Church). In 1922, it became an independent church, and his parents were charter members. Holman was baptized on his 12th birthday, and he became a member of the church on March 4, 1930. From 1922 to 1939, Holman attended Sunday school and youth programs on a regular basis. Minnehaha Baptist Chapel offered an in-depth study of the scriptures through the Pastor's Bible study class. The class did not have a minimum age limit, so at the age of six, he began attending and continued to do so for five years. Holman's parents believed

that repetition was a virtue of education, and they relied on the Bible verse "Train up a child in the way he should go and when he is old he will not depart from it ." (Proverbs 22:6)

During his high school years, Holman's mother hoped to nurture his musical education with several years of piano lessons. Although he learned to play the keyboard, he lacked the speed and agility to play well. However, he could also play the organ, accordion, and harmonica.

Holman was not an athlete as he was too small and too skinny for football; furthermore, he could not hit a baseball, and no one chose him for team games. In grade school, he was too short to reach the gymnastic rings. He preferred reading and tinkering instead. In addition to being small, he had two crooked fingers that bent inward toward the ring fingers. Holman found this abnormality to be an advantage because the fingers made better hooks for carrying things. Being an only child who was undersized and underweight had some hidden advantages; although he never learned to fight, he relied on the power of persuasion when trouble came his way.

College at Bethel

As mentioned previously, Holman took a job as janitor of the church during his senior year of high school. The job paid more in winter when making fires and shoveling snow were required duties. He was responsible for paying for his haircuts and other expenditures. By the end of the year, he had saved $25. He had taken all the math and science courses offered at Roosevelt High School, but he did not have enough money for college. He graduated from high school in June 1935—20th in a class of 420—and was a National Honor Society scholar. About a month into the summer following graduation, Franklin Nelson, Holman's pastor, asked of the young man's plans for the fall. He expressed his desire to attend the University of Minnesota but acknowledged that he did not have enough money to enroll. Nelson then asked if he had considered Bethel Junior College and went on to inquire if he could investigate some possibilities to help Holman obtain the necessary funds. Shortly thereafter, Nelson brought C. E. Carlson, Bethel's dean, to visit Holman, and in his home. Carlson explained that Bethel had a policy of offering a free second semester to a student who remained on the honor roll for his/her first semester. In his later years, Holman remarked that this policy might have been invented that day. Nelson offered to pay Holman's fees for the first semester with the condition that repayment would occur during the year. Divine intervention had brightened a dark future.

Bethel required aspiring chemists to take English, German, the New Testament, and Evangelism.

At Bethel, Ernest G. Nordstrom, a chemistry professor, handled Holman's registration and noted from his application that he wanted to be a chemist. Nordstrom warned him that the path toward the intended career would not be an easy one. Although books and fees were purchased on credit, help came with a raise in his church wages, from $3 per month in summer and $5 per month in winter to $5 per hour and $8 per month in summer and winter, respectively. Looking back, Holman recognized that his pastor had intervened again on his behalf. Additionally, Nordstrom helped Holman by giving him laboratory duties and advanced chemistry experiments. It is not surprising, therefore, that the professor's portrait hung in Holman's office at the Hormel Institute for many years before residing at the Department of Chemistry at Bethel.

Bethel required aspiring chemists to take English, German, the New Testament, and Evangelism. Enrollment for the second year included biology and psychology courses and, much to Holman's dismay, a history course that was required for graduation. He petitioned Carlson to opt out of the course. The professor (who taught history) exploded "How stupid can a kid on the honor roll be and what fools these sophomores are!" He explained that history was required for graduation and suggested that Holman take the course and return to discuss the subject's merits. Holman later agreed with Carlson about its value and went on to author the histories of several churches. After writing hundreds of articles for technical publications, he also realized that chemists and historians have much in common since "they are gathering and preserving information for future generations."

Holman was able to pay off his school debts for the freshman year, but prospects for the second year were not promising. Carlson intervened again by offering the young man a job paying 15 cents per hour to prepare buildings for the upcoming academic year. Credit would accrue for fees, books, and other charges. Holman readily accepted. During the summer of 1936 (remembered as the hottest on record with temperatures reaching 109°F), Holman and five others worked as a team washing ceilings, sanding floors, and varnishing windows and door jambs.

Although not mandatory, attendance at Bethel's chapel services was recommended, and Holman was a regular and teachable attendee. Bethel's interdenominational vision was

displayed when the entire student body walked en masse to the Hamline University Fieldhouse to hear the well-known Methodist missionary F. Stanley Jones speak. Carlson also took Holman to a downtown church to see and hear the famous African-American chemist and inventor George Washington Carver of the Tuskegee Institute.

Holman received a camera and generous supply of film for Christmas 1936, and photography became a long-time hobby. When he removed his sweater during a biology lab only to find it on a lab skeleton the next day, the ensuing photo taken by Holman was published in Bethel's 1937 yearbook. Andy Simko, the lab partner who had hung the sweater on the skeleton, later became pastor of Holman's church in South Minneapolis.

Fast forwarding to October 1998, Holman received a Distinguished Alumna Award at Bethel's homecoming festivities. He gave a 15-minute summary of his career, after which he received a 5-minute standing ovation. He remarked that 61 years before, he would not have imagined that he could hold the attention of 1,000+ students with a presentation of the Gospel according to omega-3 fatty acids! After the ceremony, Holman and his wife enjoyed a look at the excavation for the new Chemistry Laboratory, which was scheduled to open in the fall of 1999. Above the door was a sign reading, "The Bethel College Chemistry Laboratories are named in honor of 1937 graduate, Ralph Holman." Holman remarked, "Life is full of nice surprises."

Holman credited Bethel Junior College as playing "a major role in my early education, teaching me the foundations of a broad range of knowledge." He expressed his appreciation to Bethel's faculty and students for teaching him "that one can be a Christian in any walk of life." He also noted, "The foundations of chemistry which I learned here have served me well for three score years in the world of biochemistry and I am grateful to Bethel for getting me started."

After graduation from Bethel, Ralph took a position as a paid lab assistant in the Biochemistry Department at the University of Minnesota; simultaneously, he was pursuing a degree in Biochemistry. Gortner advised him of a part-time assistantship at Rutgers University for a student pursuing a master's degree, which Holman was successful in obtaining in 1939. In 1941, he received his M.Sc. degree; furthermore, his thesis was published in the *Journal of Nutrition*. However, Holman regarded his best discovery at Rutgers as Karla Calais, his future wife.

For his thesis work, Holman heeded Burr's suggestion to investigate glucose metabolism in plants. The project required heavy C13-labeled carbon dioxide provided by the Physics

Department. In August 1943, Holman walked into the Physics lab for a bottle of CO2 and found the room empty. The physicists were gone, and no one knew of their whereabouts. After WWII, it was learned they had been sent to join the Manhattan Project with its research on fissionable uranium. Consequently, Burr suggested another thesis topic involving lipid oxidation. Holman quickly began the new project, which led to three publications in the *Journal of the American Chemical Society*. He later remarked that he was never sorry for embarking on a lifelong career in lipid research.

Holman received his doctorate in 1944; then, in 1945, he was awarded a National Research Council Fellowship for studying abroad. As mentioned previously, he worked for a year with Theorell, a professor at the Medical Nobel Institute in Stockholm. During this period, he was introduced to John Sumner, the professor who received the 1946 Nobel Prize for crystallizing the enzyme urease. Notably, Holman succeeded in crystallizing the enzyme lipoxidase prior to completing his work in Stockholm. His work with lipoxidase resulted in six publications, including co-authorships with Sune Bergstrom. While in Stockholm, Holman learned of a new analytical technique (displacement analysis) developed by Tiselius, a professor at the University of Uppsala. Holman applied for and was granted a stipend from the American-Scandinavian Foundation. Within three months, he had applied the Tiselius method to separate complex fatty acid mixtures. Displacement analysis involved placing organic molecules onto adsorbents and separating them into zones of increasing affinity. Other researchers had attempted to separate fatty acids by displacement with little success. However, Holman believed that the problem could be solved with improved adsorbents. By treating charcoal with picric acid, he was able to separate C14-C18 saturated fatty acids via displacement analysis. Further, his work in this area resulted in a series of 10 publications.

After returning to the U.S. in 1948 and beginning his work at Texas A&M University, Holman and his wife became parents to son Teddy; moreover, they purchased their first car while there. It was here that Holman's interest in fatty acid metabolism began. His initial research showed linoleic acid to be the precursor of a fatty acid with four double bonds, and linolenic acid as a precursor of acids with five or six double bonds in vital tissue lipids.

In 1951, Holman was presented with the opportunity to return to the Hormel Institute, but a transfer of grant funds received from the National Livestock and Meat Board was needed. Fortunately, the request was granted. Within a short time, a new wing of the Hormel Institute had been built for animal research and nutritional studies. In this

facility, 100 rats could be caged at any given time. Soon, Holman was able to continue the work with arachidonic acid that he began at Texas A&M. Carl Widmer and Holman were the first to discover that linoleic acid fed to rats with an essential fatty acid (EFA) deficiency was the precursor of arachidonic acid in tissues; further, they discovered that alpha-linolenic acid was the precursor of the pentanone and hexanone fatty acids in tissues. Rats fed with a fat-free diet produced the trienoic C20:3ω9 acid from oleic acid and linolenic acid, which corrected EFA deficiencies and stimulated growth. At the time, the mechanism for correction was unclear; additionally, desaturases were unknown. In 1960, Holman proposed the triene/tetraene ratio as an index of EFA deficiency based on feeding studies in which rats were fed four different diets—fat-free, butterfat, cottonseed oil, and a blend of 80% butterfat/20% cottonseed oil. After 89 days, the rats were sacrificed and blood lipids (plasma, erythrocytes) and tissue lipids were examined for polyunsaturated acid composition. The control group showed a severe EFA deficiency; the group fed with the butterfat diet produced only mild symptoms; and the groups fed with pure cottonseed oil and the cottonseed/butterfat blend showed no signs of EFA deficiency. The fatty acid patterns indicated a connection to the content of linoleic acid in the diet. A plot of the percentage of trienoic acid in the endogenous PUFA versus dietary linoleate showed a break when the latter was about 1% of the caloric intake. A similar effect was observed with tetraenoic acids. Thus, a ratio of triene/tetraene of less than 0.4 indicates that the minimum requirements of linoleate (1% of calories) had been met.

In subsequent studies, Holman and his colleagues reported the dose levels of EFAs in rat liver lipids. Diets of ethyl linoleate, ethyl arachidonate, and ethyl linolenate were tested for the resulting weight gain, fat deficiency, and presence of lipids. Dietary linoleate fed in excess of 1% of the caloric intake resulted in satisfactory growth; additionally, this regimen cured EFA deficiency. Further, liver lipids showed conversions to C20:4 and C22:4 acids, while the number of C20:3 acids decreased. Dietary arachidonate cured EFA deficiency three times more effectively than linoleate. Additionally, a further conversion to C22:5w6 was observed. Dietary linolenate was shown to be less effective than linoleate or arachidonate in supporting weight gain. With linolenate, EFA deficiency could not be cured completely. Thus, biochemical changes in tissue fatty acids relative to diet were shown to be useful in determining EFA requirements.

Gas chromatography proved to be very useful in the study of dose levels of pure EFAs in rat livers and in their metabolic products. Dose response curves for dietary alpha-linolenic acid fed to rats showed that conversion to C22:6w3 increased more rapidly than

for the intermediate acids C20:5w3 and C22:5w3, suggesting that the C22:6w3 is the most important structural acid of the three metabolic products. Further work confirmed that the same phenomenon occurs in erythrocytes, depot fat, brain, and heart tissues; thus, indications are that EFA deficiency affects all tissues. The gas chromatography studies showed that two cascades of fatty acids were involved in the location changes of double bonds at each step of the cascade. The use of abbreviated Geneva chemical nomenclature became very confusing, and a new numbering system for double bond unsaturation was needed. Since biochemistry dictates that the terminal end remains unaltered, Holman relied on his biblical knowledge of Revelation 1:8 (i.e., "I am the Alpha and the Omega…") and proposed a numbering system beginning with the terminal end of the fatty acid molecule. Since omega is the last letter of the Greek alphabet, he used this nomenclature when counting from the methyl terminal end. Thus, the omega nomenclature was introduced in 1964 and has been used ever since. In fact, omega-3 acids have become synonymous with dietary fatty acids and their nutritional benefits. When Holman saw a sign hanging from a local market proclaiming, "Omega-3[s] are here," he ran home to get his camera to record it. Holman lived to the age of 94. When asked his secret to longevity, he replied that consumption of fish (rich in omega-3 acids) is "the Gospel I preach." Both Holmans had their omega-3 levels checked in their later years, and they learned that their levels were much higher than those of most Minnesota natives were.

Holman's group showed that linoleic acid (18:2w6) and alpha-linolenic acid (18:3w6) are metabolized by the same microsomal enzyme systems through alternating desaturation and elongation steps (cascades) to make metabolic products with chain lengths containing up to 22 or more carbon atoms. These processes occur in both animal and human tissue lipids. Therefore, linoleic and linolenic acids could be considered the precursors of the two main families of essential fatty acids. The pathway for linoleic acid (18:2w6) involves conversion to 18:3w6. It can be followed by chain elongation to C20:3w6, then desaturation to C20:4w6 followed by another chain elongation to yield C22:4w6. The final steps involve the Sprecher pathway and end at C22:5w6. Linolenic acid follows a similar desaturation chain-elongation sequence with the Sprecher pathway to produce C22:6w3.

Further work showed that when dietary C18:2w6 was held constant, increasing the level of dietary C18:w3 suppressed w6 products; conversely, when C18:3w3 was held constant, increasing C18:2w6 suppressed w3 products. Based on these studies, Holman proposed a general hypothesis that all fatty acids of the w3 and w6 series can compete at

all steps of the cascades since the same enzymes are involved in the above desaturation/elongation reactions.

Much of Holman's research focused on EFA deficiency in humans. An infant born with numerous medical problems was fed a fat-free total parenteral nutrition (TPN) diet, after which skin lesions appeared after three months. Analysis of the plasma phospholipids showed that the infant was deficient in EFAs, and analysis of the tissue lipids confirmed the findings, thus providing evidence that plasma and tissue phospholipid profiles can be used as a measure of EFA deficiency in humans. During the same period, an elderly woman was put on a fat-free diet, and lesions appeared within a month. Analyses of lipids at one, two, and three months indicated a severe (nearly complete) EFA deficiency. These cases showed that EFA deficiency could occur rapidly in both the young and old.

Holman reported the first case of omega-3 deficiency in a six-year-old girl who was the victim of an accidental gunshot wound. By 1982, the FDA had approved the use of 2TPN with lipid emulsions—one which contained soybean oil and the other safflower oil—to provide EFAs. The soy preparation contained C18:w3, but safflower oil was devoid of omega-3 acids, although it contained a high content of C18:2w6. Within five months on the safflower TPN diet, the girl exhibited numbness, tingling, weakness, and the inability to walk. It was suspected that the safflower TPN was inducing the omega-3 deficiency, and this assumption was confirmed by lipid analysis. After a switch to the soy oil-TPN combination, the girl's neuropathy disappeared; further, a lipid analysis confirmed that omega-3 deficiencies were restored to normal. In addition to single case studies, Holman published several larger ones, including vegetarians in the U.S. and populations from foreign countries. The control group was composed of 100 healthy vegetarians (faculty and students from the University of Minnesota), and the blood lipid data of individuals belonging to six different countries were compared. A plot of total w3-PUFA versus total w6-PUFA showed a correlation between the two acids. As w3 acids increased, w6 acids decreased. Although a wide range of dietary acids support life, it is interesting to note that the regions where fish is consumed (e.g., Northern Sweden, Kerala, and Nigeria) have populations with the highest levels of omega-3 acids. American infants and the Minnesota control group had the lowest levels of omega-3.

Furthermore, Holman found that diseased humans showed low omega-3 levels. It was discovered that foods with omega-3 oils (e.g., soybean oil) had been modified by hydrogenation to increase shelf life and functionality, thus eliminating their nutritional benefits. Currently, 50 human afflictions and diseases have been linked to essential

fatty acid deficiency. An excellent review of Holman's EFA research through 1997 can be found in the publication by the American Society of Nutritional Sciences entitled "The slow discovery of the importance of w3 essential (omega-3) fatty acids in human nutrition" (Supplement pp. 427s–433s, 1998).

In early 1951, while still at Texas A&M, Holman was invited to contribute three chapters to an updated book entitled The Chemistry of Fats, first published in 1936. Holman completed one chapter before he left Texas. Shortly after arriving at the Hormel Institute, he learned that the lead author had died and that the unfinished book had been purchased by Pergamon Press; further, the owner, Robert Maxwell, was new to the publishing business. At the encouragement of a colleague, 33-year-old Holman became the editor for the book in progress and anticipated additional volumes. Thus, with no experience in editing, Holman along with Walter Lundberg and Thomas Malkin began their collaboration on the classic *Progress in the Chemistry of Fats and Other Lipids*. The first volume was published in 1952. By 1962, the sixth volume was in preparation. By then, Holman was doing the major part of the work as Lundberg had resigned from the project. Malkin died that spring, leaving Holman with full responsibility for future volumes. Within a few years, the series evolved into a quarterly journal named *Progress in Lipid Research* to include information on other fatty materials. Furthermore, annual volumes were no longer profitable nor the best way to communicate scientific findings and news. Volume 17 was published in 1979, and it was dedicated to Lundberg, the then chair of the editorial board. The volume included manuscripts edited by Frank Gunstone, professor, entitled "Topics in Lipid Chemistry." Another volume was dedicated to Stenhagen and his wife. Holman remained editor through 1989 (Volume 28); however, Howard Sprecher, a former post-doctoral fellow from Holman's lab, and John Harwood (Cardiff, UK) assumed editorship with the publication of Volume 29 in 1990. The journal is still going strong as Volume 52 was published in 2013. Pergamon Press grew at a phenomenal rate and soon reached the ranks of top scientific publishers. When an American branch of the publisher was incorporated, Holman invested in shares that he eventually sold at a loss when a hostile takeover occurred and Maxwell lost control of the company. The takeover was successfully contested in court. When Holman and Maxwell met in the 1970s, Holman explained that his wife had remained at home to avoid additional travel expenses. Maxwell advised that Holman was to bring her next time at the company's expense, and on their next visit, Karla Holman accompanied her husband. In 1980, Holman was organizing the First International Congress on Essential Fatty Acids and Prostaglandins to be held in Minneapolis where Burr had discovered

EFA some 50 years previously. Maxwell generously supported the Congress, and proceedings were published in *Progress in Lipid Research*. The volume soon became the most respected reference book for this research field, and it remained so for several years. In 1988, Pergamon Press celebrated its 40th birthday, and Maxwell planned a lavish celebration with a formal ball. All editors and their wives were invited with all expenses underwritten by the company. Three days prior to departure, Holman became ill and was hospitalized. Unfortunately, he and his wife were not able to meet Queen Elizabeth II, the guest of honor.

The Hormel Institute

After a long and productive career of leading and conducting lipid research at the Hormel Institute, Holman moved into administration. In 1974, Lundberg requested medical leave from his position as the Institute's director until retirement. Herman Schlenk was appointed interim director, and Holman was appointed to a search committee to find a permanent director. Requests for nominations were sent to lipid chemists across the globe. Of the first 10 nominations received, six were for Holman. Therefore, he was advised to either remain on the search committee or become a candidate. Other committee members encouraged him to become a candidate, and within months, Holman was elected unanimously by the Hormel Institute Board of Directors. Before accepting, he wished to explain the conditions under which he would take the position. First, the position would no longer be a lifetime appointment. Second, the board would fix the term for five years, requiring a performance review by faculty members after four years, with reappointment pending satisfactory performance. Third, he requested more interest and involvement from board members, who agreed to the conditions. Therefore, Holman accepted the position effective July 1, 1975.

The 10 years of Holman's tenure as the Institute's director were excellent ones, despite funding cuts to research in general. From 1975–1985, funding doubled from $1.6–3.4 million, and the Institute continued publishing at a high rate. The governor of Minnesota visited Hormel, and he was so impressed that a further $550,000 was appropriated. The electronics and computer departments were expanded and updated, and a state-of-the-art mass spectrometer and other important instrumentation were purchased. In 1979, Jacques Chipault, one of the original staff members, retired; to honor him, Holman wrote the following parody based on *Genesis* 1:

> *In the beginning, the university created the Hormel Institute, this scientific heaven on earth. And the place was without form and void. Then the*

> *university said, 'Let there be a man to put order into this chaos.' And it was so. Jacques Chipault was sent to Austin and he did separate the cows from the horses. And the Hormel Institute was born in a stable and it was good.*

1981 brought good news to Holman. In April, he received a call announcing his election to the National Academy of Sciences (NAS). Holman reacted with, "You have to be kidding," because he had never entertained that possibility. Shortly after the announcement, Hormel's faculty and staff gathered in the library to celebrate. The honor was a complete surprise. In 1982, he and his wife traveled to Washington, D.C. for the NAS meeting, where Holman was inducted by signing the large book containing the signatures of all NAS members.

1985 saw the death of Lundberg and Orville Privett, both long-time faculty members associated with the early development of the Institute and its reputation as a global leader in lipid research.

Highlights of the decade included the 50th anniversary of the Institute, which was celebrated with a birthday cake baked by Holman and enriched with omega-3 acids. The computer/electronics group was expanded to cope with the increasing needs of the research staff. Additionally, the Institute developed a program to assist small biotechnology start-up companies by providing space and a distance-learning program.

Over his long career, Holman had many friends and colleagues who influenced his life—Nelson, his pastor from the Minnehaha Baptist Church; Carlson, the dean at Bethel College who was instrumental in helping him attend college; and Lundberg, the brilliant scientist who mentored Holman as a graduate student and as a valued colleague at the University of Minnesota, and later at the Hormel Institute. Lundberg was a coauthor for a number of Holman's early publications on fatty acid oxidation. Lundberg, Holman, and Malkin were coeditors of the popular *Progress in the Chemistry of Fats and Other Lipids.* Holman also considered Burr his mentor and teacher. Burr had a number of careers besides his position as a professor, which included pioneering research in essential fatty acids. Additionally, he was employed by the Hawaiian Sugar Planters Association, where he discovered that the initial photosynthetic product in sugarcane was malic acid and not the expected pyruvic acid. His first manuscripts were repeatedly rejected by editors, but within a year, confirmation of his results came from all over the world, and his work was finally published in *Plant Physiology* in 1965. Burr made major discoveries in both animal and plant biochemistry. Holman presented Burr and Lundberg copies

of his doctoral thesis, which included photographs of each of these men who had influenced Holman so profoundly.

The Hormel Institute was a mecca for attracting post docs and visiting scientists. From 1951 until 1997, 85 individuals came there to study or work, and 30 of these were from countries other than the U.S. The author's mentor H. J. Dutton became an Honorary Fellow of the Hormel Institute shortly after his retirement from the U.S. Department of Agriculture. Dutton and Holman coauthored several publications. It is a testament to the Institute that three of the visiting scientists had received or would receive the prestigious American Oil Chemists' Society (AOCS) Award in Lipid Chemistry.

Holman and his wife attended church service regularly for nearly 60 years; for more than 50 of those years, they were members of the First Congregational Church in Austin, Minnesota. Holman attributed his scientific successes to prayer; further, he maintained that as he waited for answers to these prayers, he received divine leading (which he followed). He believed that too many events in his life could be attributed to just random chance. He noted that many basic processes are common to both animals and humans, but the distinguishing difference between the two stems from man having freedom of choice, whereas animals eat, digest, excrete, decay, and die. Holman believed that choice comes from the creator who allows humans to communicate both vertically and horizontally; thus, humans were created to commune with and serve God. Holman's life was centered on his family, his church, and others. Alcohol was forbidden at functions of The Hormel Institute during his tenure as director.

The Holmans lived in a small well-furnished home in Austin. Their frugal lifestyle belied the fact that investments had brought wealth. While pursuing his undergraduate studies, Holman traveled by bicycle to and from school. He and his wife did not own a car until 1948. Yet, Holman never lost his love of bicycling, and he and his wife took many extended trips for rest and relaxation. In 1945, they embarked on a trip to northern Minnesota with the goal of traveling up Gunflint Trail to the Canadian border. Rain and flat tires spoiled the trip. Fortunately, the driver of a mail truck saved the day by taking them back to civilization.

Deuel Conference on Lipids/Travels/Honors/Awards/Editorial Service

The annual "Metabolic Conference" began in 1956 when a group of top lipid biochemists, including four Nobel Prize recipients, met in various West Coast cities. Holman was not invited in 1957, but he attended nearly every meeting from 1958

to 1987. In 1958, the conference was renamed the Deuel Conference in honor and memory of Harry Deuel for his numerous contributions to lipid biochemistry, including three volumes on lipids. One year en route to their homes, the group of biochemists had a layover in Las Vegas. To kill time, they visited the casinos to observe the gamblers. Holman did not gamble, and his friends thought his innocence would bring them luck; consequently, they coaxed him into pulling the handles on the slot machines after the coins were inserted. Ralph noted that no noticeable difference in winnings occurred; furthermore, he had not spent a nickel.

Holman's involvement over the years in the Deuel Conference extended beyond his attendance. He served on the program planning committee and chaired fundraising efforts to support the conferences. For a number of years, conference themes included numerous lipid topics other than essential fatty acids; therefore, Holman tried to convince conference leaders that too much emphasis was being placed on lowering cholesterol levels rather than increasing dietary omega-3 levels. Finally, in 1981, omega-3 acids were designated for theme topics, and it appeared that essential fatty acids were getting the attention they deserved.

Holman traveled abroad to Sweden, Norway, Italy, England, Japan, Argentina, Mexico, and Australia. His wife traveled to Sweden and Norway with him. A highlight was an invitation to attend the Nobel Prize ceremony in Stockholm when Sumner was honored for his pioneering enzyme work and crystallization of urease. Sumner discussed research regarding soybean lipoxidase with Holman, and Theorell soon joined the conversation. Holman felt that it was no coincidence that scientists from Cornell, Sweden, and the U.S. would gather in one place to discuss their common interests.

Holman was a regular attendee at American Oil Chemists' Society Meetings; in fact, he held key roles in the governance of the Society as a member of the governing board and as the organization's secretary, vice president, and president (1974). After his retirement in 1988, however, he attended very few meetings. He received the A. R. Baldwin Distinguished Service Award at the 2001 meeting held in Minneapolis. The last meeting he attended was held in Cincinnati, where he was inducted as an AOCS Fellow. This prestigious honor was initiated in 1998 (after Holman had retired). The Health and Nutrition Division of AOCS established an award in recognition of meritorious service and contributions to the health and nutrition fields, and Holman was the first recipient in 2004. Later, the award was renamed as the Ralph Holman Award. With the award,

Holman received a framed color print of orchids (dear to his heart) as well as a $1,000 honorarium.

In 1959, the North Central Section of AOCS established the Alton E. Bailey Medal to commemorate Bailey's contributions to fats and oils technology. The award is the oldest and one of the most prestigious honors given to a lipid chemist. Holman, along with Lundberg and Privett, were the few staff members of the Hormel Institute to have received the Bailey Award. However, several visiting scientists under Holman's guidance have been recipients.

The AOCS Award in Lipid Chemistry (renamed several times since) dates back to 1964 and its recipients include three Nobel laureates. The award currently carries a $10,000 honorarium. Holman received the award in 1979 for his pioneering work related to essential fatty acids and human nutrition. Upon being introduced as a recipient, he was referred to as a "guru." Holman was especially proud of this award as well as his election to the National Academy of Sciences.

Additionally, Holman was a Fellow in the American Institute of Nutrition and recipient of the society's Borden Award. The Italian Oil Chemists' Society presented him with the Fachini Medal in recognition of his accomplishments on essential fatty acids. Other international honors included an appointment to the Academy of Medical Sciences and selection as a Foreign Academic Correspondent. Holman was selected as President of the Golden Jubilee International Conference on Essential Fatty Acids and Prostaglandins held in Minneapolis in 1980. The second conference was held in London (1985), where Holman was part of the organizing committee. He was the keynote speaker at the third conference (1992) in Adelaide, Australia. In 1995, he was a guest speaker at the Meat Composition, Nutrition and Health Conference in Buenos Aires, Argentina.

In addition to the previously mentioned series that Holman edited, he served on the editorial boards of the *Journal of Nutrition, Lipids, Excerpta Medica, Journal of Parenteral and Enteral Nutrition*, and *Journal of Laboratory and Clinical Medicine*. He also served on the advisory board for the *CRC Press Handbook of Prostaglandins and Related Lipids.*

Academic activities

In addition to holding full professor appointments at the University of Minnesota and the Hormel Institute, Holman was an adjunct professor at the Mayo Medical School from 1977 to 1990. After his retirement in 1988, he became Professor Emeritus of Biochemistry (University of Minnesota).

Holman was a devout Christian who believed the Holy Scriptures to be God's word, and he applied them to his life. Although man and beast have common metabolic processes, humans are unique; Holman believed that they were created for communication and creativity with fellow humans and their creator. Whereas animals are governed by ingestion, digestion, metabolism, reproduction, decay, and death, each human possesses a spirit. Theologians state the purpose of man is to praise and glorify God through communication and in creativity and emulation of Him. Ralph paraphrased this with:

> *Our purpose in life is to engage in spiritual metabolism to partake of the nature of God by communication with him to transmit this knowledge to others, and to create new versions for old truths.*

Epilogue

Holman died in August 2012 at the age of 94 from natural causes. At the time of his death, he was living in the home that he and his wife had shared for over 50 years before her passing in 2003. Holman was not only an accomplished biochemist, but also a devoted father and husband, a man of integrity, and a role model for students and young scientists. He was humble, crediting God for his personal and professional successes. His students and colleagues held him in the highest esteem; they were beneficiaries of his friendship.

This biography is based in part from Holman's personal memoirs and a personal relationship through the American Oil Chemists' Society. Douglas Bibus was a Post-Doctoral Fellow at the Hormel Institute and has remained to continue essential fatty acid research. He credits Holman with teaching science and, just as importantly, how to live life productively.

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