Murray Rabinowitz

1927–1983

BIOGRAPHICAL *Memoirs*

A Biographical Memoir by
Godfrey S. Getz

NATIONAL ACADEMY OF SCIENCES

MURRAY **RABINOWITZ**

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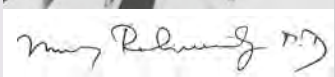

By Godfrey S Getz

For Murray Rabinowitz, 1983 was the best of years and the worst of years. In April he was elected to the National Academy of Sciences for his work on cardiac hypertrophy and mitochondrial biology. His election to the academy occasioned much pleasure and excitement among his colleagues, so great was their admiration for his achievements and his courage. The honor also pleased Murray greatly, but he had limited opportunity to savor it, for he passed away the following October at the relatively young age of 55. The following month, Murray was granted the Research Achievement Award of the American Heart Association, posthumously, at the association's annual meeting.

Murray was a gentle man of enormous intellectual energy and a wide range of interests in science, the arts, and the beauties of nature. I first met him in 1964 when I came to the University of Chicago, encouraged to make contact by a former colleague who described him as a "tough customer." We had a fast friendship and collaboration, especially on the mitochondrial biogenesis program in his laboratory. From 1964 until his death, I attended his laboratory meetings, worked with some of his students, and enjoyed being his neighbor on the Lake Michigan shore.

Prior to the University of Chicago

Murray Rabinowitz was the youngest of three siblings and a native of New York City. He obtained his undergraduate and medical degrees from New York University (NYU), which is where his interest in cardiology was initially fired.

Murray became the exemplar of a true physician scientist. After graduating with his medical degree in 1950, he completed his internship at the Beth Israel Hospital and the first of his two residencies in Medicine at the Montefiore Hospital. This was the period of the Korean War, and Murray learned during his Selective Service physical that he

had muscular dystrophy, which was, for the rest of his life, to progressively impair his mobility and his ability to carry out the daily tasks of living.

Seeking to enhance his education in cardiopulmonary pathophysiology, Murray obtained a Public Health Service fellowship to study with Lewis Dexter at the Brigham and Women's Hospital in Boston. Dexter was a pioneer in cardiac catheterization, and it was here that Murray laid the foundation for his subsequent clinical specialization. He studied pulmonary compliance in patients who had heart disease, and he studied the methods for measuring pulmonary blood flow. He then undertook his second medical residency at the Massachusetts General Hospital.

With his well-honed training in clinical cardiopulmonology, Murray began preparing himself to do research on the biochemistry and physiology of the heart. The enormous enrichment of heart muscle cells with mitochondria informed his next steps, and indeed, his scientific life.

Murray continued his postdoctoral training at the University of Wisconsin Institute of Enzymology under the direction of David E. Green. (By coincidence, 1983 was also a bad year for Green, a fellow New Yorker and NYU alum, as it was the year in which he, like Murray, passed away.) Together with Benedetto de Bernard, he published a paper on the characterization of NADH and succinate cytochrome c reductase in heart muscle. Benedetto de Bernard chaired the department of biochemistry at the university in Trieste, Italy, and was a visiting professor in Murray's laboratory on several occasions.

Murray returned from Madison, Wisconsin, to the Massachusetts General Hospital, this time as National Foundation Fellow studying with Fritz Lipmann, who was director of the hospital's Biochemical Research Laboratory. He moved with Lipmann in 1958 to the Rockefeller University, and together they published a paper in the *Journal of Biological Chemistry*, which has been frequently cited in the years since, that described a new class of protein phosphokinases exhibiting striking acceptor specificity. Some of these kinases are stimulated by cAMP.

While at the Rockefeller University, Murray began to collaborate with Ed Reich and Irving Goldberg, and their relationship continued after Murray and Goldberg moved to the University of Chicago. This collaboration resulted in a series of papers on the detailed structure-function relationship of actinomycin D and its DNA template for the inhibition of template-dependent RNA synthesis. Actinomycin D has now proven to be an extraordinarily valuable reagent for the inhibition of DNA-dependent RNA synthesis.

In the course of their studies of RNA synthesis, the collaborators showed that pseudo-uridine triphosphate could substitute for uridine triphosphate. With this in mind, they also showed that pseudo-uridine diphosphate glucose could facilitate the incorporation of glucose into glycogen, and that other pseudo-uridine diphosphate sugars could promote other transfer reactions that depend upon these activated sugars.

The University of Chicago, Department of Medicine

In 1958, Murray moved to the University of Chicago as an assistant professor of medicine and biochemistry, becoming director of the Cardiopulmonary Laboratory. He also had an appointment in the Argonne Cancer Research Hospital, which facilitated his many experiments that employed radioisotopes. Murray led two separate areas of investigation: one focused on cardiac hypertrophy and the cardiac myosins, and the other on mitochondrial biogenesis and organellar nucleic acids.

During his twenty-five years at the university, he was one of its most loyal and enthusiastic advocates, particularly on behalf of its biomedical research enterprise. He played a major role in shaping the cardiology section of the Department of Medicine, helping to ensure that it was one of the centers of biomedical science at the university. Such prominent investigators as Ernest Page, Harry Fozzard, Arnold Katz, and Hans Hecht were recruited to the section soon after Murray arrived.

Cardiac hypertrophy and its mechanisms

Murray's first work in cardiac hypertrophy reporting on the polysomal aggregates capable of protein synthesis in extracts of cardiac muscle was published in the *Proceedings of the National Academy of Sciences*. These aggregates could be disaggregated by protease treatment, yielding monosomes, which led the authors to suggest that the aggregates were held together by nascent protein. This was an era when polysomes were being characterized as the major functional units of protein synthesis *in vivo*.

Murray collaborated with Ira Wool and Radovan Zak on the polysome projects. Wool, who was Murray's colleague in the Department of Biochemistry and had been studying the effect of insulin and other hormones on protein synthesis, continued with a long and highly productive career characterizing eukaryotic ribosomes and their proteins. Zak was a postdoctoral trainee coming from Czechoslovakia via Northwestern University to join Murray's laboratory. They continued their collaboration for many years studying cardiac muscle biology and its contractile proteins. Zak went on to establish his own laboratory, ultimately becoming professor in the Department of Medicine and Physiology and of course mentoring many of his own students.

I will return to the collaboration between Murray and Zak shortly. Another of their collaborators was KG Nair (Raj), an Indian cardiologist who undertook extensive training in the basic biology of the heart at several institutions in the United States, including two stints at the University of Chicago. Nair earned a PhD in physiology with Murray's help, and he was the first cardiac fellow in Murray's laboratory. He remained at the university as an assistant professor of medicine, collaborating with Zak and Murray on the use of an aortic banding procedure to induce cardiac hypertrophy in the rat. Nair ultimately returned to India, where he prospered as a distinguished cardiologist.

The rat cardiac hypertrophy model that they developed enabled Zak, Nair, and Murray to explore some of the mechanisms by which heart muscle adapts to pressure overload.

Their research model involved placing a stainless steel constricting band round the ascending aorta to induce sudden pressure overload. While this does not precisely model clinical situations, it does provide the opportunity to examine the heart's capacity to adapt and remodel, which they, along with their students and fellows, characterized in a long series of reports and reviews that were published between 1969 and 1979.

Their initial report showed that after banding, there was a rapid increase in RNA synthesis, mostly of ribosomal RNA and transfer RNA. Each of the cellular components was shown to respond according to its own time frame, contingent on the type of model for cardiac hypertrophy studied. They also showed that there was a thirty to fifty percent increase in the mass and protein content of the heart within forty-eight hours of banding.

Another early response to banding (within twenty-four hours) was a rapid accumulation of inner mitochondrial respiratory complexes.

An increase in DNA synthesis was also observed, but the effect was somewhat later, and it peaked at about seven days after banding. The DNA synthesis occurred primarily in the nuclei of the connective tissue cells in the heart. Cardiac myocytes of the adult rodent heart do not incorporate DNA precursors. Protein synthesis in connective tissue was studied using proline as precursor, measuring its incorporation into collagen as hydroxyproline. This increased and reached a peak prior to the peak of DNA synthesis, suggesting that collagen synthesis was enhanced within pre-existing connective-tissue cells. Thus, the increment in collagen synthesis was not exclusively a property of dividing connective tissue cells.

Another major focus of their research was on the homeostasis of cardiomyocyte mitochondria. As indicated by the changes in respiratory complexes, there was an early selective accumulation of mitochondria, while myofibrillar proteins accumulated at later times after banding. To understand the basis for these changes in mitochondrial homeostasis, Nicholas Gross, a fellow, and Robert Druyan, a faculty colleague, focused on mitochondrial turnover.

Gross studied mitochondrial DNA and mitochondrial lipids, most notably cardiolipin, which, as its name suggests, is highly enriched in the heart and is particularly useful as a unique phospholipid marker of the inner mitochondrial membrane. He examined mitochondrial turnover in four body tissues: heart, liver, kidney, and brain. Turnover was quite rapid in the heart and the liver, and it was very slow in the latter two tissues. The data suggested that the inner mitochondrial membrane might turn over as a unit, presumably through uptake by the lysosomes in processes we now know to be akin to autophagy. Mitochondrial heme turnover was approached using the experience of Druyan, who pointed the laboratory to the precursor of heme, delta aminolevulinic acid, which has a turnover so rapid that it is, effectively, a pulse label.

In contrast to the inner mitochondrial membrane, the outer mitochondrial membrane and matrix components turned over more rapidly, suggesting that these components could be independently inserted and removed from mitochondrial structures. The change in the mass of mitochondria in the hypertrophic heart was the net result of both an increment in the synthesis of inner mitochondrial components and a decline in their degradation along a similar time course.

As the cardiac hypertrophy progressed, the concentration of mitochondria declined toward normal while the myofibrils increased in mass. In contrast with the inner mitochondrial membrane, the individual myofibrillar proteins turned over at different rates. The increase in heart DNA synthesis probably did not reflect a change in mitochondrial DNA, since it represented such a small portion of the total heart DNA. But carefully characterized mitochondrial DNA showed that this synthesis reached its peak two to seven days after banding.

The electron microscopic examination of isolated mitochondrial DNA showed that with pressure overload, the molecules had a marked depletion of D loops (these are loops that accumulate in steady-state mitochondrial DNA, mostly because of a rate limitation in first strand DNA replication), reflecting the increased DNA replication.

This extensive series of studies on the response of the heart to acute pressure overload indicated the complex nature of changes that result when the heart is forced to work harder. But to what extent are these changes reversible? Zak and students removed the constricting band at ten days and thirty days post banding and found that the early time of debanding, many of the changes were reversed. However, after thirty days, the changes were barely reversible.

Zak and Murray also turned their attention to the major contractile protein of cardiac muscle cells, myosin, and their work mainly addressed questions about the protein's heavy chain.

Genes for the diverse heavy chains in chick skeletal muscle had already been cloned, largely due to Patrick Umeda, who was then a graduate student and later a fellow and assistant professor at the University of Chicago. Umeda was assisted by two other trainees, Achyut Sinha and David Friedman, and their work was among the first recombinant DNA studies in the Department of Medicine.

The two cardiac myosin heavy chain genes were isolated and cloned from rabbit ventricle, with the protein products designated heavy-chain alpha and beta. These two genes were differentially expressed through development. Early in development, the level of alpha-chain and beta-chain expression were equivalent, but with maturation, the expression of the alpha chain receded and that of the beta chain increased so that in adult cardiac muscle, the ratio of beta to alpha was 4:1.

Their expression was also regulated by thyroid hormone. In hypothyroid animals, the beta heavy chain was dominant; however, with thyroid hormone administration, heavy-chain alpha synthesis increased while the beta declined. Atrial heavy-chain alpha was shown to be identical to the ventricular alpha chain. The two heavy chain genes were very similar in overall structure, with similar placement of introns, though there was considerable variation in intron lengths. Chick skeletal muscle revealed more heavy chain diversity than was described for the heart.

While the pressure overload resulted in a complex series of regulatory events, many of them involving various compartments of the mitochondria, the animal models that Murray had been using did not allow for a very detailed mechanistic analysis of these events.

Mitochondrial biogenesis in yeast

In collaboration with Hewson Swift, Murray had isolated mitochondrial DNA from chick heart and liver, reported in 1964 in the *Proceedings of the National Academy of Sciences*. This alerted him to the role of the mitochondrial genome in regulating the biogenesis of functioning mitochondria. He had the good sense to appreciate the limitations of cardiac muscle system, and he chose therefore to move to a more malleable experimental system: the yeast Saccharomyces cerevisiae. in which the mitochondrial complement is readily modified by growth, environment, and genetic engineering.

To prepare himself for the new experimental model, Murray and his wife, Smilja, took themselves for a brief sabbatical to the National Center for Scientific Research (CNRS), located in Gif-sur-Yvette, near Paris, where he established a very strong relationship with Piotr Sλonimski, the distinguished yeast geneticist, and with members of Slonimski's research group. They became fast friends and colleagues.

At the end of the 1960s and through the 1970s, the pathways of mitochondrial biogenesis were being unraveled in many laboratories in the United States and in Europe.

The pathways involved genes encoded in the nucleus and a smaller number encoded in the mitochondrial genome. The genes encoded in the nucleus are involved in protein synthesis, in mitochondrial RNA synthesis, mitochondrial respiration, mitochondrial fatty acid oxidation, the proteins of the tricarboxylic cycle, and the proteins involved in the import of these gene products through the mitochondrial membranes and into the appropriate mitochondrial compartment.

On the other hand, a few of the core proteins of the terminal respiratory chain, of ATP synthase, and the RNA machinery for intramitochondrial protein synthesis, including ribosomal RNA and most transfer RNAs, were synthesized within the mitochondria and encoded by mitochondrial DNA. Much of the elucidation of the role of nuclear genomes in mitochondrial biogenesis was being uncovered in other laboratories. Murray's laboratory focused on the mitochondrial DNA and RNA species synthesized within the mitochondria.

David Levens, one of Murray's graduate students, was the exception to this rule. He purified the yeast mitochondrial RNA polymerase, a nuclear gene product that is synthesized in the cytoplasm as a 47 kd precursor and is imported to the mitochondrial matrix, where it appears as a processed, mature, 45 kd, active protein. The availability of this purified polymerase was of immense value in the further analysis of mitochondrial transcription and transcript mapping.

Saccaharomyces cerevisiae is an excellent model organism in which to study mitochondrial biogenesis and the interaction between the nuclear and mitochondrial genomes. When wild type yeast are grown on glucose, their mitochondrial biogenesis is repressed until the available glucose is exhausted when the glucose metabolites are employed by the mitochondria to facilitate further cell growth. In the absence of functional mitochondria, this latter phase of growth is not possible, so that the colonies are small, designated petite (or cytoplasmic) mutants. The ability to grow yeast on glucose without mitochondrial function and an intact mitochondrial genome, allows one to study mitochondrial mutants without killing the organism. These mutants may include deletion of portions of the mitochondrial DNA. This is not possible for mammalian cells and organisms. Thus the study of yeast could point to functions that could play a role in the biology of mammalian cells, including heart muscle cells of greatest interest to Murray.

A variety of cytoplasmic mutants (i.e., mutants determined by the mitochondrial genome) were being studied at CNRS. The cytoplasmic petites were largely a result of deletions of different segments of mitochondrial DNA. The deletions could be small or large; indeed, in some petites, the residual DNA could be as small as 80 base pairs out of a total of 70-76 kilobases. The petite mitochondrial DNA could be the outcome of single contiguous deletions of the mitochondrial genome, or multiple deletions with possible sequence rearrangements, oligomerization, or amplification of the retained sequences. Thus, the mitochondrial DNA could be quite heterogeneous, or physically complex.

The genetic characterization of these petites was very valuable in ordering the genes on the mitochondrial genome. Much of this was accomplished by an extremely talented group of graduate students working in Murray's laboratory in the mid to late 1970s and early 1980s, including Richard Morimoto, Alfred Lewin, Joseph Locker, John C. Edwards, David Levens, James Casey, Michael Fauman, Paul Gordon (fellow), Janice Wettstein-Edwards, Thomas Christianson, Baruch Ticho, and Arthur Lustig. Several of these students were members of the Medical Scientist Training Program (MSTP) at the University of Chicago who gravitated to the laboratory.

A wide range of techniques were employed by Murray's research group, among them, DNA:RNA hybridization, DNA denaturation kinetics, the isolation of RNA initiation complexes, and the hybridization of mitochondrial DNA petite segments with charged (labeled) transfer RNA species. Using these techniques, they were able to develop a fairly comprehensive map and gene order for yeast mitochondrial genome. A particularly useful technique took advantage of the ability of guanylyl transferase derived from

vaccinia to in vitro label primary transcripts retaining their 5' polyphosphate ends. This enabled the laboratory to characterize sites of RNA transcriptional initiation.

Yeast mitochondrial DNA is different from the mitochondrial DNA of higher eukaryotes in several ways. Most eukaryotic mitochondrial DNA is enriched with the bases guanine (G) and cytosine (C), whereas yeast mitochondrial DNA is rich in the bases adenine (A) and thymine (T). Also, in contrast with the former, yeast mitochondrial DNA exhibits multiple sites of transcriptional initiation that each involve a highly conserved nonanucleotide promoter, which was defined through the work of some of the above named graduate students, as well as a few postdoctoral fellows, including Nancy Martin, Tapan Biswas, and David Mueller. The canonical promoter that they characterized is A/TA/T[aTATAa/g/cGTa/c] N at the G at the -2 position was critical and invariant; (note upper case letters refer to relatively highly conserved nucleotides; lower case letters refer to nucleotides that are not highly conserved; letters separated by / refer to alternate nucleotides at the same position; the square [ ] includes the nonanucleotide promoter from -8 to +1). Promoters may vary in strength, but strong promoters have purine/purine sequences at +2/+3 positions, while weak promoters have purine/pyrimidine dimers at these positions. Of course, rates of transcriptional initiation were shown to depend upon the strength of promoter sequences.

In summary, the researchers in Murray's laboratory used multiple studies and found that mitochondrial DNA encoded large ribosomal RNA(21S), small ribosomal RNA(14S), and 22 transfer RNA cistrons, and of course cytochrome b, cytochrome oxidase subunits, and ATPase subunit 9. Many of these originated from separate promoters, although there were some oligogenic transcripts: 21S–tRNAthr; Oxi-3-AAP-Oli-2; Oli-1–tRNAser–var; tRNAfmet-TSL; and tRNAglu-cyt b. The multiplicity of transcriptional start sites provides a mechanism for the yeast to differentially regulate the transcription of individual genes or subgroups of mitochondrial genes and hence to differentially influence the function of the mitochondria. This plasticity of transcriptional regulation is not readily available to mammalian mitochondria and cellular function.

Murray and Smilja Rabinowitz

Interestingly, Raj Nair, Murray's first fellow, had an influence on Murray's life that eclipsed any scientific contribution he made to their joint enterprise in the study of cardiac hypertrophy. He and Murray often went out for coffee after work. It was in this relaxed context that he learned of Murray's great love for music, especially Mozart and Bach.

Nair's wife, Sumi, was a pediatrician training in the human genetics section of the Children's Memorial Hospital, which was then affiliated with Northwestern University in Chicago. Working with her there was Smilja Jakovcic, a Croatian pediatrician, who had made no secret of her love of music—her brother, nephew, and niece are professional musicians. So Sumi and Raj Nair introduced Smilja to Murray, and the rest is history, as they say.

The couple shared great joy in fine music, but also in fine art, fine food, and a love of nature, as well as cordial friendships. They first met in 1961 and they married in 1963. Smilja Jakovcic had been working on inherited disorders of metabolism, particularly glucose and lipid metabolism, with David Hsia. At the time of her move to the University of Chicago, she was an assistant professor of pediatrics at Northwestern University. Her initial research at the University of Chicago, as a fellow in 1966 and 1967, was carried out in my laboratory, studying early mitochondrial development in the liver of growing rats, as well as the phospholipid markers of mitochondrial development in yeast, especially cardiolipin, that were subject to variations in genetic and metabolic context.

The detailing of scientific accomplishments is but a part of the story of Murray Rabinowitz. He was an intense, serious, and compassionate mentor. His reputation as such was widely recognized throughout the University of Chicago Division of Biological Sciences, which encompasses both clinical and basic science departments. Any member of the division may serve as a mentor for graduate students. Murray, who had appointments in the Medicine and Biochemistry departments, was a magnet for graduate students, based upon his known attentive and compassionate mentoring of students, many of whom came to be regarded as members of the Rabinowitz/Jakovcic family.

His twenty-seven graduate students were drawn from seven different departments, though most were from the Biochemistry and Biology departments. Hewson Swift, a loyal and much admired collaborator and colleague in the Biology Department, was undoubtedly responsible for referring biology students to Murray for their thesis work. Swift had an enduring interest in the "morphology" of organellar DNA. Students passed through Murray's laboratories, cramped though they were, and referred to him affectionately as "the Boss." Comments made by John Edwards at the memorial service held in Murray's honor speak to this:

> *And yet his talents as a scientist, indispensable as they were, were not the main reason that we believe that his lab was a very special place.*

Beyond that, we shared a joy which was our own unique interaction with our advisor. He had a talent for dealing with each of us as unique people, each with our strengths and weaknesses, devoting individual attention to us all. In his dealings with us he was always gracious and humane. His challenges and expectations were tremendous, but equaled by his confidence and support.

He humbled yet inspired us by the force of his personal example: his contagious enthusiasm; his persistence in achieving a job well done; his sheer joy in discovery; his intense interest in our results, being able to rejoice in success, and yet not censure us for our failures; and, most of all, his indomitable spirit in the face of what seemed to us to overwhelming adversity.

For each of these, and yet a thousand other things, he grew in our hearts and became for us a kind of personal hero. Whatever we were able to accomplish was as much for him as it was for ourselves.

As his physical disabilities progressed, Murray was unable to present his laboratory accomplishments at national and international meetings. His students became his voice. In preparation for these talks, each student was meticulously and repeatedly rehearsed by Murray and Smilja. As a result, the preparations were invariably well received. At one of these meetings, Jim Casey, then a graduate student and now a faculty member at Cornell University, was able to confidently stand his ground in the face of searching questions from Efraim Racker, who was then a professor at Cornell.

The Monday noon "lab meetings" in the Boss's office were the intellectual highlights of the week, not only for Murray and his students, but also for me. The twinkle in Murray's eye and his wry sense of humor added levity to these proceedings, which were complemented by end-of-the-day, one-on-one discussion of experimental results, to which Murray looked forward with keen commitment. In these impromptu discussions, he exercised his talents in extracting the best from his students and fellows, just as a sculptor fashions his material.

Also passing through the laboratory were thirty-seven fellows drawn from local departments and many countries, including Australia, Czechoslovakia, India, Israel, Japan, Poland, Spain, and South Africa. The last was represented by David Friedman (cloning of muscle proteins) and Arthur Rubenstein, who spent his first year in the United States in

Murray's laboratory, where, as he explained at Murray's memorial service on October 21, 1983, he came to "appreciate Murray's breadth and depth of knowledge, about all aspects of research, and the fierce loyalty of everyone who worked for him…What gave him pleasure was the challenge of scientific discovery, the beauty of rigorous experiments, the give and take about the interpretation of results, and the intellectual stimulation which each new study afforded. He reveled in competing with the best, but was always generous in his praise of excellence in others."

One cannot discourse on the life of Murray and Smilja without recognizing their pleasure in life beyond science—in music, good food, natural beauty, good conversation, and even good football. Much of this was experienced in their house by Lake Michigan, where they enjoyed the water, the sun and its setting, and the singing of the birds, about which they became quite knowledgeable. This house was an indispensable part of their lives. It was here that they relaxed for a month each summer during the last ten years of Murray's life. This period of relaxation was a tonic for him, and afterward, he returned to work tanned and rejuvenated.

Often the laboratory family was invited to join Murray and Smilja for a day in the water and sun. Also, scientific colleagues, including myself, were guests for relaxed gossip and conversation, as well as their generous hospitality. One memorable occasion involved a discourse by Piotr Slonimski on the history of yeast petites while making ratatouille.

Life was a complicated business for Murray and Smilja. Despite this, he never lost his spirited enthusiasm and his sense of humor. Murray endured his advancing illness with relative tranquility and incredible freedom from bitterness. But this would not have happened without the love, commitment, courage, and unsparing energy of Smilja. Almost single-handedly, she gave him his life, his mobility, flexibility, and ability to carry on the work to which he was devoted. She did almost everything for him. Yet, when asked about the intensity of this burden, she exclaimed that their love and devotion greatly lightened her responsibilities.

One major legacy of a distinguished scientist rests with the works and accomplishments of his trainees. In Murray's case, twenty of the graduate students and fellows who once worked in his lab now hold academic positions, many of them as full professors, while seven are very active and leading biomedical companies.

A year after Murray's death, a memorial symposium was held in his honor at the University of Chicago. It was titled, "The genetics of yeast and its mitochondria." Speakers were Gerald Fink, Ronald Davis, Edward Scolnick, David Botstein, and on the topic of mitochondria, Alex Tzagoloff, Gunter Blobel, Guiseppe Attardi, and Gottfried Schatz. The Rabinowitz alumni assembled for a second symposium in November 2007, almost twenty-five years after Murray's death, this time at Northwestern University, where Murray's former graduate student Rick Morimoto, now a member of the American Academy of Arts and Sciences, is a distinguished professor and leader. All attendees were generous in the recognition of the enormous influence Murray and Smilja had on their scientific and personal lives.

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