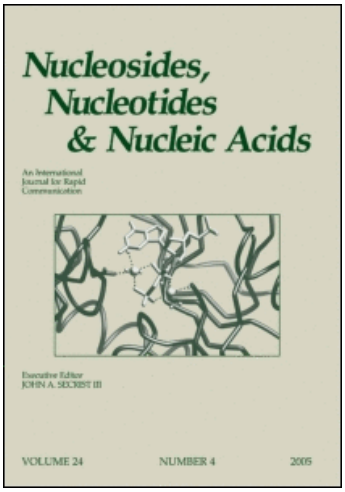

Nucleosides, Nucleotides and Nucleic Acids
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597286

John A. Montgomery, March 29, 1924-May 24, 2004

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To cite this Article Secrist, Jack(2005) 'John A. Montgomery, March 29, 1924-May 24, 2004', Nucleosides, Nucleotides and Nucleic Acids, 24: 10, 1387 — 1394
To link to this Article: DOI: 10.1080/15257770500482340
URL: http://dx.doi.org/10.1080/15257770500482340

Nucleosides, Nucleotides, and Nucleic Acids, 24:1387–1394, 2005

ISSN: 1525-7770 print/1532-2335 online
DOI: 10.1080/15257770500482340

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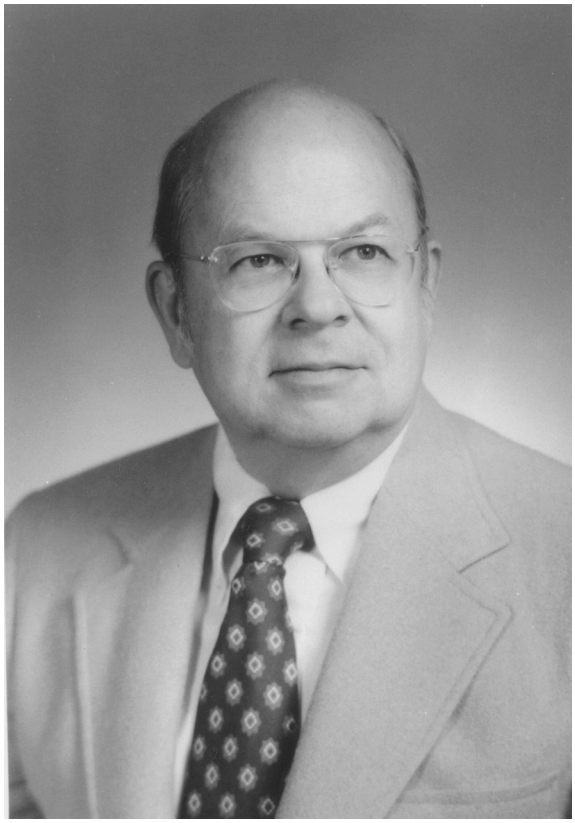

This issue of *Nucleosides, Nucleotides & Nucleic Acids* is dedicated to John Montgomery, who made major contributions to the areas of science covered by the journal. Those of us who had the pleasure of both knowing and collaborating with John over many years feel truly fortunate. Through his scientific interactions he gained friends and colleagues around the world, and that group of scientists will particularly feel his loss. The paragraphs that follow provide some information on John's illustrious career.

John was born in Greenville, Mississippi, a small town along the Mississippi River where his father was a leading physician. He attended Woodberry Forest School in Virginia, and received both B.A. (1946) and M.S. (1947) degrees from Vanderbilt University. He then attended the University of North Carolina, where he received a Ph.D. in organic chemistry in 1952. John and Jean Montgomery were married in 1947, and had four children, John, Elaine, Kirk, and Adrianne. Jean continues to live at their residence in Birmingham, Alabama.

John's career in research actually began at Vanderbilt University, where his M.S. thesis research work involved an investigation of "The Reductive Alkylation of Aromatic Amines with Noval Ketone." Today, not many of us know about noval ketone (5-diethylamino-2-pentanone), but it was well known years ago, and was a component of some antimalarial drugs. John's Ph.D. research, under the direction of Arthur Roe, was entitled "A Study of Schiff Bases." He also performed postdoctoral research with Dr. Roe on the synthesis of certain fluorine-containing heterocyclic compounds. It seems likely that his interest in the potential value of incorporating fluorine into biologically active compounds developed during this period.

In 1952, John joined the staff of a young and small group of scientists at Southern Research Institute. Interestingly, when John was completing his M.S. degree at Vanderbilt, he visited Southern Research Institute to apply for a job. The director at the time told him that if he had a desire to advance in science that he should obtain a Ph.D. before starting his career. It was because of this conversation that John went to the University of North Carolina. As the Institute grew, John's talents were recognized, and within a few years, he was appointed Director of the Organic Chemistry Research Department. Eventually, he became Vice President and later Senior Vice President, which was his title when he retired.

By the late 1940s, Southern had begun a move toward cancer research, and by the mid 1950s, a team had been assembled that included Howard Skipper, L. Lee Bennett, Frank Schabel, and John Montgomery. This team led the cancer research effort for many years, and was responsible for major advances in the area, including the discovery and development of a series of FDA-approved anticancer drugs. The concept of using drug combinations to more effectively eradicate all tumor cells was also demonstrated in animal models by this team, and was adopted by clinicians all over the world based

John Montgomery in the 1960s.

upon our data. John's role was, of course, focused on medicinal chemistry, and he made major contributions to cancer chemotherapy with a focus on purines, nucleosides, folates and alkylating agents.

John's scientific career is best reflected in his body of publications and presentations. He was an author on 450 publications, with a few more yet to come. He was an author on approximately 50 book chapters and an inventor on many patents. In addition to his major efforts devoted to cancer research, John was involved with antiviral, antibacterial and antiparasitic drug discovery. Though much of his work involved purines and purine nucleosides, he worked on many different heterocyclic systems during his career, and also occasionally on carbohydrates. He contributed not only many new compounds, but also some research on new methodology and mechanistic considerations.

John's focus was clearly the discovery of new anticancer drugs. One of his great strengths was the ability to digest all of the relevant biological knowledge and to use that information for drug design. Between John Montgomery and Lee Bennett, they knew just about everything that had ever been done of relevance to the development of new nucleosides as anticancer drugs. John was an invited lecturer on cancer chemotherapy throughout his career at meetings all over the world. He truly enjoyed interacting with other scientists, and he had friends and colleagues around the world with whom he corresponded and collaborated.

In assessing John's multitude of accomplishments, I believe that the greatest of these lies in the discovery of new anticancer agents that have

John Montgomery in the 1970s.

been and continue to be used for the treatment of cancer patients. John's record of discovery in the anticancer field is unlikely to ever be surpassed by future scientists. He was an inventor on five FDA-approved drugs used in the treatment of cancer. These are carmustine, lomustine, dacarbazine, fludarabine and clofarabine. Though he rarely mentioned it, I know that he derived great satisfaction from the contributions these drugs made to the lives of many cancer patients.

In addition to his efforts in scientific research, John spent a great deal of time participating in other professional activities. He was for many years a tour speaker for the American Chemical Society. He also served that organization in many other ways, including organizing symposia, overseeing regional meetings held in Birmingham, AL, serving on various committees, and serving as an elected Councilor for the Medicinal Chemistry Division of ACS. John served on many National Institutes of Health study sections during his career, as well as on other review bodies. He was a consultant and adviser to both companies and foundations, including serving on the Board of Scientific Consultants for the Sloan-Kettering Institute for Cancer Research, the Pharmacology Advisory Committee for M. D. Anderson Hospital and Tumor Institute, and on the National Advisory Committee for the Wesley Foundation Scholar Program in Cancer Research. John served two terms on the President's Cancer Panel from 1983–1991, serving with Vincent DeVita, Armand Hammer, and William Longmire. John served on the steering committee of the Onchocerciasis Chemotherapy Project of the World Health Organization during the early 1980s. Together with Nelson J. Leonard and George B. Brown, John was involved in the organization

The President's Cancer Panel: William Longmire, Vince DeVita, Armand Hammer, John Montgomery, ca. 1984.

of the first Gordon Research Conference on Purines, Pyrimidines and Related Substances, which was held in 1976. This conference still continues today but with a recent name change to the Nucleosides, Nucleotides and Oligonucleotides conference. These activities are merely representative of many others in which John Montgomery participated.

John served on many journal editorial advisory boards, beginning in the 1960s. The list of journals includes the *Journal of Heterocyclic Chemistry*, *Journal of Medicinal Chemistry*, *Cancer Research*, *Cancer Treatment Reports*, *Journal of Organic Chemistry*, *Nucleosides & Nucleotides*, *Anticancer Drug Design*, *Pteridines*, *Antiviral Research*, *International Journal of Purine and Pyrimidine Research*, and *Heterocyclic Communications*.

As a result of his scientific efforts, John was honored with a number of awards during his career. These include the Herty Medal (1974), the Taito O. Soine Memorial Award from the University of Minnesota (1979), the Southern Chemist Award (1980), the Cain Memorial Award of the American Association for Cancer Research (1982), the Alfred Burger Award in Medicinal Chemistry of the American Chemical Society (1986), The Madison Marshall Award (1986), and the Edward E. Smissman Bristol-Myers Squibb Award of the American Chemical Society (1995).

In 1990, John retired from Southern Research Institute, but definitely not from science. He was a co-founder of a now public company, BioCryst, Inc., based in Birmingham, AL, and he transitioned to full-time activities at BioCryst at that time. He was instrumental in guiding the scientific

directions of the company, and achieved the same high regard from its staff as he had at Southern. During many of these years he also was able to join our weekly research meetings at Southern. In his later years he reduced his efforts to part-time at BioCryst, and he continued to be active until health problems curtailed his ability to participate to the level he wished.

It is difficult to adequately summarize a scientific career with the impact that John Montgomery's had, but even what has been presented briefly here provides a measure of his contributions. Beyond the impact that he has had on scientists around the world, his efforts will live on permanently through the record of his publications. It is clear that his career indeed made the world a better place, and we can celebrate that fact.

PERSONAL RECOLLECTIONS

I first met John Montgomery at a meeting of contractors supported by the Walter Reed Army Institute of Research in 1978. He made a very positive impression on me at that time, and by the end of the following year I had joined the team. John and the other senior scientists mentioned earlier had put together a system for iterative drug discovery that still is largely in place today. The focus was always on finding promising compounds, and not spending time on the others. Thus, John always would say that we need to let the data guide us as we moved forward. In that regard, we have always looked for robust biological data, because systems that make compounds look better than they are will only delay the discovery process. This approach is, of course, used by companies routinely, and we continue to use it to guide our research today.

As I mentioned, John had friends and colleagues around the world, and he was very quick to recognize who might be a collaborator of value to the program. In that regard he did not hesitate to collaborate with younger scientists that he recognized as outstanding. Their names can be seen in his publication list. Similarly, he was quick to pick up on new techniques that could make the research effort more efficient. Thus, he was always in favor of buying the latest instrumentation, whether it was nmr equipment back in the 1960s or combinatorial chemistry equipment in the 1990s.

One of John's pleasures was dining at fine restaurants, and he always tried to arrange meals at these locations when he was attending meetings. Thus, I was introduced to many excellent establishments during our joint travels, and I have picked up this enjoyable habit myself. John would regularly arrange for a group meal at a nice restaurant for Southern personnel in attendance at an AACR or ACS meeting. Unsuspecting staff members who were significantly more frugal than John would carefully order meals and drinks only to discover to their chagrin that the check was

Jean and John Montgomery, Orange Beach, Alabama, 1988.

divided up equally at the end of the evening! These events generated many funny stories over the years.

For many years John and I spent long hours discussing medicinal chemistry, biological data, and drug discovery. Most of that time was spent with him teaching and me learning. He was very willing to impart his knowledge, and in the process we came up with many ideas, including the compound that is now known as clofarabine. These sessions were often toward the end of the day, and would drag on into the evening. It is fortunate that both of our wives had great patience during those years. In a similar vein, John recognized the value of getting our research published, and he would arrange for all of us to drop what we were doing to ensure that manuscripts were properly prepared and submitted in a timely manner. In these respects and many others, John was an outstanding mentor and a great colleague.

Jean Montgomery was always a great supporter of John's efforts and an enthusiastic traveler to many locations around the world. She accompanied John on most of his travels, and always had a great time. Even though their children are spread around the country, they always managed to get together during the year-end holiday season. These gatherings were anticipated by John with great enthusiasm, as all of us close to him could see. It was obvious that the entire family had a great time together.

Among John's great pleasures were listening to jazz music, sailing, and reading good literature. He had an extensive collection of records and CDs, and it gave him much enjoyment. During our trips to New Orleans, he would always arrange to see Pete Fountain or others perform, and he was always an enthusiastic member of the audience. Visits to the Montgomery residence would often include listening to and discussing jazz and jazz musicians.

At Gordon Research Conferences John was a regular participant in afternoon sailing expeditions, both on Lake Winnipesaukee and on Narragansett Bay. For many years the Montgomery's had their own sail boat, which was used on Lake Martin.

As noted in the first paragraph, John was born and raised in the southern part of the United States. He truly was what is known as a southern gentleman. He was always polite, pleasant and responsive. In general, he kept adverse opinions to himself in formal situations unless his input was specifically requested. Informally, of course, he was much more willing to make his views known. It generally turned out as no surprise to those of us who knew him that his opinions were often quite strong. I always marveled at the restraint that he showed in certain situations—it is a trait that more of us should have!

My own relationship with John became very close over the years. He taught me a lot about science and other topics. His influence on me, as well as on many others, continues today, and has been a very positive force in our lives. John was a wonderful colleague and a great friend, and his loss is felt very keenly by many of us.

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