

John Gergely (1919–2013): a pillar in the muscle protein field

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Abstract Dr. John Gergely passed away on July 26, 2013 after a long and distinguished career. His publications spanned 67 years. He founded the Department of Muscle Research in the Retina Foundation (which later became the Boston Biomedical Research Institute) and served as director for 34 years. Dr. Gergely served on the editorial boards of ten scientific journals. He was elected as a Fellow of both the Biophysical Society and the American Association for the Advancement of Science. Dr. Gergely made major contributions concerning muscle protein structure and function. He was best known for his work on the troponin complex. The insights of John and his associates have provided the foundation for our understanding of calcium regulation in skeletal and cardiac muscle.

Keywords Troponin · Tropomyosin · Myosin, calcium regulation of muscle contraction

Personal and professional history

Dr. John Gergely (MD; PhD) was born on May 15, 1919 and died surrounded by his family on July 26, 2013. He was born and raised in Budapest, Hungary and received his MD degree from the University of Budapest in 1942. He was appointed an Assistant Professor of Pharmacology at the same institution from 1942 to 1945. It was there, in the Biochemistry Department, that he met his mentor and friend Dr. Albert Szent-Gyorgyi. From Budapest John moved to the University of Leeds where he studied the quantum aspects of biochemical structures, receiving his PhD in 1948. A two-year fellowship at the National Institutes of Health in Bethesda, Maryland was his next stop, following Dr. Szent-Gyorgyi who already had an appointment there. John summarized his association with Albert in an extensive interview available at <http://profiles.nlm.nih.gov/ps/access/WGBBLS.pdf>. John then spent one year at the University of Wisconsin-Madison as a National Heart Institute Senior Trainee working with Dr. David Green in the Enzyme Institute. In September 1950 the family moved to Massachusetts where John assumed an appointment at the Massachusetts General Hospital, funded by an Established Investigatorship from the American Heart Association. He subsequently obtained a concurrent appointment as Associate Professor in the Department of Biological Chemistry and Molecular Pharmacology at Harvard Medical School. In 1961 he founded the Department of Muscle Research in the Retina Foundation, a new Institute created by Dr. Endre “Bandi” Balazs, his boyhood friend from Budapest, and Dr. Charles Schepens. The Muscle

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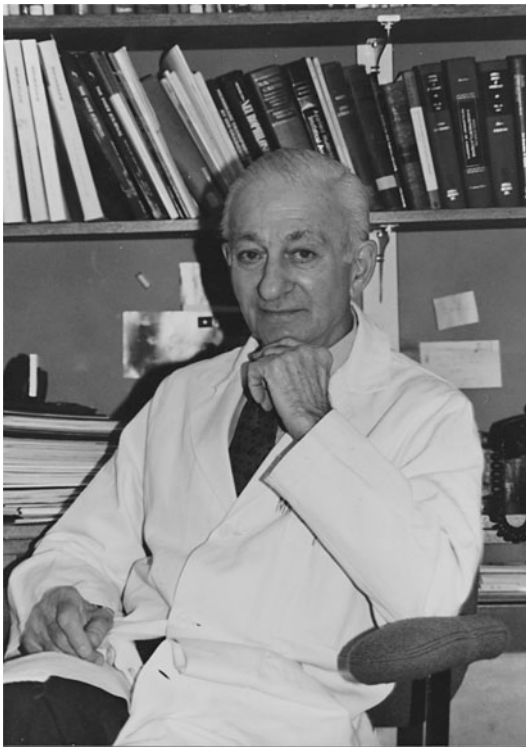


Fig. 1 A photograph of John Gergely in his Boston Biomedical Research Institute office on Staniford Street in Boston, Massachusetts. A white lab coat was his usual attire. The photo was taken about 1980

Department subsequently became part of the Boston Biomedical Research Institute in 1970, and John served as its director until semi-retiring in 1995. He remained active as a BBRI Board of Trustees member until February 2013 when the Institute closed due to shortage of funding (Fig. 1).

John married Nora Czoboly in 1944 and they had eight children (Sophia, Katherine, Julia, John Jr., Martha, Peter, Andrew, and Anna). John settled in Nahant, Massachusetts in 1951, and remained there the rest of his life. He enjoyed skiing, sailing, tennis, music, and art, and he imparted a true joy of learning to his children and grandchildren. He continued these activities into his late eighties. He loved the challenges of Manchester Guardian crossword puzzles, Sudoku, studying and discussing linguistics, politics, and religion. John took great pleasure in the art of debate and in solving math problems. He was an active member and leader on the Council of the Clifton Lutheran Church (Marblehead, MA) where he served as a lay worship assistant for many years.

Scientific contributions and professional honors

John Gergely and his co-authors published 176 refereed journal articles between 1941 and 2008. In addition he

published 63 book chapters and monographs. His first major finding was the observation that myosin could be mildly digested with trypsin but still retain its enzymatic activity (Gergely 1950, 1953). This work was extended by Szent-Gyorgyi (1953) who termed the major proteolytic fragments heavy meromyosin and light meromyosin. A series of major papers on the metal and nucleotide binding properties of actin followed in the 1960s. His work with John (Jack) Seidel and David Thomas pioneered use of spin-labeling techniques to probe the structure of myosin (Seidel et al. 1970; Thomas et al. 1975).

In 1971 John published the classic paper on the subunit structure of troponin with his postdoctoral fellow Marion Greaser (Greaser and Gergely 1971), and the studies on the structure and function of this protein and its subunits, including the naming of the subunits, Troponin C, Troponin I, and Troponin T (Greaser and Gergely 1973), would remain the central focus for the remainder of his research career. The calcium and magnesium binding properties of TnC and the troponin complex (Potter and Gergely 1974, 1975) were next established. Subsequent work using a multitude of spectroscopic (Leavis et al. 1978; Wang et al. 1982) and cross-linking (Leszyk et al. 1990; Grabarek et al. 1990; Luo et al. 2000) techniques have provided the foundation for our current understanding of the protein structural changes in the calcium control of muscle contraction.

Major contributions were also made to our understanding of tissue and fiber type differences in myosin light chains (Sarkar et al. 1971) and in myosin during muscle development (Sréter et al. 1975). In addition, John also collaborated with Noriaki Ikemoto on several papers related to the structure and function of the sarcoplasmic reticulum (see, for example, Ikemoto et al. 1974).

In recognition of his special knowledge and skills, John served on the editorials boards of more than ten different journals, including a 3-year term as editor of the *Biophysical Journal*. He was a member of numerous study sections and provided consultation advice for the National Institutes of Health. Honors included an Established Investigatorship from the American Heart Association, a Merit Award from the National Heart, Lung, and Blood Institute, an honorary Doctor of Medicine from the Semmelweis University Medical School, Budapest, and an elected Fellow of both the Biophysical Society and the American Association for the Advancement of Science.

Personal memories

Following are a collection of personal memories about John from several scientists who John trained or collaborated with.

Marion Greaser, Emeritus Professor, University of Wisconsin-Madison, Madison, Wisconsin

I arrived in Boston for an NIH Postdoctoral fellowship in October of 1968. At that time John had a talented group of scientists working in his department. Most of them were focused on the properties of myosin and actin. We decided to forge off in a new direction and study the properties of the new protein called troponin that had recently been discovered by Prof. Setsuro Ebashi in Japan. We were successful in separating troponin's three subunits and reconstituting the functional complex using an ATPase assay. I can vividly remember John's reaction when I first showed him the data—he was complimentary but extremely cautious and careful, and had several suggestions on ways to solidify the conclusions. This caution in data interpretation was a valuable lesson that I have carried with me throughout my scientific career.

I also have etched in my memory how rapidly John's mind worked; it processed information so rapidly that his speech often couldn't keep up. His penetrating gaze during conversations could also be intimidating until you got to know him. John had a brilliant grasp of many scientific fields (physics, mathematics, chemistry, biochemistry, etc.), and this willingness and ability to seamlessly combine these various fields led to many successes throughout his career. He was an inspiration to all of us that had the opportunity to work with him.

Jim Potter, Emeritus Professor, University of Miami Miller School of Medicine, Miami, Florida

When I was finishing my PhD in Biochemistry in 1970 at the University of Connecticut studying tropomyosin expression during muscle development, I started looking for a good muscle research lab for a Postdoctoral position. I decided to leave the muscle development field, and pursue a more biophysical approach to learn more about how tropomyosin and the newly discovered protein troponin controlled muscle contraction. Several opportunities presented themselves but in the end I chose John Gergely's lab because I thought the Muscle Research Department at the BBRI offered tremendous opportunities for my future development. At the time, the Department had many outstanding muscle researchers to interact with, e.g., Marion Greaser, Jack Seidel, John Collins, Marshall Elzinga, Noriaki Ikemoto, Fred Julian, Sam Lehrer, Bela Nagy, Frank Sreter and many visitors to the lab, e.g., Witold Drabikowski as well. Thus, I accepted John's offer to join the BBRI.

Upon arrival at John's lab, I was introduced to Marion Greaser, who had done outstanding work on troponin and showed conclusively that it contained three subunits, not

one or two as was suggested by other labs at the time. Marion and John suggested that I study the calcium binding properties of one of the subunits, troponin C. I had no idea how to do this and after many attempts at different techniques, came up with an excellent method utilizing equilibrium dialysis and calcium chelators and, as they say, the rest is history. This work exemplified John's amazing capabilities and taught me the importance of objectively analyzing data. This was before the days of the PC or even a simple math hand-held calculator, but John was at the forefront of computational capabilities at the time, utilizing a telephone connection to a remote computer at Harvard. We would enter the data via ticker tape (some taken directly from a scintillation counter) and this would be processed using programs John had developed. He had also developed programs to calculate free calcium concentrations, variants of which are still used today. John was the consummate editor of manuscripts and I know of at least one that we wrote that went through seven revisions!!! And all this without word processing, just red marked hand typed copies! But, this was important training for not just me, but for all who passed through his department. John always insisted on excellence in everything and this has carried over into all aspects of my life. John was a giant in the muscle field and unfortunately with his loss, it is the end of an era in muscle research. I will be forever grateful for the wonderful and exhilarating times I spent with John at the BBRI.

David D. Thomas, Professor, Department of Biochemistry, University of Minnesota, Minneapolis, Minnesota

One of the most important measures of a scientist is the number of scientists they train and inspire. I can't begin to count the number of young scientists that John Gergely advised, many of whom are now leaders in muscle research. This was partly due to his scientific brilliance, but even more to his generosity, his selflessness, his empathy. We are all so lucky to have been inspired and encouraged by John.

John Gergely was a great mentor and friend to me. I met him in 1972 when I was a first-year grad student, attending my first scientific meeting—the International Biophysics Congress in New York. I was a physicist, developing new magnetic resonance techniques for studying large molecules, but not too sure where to apply it. John saw right away that myosin was the perfect system for me. He and Jack Seidel had already been spin-labeling myosin, so they mailed me the samples I used for my PhD thesis. So it was a natural that I joined John and Jack at the BBRI for a postdoc. Without even telling me, John ordered the very first of a new generation of EPR spectrometers that was

based on my PhD work. It arrived in Boston a week after I did, and I never turned it off for the next 2 years. It was a very productive 2 years. John was not a schmoozer, and he was famous for being quite inarticulate in conversation, but his intellect was impressive—he could synthesize so many disparate ideas and concepts and technologies into a coherent research plan, and I have carried his influence throughout my career. On the personal side, he was very generous. My favorite non-scientific adventure with John was a sailing trip. The Tall Ships (several hundred giant sailing ships of 18th and 19th century vintage) appeared in the summer of 1976 to help celebrate the Bicentennial. John suggested that we join them. So we drove to his home at Nahant on the coast north of Boston, got into his TINY sailboat, and sailed off to see the ships. The seas were rough that day, and we barely survived the wakes from those big ships, but although John was an able skipper, I vowed to stay in the lab after that where it was much safer. I will always cherish John's mentoring and his friendship.

Gale Strasburg, Professor, Department of Food Science and Human Nutrition, Michigan State University, East Lansing, Michigan

John Gergely was the reason I came to BBRI in 1981 to begin my postdoctoral work. But it was not only to work with John, whom I regarded as one of the titans of muscle research, but it was also to join the scientific community that he was largely responsible for creating at BBRI. A community that included eminent, established scientists in the muscle field including Jack Seidel, Satu Sarkar, Sam Lehrer, Paul Leavis, Noriaki Ikemoto, Walter Stafford, Fred Julian, as well as a talented new generation of post-doctoral fellows and new investigators including Zenek Grabarek, Phil Graceffa, Renne Lu, Terry Scott, Terry Tao, and Albert Wang. John was largely responsible for fostering an environment where people wanted not only to join, but also to stay, despite the pressures of generating their salaries from grants. I learned a great deal from my interactions with John and a significant part of my career success stems from Boston training. I'll never forget the 3 years I spent at the BBRI, or the people with whom I worked.

Sam Lehrer, Senior Scientist Emeritus, Boston Biomedical Research Institute, Boston, Massachusetts

John was a many-faceted person with multiple talents. He was first a mentor, particularly for those writing scientific grant proposals and journal articles. His post-docs and collaborators will remember long hours sitting at his desk discussing his red mark edits on their first drafts. Many versions got the same treatment which illustrated the

proverb that “no piece of writing is ever finished”. His English was the King's English that he learned in Hungary along with Latin before practicing it in England. Despite the apparent tediousness of the process, it was quite useful, particularly for the post-docs from abroad—they learned English writing in addition to clear scientific writing lessons. John tutored me on my first NIH grant proposal written 6 months before I arrived at BBRI, so when the grant was awarded soon after my arrival, I had my salary. He was the mentor to many visiting post-docs and collaborators from all over the world: Hungary, Poland, Czech Republic, England, Russia, Japan, Taiwan, and to some he was helpful in obtaining residency and citizenship.

His knowledge seemed to be endless. When apropos, he would quote Latin sayings and expect us to understand them. Or he would tell us of the interesting Hungarian word that was different from the Polish or the German that was being used. He was particularly gifted in mathematics to the extent that he sent in corrections to equations that he noted in scientific articles. Or, he would pose a math problem for us to solve and leave it on the blackboard until we gave up. He was not afraid of using computers, even the early ones that required punch cards. I remember his help in extrapolating data which I used in a review article with a program that he devised.

Owing to his medical school education, he was often called upon to advise a person with a medical problem or an emergency, and helped even though he had no clinical experience. John was a hard worker and expected similar diligence from others. He was in early, left late and came in on Saturday. He expected similar time spent from all. But he learned that some of us needed flexibility because we did not have a wife like Nora who took care of family and house.

John was an old world scholar who evolved in his policies and ideas as BBRI matured and grew to house more investigators with grants. He was active in providing advice to all during his frequent visits to his office up to the last months of BBRI's existence which eventually suffered the fate of many basic research programs caused by cut-backs in government spending. He was happy in the knowledge that several of his associates obtained research positions in neighboring institutions. In their positions they will be continuing some of the useful traditions and approaches that were influenced or instilled by John.

Albert Wang, Department of Physiology and Biophysics, Boston University School of Medicine, Boston, Massachusetts

John was not only my mentor, but also like a father to me; he also treated me almost like his own son, in addition to one of his colleagues. Several years ago he invited my wife

and me to their Nahant home on a beautiful autumn afternoon. He took me for a sailboat ride, while my wife chatted with Nora. Since I had never sailed before, he painstakingly explained every procedure to me as he maneuvered the boom. We went quite far offshore and only turned back when the water became really choppy. Later he kept on saying we should go sailing more often, but we never did it again.

John had a very organized way of thinking, although his office was always cluttered. I learned from him to make a table whenever there were multiple variables to consider. When I was a postdoctoral fellow with John, we used to write manuscripts together. That is, I wrote the first draft and went over it with him, typically in the afternoon. He would use a red pen to mark the changes. He taught me how to use “viz.” and “owing to” (rather than “due to”), and he hated redundant or ambiguous adjectives. He also told jokes to illustrate his point. We would go on till well past 6 pm when I became antsy for being late to pick up my daughter from the day care. We would repeat this process many, many times, until finally he began to correct his own writing or got tired of seeing it again. With this kind of internal scrutiny, our manuscripts were often accepted without the need of revision. John also facilitated many of my extramural collaborations. It was he who paid for my first trip to meet with Joe Bryan in Texas that eventually led to a 15-year program project grant.

John was a modest person, perhaps because he was very critical of himself, much more so than of others. He applied high standards to his students and post-doctoral fellows as well. He would not approve any act of self-promotion. Instead, he kept us doing solid work, which eventually brought about recognition. He believed that a true leader should be “the first among equals with his leadership”, BBRI became like a law firm, with each principal investigator as a partner. After his retirement, John remained a regular faculty member.

I was always envious of John’s good health. Compared with my own father, who is about the same age as his, John looked so youthful and energetic. Besides jogging and skiing during conferences, John also exercised regularly in the institute gym. He and I both preferred using the elliptical trainer in late afternoons, so we often ran into each other. Only during the past year did age finally catch up with him and he stopped the routine workouts. After BBRI closed, he came to visit my lab at Boston University, and I am so glad he did. That was the last time I saw him.

Zenon Grabarek, Department of Molecular Biology,
Massachusetts General Hospital, Boston, Massachusetts

Dr. John Gergely had a profound role in my research career and in the life of my family. He was the reason why I came to

Boston from Warsaw. The most valuable skills I have learned from John during my many years of working with him were rigorous, logical thinking and critical analysis of experiments. In the late seventies the Muscle Research Department at BBRI created by John was a vibrant, intellectually stimulating, and internationally famous research center. It was the place to go if you were serious about muscle research. Indeed, post-docs from all around the world were coming to BBRI to study muscle biochemistry and to obtain top rate training in biophysics. The mechanism of calcium dependent thin filament regulation was the hot topic that was studied with great intensity at BBRI at that time.

I was introduced to John at the European Muscle Club in Warsaw in 1978 by my PhD thesis advisor Prof. Witold Drabikowski, who himself had forged a friendship with John a decade earlier. There was an ongoing collaboration between the two laboratories and the TnC peptides that I prepared in Warsaw have already made the trip across the Atlantic on more than one occasion. My going to Boston was inevitable. When I arrived in Boston with my wife and two children in October 1979 my MDA postdoctoral fellowship awarded just a few months earlier was waiting for me in the form of a check for \$13,500, which John handed to me. That was my complete first year salary and an equivalent of about 30 years of the graduate student pay I was receiving in Warsaw. Suddenly, I felt very rich. Luckily, John understood perfectly well how long that money would last. So, a week later he asked when my wife, who had a PhD in chemistry, would show up for work. That was his way of making a formal offer of employment and, of course, a great help to our family, which we were happy to accept. This, very low key, yet highly sensitive and perceptive way was very characteristic of John and we experienced it later on several occasions.

John was a very humble person despite the well-deserved fame and broad recognition. The philosophy that he followed and tried to instill in his students was that the scientist’s work should speak for itself. He despised any form of self-promotion. He was very critical of himself and of his students, a characteristic most apparent at the time of writing a manuscript. His leadership style as the Director of BBRI was honest and straightforward. Getting a semi-positive head nodding from John was a perfectly valid form of endorsement in any official business. It was very difficult for John to witness the gradual collapse of the BBRI in recent years.

He was very concerned about the future of the BBRI scientists and, despite his declining health; he wanted to know about every detail of our situation after the institute closed. John always had a positive outlook concerning people and events. He summed up the BBRI dissolution with his philosophical: “*Tempora mutantur, nos et mutamur in illis*”, meaning “*Times change, and we change with them*”.

We will all miss this pillar of the muscle field.

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