Gone but not Forgotten

In memoriam of those muscle researchers who have gone since the last EMC meeting in Canterbury in September 2019

John M. Squire (†January 31, 2021)

Professor John Michael Squire, 1945-2021

John Squire, Professor of Structural Biophysics in the University of London and Visiting Professor at Imperial College London, was one of the leading scientists in the field of muscle contraction. Understanding the mechanism of muscular contraction at the molecular level has required expertise from all fields of science and John Squire was an exemplar physicist who made fundamental contributions towards this goal. He was cruelly snatched from our midst earlier this year by Covid-19. He was 75 and still actively contributing to science.

John Squire in early 2000 showing his model of thin filament with tropomyosin and troponin (photo by Pradeep Luther)

John Squire's reputation in the muscle community was initially due to his 700-page monograph "Structural Basis of Muscular Contraction". This comprehensive exposé covers structural analysis methods like X-ray diffraction and electron microscopy, describes the main components of muscle, the myosin and actin filaments and discusses the then current ideas on the molecular events during contraction. Though written in 1981, prior to some major discoveries in muscle like crystal structures of actin and myosin S1, it has remained the go-to bible for many researchers. Throughout his career John wrote several clear and detailed reviews which were highly cited. John's grasp of the field saw him writing News & Views and Commentaries for various journals. John was an active participant at muscle conferences, giving insightful contributions and helping to clarify theoretical issues.

John made many significant contributions to muscle research. Here are just two. In 1973, following analysis of X-ray diffraction patterns of muscle, he proposed, together with David Parry, the steric blocking mechanism for muscle contraction. Early in his career, he proposed a general model for the packing of myosin molecules into all types of myosin-containing filament. This has been verified for the consequent myosin filament symmetry for various muscles. Very recently the backbone packing hypothesis was verified spectacularly by cryo-EM analysis of insect flight muscle thick filaments by the group of Ken Taylor.

Most of all, John was friendly and approachable. He will be sorely missed by all his past PhD students, associates and collaborators. He is survived by his wife, Melanie, and their four daughters and ten grandchildren.

(by Pradeep Luther, Imperial College London)

Hanna Strzelecka-Gołaszewska (†April 13, 2020)


Hanna Strzelecka-Gołaszewska in 2005 (J. Redowicz's archive)

Studies on actin and myosin were her passion and joy.

Professor Strzelecka-Gołaszewska, or Hanka for those who knew her well, died suddenly on April 13th, 2020. She was a muscle biochemist, widely recognized for her research on contractile proteins, actin and myosin. Born in Lviv (now Ukraine), she moved with her parents to Warsaw, where she survived World War II and the Warsaw Uprising. During the difficult post-war times, she received the solid education and graduated from the University of Warsaw, Faculty of Natural Sciences. Already at this early stage of her scientific career, she became interested in muscle proteins. Her master thesis concerned nucleotide binding to muscle proteins and it was inspired by Prof. Włodzimierz Niemierko, the head of the Department of Biochemistry at the

Nencki Institute of Experimental Biology and the Department of Animal Physiology at the University of Warsaw. Since then, Hanka became a prominent member of the muscle community and was associated with Nencki Institute for the rest of her life. Her doctoral thesis entitled: "Studies on binding of ATP, Ca2+ and other divalent cations to G-actin" was written under supervision of Dr. Witold Drabikowski, the founder of the Polish school of muscle biochemistry.

After receiving the Ph.D. degree (in 1965), she spent two years in the laboratory of Dr. John Gergely in Boston Biomedical Research Institute (at that time Department of Muscle Research at the Retina Foundation), where she continued her research on the structural an functional importance cation and nucleotide binding to actin. Her exceptionally meticulous and detailed analyses led her later to the discovery of cation- and nucleotide-dependent conformational changes in the DNase I-binding loop, which are crucial for stabilization of the actin filament. Functionality of these changes were later confirmed by crystallographic studies as to be fundamental for stabilization of the actin filament. Although actin has always remained at the center of her scientific interests, Hanka also included myosin in her research. She investigated the enzymatic properties of myosin, showed the differences between myosin isoforms found in slow and fast skeletal muscles and conformational changes occurring in the myosin head during contraction. She has published over 60 articles and 3 book chapters; she co-edited two scientific monographs. For more than 30 years, she was a group leader and mentor of ten Ph.D. students, among which are authors of this memory. Hanka had many international collaborations, was a frequent participant of the muscle conferences and co-organizer of the 7th European Muscle Conference in 1978.

For us, the best memory of Prof. Strzelecka-Golaszewska is her strength and perseverance. No matter how difficult the problem was, she always created the atmosphere of confidence and hope that everything would be fine. We really miss those times.

(by Joanna Moraczewska, Kazimierz Wielki University in Bydgoszcz and Jolanta Redowicz, Nencki Institute of Experimental Biology)

Terence C. Tao (†April 2, 2020)

Terence Tao (1944-2020)

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Dr. Terence Tao was a biophysicist recognized for his studies of the muscle proteins. Terry was born on August 4, 1944 in Shanghai, China. He attended secondary school at St. Francis Xavier's College, Hong Kong, where he graduated in 1960. He earned his undergraduate degree from University of California, Berkeley in 1964, and a PhD in chemical physics from Columbia University in 1969. After completing his post-doctoral training at Yale University and then at MRC Laboratory of Molecular Biology, Cambridge, England, Terry returned to New York, where he was teaching for 3 years at New York University. In 1977 Terry moved to Boston to accept a Staff Scientist position in the Department of Muscle Research, Boston Biomedical Research Institute (BBRI). At that time BBRI was a vibrant muscle research center under the leadership of John Gergely. Just a few years earlier the three components of troponin have been isolated and reconstituted into an active complex. The mechanism of thin filament regulation of contraction posed a formidable challenge which attracted Terry's imagination and talent. He spent the next 37 years at BBRI, where he contributed in many ways to the research and leadership. Terry's expertise was the biophysics and biochemistry of protein-protein interactions. Following his early seminal contribution into the area of time-dependent fluorescence anisotropy he focused on muscle proteins, primarily the troponin components. He applied Forster resonance energy transfer, chemical and photo-activated protein crosslinking and site-directed mutagenesis to map the topology of muscle regulatory complexes and to uncover the molecular mechanisms underlying their function. His work greatly contributed to our current understanding of the mechanism of muscle thin filament regulation by the troponin complex. Terry was a brave man. Having suffered a serious accident in 1996, causing him to become a quadriplegic and wheelchair bound, Terry forged ahead with his work with vigor and enthusiasm. Terry died on April 2, 2020 after a brief illness. He will be fondly remembered by his colleagues and friends.

(by Zenon Grabarek, Massachusetts General Hospital, Harvard Medical School)

Richard Tregear (†May 1, 2020

Co-founder of the Journal of Muscle Research and Cell Motility

Richard Tregear died 1st May 2020, he was 88 years old. He will be remembered as a significant contributor to our understanding of muscle contraction, particularly in the 1960s and 1970s but more especially as a cofounder of The Journal of Muscle Research and Cell Motility.

Richard Tregear at Alpbach, March 1974; (photo by Clive Bagshaw)

Richard studied physics at Cambridge and to started muscle research in the ARC Unit of Insect Physiology in the Zoology Department of Oxford University. The fundamental research done by this group exploited the unique properties of the 'fibrillar flight muscle" of the giant water bug Lethocerus.

Richard's research contributions were seminal in many areas and include the first direct demonstration of stretch-activation of actomyosin ATPase (Rüegg and Tregear 1966) and the direct visualisation of rigor and relaxed crossbridges in muscle by EM and X-ray techniques (Miller and Tregear 1970; Reedy et al. 1965; Tregear and Miller 1969.

He was a modest and very thoughtful man who revelled in scientific arguments; he was closely involved in the challenges and controversies of this exciting era of muscle research. He achieved much by asking questions and motivating others to find answers rather than as an individual experimenter

Although he rarely spoke at scientific meetings and he had only a few PhD students, he was a great promoter of scientific discussions in less formal situations. He was involved in reviving the Muscle Club Dinners in the 1970s and promoting the Alternative Muscle Club for student and postdocs, founded by his student, Maxine Clarke in 1980

His enthusiasm for scientific discourse culminated in the founding of the Journal of Muscle Research and Cell Motility with Chris Ashley in 1980. The first issue editorial starts with a passage that is quintessential Richard Tregear "This JournaI is intended for everyone interested in the problems of biological motion, whether in proteins or in plants. We believe that there are enough interests in common throughout this range of work to justify pulling all of them together in one place. The contents of the first issue confirm our prejudice - the range is enormous, the enthusiasm common to all. "

(by Steven Marston, Imperial College London)

Gerta Vrbová (†October 2, 2020)

A memorial tribute to Gerta Vrbová

Gerta Vrbová in 2015 during the Symposium in Warsaw (Urszula Sławińska archive)

Gerta Vrbová started her scientific career in 1950 in Prague (then Czechoslovakia) working at the Institute of Physiology of the Czechoslovak Academy of Sciences (CAS) in the group headed by Ernest Gutmann together with several other great young scientists carrying out basic research in neuromuscular physiology. Gerta's research was focused on muscle and control of movement, and this topic was closely related to some very ingenious experimental work carried out in Warsaw (Poland), by Jerzy Konorski's group at the Nencki Institute of Experimental Biology. Also, some members of Gutmann's group worked on nerve regeneration and developed collaborative work with Liliana Lubińska, also at the Nencki Institute. It was for these reasons that very productive scientific contacts and many long-lasting friendships developed between the scientists of the Nencki Institute and the Institute of Physiology CAS. During those years, members of both Institutes attended several joint meetings and visited one another's laboratories. In September 1958, the Polish Academy of Sciences organized a meeting in Osieczna and invited scientists from Gutmann's group, including Gerta. The timing of that meeting coincided with her intention to escape from Czechoslovakia. And she made it; she escaped to Great Britain, what she described in her book: "Betrayed Generation".

At Kings College London, Gerta Vrbová started her studies on the role of neuromuscular activity in controlling skeletal muscle properties. She put forward the hypothesis that activity has an impact on the phenotype of skeletal

muscle. In her study on rabbits, she demonstrated that a reduction of soleus muscle activity achieved by tenotomy had changed the time course of contraction from slow to fast muscle. Next, she demonstrated that by applying external electrical stimulation on such a tenotomized muscle its natural slow contractile characteristics can be recovered. For further validation of this hypothesis, electrical stimulation with a pattern of activity resembling that delivered by the nerve to the slow soleus muscle was applied to the fast ankle dorsiflexors and had a slowing effect on the time courses of contraction and relaxation. By these experiments, Gerta Vrbová initiated a series of investigations elucidating activity-induced changes of the skeletal muscle properties and introduced the ideas of the great concept of activity-related neuromuscular plasticity. More details about the contributions of neuromuscular activity in muscle plasticity can be found in the review written by Gerta Vrbová and Dirk Pette with whom she cooperated since the very beginning in this matter (Pette & Vrbová 1999; 2017).

Neonatal neuromuscular plasticity became a key subject of Gerta's investigations from the very beginning as well. Gerta and her group demonstrated that motoneurons and muscle fibers are critically dependent on each other during early postnatal development. Motoneurons die if their axons by a certain stage of postnatal development fail to establish contact with the target muscle. Moreover, the immature muscle fibers, like innervating them motoneuron must become capable to cope with the increased activity due to developing locomotor functions, otherwise, they die. The survival of motoneuron as well as muscle fibers depends on the accurate timing of changes in their molecular compositions during postnatal development. The possible mechanisms responsible for the development of motoneurons and muscles, related to the predisposition of immature motoneurons to cell death before the maturation of synaptic transmission between the nerves and their muscle fibers are established, were proposed by Lowrie & Vrbová in 1992.

It is important to emphasize that, as a great neuroscientist with a medical background, Gerta made a unique contribution in translating experimental data to understanding the mechanisms of neuromuscular disorders. Her research brought many results constituting a basis for creating key ideas of potential treatments for childhood genetic diseases of Duchenne muscular dystrophy or spinal muscular atrophy.

In 2015, I had the great privilege and honor to present the Diplome d'Honoure of the Nencki Institute to Gerta Vrbová. It was at the Neuromuscular Symposium in honor of Gerta organized in the frame of the 44th European Muscle Conference in Warsaw.

Gerta Vrbová, a great neuroscientist, whose more than half a century of research contributed to our understanding of neuromuscular interactions in norm and pathology, died in London on October 2, 2020, aged 93. She left us her wisdom and her heart.

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(by Urszula Sławińska, Nencki Institute of Experimental Biology)