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TRIBUTE TO MAVIS AGBANDJE-MCKENNA A Beautiful Mind and the Heart of an Explorer

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Dr. Mavis Agbandje-McKenna
A Beautiful Mind and the Heart of an Explorer

The end of life is always difficult to accept, even more so when it arrives prematurely in nature and reaches a person like Mavis Agbandje-McKenna, a woman filled with an exceptional capacity to dedicated research and full enjoyment of life. So many shared moments and days to remember come to my mind and to my heart now.... I should perhaps mention when I first met Mavis and her husband Rob in Warwick (UK), we immediately realized how complementary our respective fields of expertise were, and so that visit set a fruitful collaboration of several years on structure-function analysis of parvovirus MVM capsid. Mavis turned out to be a surprising collaborator, not only because of her wide range of knowledge, but mainly because her unique scientific passion. She never stopped questioning assumed principles, asking for fine details of any kind of methodology, or proposing sophisticated experiments to address the most intricated aspects of parvovirus biology. And all that came mixed up with a positive attitude and frequent laughs that made challenging science a job easy to enjoy.

It is also impossible not to remember Mavis's openings of Parvovirus meetings, as happened for example in Granada and Cordoba, when I felt tied up by the unavoidable rigid atmosphere of the meeting start up. Amazingly, she lightened the mood from the very first second with her powerful enthusiasm and warm manner of presenting data, which relaxed everyone in the hall at once, and miraculously drove an easy flow of science and friendship among us along the rest of the meeting.

As successful person in life, Mavis also grew a lovely family with Rob. It has been a pleasure to follow some hallmarks of their lives from the distance by the "McKennas' letters" that they always sent at the end of every year or at the dawn of the next. I was also able to witness their happiness when I visited them in Florida, playing in the pool with their (by then) kids Nicole and Sean, and it was easy to notice that such a big house was filled with love.

Mavis developed an impressive scientific career, starting from the fundamentals of how Parvovirus capsids are built, she reached a wide and comprehensive structural view of the diversity and complexity of these viruses in nature. From this solid platform, she then became involved in gene therapy approaches with parvovirus vectors, a long period of research that yielded many of her outstanding contributions until the very end. In perspective, her work has illuminated insights and technical avenues that may become essential concepts to build a successful gene therapy field.

Her legacy for our current and future understanding of Parvovirus structural biology is therefore enormous, and her emotional impact in our life will last forever. Mavis's scientific achievements and human generosity deserve lasting memory in meetings and related academic activities.

José M. Almendral
Centro de Biología Molecular Severo Ochoa (CSIC-UAM)

Mavis saw viruses in a way that only she could. Every loop, every turn, every single amino acid residue spoke to her. No detail was too trivial. She always believed that if we unlocked the secrets of the AAV capsid, we would find solutions to some of the biggest challenges facing gene therapy. She extended this philosophy seamlessly to the relationships she nurtured with her students, collaborators and colleagues. Every interaction was thought provoking and left a lasting influence on your life. People who were

fortunate to spend time with her will remember her welcoming smile, her warmth and genuineness, forever conversations at conferences and late nights pouring over data (or on the dance floor), long early morning walks, and a gentle scolding every now and then, reminding you to do the right thing. Her passion for science and her legacy are simply unmatched. Every time we look at that AAV capsid that continues to enamor all of us, we will remember you, Mavis.

Aravind Asokan
Duke University

I always considered Mavis a gift from Heaven. One of my first goals when I became Dean of the UF College of Medicine was to enhance our strength in structural biology. There were no crystallographers. So when I heard that Mavis and Rob were looking to return to the US, we immediately invited them to visit. I knew Mavis from her work on parvoviruses as a fellow with Michael Rossmann at Purdue, so she was a great recruit because she not only was a structural biologist, but had worked with parvoviruses. Her visit was a great success, both she and Rob were recruited to the Biochemistry department. When I made the offer on their second visit, I asked for an answer in two weeks. They replied that they had already closed on a new home. So they were off and running and the pace was dazzling. The lab was always full of students, including undergraduates who published in major journals. Mavis's many contributions to the determination of AAV structure and the implications for gene therapy are legendary.

Mavis was one of my most successful appointments; as a dean your legacy is to a large extent the people you brought in. I will be forever grateful to her and incredibly proud of her success.

Kenneth I. Berns
University of Florida

Mavis and her husband Rob arrived in Lafayette, Indiana in 1989. Rob and I were to share an office, while Mavis and I were to work on the first parvovirus structures in a team mentored by Michael Rossmann. These were exciting times both scientifically and personally. My shared experiences with Mavis and Rob included long journeys to X-ray sources, snow storms, all-night shifts and 24-hour diners, and eventually balancing as our respective family responsibilities as our families grew. Our paths crossed again when Mavis and Rob came to Gainesville in 1999. The Chapmans had moved to Tallahassee and Florida State University in 1993, and long struggles looked like they would finally pay dividends with an AAV structure. I was delighted to have colleagues "down the street." However, gene therapy was growing exponentially, impatient for structures that had taken eight years, and, with regrets, I don't think that we foresaw the pressures of increasingly overlapping interests. Mavis has been not only an exceptional scientist, but an ambassador. Beyond her many scientific achievements, the understanding of structural implications by our community is due to her infectious enthusiasm and unique skills in engagement that opened new initiatives and inspired a new generation. She has been the structural biologist that gene therapy needed. Finally, she and Rob are leaving us an example of how to live through adversity, unimaginable to most of us, with grace and love. Meetings will seem quiet, but long may the memory of Mavis's infectious laugh be a clarion call to us all.

Michael Chapman
University of Missouri

I will always remember Mavis Agbandje-McKenna as a brilliant, energetic, vivacious, indefatigable scientist and colleague. I met her for the first time at the International Parvovirus Workshop in Montpellier, France. We kept loosely in touch until we started collaborating on the structure of AAVHSCs. Her profound scientific insights and contributions on AAV structure and cellular interactions are legendary. Her scientific work was only matched by her quick wit and repartee. We got to know each other well during her frequent trips to the west coast and as she helped her daughter transition to and eventually from LA. She served as the external PhD examiner for Laura Smith, who was doing her graduate work in my group at the time. It was during one of Mavis' trips that she told us of her ALS diagnosis while she was in training to climb Mount Kilimanjaro. I will never forget the profound sense of shock that we felt on hearing the news. But Mavis continued undeterred, as enthusiastic about science and AAV and full of life as ever. She was not about to let anything slow her down, with Robert McKenna, her dedicated husband, always by side to help make that a reality. Not only did Mavis continue to make significant scientific contributions for many years after her diagnosis, but she also ventured into biotech, cofounding Stridebio. To me, Mavis will always embody the spirit of an exceptional fighter who overcame many odds to not only achieve her dreams and make exceptional scientific contributions without ever losing her exuberance for life and her sense of humor. I am sure that she will continue to inspire many young scientists for years to come.

Sawati Chatterjee
City of Hope

As a long time collaborator to work with Mavis was a dream. She was exciting, funny, engaging, and eager to share her knowledge with all. She was a fixture at the parvoworkshop engaging all in science discussions during the day and on the dance floor in the evening. Mavis's love of science was only equaled by her love of family and friends. She was a constant and reliable friend and I feel very fortunate to have collaborated with her for over 17 years and will always value the experience.

Jay Chiorini
National Institutes of Health

I first got to know Mavis and Rob when they were considering coming to the University of Florida to join our ensemble cast of AAV researchers. What became clear as I got to know Mavis better was that she was a remarkable woman and scientist in every respect. She was literally bursting with enthusiasm for her work of bringing structures into sharper and sharper focus, and helping us all to interpret every lump, bump, groove and valley on every facet of the complex jewel that is the AAV capsid. It was in this context that I called her "a beautiful mind" when I introduced her as the winner of 2020 ASGCT Outstanding Achievement Award.

The sheer joy that Mavis exuded as she led colleagues and trainees in this exploration was infectious. Her purity of heart, the heart of an explorer, enabled Mavis to move the science of AAV structure

forward rapidly and inclusively of every collaborator who ever approached her. Tragically, her stellar scientific career has been cut short by her battle with ALS. In facing such a terrible and progressive disease over the last few years of her life, Mavis displayed a greatness of spirit that exceeded all of her prior achievements. Keeping her work going for as long as possible, I never once heard her express even a hint of self-pity. She faced the ultimate challenge of death with the same courage and transcendence that she brought to every aspect of her life. She is sorely missed, but also unceasingly admired. We are all better for having known her.

Terry Flotte
University of Massachusetts Medical School

I had the great pleasure to have known Mavis for many years as a collaborator and friend. She was an impressive and hard-working scientist as well as a very kind, genuine and generous person. She had a special gift for visualizing highly complicated viral structures and for effortlessly communicate her ideas and understanding to others that was truly remarkable. She was an inspiration to many people in both science and life, and she will be greatly missed.

Guangping Gao
University of Massachusetts Medical School

When I entered the AAV vector field as a PhD student in the mid 90's, one of the first key opinion leaders that my mentor (Jürgen Kleinschmidt) introduced me to and who would accompany me throughout my entire career was Mavis. Over two decades later, I feel very honored that I was allowed to collaborate and publish with Mavis on numerous projects, and that I was able to introduce several of my own students to this exceptional colleague, human being and mentor. It speaks for Mavis' spirit, passion and constant care for the next generation of scientists that she has continued to guide my students and to foster their careers up until very recently. My lab including Julia Fakhiri, Jad El Andari and I feel grateful and blessed by these opportunities, and we will always fondly remember and sorely miss Mavis for the extraordinarily positive impact she has had on our personal and professional lives.

Dirk Grimm
Heidelberg University

Having known and worked sporadically with Mavis for about 20 years I came to greatly admire her intelligence and focused determination. She always seemed in good humor and willing to talk about anything whether it be of mutual interest or not. Most importantly, Mavis is perhaps the bravest person I have ever met, willing to overcome great physical limitations to achieve a unique standing in the field of understanding AAV capsid structure and biology. She will be sorely missed by all who knew her.

William Hauswirth
University of Florida

I heard the sad news from Mario Mietzsch, a former PhD student in my lab, who went on to do a Postdoc with Mavis and then was promoted to Assistant Professor at the University of Florida. When I first met Mavis, years back at the bi-yearly Parvovirus Workshop she started stirring up the field with her biophysicist perspective. I was impressed by how she sincerely, yet cheerfully bridged the knowledge gap to the virology field, initiating numerous lasting interactions. My lab's collaboration with Mavis took off years later, when Mario had developed a baculovirus-based production system for AAVs of different serotypes and her lab helped characterize the vectors. She was absolutely passionate about new scientific questions, full of ideas, responsive almost 24/7, even when she was already struck with her devastating disease. The latest manuscript we coauthored just dates back a couple of months, she still corresponded with the authors to discuss relevance and outlook. Others would have retired early, not Mavis, it likely helped her to see purpose in her doings. We will keep her on our minds as a brilliant scientist and compassionate, cheerful personality.

Regine Heilbronn
Charité-Universitätsmedizin Berlin

I very much admired Mavis for her enthusiasm and dedication to her research even in the last year of her life.

Jürgen Kleinschmidt
University of Munich

I first met Mavis in the early 90s and have seen her frequently since. Each meeting was interesting and memorable. Mavis was extraordinarily collegial, and she was always generous with her time to discuss and help others with science. Once while visiting the NIH, Mavis stopped by my lab and spent a half-day teaching me how to use more advanced features of the Chimera molecular modeling programs. Her substantial body of work is obvious from her publications, but her contributions to science cannot be reduced to an h-factor. Mavis mentored and provided opportunities to women and other under-represented groups in science. Now her protégées are among the most successful and sought-after structural biologists.

Over the last five years we collaborated on a paleovirology project and had regular contact to discuss the analysis of data and development of manuscripts, among other topics. Mavis was a lively and knowledgeable correspondent, I was always elated when she agreed with me over a hypothesis or result, and I still chuckle from some of our recent exchanges:

Dear Rob,

I am glad that I am not the only person unable to read papers that I think are going to be upsetting/based on incomplete data or lacks head-to-head data.

Bye for now,

Mavis

Robert Kotin
University of Massachusetts Medical School

We were among the many who had the immense privilege of not only crossing Mavis's path, but also to walk a few treasured steps with her along the way. She was both an outstanding scientist and extraordinary person. Her profound insights into AAV structure and function were legendary. To many of us, virions look like a tangled mess of spaghetti, but Mavis seemed to know intuitively how it all fits together. She was like the "Google Maps of capsid structure" and quite correctly called it her superpower. What inspired us most, however, was Mavis's strength in the face of adversity. Despite declining health she didn't slow down and continued to work fearlessly to expand our understanding of AAV biology. She was as active as ever, joining tele-conferences, coming up with project ideas and developing strategies to resolve unanswered questions. And through all of this Mavis remained a fount of positivity, unfailingly generous, passionate about science and always smiling.

We have lost a doyen in our field all too soon and send our deepest condolences to her husband Rob, her family and her research team.

Leszek Lisowski, Grant Logan and Ian Alexander
Sydney, Australia

I was fortunate to know Mavis as a colleague, mentor, collaborator, and friend. With my office just three doors down from hers, I saw daily her dedication as a scientist and how she inspired those around her. She approached structural biology with a keen sense of the innate complexity of biological systems and the relationship between samples, techniques, and the insights one could gain. As a virologist, she had in her mind's eye a unique and ever-refining model of how viral particle scaffolds elegantly supported the peripatetic existence and propagation of a host of different viruses through their dynamic and adaptive structures. She guided her many students and postdocs in pursuing the joys of rigorous, ambitious scientific research in balance with the day-to-day responsibilities and rewards of having a family and being part of a community by both her personal example as well as through her conscientious mentoring. Her optimism, wry sense of humor, pragmatism, and clear sense of purpose encouraged all of us around her to pursue our research interests with passion while appreciating individual strengths and areas for growth. Mavis loved her family, community, and kindred spirits. I will dearly miss our conversations and hearing her laugh from down the hall.

Joanna Long
University of Florida

Mavis was a pioneer who broke grounds in and beyond science. Her work was characterized by true depth and focus. She understood molecular structure, but more importantly, she knew how to use structure to gain functional insights with real therapeutic implications. She made seminal contributions to our understanding of ssDNA viruses, such as AAV, and her gene therapy work will benefit many people in the ensuing years. Mavis was also an inspirational mentor, and she contributed to the

development of many bright scientific minds. This quality of hers is impossible to measure but leaves a long-lasting legacy among her peers and trainees. I had the distinct pleasure to work with Mavis and her husband Robert. Our collaboration was unexpected, but very rewarding. We used her AAV2 specimen to develop novel cryo-EM tools and overcome technical challenges with cryo-EM data analyses. Mavis, in turn, contributed with biological insights that substantiated and complemented our findings. Our collaborative work impacted multiple fields and also played a major role in my own career development. I am where I am today, in part, thanks to Mavis. I'm sure many others can say the same. She was an amazing scientist, researcher, mentor, and person. She will be missed.

Dmitry Lyumkis
The Salk Institute for Biological Studies

Mavis and I worked together on the anti AAV capsid antibody response mounted by patients treated with AAV8 vectors. She had done some wonderful work around this issue in murine anti-AAV antibodies and so she was the best person, globally, for my group to interact with. Mavis was an absolute pleasure to work with and amongst the best collaborators I have ever interacted with. She was a great thinker with a deep insight into AAV vectorology. She was always full of energy and extremely hardworking. She generously shared her knowledge and expertise and guided us on to the right path without expecting anything back in return. Hers was a life exemplified by friendship, brilliance and humility. She will be greatly missed.

Amit Nathwani
University of College London

I worked with and was friends with Mavis (and Rob) for over 30 years. We first met when she joined Michael Rossmann's lab at Purdue, then continued to collaborate when she was at Warwick University and after she moved to the University of Florida. During that time we shared both science and family life, and she was the most kind and thoughtful person, as well as being an excellent scientist who helped to put the entire AAV gene therapy field on a solid structural footing. The world and science have lost a leading light - who will not be replaced.

Colin Parrish
Cornell University

I was fortunate to know Mavis during our time together at StrideBio, the company that she co-founded. Mavis and her husband Rob made regular trips up to North Carolina to visit the StrideBio offices and on those trips, Mavis would always spend time talking to and engaging with the entire company. She was happy when discussing science and mentoring the team. Mavis was always outgoing, quick to smile and laugh, and always had words of encouragement. She was so positive in her outlook on life. Mavis had a rare combination of personal warmth, scientific brilliance and humility which inspired so many. She will be forever missed.



Pat Ritschel
Atsena Therapeutics

Mavis was for us the inspiration for us to work on her pet molecules, Adeno-associated viruses (AAVs). As mass spectrometrists we continuously develop new technologies to detect and mass analyze intact viruses and virus-like particles. While meeting her at one of the Gordon Research Conferences on Physical Virology she infected and challenged us to take on AAVs. Being naïve, we thought this might be easy, as it represents a highly symmetric and rather small virus. Mavis and her lab provided us with great samples, but their mass spectra actually turned out to be extremely complicated (Snijder et al., *J Am Chem Soc* (2014)). With her help, we first took a step back and analyzed a Vp3-only particle that she made especially for us, which made us understand why the wild-type AAV spectra looked so complicated. This led us together to study AAV assembly by high-resolution native MS, from which we concluded that the assembly process is highly stochastic, leading to a very diverse panel of co-occurring stoichiometries in every AAV preparation (Wörner et al., *Nature Communications* (2021)). Also made possible by Mavis, we turned from empty AAVs (Virus-Like Particles) to genome-encapsulated AAVs, which we used to demonstrate the power of another new mass spectrometry-based technique, Orbitrap-based charge detection single particle mass spectrometry, which allowed us to simultaneously qualitatively and quantitatively measure and mass analyze empty and genome-encapsulated AAVs (Wörner et al., *Nature Methods* (2020)). The acceptance of the paper on the AAV assembly, normally a moment of joy, coincided with the devastating news about her passing away. For us, Mavis was an extremely nice and knowledgeable collaborator who taught us a lot about her favorite virus with her characteristic enthusiasm for science. She will be truly missed.

Joost Snijder and Albert J.R. Heck
Utrecht University

Mavis was a brilliant star shining a light on the scientific unknown. She was inspirational and uplifting to her students and colleagues, and the chemistry she had with people established the tightest bonds. I am so honored to have learned from and laughed with Mavis.

Richard Snyder
Thermo Fisher Scientific

One of the highlights for me has always been the biennial Parvovirus Workshops. I always looked forward to seeing all “parvo friends”. There I also met Mavis, I think the first time was in 1991 in Elsinore, Denmark. I always thought Mavis was very active in providing talks and also in the discussions, showing her broad understanding of also other fields of virology than her own. I really enjoyed her talks and was amazed of her knowledge of viral structures, and she also got me interested in the topic. I certainly learned a lot from her. Now, in the past 7 years, we have been actively collaborating on diverse human and primate parvoviruses, resulting in 9 joint publications, the two most recent ones in 2021.

After the shocking news of her passing, I feel one era is now gone, but she will be in my heart forever. A few years ago, I received a parcel from her; it was a 3D-printed multicolored detailed human bocavirus, an exact replica of the structure she and her lab had constructed. I was so happy and honored, it truly touched me deep. Another example of her genuine caring and warmth was her greeting cards, with pictures and stories of her loving family. I was also happy to meet and learn to know her husband Rob at these meetings. I truly admire the love, respect, and humor that glowed from this couple, even despite the devastating disease Mavis was battling.

Mavis is indeed a role model for us all with her combined enthusiasm and friendliness. She was a truly amazing person, friend, collaborator and scientist. Her passing is a huge loss, not only to her family and friends, but to the whole parvovirus community, since she was a true visionary and gathering force and a wonderful, kind and warm person. I will never forget her humor and laugh.... Thank you Mavis for being one of my closest “parvo friends” and a marvelous collaborator, rest in peace.

Maria Söderlund-Venermo
University of Helsinki

I first met Mavis and her husband Rob at the 1991 International Parvovirus Workshop in Helsingor, Denmark, and took an instant liking to them for their gentle and mild demeanors. Every two years since then, it was a pleasure to see them at every Parvovirus Workshop, and listen to Mavis’s masterful presentations on parvovirus structures, usually as the very first speaker. I must acknowledge, however, that other than the 2-fold, 3-fold, and 5-fold- axes of parvovirus capsids, I understood very little. When Terry Flotte recruited me back to the University of Florida, I reached out to Mavis in 2006, and sought to initiate a collaboration with her. However, in a moment of either utmost honesty or extreme stupidity (or both), I also said to Mavis that I did not see how structure biology would contribute to the development of the next generation of AAV vectors. Rather than laughing at me, ridiculing me, or dismissing me outright, she did something amazing that I realized only after she passed away. Starting in 2007, Mavis asked me to serve on the research advisory committees of 10 of her graduate students (Brittney Gurda, 2007-2010; Lawrence Tartaglia, 2009-2014; Robert Ng, 2009-2012; Lauren Drouin, 2009-2014; Harald Messer, 2010-2012; Shweta Kailasan, 2011-2016; Bridget Lins, 2012-2016; Lin-Ya Huang, 2012-2017; Nikea Pittman, 2014-2019; and Victoria Fielding, 2016-2017), from all of whom I learned a great deal. I also noticed that all of her graduate students truly revered Mavis.

What I finally realized is that this was Mavis’s subtle and unique way of educating me, for which I shall remain eternally grateful. From 2007-2020, Mavis and I also co-authored 13 publications, and we were

actively collaborating on a joint research project which we discussed in a video conference call with Mavis and Rob on December 21, 2020, when I saw her for the last time. Mavis was also a highly sought-after collaborator, nationally and internationally – she had 63 different co-authors from 14 countries, among her more than 215 scientific publications.

It was also an absolute privilege and honor to co-organize with Mavis the 2018 International Parvovirus Workshop, which was held in Miami Beach, Florida (*Human Gene Therapy*, 30: 252-256, 2019).

Rest in peace, Mavis.

Arun Srivastava
University of Florida

A few years into my academic career as a rookie assistant professor, I met Mavis at a Gordon Conference in 2011. She was a rockstar in AAV biology, and I knew I had to work with her if I was going to get any insights on AAV structure. She had no reason to agree to work with someone who she barely knew, but she did. She agreed with enthusiasm – I counted two exclamation marks from her in that first email exchange! Over the next ten years, our two labs worked together on designing AAV capsids to do unnatural things, like become activated by extracellular proteases that are elevated in disease. I used to say we work on things we can't see. Mavis made that statement simply not true. She brought structural clarity to what we were attempting to do, making real the designs that only existed in our minds. I will miss you Mavis. You have inspired a whole generation of virus researchers. And as you often ended your messages - Bye for now.

Junghae Suh
Biogen

In the 1990's our lab was collaborating with Michael Rossmann to determine the structure of Minute Virus of Mice (MVM). We were sending several milligrams of virus to a graduate student at Purdue every month or two, without any significant progress. During a timely visit by Michael to Yale, we discussed this problem, and he suggested giving the project to a post-doc in his lab who was showing particular enthusiasm and talent for solving parvovirus structures. Thus began our collaboration with Mavis, and our introduction to the world of real, rather than imagined, parvovirus structure, a field that she illuminated so successfully over the next quarter century or so. Within a few short weeks she had crystals and subsequently refined a molecular model for our favorite virus. On his several visits to West Lafayette, Mavis patiently guided Peter through visualizing the virus, using the then cutting-edge, and aptly named, "CrystalEyes" imaging package. This was a transformative experience!

It would be impossible to overestimate the importance of her contribution to our understanding of puzzling observations from the past, and to the subsequent experimental approaches that we pursued in efforts to understand parvoviral capsid dynamics at all stages of the viral life cycle.

Mavis was a wonderfully welcoming and generous person, who faced adversity with great bravery and determination. She will be cherished and honored by all associated with the parvovirus field, for her boundless warmth and her many seminal contributions across all genera of the parvovirus family.

Peter Tattersall and Susan Cotmore
Yale University

One high point of my career was my one and only sabbatical which was conducted in Gainesville Florida in the lab of Mavis McKenna studying AAV structure. As part of her “laboratory” I was able to learn first-hand how she conducted herself as a scientist, a colleague and a mentor. As a scientist she was creative and meticulous. I appreciated how thorough she was when it came time to write up our work. As a colleague she was generous and engaging. Mavis knew what she knew but had an appetite to always learn more. What impressed me the most though was her commitment to her students. She was all in – taking care of their professional and personal needs. Every time I see a structural model of an AAV particle, I think very fondly of my time as her “student”! She will be sorely missed.

Jim Wilson
University of Pennsylvania