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Remembering Austin L. Hughes

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Dear Editor,

Over tea in a New York November
seems an odd place to weep for you,
straight Catholic man.
Your most honest of intellects
and most awkward of greetings
—a look up, a nod—are needed now,
my guide and muse.
How could you bow?
I am unfit to tell the brilliance you knew.
The clack of a 1 train your parting knell,
a gesture too quick. The last words too few.
Dr. Austin L. Hughes.

[—C. W. N., 2 November 2015]

Dr. Austin L. Hughes, esteemed evolutionary biologist, husband, father, and teacher, passed away on 31 October 2015. Like so many early deaths in his field, including those of Motoo Kimura and Takeo Maruyama, the 66-year-old University of South Carolina Distinguished Professor succumbed to an unexpected heart attack, leaving those under his tutelage floundering. Hughes' expertise covered multiple languages—Welsh, French, Latin, Greek, Italian, and English—and a host of disciplines from philosophy to matrix algebra. He produced an enormous body of work in his own profession, including the books *Evolution and Human Kinship* (Hughes, 1988) and *Adaptive Evolution of Genes and Genomes* (Hughes, 1999), as well as over 300 peer-reviewed studies.

Hughes became a member of the American Association for the Advancement of Science in 2010, owing largely to his work on the evolution of genes encoding the major histocompatibility complex (MHC). While a postdoctoral researcher with Masatoshi Nei, he used the recently published structure of the MHC molecule (Bjorkman et al., 1987) to support the hypothesis that overdominant positive selection (i.e., heterozygote advantage) maintains the high polymorphism observed at these loci (Hughes and Nei, 1988). Subsequent work confirmed his conclusions (Hughes and Yeager, 1998), and his focus quickly expanded to the role of selection in shaping the genomes of pathogens. His last article in these pages discusses an approach for such studies using pooled next-generation sequencing (NGS) variant data from viruses (Nelson and Hughes, 2015).

Hughes made several other major contributions to evolutionary theory. For example, his work on gene duplication stressed the ancestral multi-functionality of duplicated genes which later experience sub-functionalization (Hughes, 1994), and he demonstrated a preponderance of gene family loss in the evolution of animals (Hughes and Friedman, 2004). He also criticized the use of inappropriate statistical tests for detecting positive selection (Hughes, 2007) and, as a proponent of the nearly neutral theory (Hughes, 2008), he argued that phenotypic plasticity plays a central role in adaptive evolution (Hughes, 2012a). Regardless of complexity, there seemed to be no dataset from which he could not extract conceptual generalities and meaningful patterns. A full review of his scientific work is in preparation elsewhere.

Beyond science, Hughes had penned a book on philosophy, a sample of which can be found in his essay "The Folly of Scientism" (Hughes, 2012b). He was a staunch opponent of those who treat religion and science as incompatible (Hughes, 2015). He was also writing a new work on environmental ethics, and published several essays on society, philosophy, and ethics (e.g., Hughes, 2013). Although he was quite shy on a personal level—a quality often misinterpreted as ego—things changed when the focus was science. In lab meetings, he would visibly metamorphose into a creature of childlike alacrity, streaming ideas and opinions that revealed his true nature: a gleeful mind, an incisive wit, a learned jokester. He was an incredible advisor, at once responsive, creative, and selfless. Some could be offended by his candor, but his simplicity and straightforwardness were some of his greatest qualities. They also made for elegance in his writing, if awkwardness in his interactions.

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Besides family, including Andrea Hughes (his wife of six years) and his children and grandchildren, Hughes also deeply impacted those he mentored in science. These include seven Ph.D. students, three M.S. students, seven postdoctoral researchers, and many more undergraduates and high schoolers. Thus, while I knew Hughes for about five years and have contributed a personal memoir elsewhere (Nelson, 2015), I had only begun to appreciate his rich scholarship and shy personality. It therefore seems fitting to remember him with the words of some of his other students, colleagues, and friends, many of whom knew him for decades. Although important individuals are not represented here (e.g., Masatoshi Nei was unable to comment due to severe health concerns and Charles P. Poole, Jr. passed the day after Hughes), these reflections help to paint the memory of a man who touched hearts as profoundly as he did minds. The broad swathe of personalities included—scientists and philosophers, atheists and theists, young and old—is a testament to the truly liberal nature of his personality and thought.

It is impossible to exaggerate the importance of Austin Hughes' fundamental contributions to molecular evolutionary theory and practice. He was a prolific researcher whose work covered such disparate topics as coevolution, phylogenetics, repetitive DNA, and more recently the application of population genetics to clinical research. Austin had an incredibly sharp mind, an imitable scientific intuition, and an abundance of impatience for bad science, faulty logic, and demagoguery. Debunking unwarranted generalizations and "accepted" theories was one of his fortes. His writing was crystal clear; I wish he had written a manual of writing style for scientists. He was also fluent in the Welsh language (Cymraeg) and wrote both poetry and prose in this ancient tongue. His untimely death deprived me of a friend and colleague; science was deprived of a great biologist who knew living systems inside and out at all levels, from the molecular to ecological. I'll miss you, Austin. Gorffwys mewn hedd.

[—Dan Graur, University of Houston]

I first met Austin in Houston when he was a fellow at the University of Texas. It was an exciting time for those studying molecular evolution and immunogenetics, as Drs. Hughes and Nei had recently published important papers on the MHC loci. I was lucky enough to take part in their work as a graduate student. Austin was a man with a sense of humor, and his words helped me to live in a foreign land as a non-native speaker. The unexpected loss shocked me and those who know him. We once again thank him for being a role model for young scientists; no one can replace him.

[—Tatsuya Ota, SOKENDAI, Japan]

Austin Hughes was a thinker, a theorist, and a highly original scientist. Trained as an ecologist, he started to pursue molecular evolution in his postdoctoral years and soon became a leader in the field. Anyone who had a conversation with him would have been impressed by his critical thinking and broad knowledge. His passing is a big loss for science.

[—Wen-Hsiung Li, University of Chicago; National Academy of Sciences, USA; Academia Sinica, Taiwan]

Dr. Austin L. Hughes' work on the MHC was the first of many subsequent attempts to discover adaptive evolution at the level of protein structure and function. He conducted this research with Dr. Masatoshi Nei, with whom I have had a long-lasting debate on issues such as the near-neutrality of molecular evolution. After Dr. Hughes moved to South Carolina, he performed many relevant analyses, finding that many genome data indeed show the prevalence of slightly deleterious mutations, supporting near neutrality. I have always been much impressed by his work, and grateful for his fair presentation.

[—Tomoko Ohta, National Institute of Genetics, Japan; National Academy of Sciences, USA]

I first met Dr. Austin Hughes in the late 1990s at a symposium on molecular evolution in Mishima, Japan. He was one of the invited speakers, yet when the welcome party commenced, he did not show up. I went to his hotel room and asked him to join us. He replied, "I was not invited to the party." It was my oversight—but even without invitation, other invited speakers had thought it natural to attend. I think that this episode reveals Austin's sincere and straightforward attitude toward everything. Besides MHC work, he is known as a staunch opponent of the two-round genome duplication hypothesis in the vertebrate common ancestor. Even if his conclusions were sometimes different from what I believe, I always respected his papers because of his clear logic and thorough analysis. I regret his sudden and early death.

[—Naruya Saitou, National Institute of Genetics; SOKENDAI; University of Tokyo, Japan]

I remember Austin fondly—an unusual individual to say the least. He held deep religious convictions and yet was a rigorous scientist. I would call Austin, talk to him about whatever subject, and he would come up with some form of analysis. He was a rare scientist who bridged both biology and computing; his passing is such a loss to the field. It's not that his relationship with my lab members was always plain sailing. His intolerance of naïve graduate students was legendary! I would ask them, with a smile on my face, to talk to Austin about their ideas. Almost always, they would be back in my office, despondent and demoralized! But once they got to know Austin, their disposition would change. I never, ever, had a single issue with Austin. He was always ready and excited to help with new analyses, and entertaining to talk to—really a wonderful colleague and friend.

[—David I. Watkins, University of Miami]

I feel lucky and honored to have known and collaborated with Austin Hughes for over ten years. In the early 2000s, we made some puzzling findings, showing that certain specificities of MHC molecules were coming up repeatedly in rather different animal species. When we tried to establish whether this was due to common ancestry or convergent evolution, we could not find a way out—that is, until Austin came into the picture. By doing the analysis "his way", which was "the right way", he showed us that in fact both convergent evolution and common ancestry were at play. That was a remarkably simple, brilliant and unexpected explanation for a complex problem. I appreciated him so much.

[—Alessandro Sette, La Jolla Institute for Allergy & Immunology]

We were fortunate to meet Austin Hughes 20 years ago when he helped us understand the molecular evolution of MHC introns in primates. Austin was one of the most brilliant scientists we ever met. His insight into and explanations for our seemingly complex questions were simple but precise. After a long gap, we had just reconnected this year to work on the population genetics of HLA and other immune response genes. His sudden death came as a shock. We will miss him immensely, his down to earth personality, and his brilliant and creative mind.

[—Soo Young Yang & Nezih Cereb, HistoGenetics LLC]

Austin Hughes was a valued collaborator and friend, distinguished by his incisive understanding of quantitative evolutionary biology.