2020 William Allan Award introduction: Mary-Claire King

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This article is based on the address given by the author at the 2020 virtual meeting of the American Society of Human Genetics (ASHG) on October 26, 2020. The video of the original address can be found at the ASHG website. Photo credit: Clare McLean.

The William Allan Award is the highest and most prestigious honor that the American Society of Human Genetics can bestow on any scientist. This award was established in 1961 in memory of William Allan, a physician-scientist who helped develop one of the first courses on human genetics and who was dedicated to the study of human hereditary disease. The award is given each year to a scientist who has had far-reaching and substantial scientific contributions to the field of human genetics demonstrating a sustained period of productivity over their lifetime. Few people are as well qualified as this year's awardee who has had an outstanding record of accomplishment over the last 50 years. It is my great honor and pleasure to introduce to you the 2020 recipient of this award, Dr. Mary-Claire King.

Mary-Claire was born in 1946 in Wilmette, Illinois; she and her younger brother Paul King grew up on the shores of Lake Michigan—regarded as one of the top ten places to raise a family. In 1963, she attended Carleton College, a small liberal arts college of 2,000 undergraduates, where she received her bachelor's degree (cum laude in 1966). She attended UC Berkeley to pursue her doctoral studies at the height of the Vietnam War. Although she became politically active, she never lost her scientific focus. In 1967, she heard a lecture from human geneticist Curt Stern, which convinced her to switch from statistics to human genetics. Human genetics would never be the same. She graduated in 1973 with her PhD from UC Berkeley where she worked with Alan Wilson on comparative protein analysis between chimpanzees and humans. From 1974–1976, she completed her postdoctoral work at UCSF, during which time her daughter Emily was born. In 1976, Mary-Claire accepted a faculty appointment at UC Berkeley as Professor of Genetics and Epidemiology (1976–1995). It was here that she began much of her groundbreaking work on *BRCA1* and the genetic architecture of breast cancer. In 1995, Mary-Claire King made the move to Seattle where she continues to teach, train, and work as an American Cancer Society Professor within the Division of Medical Genetics and Department of Genome Sciences at the University of Washington.

Over her entire career, Mary-Claire has been a leader in the field of human genetics. Her PhD thesis work with Alan Wilson, for example, was among the first to highlight the remarkable high degree (99%) of similarity between human and chimpanzee proteins.[1] She argued then that regulatory mutation and structural variation likely contribute more to morphological and behavioral differences between the species. This hypothesis has largely been borne out by numerous studies since the chimpanzee draft genome was sequenced in 2005. In the field of breast cancer, her discoveries are legendary. She mapped *BRCA1* and proved it was the major gene responsible for inherited breast cancer.[2,3] This disrupted the commonly held view at that time that cancer could not be readily dissected genetically. She built on this work to develop some of the most accurate genetic models to explain its underlying etiology and become an internationally recognized advocate for cancer patients and the importance of genetics more broadly. She further demonstrated that rare and *de novo* mutations in these and other genes were responsible for dramatically increased risk even among individuals for whom there was limited or no family history of the disease.[4] Her work made it possible to develop life-saving diagnostic tests for early detection of breast and ovarian cancer.

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This work was critical to the field of genetics because it helped shape a paradigm of "individually rare but collectively common" variants to explain not only cancer risk but also the genetics underlying other complex diseases. More recently, she applied this paradigm to understanding the genetics of schizophrenia. Working with Drs. Walsh and Gulsuner, Dr. King demonstrated the importance of rare copy number variants[5] as well as private and *de novo* truncating mutations[6,7] in neurodevelopmental genes contributing to schizophrenia. The research is particularly important because it has highlighted the prefrontal cortex and neurogenesis as contributing to these adult psychiatric diseases.

In addition to her major scientific contributions, Dr. King has been an advocate and a role model for "the global citizen scientist"—the topic of her 2012 presidential address to the ASHG.[8] She fundamentally believes that human geneticists have a unique responsibility to use their talents to engage society, redress civil rights abuses, and build bridges between groups. Here, she has led by example. She pioneered efforts to use HLA and forensic mtDNA to reunite grandmothers with kidnapped grandchildren after the Argentinian Dirty War.[9,10] Similarly, she actively maintains close collaborations with Israeli and Palestinian investigators studying rare Mendelian diseases (especially around the genetics of hearing loss) in an effort not only to foster research collaboration but to build connections based on science rather than politics.[11–13] She is deeply committed to this effort and every year spends at least two to three weeks teaching courses, giving lectures, and working on papers with her colleagues in the Middle East. Her scientific contributions were recognized by President Obama when she received the Presidential Medal of Science in 2016.

Perhaps the best testament to her remarkable career and contributions to field can be found in a few comments from her peers—many of whom were former presidents of our society. David Page, for example, commented: "Mary-Claire's contributions to genetics stand far apart from others in the field because they are the production of a sustained brilliance, an insatiable curiosity, uncompromising rigor and scholarship." Lynn Jorde wrote: "I have always been struck by the energy and passion with [which] she approached everything we discussed. She is a wellspring of great ideas and plans." Aravinda Chakravarti noted: "Her major successes have arisen from unique observation where all others working in an area have missed." From my own perspective working with her as a colleague over the last 16 years, I have frequently met with Mary-Claire for advice, especially when faced with difficult problems. Time and time again, she has demonstrated a remarkable clarity of thought to see through complex problems to get to its essence. Once she makes an informed decision, she is resolved and seldom waivers in her convictions. With Mary-Claire, one can have no better advocate or critic. She is fearless and rigorous in her science. She is committed and passionate in her training of the next generation of scientists, often regarding the students and postdocs under her mentorship as family.

In summary, Dr. King is a recognized pioneer and visionary leader in the field of human genetics. Her research bridges genomics, genetics, and statistics to develop concepts and new paradigms that have transformed our field. She is among the most passionate advocates of human genetics and has used her talents not only to drive research but to make a bigger impact in our society at large. She is a role model both to other scientists and to hundreds of students and trainees with whom she has interacted over the years. Recognition of her productivity, excellence, and unparalleled contribution to our field with the William Allan Award is long overdue. On behalf of the Society, let me thank you for your scientific contributions, your insight, and your leadership over the years. Ladies and gentlemen, please join me in welcoming the 2020 recipient of the William Allan Award: Dr. Mary-Claire King.

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