

## Genetics as a Tool for Generational Empowerment

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I can still remember the geneticist's face, sweet and round like a grandmother's, as she asked how my mom was recovering from her surgery. Then she opened the envelope to read the results of my *BRCA* analysis. It was a search for the same mutation that had spurred my mom's ovarian cells to overwhelm her body like a swarm of bees, as had happened to her mother and three sisters. I was a first-year laboratory technician at the time, focused on pipetting techniques and PCR reagents, and I hadn't yet made the connection of how the genes I studied on the bench translated into the real-life, punch-you-in-the-gut consequences that can devastate an individual. In fact, looking back now, my 23-year-old self was fairly nonchalant going into that meeting, just a little nervous—more from the anticipation of such an official meeting with a real adult than the consideration of how her report might change my life. However, that moment with the geneticist was a turning point: it was a pindrop of a moment, one I would revisit multiple times as I charted my personal journey as a physician scientist.

In my journey, I was drawn to work on cancer prevention, but it took several years in lab and a medical degree to learn of Dr. Mary-Claire King, the person whose work changed our lives. I was drafting clinical guidelines for hereditary melanoma and knee-deep in tumor suppressors and oncogenes when I learned of Dr. King, who hypothesized more than 30 years ago that a complex disease like cancer could be explained by permutations in a single gene. I was surprised that many were very skeptical of this idea, and that she faced significant challenges, especially as a young female in the field.<sup>(1)</sup> Yet she persisted, and has stated, "I have come to realize that there was a great freedom in being ignored, that you could go after huge questions, because nobody noticed."<sup>(1)</sup>

The results of going after the huge questions were deep and far-reaching. Building on the mathematical work of Morton and Elson, Dr. King utilized a multivariate, complex segregation analysis to show that the hereditary pattern of 4% of cases in their 1,579 family cohort was an autosomal dominant pattern of inheritance, then linked this risk to a gene on chromosome 17.<sup>(1-3)</sup> This ultimately led to the identification and cloning of *BRCA1* and the ability for individuals to understand and act on their risk for breast and ovarian cancer.

If the Lasker Award, National Medal of Science, Shaw Prize and membership to the National Academy of Science represent a consensus, then it is agreed that Dr. King's scientific achievements are nothing short of a landmark. Multiple generations of women and men have been empowered by the gift of knowledge for family planning, prophylactic interventions, and enhanced screening. It is not only the ability to take action and prevent morbidity and mortality, but also the understanding of how and why this happens that can bring peace to a family, like it did to mine.

Science is on the backs of many, but Dr. King is testament to what one individual, with persistence, leadership, and vision can achieve with translational science. While productively filing many scientific achievements into the folds of medical literature, she elevates her discoveries to empower the individual. Another example of her extraordinary bench-to-bedside work is the Abuelas de Plaza de Mayo project, in which Dr. King utilized genetics to reunite grandparents with their grandchildren who had been abducted from their homes and trafficked during the Argentine dictatorship.(4) She has stated that “the most important questions come from people on the front lines,” which as a guiding doctrine enables the fruit of her discoveries to remain hand-in-hand with those she studies.(5)

Dr. King’s work in the lab and dedication to the people on the front lines made possible the moment my mom learned that both my sister and I had a normal locus. I picture my mom clearly: she was wheelchair-bound, her head wrapped in a scarf, an initial look of startled disbelief on her face, followed by relief and tears of happiness. Her facial features were lit up with the first glint of strength I had seen in months. It was a moment of victory. Victory for her, for us, and, though she has never met me or my family, for Dr. King. She has touched my life through her *BRCA1* discovery, but also in ways she may not have imagined. She inspires me to use science to empower the individual, and hitch the front lines of my clinic to the expanding scientific frontier, a value that fits hand-in-glove with my work utilizing functional genomics to bring individualized care to my patients with cancer. And, to live by the tenant that landmark progress occurs by thinking extraordinarily.

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2. Hall JM, Lee MK, Newman B, Morrow JE, Anderson LA, Huey B, et al. Linkage of early-onset familial breast cancer to chromosome 17q21. *Science.* 1990;250(4988):1684-9.
3. Newman B, Austin MA, Lee M, King MC. Inheritance of human breast cancer: evidence for autosomal dominant transmission in high-risk families. *Proc Natl Acad Sci U S A.* 1988;85(9):3044-8.
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