Peripatetic southern cytogenetics

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I was raised in southwestern Oklahoma near Lawton, began my education in a one-room school for grades 1–5, and graduated from a similarly understated high school. As a youngster, genetics never crossed my mind! My undergraduate interest in genetics resulted from the general biology training required for my teaching certificate. Pursuit of a medical degree was not viable for a female with no connections to medical education in Oklahoma. My first effort to influence the world was as a secondary school teacher. That lasted for not quite a year and a half. In 1964, I was a biochemistry technician in the Division of Biology at Oak Ridge National Laboratory in Tennessee. I soon concluded that if I was going to do research, I could be doing it for myself, and thus I enrolled in the graduate school at the University of Texas in Austin. My mentor, fortunately, was H. Eldon Sutton, PhD, a human biochemical geneticist.

After acquiring my PhD (zoology–genetics) in 1969, I completed a two-year postdoctoral fellowship with Dr Robert Krooth, focusing on somatic cell genetics. The first year was spent at the University of Michigan in Ann Arbor, in the Department of Human Genetics. In the meantime, Dr Krooth moved to the Department of (Human) Genetics and Development at the College of Physicians and Surgeons of Columbia University in New York City. I preceded him there to set up his laboratory, and along the way I met and worked with Georgiana Jagiello, MD, who, serendipitously, had just arrived in New York City from Boston. Under her direction, I came to appreciate the "vehicles of genetics—the chromosomes" and became proficient in basic human chromosome technology. I also was able to interact with other like-minded department members, Drs O.J. and Dorothy Miller and Dr Dorothy Warburton. That year, 1971, chromosome banding burst onto the scene, utilizing quinacrine mustard as the cytogenetic stain. These people and this new technology sealed my newfound love for chromosomes.

My first academic faculty position was in the Department of Pediatrics at the University of Oklahoma Medical School in Oklahoma City. I was the assistant director of the Cytogenetics Laboratory and worked with the Obstetrics and Gynecology faculty to develop techniques for culturing amniotic fluid cells. In 1973, I accepted a position in the Institute of Genetics, Department of Microbiology, at the University of Southern Mississippi in Hattiesburg, where I established a clinical cytogenetics laboratory and filled a genetic consultant position at the Ellisville State School. At this state institution for the mentally handicapped, I devoted two or three days a week to reviewing residents' charts and selecting subjects for chromosome analysis.

During that period, I developed an interest in X-linked mental retardation, keying off a large, multigeneration family. The result was the most "fun" publication of my career (Yarbrough and Howard-Peebles, 1976). Diligence and imagination, combined with new chromosome-banding techniques and extraordinary access to a population of developmentally delayed persons, resulted in a series of clinical research papers from our institute over the next six to seven years. In 1977, Grant Sutherland published his initial work re-identifying the "marker X chromosome," later called the "fragile X chromosome." (The fragile X cytogenetics phenomenon was originally identified by Herbert Lubs, MD, in 1969.) Using this culture medium–sensitive technique, I identified my first families with fragile X syndrome at Ellisville State School from among the X-linked families previously documented. Of five such families, three had the fragile X chromosome in their cytogenetic preparations. We were on our way!

Through discussions at international workshops and a series of strategic collaborations, the molecular basis for fragile X syndrome was determined much sooner than usual. In short, the phenotype was caused by the expansion of a triplet repeat (CGG) in the *FMR1* gene, such that the FMR protein was not produced. This distinctive inheritance pattern explained why both males and females could be affected and how males could be carriers of an X-linked disorder. By 1994, fragile X laboratory testing moved from the cytogenetics laboratory to the molecular laboratory, but my "cytogeneticist" interest did not waver. Molecular testing was more accurate, allowing for reliable evaluation of both affected and carrier status, vastly improving genetic counseling for affected families—a real plus. Moreover, as a result of the breakthrough in fragile X syndrome, a new category of genetic neurological disease was identified: triplet-repeat expansion disorders. Other such disorders include Huntington disease, myotonic dystrophy, Friedreich ataxia, spinocerebellar ataxia (numerous types), and Kennedy disease. I had declared early in my involvement with fragile X that "this disease is trying to tell us something special." It definitely did!

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My clinical research interest and publications regarding the fragile X syndrome continued during my last three clinical cytogenetic positions (University of Alabama at Birmingham, University of Texas Health Science Center–Dallas, and the Genetics & IVF Institute (GIVF), Fairfax, Virginia), including early prenatal cytogenetic studies and premature ovarian failure in fragile X carriers. At the University of Alabama at Birmingham, my colleagues and mentors, Drs Sara and Wayne Finley, particularly influenced my development as a clinical cytogeneticist and as a member of the medical community, serving me well for the rest of my career. During my time at GIVF, I was also involved in the clinical cytogenetic studies of confined placental mosaicism in chorionic villus samples. Fluorescence in situ hybridization broke onto the cytogenetic scene in the late 1990s as an exciting and innovative new technique and yet another "beginning" for molecular clinical cytogenetics. GIVF also afforded me the opportunity to merge my academic background with the benefit of working in a nonacademic environment.

In 2000, I semiretired and have since pursued part-time "locum tenens" clinical cytogenetics, working in many locations and laboratories, both academic and commercial. Not only have I had the opportunity to interact with many clinical cytogeneticists and cytogenetic technologists and learn new approaches, I have also been able to concentrate on "the chromosomes" instead of all the other details of running a modern clinical cytogenetics laboratory. This has been rewarding and has kept me involved as clinical cytogenetics has "sprinted" into the twenty-first century. Meanwhile, cytogenetic technology has continued to progress as banding has been supplemented by fluorescence in situ hybridization. Microarray analysis of chromosome structure followed soon thereafter. Genomic medicine and research continue to offer a bright future for both clinical and basic-research geneticists. Determining gene function and application of whole-genome sequencing have become the foundations of personalized medicine.

Of the lessons learned, I consider collaboration with other scientists and the interactions/experiences at genetics meetings vital for professional growth and development of young scientists. Another lesson is to immerse yourself in your work. It was thus that I enjoyed all aspects of my work on fragile X, from the laboratory to the clinic, and especially my interaction with the families who contributed significantly to my success. Go for it!

DISCLOSURE

The author declares no conflict of interest.