2012 William Allan Award Introduction: Uta Francke[1]

Tayfun Özçelik[2,*]

Ladies and gentleman,

There are many great geneticists, but few are truly exceptional in the way that Dr. Uta Francke is. I had the enormous privilege of entering into the world of human genetics under her mentorship and the great honor of working with her. Dr. Francke is a pioneer in the field of molecular and genomic medicine. Her name is synonymous with human and mouse chromosome identification and gene mapping, discovery of genes involved in heritable disorders, and studies of their functions and disease-causing mechanisms.

Today, we have a comprehensive understanding of genomic architecture, but this was not so only two decades ago. In the early 1990s, chromosomal localizations of approximately 10% of the expressed genes were known. Of those, Dr. Francke mapped more than 10% single-handedly, just as in fine-needle embroidery. These genes include those encoding insulin and its receptors, insulin-like growth-factor receptors 1 and 2; low-density lipoprotein and its receptors, α-β-γ-globins; epidermal and nerve growth factors; transforming growth factors α and β; C-reactive protein; synapsins; serotonin receptors; adrenergic receptors; lactate dehydrogenase; thymidine kinase; α1-antitrypsin; glucocorticoid receptor; the major histocompatibility complex; and many more.

Dr. Francke was raised in a small town in Germany. She obtained her baccalaureate from Aufbaugymnasium Idstein and studied medicine at the Universities of Frankfurt, Marburg, and Munich. After a 2 year internship at Klinikum rechts der Isar in Munich, she moved to the United States in 1969 and completed her residency training in pediatrics at Children's Hospital Los Angeles. It was during her postdoctoral years at the University of California in Los Angeles and San Diego that she began studying chromosomes. Her remarkable ability in pattern recognition and her phenomenal drive for editing and educating herself to achieve perfection soon led to her unsurpassed command of cytogenetics. In the four decades that have passed since then, her achievements culminated in an exemplary career and she became an elected member of the European Molecular Biology Organization, the Institute of Medicine (National Academies), the American Association for the Advancement of Science, and the American Academy of Arts and Sciences and was an original member of Highly Cited Researchers (Institute of Science Index). Using somatic cell hybrids, she defined conservation of autosomal gene synteny groups in mice and humans, established that the order of loci on the X chromosome is different between mice and humans, and demonstrated cytogenetic approaches to mouse models of human genetic diseases. On the clinical front, Dr. Francke was and continues to be a fabulous clinical geneticist: she delineated several new syndromes, such as 2p partial trisomy syndrome, duplication 12p mosaicism, and proximal 4p deletion syndrome.

Dr. Francke moved to Yale University in 1978, and for the next decade, her laboratory became a mecca for gene-mapping studies. This was the age of gene hunters as described in late Arthur Kornberg's book *For the Love of Enzymes: The Odyssey of a Biochemist*. Her group defined microdeletions associated with chronic granulomatous disease, adrenal hypoplasia, glycerol kinase deficiency, and last but not least, Duchenne muscular dystrophy. It was during that period that I met Dr. Francke when I was a visiting medical student giving a presentation of a patient

[1]This article is based on the address given by the author at the meeting of the American Society of Human Genetics (ASHG) on November 9, 2012, in San Francisco, CA, USA. The audio of the original address can be found at the ASHG website.

[2]Department of Molecular Biology and Genetics, Bilkent University, Ankara 06800, Turkey
*Correspondence: tozcelik@bilkent.edu.tr

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with lissencephaly at Yale Genetics Grand Round. She made a few key comments, and its effect was literally like the American R&B singer Doris Troy's song "Just one look, that's all it took." I knew who my mentor was going to be once I graduated from Istanbul Medical School. This of course is a direct reflection of Dr. Francke's contagious enthusiasm, encouragement and optimistic approach to well-defined scientific questions, and elegantly formulated hypotheses. In 1999, when she was the president of the American Society of Human Genetics and the Annual Meeting convened in San Francisco like now, the party at the presidential suite was filled with members of her group from the 1970s, 1980s, and 1990s, and the air was full of joy and good memories of the years spent in her lab.

Going back to the 1980s, linkage analysis, like physical mapping, was moving toward the center stage of human genetics, and Dr. Francke was laying the foundations of her research activities for the 1990s and beyond. This time, as a Howard Hughes Medical Institute investigator at Stanford University, she pioneered the merging of the two maps—that of loci of disease phenotypes through linkage analyses and that of physical localizations of expressed genes to chromosomes. Those genes with a map location overlapping a disease locus would then become a candidate gene for that particular disorder. Using this strategy and various other positional-cloning and mapping approaches, her group discovered or collaborated in the discovery of genes responsible for Prader-Willi, Rett, Williams-Beuren, Wiskott-Aldrich, and Laron syndromes and Charcot-Marie-Tooth disease type 1A. Please visit Stanford University's recently dedicated "Discovery Walk," which stretches the entire length of the Medical School Campus, and see the promenade that features significant scientific discoveries made at Stanford and elsewhere during the past 150 years; all are engraved on nearly 350 black granite panels lining more than 20 benches. On one of the benches facing the Beckman Center for Molecular and Genetic Medicine, where Dr. Francke's laboratory was located, you will see the stories of Rett and Prader-Willi syndromes.

As we heard at the presidential address of this meeting, scientists are citizens of the world. Dr. Francke is indeed a citizen of the world. She collaborated with many different groups and also explored the globe by experiencing the natural beauties and different cultures of all the continents.

It is not possible to ask Columbus to discover America. But it is possible to set the direction to sail. During a lifelong journey in science, Dr. Francke always knew in which direction to sail. Today, she sails toward the new world of personal genetic information. For geneticists around the world, she has always been and will continue to be an inspiration and a role model as a researcher, educator, clinician, and leader. It is with great honor, admiration, and humility that I introduce Dr. Uta Francke as the recipient of the 2012 William Allan Award.