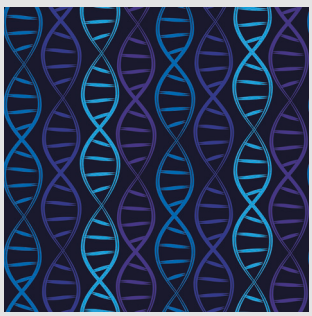
NEWS

ACMG announces new chief executive officer

Following a nationwide search, the American College of Medical Genetics and Genomics is delighted to announce that Maximilian Muenke, MD, FACMG, will become its new chief executive officer on October 7. An esteemed physician–scientist and dedicated clinical and research mentor, Dr. Muenke brings more than three decades of experience to the ACMG, including nearly 20 years as senior investigator, head of the Human Development Section, and chief of the Medical Genetics Branch at the National Human Genome Research Institute (NHGRI) of the National Institutes of Health (NIH). Dr. Muenke's research centers on identifying the underlying causes of craniofacial and related anomalies in humans thanks to a clinical encounter with two newborns during an early-career research fellowship. The two patients—one with a severe brain abnormality, the other with an unusually shaped skull—set the course for Dr. Muenke's research trajectory, which investigates holoprosencephaly, a common birth defect in which the brain fails to divide into the right and left hemispheres, and craniosynostosis, a birth defect in which skull bones join together prematurely. Dr. Muenke's laboratory uncovered the genetic basis of a common craniosynostosis condition, which is now called Muenke syndrome. Dr. Muenke earned his MD degree from the Free University of Berlin School of Medicine in Germany in 1979. He then completed residency in pediatrics at the Christian-Albrechts University in Kiel, Germany, and a postdoctoral fellowship in human genetics at Yale University. Before joining the faculty of the University of Pennsylvania School of Medicine for 10 years, Dr. Muenke completed a clinical genetics fellowship at the Children's Hospital of Philadelphia. He is board certified in clinical genetics, clinical cytogenetics, and clinical molecular genetics by the American Board of Medical Genetics and Genomics. In addition to his many research accomplishments, Dr. Muenke has worn several other hats, including mentoring the next generation of research leaders as the director of the NIH Medical Genetics and Genomic Medicine Residency and Fellowship Training Programs and as editor-in-chief of the *American Journal of Medical Genetics Part A* and *Part C*. For his outstanding contributions, Dr. Muenke has received several awards including three NHGRI Genome Recognition Employee Accomplishments and Talents (GREAT) Awards, the NIH Director's Award for establishing the International Summit in Human Genetics and Genomics, and the Samuel Pruzansky Memorial Lecture Award from the March of Dimes Birth Defects Foundation. Dr. Muenke will work closely with the College's current executive director, Michael S. Watson, MS, PhD, FACMG, and board leadership to ensure a smooth transition before Dr. Watson departs the ACMG at the end of the year.

—V. L. Dengler, News Editor

FMR1 premutation carriers display unique clinical profile



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Fragile X syndrome is a developmental disorder that affects approximately 1 in 4000 males and 1 in 8000 females. Among other traits, the condition leads to mild to moderate intellectual disability and occasionally anxiety and hyperactivity. Variations in the fragile X mental retardation 1 (*FMR1*) gene are causative. *FMR1* encodes a protein responsible for regulating the translation of nearly a third of synaptic transcripts. Whereas healthy individuals usually possess 5 to 50 trinucleotide CGG repeats in *FMR1*, patients with fragile X syndrome (FXS) typically harbor more than 200 repeats. The large expansion of CGG repeats in FXS patients leads to hypermethylation and silencing of the gene. People with 55 to 200 CGG repeats have what is known as an *FMR1* premutation. Considerable debate surrounds whether the premutation renders this population more susceptible to clinical characteristics beyond intellectual disability. As reported in a recent article in *Science Advances* (https://doi.org/10.1126/sciadv.aaw7195), Movaghar et al. found that *FMR1* premutation carriers possess a distinct clinical profile that is evident throughout adulthood. The researchers used a machine-learning approach to mine the electronic health records (EHRs) of nearly 20,000 participants in the Personalized Medicine Research Project at the Marshfield Clinic in Wisconsin. A screen of participants' DNA identified 98 premutation carriers. The team then selected about 1000 participants with CGG repeats in the normal range matched by age and duration of receiving medical care from Marshfield Clinic to serve as control subjects. Researchers and participants were blind to subjects' genotypes. By examining diagnostic codes from EHRs with a random-forest machine-learning approach, the researchers were able to distinguish premutation carriers from healthy participants. The analysis also allowed Movaghar and colleagues to identify the specific clinical diagnoses that differentiate premutation carriers from controls. The team then linked diagnostic codes to clinical phenotypes. Diagnostic codes related to anxiety such as agoraphobia, social phobia, and panic disorder associated with *FMR1* premutation status in women as did codes related to reproductive issues, including infertility, dysmenorrhea, and premature reproductive aging, and diagnoses related to injuries (e.g., fractures and sprains). In total, the team identified 37 significant phenotype–premutation status associations in women. In men, diagnostic codes related to abnormal blood chemistry, mental health disorders such as major depressive disorder, respiratory conditions like chronic sinusitis, and genitourinary disorders including urinary incontinence associated with *FMR1* premutation status. Significant associations in men totaled 22, the researchers report. Altogether, the team's investigation reveals *FMR1* premutation association with a unique clinical profile. The researchers conclude that understanding how *FMR1* premutation status affects disease risk could facilitate the development of personalized health plans and preventive care.

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