http://dx.doi.org/10.7124/bc.000AF8

The GIWU-CF study: exploring genetic modifiers in cystic fibrosis

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Background/Aim. Genome-wide association studies (GWAS) effectively identify links between genetic variants and diseases. Cystic fibrosis (CF) results from the *CFTR* (Cystic Fibrosis Transmembrane Conductance Regulator) gene mutations; however, disease severity varies among patients with the same mutations because of other genetic factors. We launched the GIWU-CF study (Genetic Investigation into Western Ukrainian CF) to explore CF's genetic foundation. **Methods.** We compiled a dataset of Ukrainian CF patients who provided informed consent to participate in the study. DNA was extracted from blood samples for high-quality analysis. PCR and registration analysis screened for the 35 most common *CFTR* mutations. Genotyping was done using the Illumina Global Screening Array (GSA), analyzing hundreds of thousands of SNPs across the genome. The study group comprised 184 males and 177 females. The average age at diagnosis was 4.93 years [SD = 6.36], ranging from 0 to 35 years. The body mass index (BMI) averaged 16.72 [SD = 2.89], with no significant difference between males (16.95 [SD = 3.18]) and females (16.52 [SD = 2.63]). **Results.** A comprehensive dataset of 381 Ukrainian CF patients was compiled. Genetic testing revealed 30 different *CFTR* variants, with the most common being F508del (c.1521_1523delCTT) at 58.96%, 2184insA (c.2052_2053ins) at 7.65%, N1303K (c.3909C>G) at 3.75%, CFTRdele2,3 (c.54–5940_273+10250del) at 3.26%, and G542X (c.1624G>T) at 2.93%. It was established that in 122 patients, F508del was the most common in both alleles of the *CFTR* gene. Among the CF individuals, 38.01% were F508del homozygous (F508del allele frequency, AF = 62.31%), while 60.12% were compound heterozygotes for the *CFTR* mutations. To delve deeper into the genetic factors influencing CF, we performed genotyping. After stringent bioinformatic quality control measures, we focused on 725,497 SNP variants for detailed analysis. The study also highlighted various complications among GIWU-CF patients, including diabetes mellitus observed in 4 patients, liver disease in 18 patients, and other complications such as bronchiectasis, cirrhosis, distal intestinal obstruction syndrome, and malignancies. **Conclusions.** This research seeks to advance our understanding of CF genetics by integrating individual genetic profiles, thereby contributing to a more nuanced approach to managing and understanding the disease and its complications.

Keywords: cystic fibrosis (CF), genetic variants, GWAS (Genome-Wide Association Study), mutation, PCR, sequencing, bioinformatics.