Alleges polymorphism of microsomal epoxide hydrolase gene (mEPHX) as modifier factor in cystic fibrosis

N. Rohovyk1,2, N. Vishnuk1, H. Makah1, L. Bober1, O. Lyva1, Danylo Halystky
Lviv National Medical University, Lviv, Ukraine; 2Western Ukraine Specialized Children’s Medical Centre and Cystic Fibrosis Regional Centre, Lviv, Ukraine; 3Institute of Hereditary Pathology of National Academy of Medical Sciences of Ukraine, Lviv, Ukraine; 4Western Ukrainian Specialized Children’s Medical Centre and Cystic Fibrosis regional centre, Lviv, Ukraine

Introduction: mEPHX enzyme activity and stability are strong factors for resistance to development of chronic obstructive pulmonary disease. The mEPHX allelic polymorphism T337C and A415G could be considered as a modifying the severity of chronic pulmonary disease in CF patients.

Aim: To establish mEPHX T337C and A415G alleles and genotypes distribution among CF patients F508del homozygotes.

Methods: The amplification of DNA sequences using PCR was carried on. Amplified products were subjected to digestion and electrophoresed on 2% agarose gel.

Results: We analyzed 35 CF patients homozygotes for F508del and 157 no-CF persons as control. In patients with mild form of CF 415AA genotype is more common (75.0%) than among patients with severe form (52.6%). mEPHX 415GG genotype was recorded in half rarely in patients with CF mild form than in patients with severe form (26.3%). The frequency of 415GG genotype was higher among patients with CF (OR = 2.77, p < 0.05) as compared to control group.

Conclusions: The association between mEPHX alleles and the severity of the disease among CF patients was not confirmed. To clarify the higher frequency of mEPHX 415GG genotype among CF patient the mEPHX enzyme activity shall to be studied.

Genome sequence of the Danish epidemic strain of Achromobacter ruhlandii

K.J. Handberg1, T. Andreassen1, M. Wang1, W. Ridderberg1, N. Norskov-Lauritsen1, Aarhus University Hospital, Clinical Microbiology Department, Aarhus N, Denmark

Objectives: Achromobacter xylosoxidans and other Achromobacter species can chronically colonise the airways of cystic fibrosis (CF) patients. These bacteria are increasingly reported from CF centres and have propensity to develop resistance to all antimicrobial agents. The Danish epidemic strain (DES) is a transmissible strain of A. ruhlandii that has spread between patients from both Danish CF centres causing 17 of 68 (25%) primary infections with Achromobacter from 2000 to 2011. The DES is, or has become, an exceptionally resistant clone, and infection with DES is suspected if a patient presents with a first-time isolate of Achromobacter showing pan-resistance. As no genome sequence is publicly available for A. ruhlandii we sequenced a representative of DES.

Methods: Next-Generation-Sequencing.

Results: The investigated strain was a first-time isolate cultured in 2002 from a patient at the CF centre at Aarhus University Hospital. By de novo assembly and RAST analysis the genome size was estimated to 6.35 Mbp with a GC-content of 67.6%. The closest neighbour in the RAST database was Achromobacter piaeaudartii. The number of protein encoding genes was estimated to 5,895. The GC-content of DES A. ruhlandii is similar to that of A. xylosoxidans strain NH44784–1996, but the genome size and number of genes were slightly lower for A. ruhlandii. The genome contained several potential antimicrobial resistance genes.

Conclusion: The data will serve as a framework for a comparison of all strains involved in the DES outbreak to elucidate the molecular epidemiology and the spread of the strain, as well as the putative acquisition of antimicrobial resistance genes.

Prevalence of ΔF508 mutation in patients with cystic fibrosis in a miscegenated population of the Brazilian Northeast

E.L. Souza1, C.H.S. Pinheiro2, N.A. Sena2, P.H. Bittencourt2, L.R. Mota2, R.L.F. Lima2, 1Federal University of Bahia, Pediatrics, Salvador, Brazil; 2Federal University of Bahia, Salvador, Brazil

Cystic Fibrosis (CF) is an inherited autosomal recessive disease. There are more than 1,900 mutations associated with this disease and the AF508 mutation is the most common in Caucasians. In Brazil, the frequency of the AF508 mutation varies according to geographic and ethnic origin of patients. The population of the state of Bahia, in Northeastern Brazil, is highly mixed and a previous study has shown that the frequency of DE508 mutation was 11.8% in cystic fibrosis patients.

Objectives: To determine the prevalence of AF508 mutation in CF patients followed up at the Professor Edgard Santos School Hospital Complex, Salvador, Bahia, Brazil.

Methodology: It was conducted a cross sectional study. The population studied was composed of CF patients, from 0 to 20 years. After inclusion in the study, a questionnaire was applied to collect clinical data and laboratory results and patients underwent blood sampling to investigate AF508 mutation.

Results: Forty-four patients were included, with a mean age of 9.4 ± 5.7 years, median of 8.5 years, and 22 (50%) were male. The AF508 mutation was found in 14 patients (31.8%). Of those, six (42.9%) were homozygotes and eight (57.1%) were heterozygotes. Regarding the alleles, there were 20 carriers (20/88 or 22.7%) and 68 non-carriers (68/88 or 77.3%).

Conclusions: The frequency of the AF508 mutation is lower than that found in populations from Brazilian Southeast, but higher than a previous study in Salvador. The CF diagnosis was delayed and patients with the DF508 mutation had symptoms with early onset and presented pancreatic insufficiency.