

#### 423 The genealogical contribution to the understanding of the diffusion processes of the CFTR mutations: the case study of 1717-1G → A in Brittany (France)

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**Objectives:** The aim of this study is to show that the historical data, through genealogies, can help understanding the spreading process of the CFTR mutations on a determined territorial area.

**Methods:** The panel is composed of 1264 CF patients. 674 were born or have lived in Brittany within the past 50 years. Since these patients have been taken care of by local caring centers, we know all their diagnostic and clinical characteristics. Moreover, thanks to the registry office and the local archives we have managed to follow their direct line ancestors, leading to the identification of an ancestral population of 60000 individuals.

The database, validated by the CNIL, is endowed with an algorithm which can find the parental relationships between the individuals.

The results presented in this study are limited to the genealogical links found between the 6 patients who carry the 1717-1G → A mutation in the heterozygous compound state, used here as an example because no ancestral study was made in carriers of this mutation.

**Conclusions:** 4 out of the 6 patients have been aggregated to the 13th generation, to a founder couple living in the 17th century in the Breton town of Plouhinec.

Nevertheless, the other 2 patients do not have all their ancestors localized in Brittany and do not seem to be related.

Due to the same origins of the mutations, a classification can thereby be established, between “family forms” and “theoretically sporadic forms” of CF, where one of the practical applications is to guide the genetic advice given to the families.

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#### 425 Polish National CF Registry – preliminary report

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Works on setting up Polish National CF Registry has been pursued for the last few years. The preliminary data have been collected from 20 centers. Three and two centers care exclusively for children or adults, respectively. The remaining 15 centers provide care for patients with no regard to age. Six centers care for more than 50 patients. There are 1303 patients registered at present, among them 1250 are alive. 30% of patients are adults. In a significant percentage of subjects diagnosis was made in early childhood – in 61% within first year of life. Late diagnosis is rather scarce, only 1.4% of patients were diagnosed as grown-ups. F508del is predominant mutation and was found on 69% of alleles. 47% of all patients were homozygous for this mutation. Consecutive mutations in terms of frequency are: 3849+10kbC-T(6%), N1303K(4%), G542X(4%), 1717-1G-A(3%). 21% of subjects are pancreatic sufficient while remaining 79% of patients have severe exocrine insufficiency resulting in steatorrhea. In registered clinical assessments, the presence of *Pseudomonas aeruginosa* infection was proved in 60% of patients. In 62% it was mucoid strain, in 36% – non-mucoid and 3% – drug resistant. Gastrostomy was placed and vasoput was implemented in 2% and 5% of patients, respectively. Supported by: Roche Poland (in part).

#### 424\* UMD-CFTR: a database dedicated to CF and CFTR-related diseases

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With the increasing knowledge of CF and CFTR-related diseases (CF-RD) the number of sequence variations in the CFTR gene is constantly raising. CF and particularly CFTR-RD provide a particular challenge for molecular diagnostic because of many unclassified (missense or putative splice site) variants and identical genotypes associated with different phenotypes. An exhaustive and manually-curated database (containing not only disease-causing genotypes but also haplotypes) is crucial for accurate interpretation of pathogenicity.

Using the Universal Mutation Database (UMD<sup>®</sup>) software, a freely available tool internationally recognized, we have constructed the UMD-CFTRbase dedicated to sequence variations of the CFTR gene. The UMD-CFTRbase currently contains molecular data on 771 patients studied in our laboratory: 541 CF and 216 CFTR-RD. Besides disease-causing mutations, the database contains unclassified variants and non-pathogenic polymorphisms (252 different sequence variations) representing 3900 entries.

Tools, such as UMD-Predictor, are provided to assess the pathogenicity of mutations (combining splicing effect, conservation, biochemistry and structure of amino acids) and integrate haplotypes. UMD-CFTR is unique as it offers a way to compile any mutational data of the CFTR gene in order to help the contributing scientific community to improve sequence variation interpretation, evaluate the putative influence of haplotypes on mutations and correlate with phenotypes.

We are now collecting and curating data from 9 expert laboratories. The large amount of information collected from CF or CFTR-RD patients will increase the power of analysis of correlations between genotype/haplotype and phenotype.

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#### 426 CF registry in Northern Greece

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The Aristotle University Cystic Fibrosis (CF) Center consists of two paediatric and an adult CF Unit in Thessaloniki, using the same protocols, serving a whole population of about 2.5 million inhabitants living in Northern Greece.

**Aim:** To evaluate the epidemiologic data of CF in Northern Greece.

**Method:** Demographic, genetic and clinical symptoms were collected in a database, according to the European CF Registry. Data collection was completed in a three-months period (February-April 2008). All the information was obtained from patients' clinical notes.

**Results:** Totally 191 CF patients (both children and adults) were identified with mean age 16.81±9.21 years. The older CF patient was 40 years old, while 43.5% of patients were older than 18 years. Mean age of diagnosis was 1.16±0.53 years. Eighty percent of patients were identified with the ΔF508 mutation (23.75% were homozygous). Thirty percent of our patients were chronically colonized with *Pseudomonas aeruginosa*; Burkholderia cepacia was not isolated in any of our patients. 94% had pancreatic insufficiency and 30% were malnourished (BMI < 18.5 kg/m<sup>2</sup>), 3.66% had meconium ileus and 3% had CFRD. The FEV1 among patients aged 6–18 years, was 90.67±29.28%, while the FEV1 among older patients (>18 years) was 68.64±25.87%. None of our patients had undergone lung or liver transplantation.

**Conclusions:** In the first Registry of Greek patients with CF, the health status of the patients is presented.