Title	***3. Longitudinal study of Pseudomonas aeruginosa resistance: selection and evolution of resistance mechanisms in relation to antibiotic treatment in cystic fibrosis patients***
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Study design	Prospective study in collaboration with the Laboratory of Microbial Physiology and Biotechnology, Department of Molecular Biology, Policlinico "S. Maria alle Scotte", Siena (Prof. G.M. Rossolini)
Grant by	Italian Cystic Fibrosis Research Foundation (FFC #14/2006 and FFC #9/2008; 3 years; E. 60.000)
Background and aims	*P. aeruginosa* (*Pa*) is the most important opportunistic pathogen in Cystic Fibrosis (CF) patients. Recent advances in antimicrobial therapy have dramatically contributed to increase life expectancy of CF patients. However, frequent and prolonged antibiotic courses are likely to be a major factor in selection of resistant Pa strains, which are difficult to treat and apparently associated to a more severe prognosis. This project has the following objectives: 1. Identification of resistance mechanisms to β-lactams (βLs), aminoglycosides (AGs) and fluoroquinolones (FQs) in Pa isolated from a cohort of CF patients; 2. Analysis of the correlation between antibiotic treatment and the selection/evolution of resistance mechanisms to the above classes of drugs in Pa; 3. Analysis of the correlation between *P. aeruginosa* carrying known resistance determinants and clinical outcome in CF patients.
Inclusion Criteria	A selection of Pa isolates collected from CF patients followed over a 10-year period and chronically infected by Pa will be analyzed for the most important resistance mechanisms. Pa isolates obtained from CF patients that have received eradication therapy for the first colonization and for the subsequent episodes will be assessed.
Exclusion criteria	Patients with CF and airway chronic infection by bacteria different from Pa will be excluded.
Methods	Analysis of mutation-mediated resistance mechanisms will be performed. The antibiotic treatment received was analyzed with quantification of the used drugs as oral or intravenous or nebulized antibiotics (mean annual dose of the most frequently used classes of antipseudomonal antibiotics). The clinical parameters considered were: the decline of the FEV1 over time (expressed as ΔFEV1 % pred./year), the number of pulmonary exacerbations/year suffered by patients, the nutritional status (expressed as BMI).
Expected results and anticipated output	To propose suppressive antibiotic treatment for chronic Pa, considering the relationship between resistance mechanisms and used drugs.
Start of recruitment	September 2006
End of experimental plan	March 2010
Pubblication on medical Journal	December 2010