PROGRAM - ABSTRACT BOOK

2nd Italian Young Investigator Meeting in Cystic Fibrosis

Rome, April 15th-16th 2016

Welcome Piram Hotel
Via Giovanni Amendola, 7 – 00185 Roma

SIFC

Second Italian Young Investigator Meeting

Rome April 15th-16th 2016

Organizing Committee:
Italian Society of Cystic Fibrosis
(Committee for Basic Research)

Chairpersons

Cirilli Natalia

Esposito Speranza

Maiuri Luigi

Tosco Antonella

Vilella Valeria

April 15

1:00 pm – 2:00 pm Light Lunch

2:00 pm - 2:30 pm: Welcome / Introductory Comments

2:30 pm - 4:00 pm: Oral presentations 1-4 (15 min + 5 discussion each)

1. Development of inhalable hyaluronal/mannitol composite dry powders to reposition flucytosine for antivirulence therapy of lung infections. (Costabile G.)
2. Cysteamine and epigallocatechin gallate improve deficient expression of the CFTR in mice. (Saluzzo F.)
3. The Activation of Calpain and Protein Kinase C is Involved in the Abnormal Release of Matrix Metalloproteinases 9 from Cystic Fibrosis Peripheral Blood Mononuclear Cells". (Bavestrello M.)
4. Restoration of CFTR function in cystic fibrosis patients by combined treatment with cysteamine and epigallocatechin gallate. (Casale A.)

4:00 pm - 4:30 pm: Coffee Break

4:30 pm - 5:30 pm: Oral presentations 5-7 (15 min + 5 discussion each)

5. Novel aminoarylthiazole derivatives as correctors of the chloride transport defect in cystic fibrosis computer assisted drug design synthesis and biological evaluation. (Liessi N.)
6. Clinical implication of cellular senescence on CFTR expression. (Comegna M.)
7. Olfactory performance in Cystic Fibrosis patients. (Di Lullo A.M.)

5:30 pm - 6:00 pm: Talk: Sweat test: is it a reliable "surrogate" marker of CFTR function? PROS and CONS

6:00 pm - 6:30 pm: Round Tables: Methodological Approach to Research.

April 16

9:00 am - 11:00 am: Oral presentation 8-13 (15 min + 5 discussion each)

8. Development of a CFTR functional test suitable for human primary leukocytes. (Vercellone S.)

9. Relationship between *Pseudomonas aeruginosa* and defective autophagy in Cystic Fibrosis bone marrow derived murine macrophages. (Ferrari E.)

10. The distribution pattern of metabolic modules and antibiotic resistance genes reveals differences in the airway microbiome of cystic fibrosis patients. (Bacci G.)

11. Evidence of *Bdellovibrio bacteriovorus* predation against Cystic fibrosis bacterial isolates. (Iebba V.)

12. Genetic background of Methicillin-Resistant *Staphylococcus aureus* (MRSA) isolates from persistently infected Cystic Fibrosis patients. (Dolce D.)

13. Individuation and evaluation of new bacteriophages for the treatment of cystic fibrosis lung infection caused by *Pseudomonas aeruginosa.* (Rossitto M.)

11:00 am - 11:30 am: Coffee Break

11:30 am - 12:30 am: Talk: Highlights from the European CF Basic Research Conference

12:30 pm- 1:00 pm: Conclusions

CLINICAL IMPLICATION OF CELLULAR SENESCENCE ON CFTR EXPRESSION

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Background: Cystic fibrosis trans-membrane conductance regulator (CFTR) is a cAMP-modulated chloride/bicarbonate channel with different functions in various organs and tissues. Patients with CF are characterized by recurrent infections and by chronic neutrophilic airway inflammation as well as increased levels of neutrophil elastase (NE) in the airways. NE triggers cell cycle arrest that can lead to senescence. Moreover, it is well demonstrated that the CFTR expression get decreasing from embryogenesis to adult/elder age. Transcriptional, posttranscriptional and epigenetic regulatory mechanisms play a key role in decreasing the CFTR expression during life and recent evidences show that some CFTR-regulating microRNAs, i.e, mir-494, is up regulated during cell senescence. Cellular senescence is a permanent cell cycle arrest. In young cells it can be induced by different stimuli both exogenous and endogenous such as the physiological shortening of telomeres, the activation of oncogenes as well as oxidative stress. Furthermore, senescent cells are associated with modifications in the gene expression profile based on transcriptional, posttranscriptional and epigenetic regulatory mechanisms.

Aims: To assess whether CFTR might be involved in cellular senescence and understand its role in the cellular senescence.

Methods: To induce premature senescence, IMR90 cells at PDL34 were treated with 100 μM diethylmaleate (DEM) (Sigma-Aldrich) in complete medium on alternate days for ten days. Western Blot and Real Time-PCR analysis were performed to assess either the CFTR and the microRNAs expression in: i) IMR90 cells at different population doubling levels (PDL); ii) IMR90 cells at different days after DEM treatment.

Results: We found that: i) the CFTR expressions significantly decreased in IMR90 cells during replicative senescence (PDL58 versus PDL35); ii) the CFTR expression significantly decreased in IMR90 cells after DEM treatment; iii) there was an inverse relationship between CFTR and miRNA 494 expression either in IMR90 cells during replicative senescence and in IMR90 cells after DEM treatment.

Conclusions: Our preliminary data show that CFTR is physiologically down-regulated during cellular senescence and this may (at least partially) depend on the up-regulation of miR-494. To better investigate the role of CFTR in cellular senescence, we are performing the over-expression of CFTR protein in pre-senescent/senescent IMR90 and the silencing of CFTR in IMR90 young cells. Furthermore, we are now validating such results on primary epithelial nasal cells from different subjects.