13th CONVENTION OF FFC INVESTIGATORS IN CYSTIC FIBROSIS

26-28 novembre 2015
Hotel Poiano, Garda (Verona)

Final Program

Thursday, 26th

10:30-13:30

Satellite Meeting

Biomarkers to personalize treatment of the basic defect and to monitor early response

Chairman: Luigi Maiuri - Co-chairman: Carlo Castellani

10:30-10:35 Opening remarks (G. Mastella)
10:35-10:50 Introduction: Biomarkers, certainties and doubts. What, when, where, how (Luigi Maiuri).

10:50-12:15

Biomarkers for monitoring the effectiveness of drugs to treat the basic defect in clinical trials and in the individual patient

- What and how markers are currently used in clinical trials: appropriateness and limits (Cesare Braggion, 15 min).
- The classic sweat test: is it a reliable "surrogate" marker of CFTR function? Methodological problems and applications (Natalia Cirilli, 15 min)
- Are there alternative procedures that can be implemented for the sweat test? The "spot test" (Paola Melotti, 10 min)
- Nasal potential difference (NPD): reliability and applicability (Paola Melotti, 10 min)
- CFTR function of monocytes: is it a possible marker of treatment efficacy? (Claudio Sorio, 10 min)
- Rectal biopsies and organoids: what can we expect from these tests? Sara Caldera, 10 min)
- Biomarkers in nasal brushing (Valeria Raia, 15 min)

12:15-13:20

Biomarkers as potential predictors of treatment effectiveness before therapy in individual patients

- May appropriate locations and appropriate biomarkers allow for personalized medicine? Can they direct the decision to a specific clinical treatment? The reasons why we need them (Carlo Castellani, 10 min)
- Polarized bronchial epithelia for in vitro evaluation of CFTR correctors and potentiators (Luis Galietta, 15 min)
- Intestinal organoid (Sara Caldrer, 15 min)
- Nasal brushing (A. Tosco, 15 min)
- Monocytes (Claudio Sorio, 10 min)

13:20-13:30

**Take home message**

- Can a versatile test or a combination of tests for both predicting and early monitoring the effectiveness of therapy exist? (Luigi Maiuri, Carlo Castellani, Cesare Braggion)

*Note. The above time-frames include discussion among speakers and with the audience*

13:30-14:30 Lunch

14:30-14:35 *Wellcome Message* (Vittoriano Faganelli, FFC President)

14:40-16:40

**Plenary session 1**

**Preventive and clinical perspectives**

Chairman: Roberto Buzzetti - Co-chairman: Cesare Braggion

*Introduction (5’)*

1. Mosconi P, Castellani C
   Citizens’ jury and decision making on cystic fibrosis carrier screening: to screen or not to screen? (FFC#22/2013, Concluded)

2. Castellani C
   Outcomes of spontaneous application of carrier screening for cystic fibrosis: follow-up of its effects on birth prevalence, neonatal screening and reproductive behaviour of carrier couples. (FFC#26/2015, New, see poster session 4, abstr. n. 65)

3. Battezzati A
   Clinical implications of the natural history of insulin secretory and sensitivity defects in cystic fibrosis (FFC#21/2013, Concluded)

4. Zegarra-Moran O, Vassalli M
   Properties of airway mucus in cystic fibrosis: their modification by changes in the activity of CFTR and after application of bicarbonate (FFC#29/2014, Concluded)

5. Zaza G, Chilosi M
   In vitro study of potential pro-fibrotic effect of Everolimus in different human airway cell lines. Searching for new biomarkers to optimize MTOR-inhibitor immunosuppressive treatment of cystic fibrosis patients undergoing lung transplantation (FFC#28/2014, In progress, see poster session 4, abstr. n. 72)

6. Tortoli E, Cariani L, Di Serio C, Niemann S
   Transmissibility and clinical significance of *Mycobacterium abscessus* in patients with cystic fibrosis (FFC#27/2014, In progress, see poster session 4, abstr. n. 71)
16:40 – 16:50 Institutional communications (Gianni Mastella)

16:50 – 17:20 Coffee break

17:20 – 19:20

Parallel Poster Sessions

<table>
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<tr>
<th>1. CFTR</th>
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<td>Chairman: Nicoletta Pedemonte</td>
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7. Atlante A  
Relationship between mitochondria and F508del-CFTR in Cystic Fibrosis (FFC#1/2015, New)

8. Cavalli A, Pedemonte N  
RNF5/RMA1 ubiquitin ligase as a drug target for mutant CFTR rescue (FFC#2/2015, New)

9. de Jonge H, Calder S  
Assessment and pharmacological correction of abnormalities in bicarbonate (HCO3-) and mucus transport in intestinal biopsies and organoids of CF patients (FFC#3/2015, New)

10. De Stefano D, Maiuri MC  
Metabolic dysfunction in CF: implications for a drug discovery program (FFC#4/2015, New)

11. Duga S, Costantino L, Orrenius C  
The plant cytokine kentin and its analogues as potential therapeutic agents to correct CFTR splicing defects (FFC#5/2015, New)

12. Messina G  
Evaluation of the biological and therapeutic properties of Mesoangioblasts -vessel associated progenitor cells- in the cell based therapy of Cystic Fibrosis (FFC#6/2015, New)

13. Millo E, Cichero E  
Novel aminoarylthiazole derivatives as correctors of the chloride transport defect in cystic fibrosis: computer assisted drug design, synthesis and biological evaluation (FFC#7/2015, New)

14. Piacentini M, Maiuri L  
Dissecting the role of TG2 in cystic fibrosis pathogenesis: identification of possible novel therapeutic targets (FFC#8/2015, New)

15. Tamanini A, Aureli M  
Identification of molecular targets to reduce the side effect of gating potentiators on the F508del-CFTR plasma membrane stability (FFC#9/2015, New)

16. Lentini L, Pibiri I *  
Identification and validation of novel molecules obtained by integrated computational and experimental approaches for the read-through of PTCs in CF cells (FFC#1/2014, In progress)

17. Luini A *  
A systems biology approach to the correction of Cystic Fibrosis: from building a network of proteostasis regulatory pathways to combinatorial targeting (FFC#2/2014, In progress)

18. Moran O *  
The molecular structure and the folding of the whole Cystic Fibrosis Transmembrane Conductance Regulator (CFTR): correctors sites (FFC#4/2014, In progress)
19. Pagani F *
   An RNA based approach based on ExSpeU1 for correction of CFTR splicing defects: analysis of efficacy in primary bronchial cells (FFC#5/2014, In progress)

20. Venerando A, Villella VR *
   A kinase-directed approach to rescue functionality of F508del CFTR (FFC#7/2014, In progress)

21. Galietta LJv, Bandiera T *
   Task Force for Cystic Fibrosis (In progress)

2. INFLAMMATION

Chairman: Mariacristina Dechecchi

22. Lleò MM *
   A CF, IL-8 transgenic mouse model for the in vivo, long-term monitoring of the anti-inflammatory role of metallo-protease inhibitors and antibiotics with mechanisms of action similar to that of azithromycin (FFC#10/2015, New)

23. Dechecchi MC, Aureli M
   A systematic investigation of miglustat-derivative iminosugar clusters as possible anti-inflammatory agents for Cystic Fibrosis lung disease (FFC#22/2015, New)

24. Hirsch E, Laudanna C *
   Targeting PI3Kγ scaffold function to activate airway CFTR, limit lung inflammation and promote bronchorelaxation in cystic fibrosis (FFC#23/2015, New)

25. Rimessi A
   Mitochondrial quality control machinery: a role in the P. aeruginosa-triggered inflammatory response in Cystic Fibrosis (FFC#20/2015, New)

26. Strazzabosco M
   CFTR-defective biliary cells from human induced pluripotent-stem cells (iPSC) as a model to study the role of innate immunity in cystic fibrosis liver disease (FFC#24/2015, New)

27. Cabrini G, Nassini R
   TRPA1 channels as novel molecular targets for anti-inflammatory therapies in CF lung (FFC#17/2014, In progress)

28. Pinton P
   Mitochondrial Ca2+-dependent inflammasome activation exacerbates the P. aeruginosa-driven inflammatory response (FFC#19/2014, In progress)

29. Pizzo E, Pedone EM
   Identification and characterization of LPS-neutralizing human peptides: potential tools to control inflammation in cystic fibrosis lung disease (FFC#20/2014, In progress)

30. Romano M, Totani L, Marchisio M
   Mechanisms and clinical implications of endothelial dysfunction in cystic fibrosis (FFC#23/2014, In progress)

31. Sonnino S
   The role of Glucocerebrosidase GBA2 in cystic fibrosis lung inflammation: from molecular mechanism to therapeutic strategies (FFC#24/2014, In progress)

32. Pilette C, De Rose V
Impaired secretory IgA and mucosal immunity in cystic fibrosis: contribution to lung pathology and impaired defence against bacterial infection, and role of CFTR-related epithelial changes in the regulation of the receptor-mediated IgA transcytosis (FFC#26/2014, In progress)

33. Recchiuti A
   Resolvin D1 for Targeting Chronic Lung Inflammation and Infection in Cystic Fibrosis (FFC#21/2014, In progress)

34. Romani L *
   Targeting pathogenic pathways leading to inflammatory Th17 responses in cystic fibrosis: from drug discovery to preclinical validation (FFC#22/2014, In progress)

(*) Project presented also in Plenary Sessions

Friday, 27th

8:30-10:40

Plenary Session 2

Rescuing F508del-CFTR

Chairman: Luis Galietta - Co-chairman: Valeria Casavola

Introduction (5’)

35. Casavola V
   Mechanism of action of trimethylangelicin in rescuing F508del CFTR functional expression (FFC#1/2013, Concluded)

36. Gambari R, Chilin A
   Design and synthesis of improved analogs of trimethylangelicin (TMA) for personalized treatment of cystic fibrosis (FFC#8/2014, Concluded)

37. Mazzei M, Fossa P, Pascale M
   ΔF508-CFTR correctors deriving from computational design and from safe natural compounds for a prompt clinical application (FFC#3/2013, Concluded)

38. Rusnati M, Fossa P, Orro A
   Development of novel methodologies for the identification of CFTR-targeted drugs: a multidisciplinary approach using Real Time Surface Plasmon Resonance interaction assay supported by bioinformatics strategies on HPC infrastructures (FFC#6/2014, Concluded)

39. Moran O
   The molecular structure and the folding of the whole Cystic Fibrosis Transmembrane Conductance Regulator (CFTR): corrector sites (FFC#4/2014, In progress, see poster session 1, abstr. n. 18)

40. Galietta LJV, Bandiera T
   Task Force for Cystic Fibrosis (FFC/TFCF, In progress, see poster session 1, abstr. n. 21)

10:40 – 11:10 Coffee break
Plenary Session 3

Other approaches for correcting basic defect

Chairman: Paola Bruni - Co-chairman: Giuseppe Castaldo

Introduction (5’)

41. Lentini L, Pibiri I
Identification and validation of novel molecules obtained by integrated computational and experimental approaches for the read-through of PTCs in CF cells (FFC#1/2014, In progress, see also poster session 16)

42. Pagani F
An RNA based approach based on ExSpeU1 for correction of CFTR splicing defects: analysis of efficacy in primary bronchial cells (FFC#5/2014, In progress, see poster session 1, abstr. n. 19)

43. Luini A
A systems biology approach to the correction of Cystic Fibrosis: From building a network of proteostasis regulatory pathways to combinatorial targeting (FFC#2/2014, In progress, see poster session 1, abstr. n. 17)

44. Venerando A, Vilella VR
A kinase-directed approach to rescue functionality of F508del CFTR (FFC#7/2014, In progress, see poster session 1, abstr. n. 20)

New diagnostic proposals

Chairman: Paola Bruni – Co-chairman: Giuseppe Castaldo

45. Castaldo G
Nasal epithelial cells as a novel diagnostic approach for Cystic Fibrosis and CFTR related-disorders (FFC#7/2013, Concluded)

46. Melotti P, de Jonge H
Testing CFTR in epithelial organoids for drug development and diagnosis of cystic fibrosis (FFC#3/2014, Concluded)

13:10 – 14:30 Lunch

14:30 – 15:30

Plenary Session 4

Advances in clinical microbiology

Chairman: Gianmaria Rossolini - Co-chairman: Livia Leoni

Introduction (5’)

47. Bevivino A, Mengoni A, Taccetti G, Fiscarelli EV, De Alessandri A
Investigating the airway microbiome in cystic fibrosis patients with a severe decline in lung function: an opportunity for a personalized microbiome based therapy (FFC#10/2014, Concluded – FFC#14/2015, New, see poster session 3, abstr. n. 55)

48. Leoni L, Ungaro F, Imperi F, Fiscarelli EV
Anti-virulence therapy against *Pseudomonas aeruginosa*: identification of antibiofilm drugs and development of inhalable Niclosamide and Flucytosine formulations (FFC#10/2013, Concluded)

49. Garlanda C
Infections in cystic fibrosis patients: effect of PTX3 genetic variants on endogenous PTX3 production and function (FFC#15/2014, Concluded)

50. Pacello F
Targeting extracellular Protein Disulphide Isomerase to control *Burkholderia cenocepacia* lung infections (FFC#13/2014, In progress, see poster session 3, abstr. n. 62)

15:30 – 17:00

**Plenary Session 5**

**State of the art and future challenges in CF Microbiology**

Chairman: Gianmaria Rossolini
- Lecture by Eshwar Mahenthiralingam (University of Cardiff, UK) (45’)
- General discussion

17:00 – 17:30 Coffee break

17:30 – 19:30

**Parallel Poster Sessions**

3. **Microbiology**

Chairman: Annamaria Bevivino

51. Berlutti F *
Anti-inflammatory and anti-bacterial activity of bovine lactoferrin administered by aerosol in airway infections of pre-clinical wt and CF mouse models (FFC#12/2015, New)

52. Bragonzi A, Iraqui F
Cystic fibrosis modifier genes related to *Pseudomonas aeruginosa* lung disease (FFC#9/2014, In progress)

53. Lorè NI
Genetically diverse mice as innovative model for cystic fibrosis (FFC#11/2015, New)

54. Bertoni G
Role of small RNA-based regulatory systems in cystic fibrosis airways infection by *Pseudomonas aeruginosa*: a new frontier in the identification of molecular targets for novel antibacterials (FFC#13/2015, New)

Investigating the airway microbiome in cystic fibrosis patients with a severe decline in lung function: an opportunity for a personalized microbiome based therapy (FFC#14/2015, New)

56. Cirillo DM
Impact of anti-*Staphylococcus aureus* treatment on *Pseudomonas aeruginosa*-induced lung damage (FFC#15/2015, New)

57. Gemma S, Docquier JD
Development of metallo-enzyme inhibitors to overcome *Pseudomonas aeruginosa* antibiotic-resistance in cystic fibrosis patients (FFC#16/2015, New)

58. Ghisotti DE
Phage Therapy against *Pseudomonas aeruginosa* Infections in Cystic Fibrosis Patients (FFC#17/2015, New)

59. Landini P
Antimetabolite drugs as inhibitors of *Pseudomonas aeruginosa* biofilm growth and virulence: potential chemotherapics and tools in target identification for new antimicrobials (FFC#18/2015, New)

60. Riccardi G, Ungaro F
Inhalable formulations of new molecules effective against *Burkholderia cenocepacia*: from *in vitro* to *in vivo* applications (FFC#19/2015, New)

61. Visca P, Peri F, Sorrentino R
Exploiting the potential of gallium for the treatment of *Pseudomonas aeruginosa* pulmonary infection (FFC#21/2015, New)

62. Pacello F *
Targeting extracellular Protein Disulphide Isomerase to control *Burkholderia cenocepacia* lung infections (FFC#13/2014, In progress)

63. Mangoni ML *
Development and preclinical testing of a novel antimicrobial peptide to treat *Pseudomonas aeruginosa*-induced lung infections (FFC#11/2014, In progress)

### 4. Epidemiology and clinical research

**Chairman:** Giovanni Taccetti

64. Braggion C
CF Clinical guidelines (FFC#25/2015, New)

65. Castellani C *
Outcomes of spontaneous application of carrier screening for cystic fibrosis: follow-up of its effects on birth prevalence, neonatal screening and reproductive behaviour of carrier couples (FFC#26/2015, New)

66. Cirilli N, Raia V
Intra-individual biological variation in sweat chloride concentrations (FFC#27/2015, New)

67. Padoan R
Cystic fibrosis and meconium ileus: a multicentric study on risk factors for adverse outcome in infancy (FFC#28/2015, New)

68. Sorio C, Averna M
Testing CFTR repair in cystic fibrosis patients carrying nonsense and channel gating mutations (FFC#29/2015, New)

69. Corti A
GSH inhalation therapies in CF: how useful, how safe? Set-up of a CF murine model for monitoring of inflammation in vivo and assessment of convenient alternatives (FFC#18/2014, In progress)

70. Taccetti G
*Pseudomonas aeruginosa* eradication in patients with cystic fibrosis: a randomised multicentre study comparing classic treatment protocols with classic treatment combined with antibiotic treatment of upper airways (FFC#30/2015, New)

71. **Tortoli E, Cariani L, Di Serio C, Niemann S** *
Transmissibility and clinical significance of *Mycobacterium abscessus* in patients with cystic fibrosis (FFC#27/2014, In Progress)

72. **Zaza G, Chilosi M** *
In vitro study of potential pro-fibrotic effect of Everolimus in different human airway cell lines. Searching for new biomarkers to optimize MTOR-inhibitor immunosuppressive treatment of cystic fibrosis patients undergoing lung transplantation (FFC#28/2014, In progress)

(*) Project presented also in Plenary Sessions

20:30 – 23:30

**Social dinner and entertainment**

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**Saturday, 28th**

9:00 – 11:00

**Plenary Session 6**

**New targets for anti-inflammatory therapies**

Chairman: **Giorgio Berton** - Co-chairman: **Giulio Cabrini**

*Introduction (5’)*

73. **Hirsch E, Laudanna C**
Targeting PI3Ky scaffold function to activate airway CFTR, limit lung inflammation and promote bronchorelaxation in cystic fibrosis (FFC#25/2014, Completed – FFC#23/2015, New, see poster session 2, abstr. n. 24)

74. **Romani L**
Targeting pathogenic pathways leading to inflammatory Th17 responses in cystic fibrosis: from drug discovery to preclinical validation (FFC#22/2014, In progress, see poster session 2, abstr. n. 34)

75. **Cigana C, Naggi A**
Pathophysiological relevance of glycosaminoglycans in *Pseudomonas aeruginosa* chronic lung infections and validation of new therapeutic approaches to modulate inflammation and tissue remodelling (FFC#14/2013, Concluded)

76. **Signorelli P, Borghi E, Sozzani S**
Sphingolipid targeting in inflammation and fungal infection (FFC#20/2013, Concluded)

77. **Berlutti F**
Lactoferrin-loaded niosomes in reducing inflammation and infection of cystic fibrosis airways (FFC#16/2014, Concluded – FFC#12/2015, New, see poster session 3, abstr. n. 51)

78. **Lleò MM**
Development of a CF, IL-8/NF-KB transgenic mouse model for the in vivo long-term monitoring of the inflammatory response induced by bacteria treated or not with azithromycin (FFC#18/2013, Concluded – FFC#10/2015, New, see poster session 2, abstr. n. 22)

11:00 – 11:30 Coffee break

11:30 – 12:50

**Plenary Session 7**

### Antimicrobial peptides

**Chairman:** Alessandra Bragonzi - Co-Chairman: Marialuisa Mangoni

*Introduction (5’)*

**79. Pini A**
Preclinical development of the antimicrobial peptide M33 and onset of regulatory procedures for clinical trials (FFC#12/2013, Concluded)

**80. Mangoni ML**
Development and preclinical testing of a novel antimicrobial peptide to treat *Pseudomonas aeruginosa*-induced lung infections (FFC#11/2014, In progress, see poster session 3, abstr. n. 63)

**81. Scocchi M**
Development of BMAP18 as a peptide drug in the lung bacterial infections: a study to improve its effectiveness in the CF-pulmonary environment (FFC#14/2014, Concluded)

**82. Notomista E, Ungaro F**
Inhalable dry powders for chemically-modified human Cationic AntiMicrobial Peptides (CAMPs): moving toward in vivo application (FFC#12/2014, Concluded)

12:50 – 13:00

*Conclusive remarks* (Giorgio Berton, President FFC Scientific Advisory Board)

Note. The names of the speakers above are relative to the Principal Investigators (first name) and Partners of the presented FFC projects

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