Fondazione Ricerca
Fibrosi Cistica - Onlus
italian cystic fibrosis research foundation

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* (**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 Caldrer**, 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

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13:30-14:30 Lunch

14:30-14:35
Welcome 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

1. CFTR

Chairman: **Nicoletta Pedemonte**

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, Caldrer S**
   Assessment and pharmacological correction of abnormalities in bicarbonate (HCO_3^-) 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 kinetin 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

11:10 – 13:10

Plenary Session 3

Other approaches for correcting basic defect

Chairmam: **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, Villella 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 – 14:10 Lunch

14:10 – 15:30

Plenary Session 4

Advances in clinical microbiology

Chairman: **Gian Maria 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: **Gian Maria 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*)

55. **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#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

Saturday, 28th

9:00 – 11:00

Plenary Session 6

New targets for anti-inflammatory therapies

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

Introduction (5')

69. Hirsch E, Laudanna C
Targeting PI3Kγ 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***)

70. 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***)

71. 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*)

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

73. 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***)

74. 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')

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

76. 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***)

77. 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*)

78. 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)

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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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