

Annamaria Fra – Curriculum Vitae

PRESENT POSITION Assistant professor in General Pathology and Immunology
Group leader at the Dept. Molecular and Translational Medicine
University of Brescia

EDUCATION		
10/03/1994	Specialty School Degree in Applied Biotechnology, University of Milan, Italy.	50/50 cum laude
14/11/1990	Laurea in Pharmacy, University of Milan, Italy	110/110 cum laude
10/03/1989	Laurea in "Pharmaceutical Chemistry and Technology" University of Milan, Italy.	110/110 cum laude

LANGUAGES
Mother tongue: Italian
Other languages: English
2012 - Certificate in Advanced English (CAE), University of Cambridge (UK). Grade B. CEFR: C1.

RESEARCH EXPERIENCE	
Since 22/01/2014	National Abilitation (ASN) to Associate Professor in Applied Biology – (SC 05/F1 - SSD BIO/13 – Biologia applicata)
From 1/10/2002 to today	Assistant professor of General Pathology and Immunology (SC 06A2 - SSD MED/04)
From 01/02/2000 to 01/04/2002	Research fellow at the Dept. Biomedical Sciences and Biotechnology, University of Brescia, Italy
From 01/08/1995 to 1/03/1999	Staff scientist at DIBIT- San Raffaele Institute, Milan, Italy.
From 01/07/1993 to 30/06/1995	Post-Doctoral Fellow of the European Community "Human and Capital Mobility Programme" in the laboratory led by Kai Simons, EMBL, Heidelberg (Germany).
From 01/01/1990 to 1/6/1993	Fellow of the Italian Cancer Research Association (AIRC) in the laboratory led by Roberto Sitia at DIBIT- San Raffaele Institute, Milan, Italy
From 01/01/1989 to 31/12/1989	Research fellow in the laboratory led by Cristina Alberini, Dept. Of Biochemistry, University of Brescia, Italy
From 07/08/2017 to 07/09/2017	Visiting scientist at the "Center for Respiratory Biology", UCL, London, UK

OTHER WORK
EXPERIENCES

Since 2002-Tutor of PhD students and research fellows

Since 2002-Thesis supervisor of 16 BD and MD students

Since 2011- Member of PhD programs and dissertation commissions

2011-2012 – Teacher committee of PhD programme in “Cellular and Molecular Biotechnology applied to biomedicine”.

2013-today - Teacher committee of PhD programme in “Molecular Genetics, Biotechnology and Experimental Medicine”.

12/02/2016 – Member of the dissertation commission of the PhD programme in Cellular and developmental Biology – Università degli Studi di Roma “La Sapienza”, Rome, Italy

Chairs

-Chair of the “Basic Research” session of the “1° meeting on the Italian research in alpha-1- antitrypsin deficiency”, 2017 February 25th, Centro Paolo VI, Brescia, Italy

-Chair of the session “Glycosylation and its biological implication in serpinopathies” in the meeting “The role of glycosylation in serpin biology and conformational diseases”, 28 September 2017, Orléans (France).

Membership in Scientific societies:

ABCD, Associazione di Biologia Cellulare e del Differenziamento

FISV, Federazione Italiana Scienze della Vita

SIICA, Società Italiana di Immunologia, Immunologia Clinica ed Allergologia

ASHG, American Society of Human Genetics

Teaching in courses of Bachelor's and Master's degrees

2002-2003

- Molecular Immunology (35 hours), MED04, BD in Biomedical Laboratory Techniques.
- General Pathology (25 hours), MED04, BD in Professional Education.

2003-2004

- Molecular Immunology (35 hours), MED04, BD in Biomedical Laboratory Techniques.

2004-2005

- Molecular Immunology (35 hours), MED04, BD in Biomedical Laboratory Techniques.
- Immunopathology (10 hours), MED04, BD in Biotechnology.

2005-2006

- Molecular Immunology (35 hours), MED05, BD in Biomedical Laboratory Techniques.
- Immunopathology (10 hours), MED04, BD in Biotechnology.
- General Pathology (20 hours), MED04, BD in Professional Education.

2006-2007

- Molecular Immunology (35 hours), MED05, BD in Biomedical Laboratory Techniques.
- Immunopathology (10 hours), MED04, BD in Biotechnology.
- General Pathology (12 hours), MED04, BD in Professional Education.
- General Pathology (16 hours), MED04, BD in Exercise and Sport Sciences (Coordinator).

2007-2008

- Molecular Immunology (35 hours), MED05, BD in Biomedical Laboratory Techniques.
- Immunopathology (10 hours), MED04, BD in Biotechnology.
- General Pathology (12 hours), MED04, BD in Professional Education.
- General Pathology (16 hours), MED04, BD in Exercise and Sport Sciences (Coordinator).

2008-2009

- Molecular Immunology (35 hours), MED05, BD in Biomedical Laboratory Techniques.
- Immunopathology (10 hours), MED04, BD in Biotechnology.
- General Pathology (12 hours), MED04, BD in Professional Education.
- General Pathology (16 hours), MED04, BD in Exercise and Sport Sciences (Coordinator).
- Immunology (10 hours), MED04, BD in Environment and Workplace prevention Techniques.

2009-2010

- Molecular Immunology (35 hours), MED05, BD in Biomedical Laboratory Techniques.
- General Pathology (16 hours), MED04, BD in Exercise and Sport Sciences (Coordinator).
- Immunology (10 hours), MED04, BD in Environment and Workplace prevention Techniques.

2010-2011

- Molecular Immunology (35 hours), MED05, BD in Biomedical Laboratory Techniques.
- Immunology (10 hours), MED04, BD in Environment and Workplace prevention Techniques.

2011-2012

- Molecular Immunology (35 hours), MED05, BD in Biomedical Laboratory Techniques.
- Immunology (35 hours), MED04, BD in Biomedical Laboratory Techniques.

- Immunology (10 hours), MED04, BD in Environment and Workplace prevention Techniques.

- General Pathology (16 hours), MED04, BD in Exercise and Sport Sciences.

2012-2013

- Immunology (12 hours), MED04, BD in Biomedical Laboratory Techniques.

- Laboratory of Clinical Pathology (30 hours), MED05, CL in Biotechnologie.

- General Pathology (16 hours), MED04, BD in Exercise and Sport Sciences.

2013-2014

- Laboratory of Clinical Pathology (30 hours), MED05, BD in Biotechnology.

- General Pathology (16 hours), MED04, BD in Exercise and Sport Sciences.

2014-2015

- Laboratory of Clinical Pathology (30 hours), MED05, BD in Biotechnology.

2015-2016

- Laboratory of General Pathology (30 hours), MED04, BD in Biotechnology.

- General Pathology (24 hours), MED04, BD in Environment and Workplace prevention Techniques.

2016-2017

- Laboratory of General Pathology (30 hours), MED04, BD in Biotechnology.

- General Pathology (24 hours), MED04, BD in Environment and Workplace prevention Techniques.

2017-2018

- Laboratory of General Pathology (30 hours), MED04, BD in Biotechnology.

- General Pathology (24 hours), MED04, BD in Environment and Workplace prevention Techniques.

- Techniques in Clinical Pathology (36 hours), MED05, BD in Biomedical Laboratory Techniques.

Specialty courses

-1999-2000

Course of "Elementi di Chimica Analitica e Analisi Strumentale" in the Specialty School of "Biochemistry and Clinical Chemistry".

PhD courses

16/07/2014 – PhD Seminars on Protein Folding and misfolding. Title: "Alpha1-antitrypsin deficiency as a prototypical ER conformational disease". PhD program in on Research in Biomedical Science and Translational Medicine and PhD program in Neuroscience.

12 and 26 May 2016– Lessons in the PhD program of Molecular Genetics, Biotechnology and Experimental Medicine on "Protein folding in cells"

PUBLICATIONS

Scientific publications in peer-reviewed international journals:

1. M. Laffranchi, E.L.K. Elliston, F.Gangemi, R. Berardelli, D.A Lomas, J A Irving, A. Fra. (2019) Characterisation of a type II functionally-deficient variant of alpha-1-antitrypsin discovered in the general population. *PlosOne*,14 (1):e0206955.
2. Annamaria Fra, Emanuela D'Acunto, Mattia Laffranchi, Elena Miranda. (2018) Cellular Models for the Serpinopathies. Contributo in volume in *.Methods Mol Biol.* 1826:109-121.
3. Giacomuzzi,E., Laffranchi,M., Berardelli,R., Ravasio,V., Ferrarotti,I., Gooptu,B., Borsani,G. and Fra,A. (2018) Real-world clinical applicability of pathogenicity predictors assessed on SERPINA1 mutations in alpha-1-antitrypsin deficiency. *Hum. Mutat.* 39(9):1203..
4. Laffranchi M, Berardelli R, Ronzoni R, Lomas DA, Fra A. (2018) Heteropolymerization of α -1-antitrypsin mutants in cell models mimicking heterozygosity. *Hum Mol Genet* 27:1785.
5. Caccia Sonia, Suffritti Chiara, Carzaniga Thomas, Berardelli Romina, Berra Silvia, Martorana Vincenzo, **Fra Annamaria**, Drouet Christian, Cicardi Marco. (2018) Intermittent C1-Inhibitor Deficiency Associated with Recessive Inheritance: Functional and Structural Insight. *Sci Rep.* 8:977.
6. **Annamaria Fra**, Edgar Djaha Yoboue and Roberto Sitia. (2017) Cysteines as redox molecular switches and targets of disease. Review. *Frontiers in Molecular Neuroscience* 10:167.
7. Elena Miranda, Ilaria Ferrarotti, Romina Berardelli, Mattia Laffranchi, Marta Cerea, Fabrizio Gangemi, Imran Haq, Stefania Ottaviani, David A. Lomas, James A. Irving, **Annamaria Fra** (2017). The pathological Trento variant of alpha-1-antitrypsin (E75V) shows nonclassical behaviour during polymerization. *FEBS J.* 284:2110.
8. **Fra A**, Cosmi F, Ordoñez A, Berardelli R, Perez J, Guadagno NA, Corda L, Marciniak SJ, Lomas DA, Miranda E (2016). Polymers of Z α 1-antitrypsin are secreted in cell models of disease. *Eur Respir J.* 47:1005.
9. Ronzoni R, Berardelli R, Medicina D, Sitia R, Gooptu B, **Fra AM**. (2016) Aberrant disulphide bonding contributes to the ER retention of alpha1-antitrypsin deficiency variants. *Hum Mol Genet* 15:642. Epub 2015 Dec 8.
10. Ferrarotti, I., Carroll, T. P., Ottaviani, S., **Fra, A. M.**, G, O. B., Molloy, K., Corda, L., Medicina, D., Curran, D. R., McElvaney, N. G., and Luisetti, M. (2014) Identification and characterisation of eight novel SERPINA1 null mutations. *Orphanet J Rare Dis* 9, 172.
11. Tiberio, L., Nascimbeni, R., Villanacci, V., Casella, C., **Fra, A.**, Vezzoli, V., Furlan, L., Meyer, G., Parrinello, G., Baroni, M. D., Salerno, B., and Schiaffonati, L. (2013) The decrease of mineralcorticoid receptor drives angiogenic pathways in colorectal cancer. *PLoS One* 8, e59410.
12. **Fra, A. M.**, Gooptu, B., Ferrarotti, I., Miranda, E., Scabini, R., Ronzoni, R., Benini, F., Corda, L., Medicina, D., Luisetti, M., and Schiaffonati, L. (2012) Three new alpha1-antitrypsin deficiency variants help to define a C-terminal region regulating conformational change and polymerization. *PLoS One* 7, e38405. Fra AM is corresponding author.
13. Masciarelli, S., **Fra, A. M.**, Pengo, N., Bertolotti, M., Cenci, S., Fagioli, C., Ron, D., Hendershot, L. M., and Sitia, R. (2010) CHOP-independent apoptosis and pathway-selective induction of the UPR in developing plasma cells. *Mol Immunol* 47, 1356-1365.
14. Lanzi, G., Ferrari, S., Vihinen, M., Caraffi, S., Kutukculer, N., Schiaffonati, L., Plebani, A., Notarangelo, L. D., **Fra, A. M.**, and Giliani, S. (2010) Different molecular behavior of CD40 mutants causing hyper-IgM syndrome. *Blood* 116, 5867-5874. **Fra and Giliani are senior co-authors and co-corresponding authors.** Commentary in InsideBlood "A new guise for Hyper-IgM syndrome" by Garnett Kelsoe and Derek Cain (Duke University).

15. Medicina, D., Montani, N., **Fra, A. M.**, Tiberio, L., Corda, L., Miranda, E., Pezzini, A., Bonetti, F., Ingrassia, R., Scabini, R., Facchetti, F., and Schiaffonati, L. (2009) Molecular characterization of the new defective P(brescia) alpha1-antitrypsin allele. *Hum Mutat* 30, E771-781
16. Fanzani, A., Stoppani, E., Gualandi, L., Giuliani, R., Galbiati, F., Rossi, S., **Fra, A.**, Preti, A., and Marchesini, S. (2007) Phenotypic behavior of C2C12 myoblasts upon expression of the dystrophy-related caveolin-3 P104L and TFT mutants. *FEBS Lett* 581, 5099-5104
17. Cenci, S., Mezghrani, A., Cascio, P., Bianchi, G., Cerruti, F., **Fra, A.**, Lelouard, H., Masciarelli, S., Mattioli, L., Oliva, L., Orsi, A., Pasqualetto, E., Pierre, P., Ruffato, E., Tagliavacca, L., and Sitia, R. (2006) Progressively impaired proteasomal capacity during terminal plasma cell differentiation. *Embo J* 25, 1104-1113
18. Sironi, M., Conti, A., Bernasconi, S., **Fra, A. M.**, Pasqualini, F., Nebuloni, M., Lauri, E., De Bortoli, M., Mantovani, A., Dejana, E., and Vecchi, A. (2006) Generation and characterization of a mouse lymphatic endothelial cell line. *Cell Tissue Res* 325, 91-100
19. Tiberio, L., Tiberio, G. A., Bardella, L., Cervi, E., Cerea, K., Dreano, M., Garotta, G., **Fra, A.**, Montani, N., Ferrari-Bravo, A., Callea, F., Grigolato, P., Giulini, S. M., and Schiaffonati, L. (2006) Mechanisms of interleukin-6 protection against ischemia-reperfusion injury in rat liver. *Cytokine* 34, 131-142
20. Bonecchi, R., Locati, M., Galliera, E., Vulcano, M., Sironi, M., **Fra, A. M.**, Gobbi, M., Vecchi, A., Sozzani, S., Haribabu, B., Van Damme, J., and Mantovani, A. (2004) Differential recognition and scavenging of native and truncated macrophage-derived chemokine (macrophage-derived chemokine/CC chemokine ligand 22) by the D6 decoy receptor. *J Immunol* 172, 4972-4976
21. **Fra, A. M.**, Locati, M., Otero, K., Sironi, M., Signorelli, P., Massardi, M. L., Gobbi, M., Vecchi, A., Sozzani, S., and Mantovani, A. (2003) Cutting edge: scavenging of inflammatory CC chemokines by the promiscuous putatively silent chemokine receptor D6. *J Immunol* 170, 2279-2282
22. **Fra, A. M.**, Pasqualetto, E., Mancini, M., and Sitia, R. (2000) Genomic organization and transcriptional analysis of the human genes coding for caveolin-1 and caveolin-2. *Gene* 243, 75-83
23. Mancini, R., Fagioli, C., **Fra, A. M.**, Maggioni, C., and Sitia, R. (2000) Degradation of unassembled soluble Ig subunits by cytosolic proteasomes: evidence that retrotranslocation and degradation are coupled events. *Faseb J* 14, 769-778
24. **Fra, A. M.**, Mastroianni, N., Mancini, M., Pasqualetto, E., and Sitia, R. (1999) Human caveolin-1 and caveolin-2 are closely linked genes colocalized with WI-5336 in a region of 7q31 frequently deleted in tumors. *Genomics* 56, 355-356
25. Scheiffele, P., Verkade, P., **Fra, A. M.**, Virta, H., Simons, K., and Ikonen, E. (1998) Caveolin-1 and -2 in the exocytic pathway of MDCK cells. *J Cell Biol* 140, 795-806
26. Maggioni C., Carelli S., Cabibbo A., Fagioli C., Fra A.M. and Sitia R. (1998) Assembly and Secretion of antibodies during B cell development. *Bratisl Med J-Bratisl Lek Listy* 99, 419-25.
27. Isidoro, C., Maggioni, C., Demoz, M., Pizzagalli, A., Fra, A. M., and Sitia, R. (1996) Exposed thiols confer localization in the endoplasmic reticulum by retention rather than retrieval. *J Biol Chem* 271, 26138-26142
28. **Fra, A. M.**, Williamson, E., Simons, K., and Parton, R. G. (1995) De novo formation of caveolae in lymphocytes by expression of VIP21-caveolin. *Proc Natl Acad Sci U S A* 92, 8655-8659
29. **Fra, A. M.**, Masserini, M., Palestini, P., Sonnino, S., and Simons, K. (1995) A photo-reactive derivative of ganglioside GM1 specifically cross-links VIP21-caveolin on the cell surface. *FEBS Lett* 375, 11-14
30. **Fra, A. M.**, Williamson, E., Simons, K., and Parton, R. G. (1994) Detergent-insoluble glycolipid microdomains in lymphocytes in the absence of caveolae. *J Biol Chem* 269, 30745-30748
31. Guenzi, S., Fra, A. M., Sparvoli, A., Bet, P., Rocco, M., and Sitia, R. (1994) The efficiency of cysteine-mediated intracellular retention determines the differential fate of secretory IgA and IgM in B and plasma cells. *Eur J Immunol* 24, 2477-2482
32. **Fra, A. M.**, Fagioli, C., Finazzi, D., Sitia, R., and Alberini, C. M. (1993) Quality control of ER synthesized proteins: an exposed thiol group as a three-way switch mediating assembly, retention and degradation. *Embo J* 12, 4755-4761
33. **Fra A. M.**, Alberini C., Bet P., Finazzi D., Valetti C., and Sitia R. (1991) Modulating secretion of antibodies. *Ann Biol Clin (Paris)* 49, 283-286.
34. Sitia, R., Neuberger, M., Alberini, C., Bet, P., **Fra, A.**, Valetti, C., Williams, G., and Milstein, C. (1990) Developmental regulation of IgM secretion: the role of the carboxy-terminal cysteine. *Cell* 60, 781-790

Book chapter:

-**Fra A.**, and Sitia R. (1993) The endoplasmic reticulum as a site of protein degradation, Chapter 7 in *Subcellular Biochemistry Volume 21: Endoplasmic reticulum*, pages 143-168. Edited by N. Borgese and JR Harris. Plenum Press, New York, USA.

Published Meeting Abstracts (in ISI-WOS):

- 1) Jagger, AM; Elliston, ELK; Wroe, EI ; Wort, JL; Poeschla, M; Nanda, AS; Motamedi-Shad, N; Faull, SV; Salvadori, E; **Fra, A**; Miranda, E; Kay, CMW; Lomas, DA; Irving, JA (2017) Stability and structural change in the pathological polymerisation of alpha 1-antitrypsin. *European Biophysics Journal with Biophysics Letters* 46: S239.
- 2) Caccia, S., Suffritti, C., Carzaniga, T., Berardelli, R., **Fra, A.**, Drouet, C., and Cicardi, M. (2015). A case of remittent c1-inhibitor deficiency. *Molecular Immunology* 67, 128–128.
- 3) Lanzi, G., Ferrari, S., Kutukculer, N., Plebani, A., Notarangelo, L.D., **Fra, A.M.**, and Giliani, S. (2008). HIGM3 patients: understanding the mutation effect to develop a therapeutic approach. *Clinical and Experimental Immunology* 154, 67–67.
- 4) Ottaviani, S., Carroll, T.P., Ferrarotti, I., **Fra, A.M.**, O'Brien, G., Molloy, K., Corda, L., McElvaney, N.G., and Luisetti, M. (2014). Identification and characterisation of seven novel SERPINA1 null mutations. *European Respiratory Journal* 44, Meeting Abstract: 2932.
- 5) Mancini, R., Fagioli, C., **Fra, A.**, Maggioni, C., and Sitia, R. (1998). Degradation of soluble proteins from the ER: Some substrates require active proteasomes for translocation to the cytosol. *Molecular Biology of the Cell* 9, 459A–459A.
- 6) Mastroianni, N., Sitia, R., and **Fra, A.M.** (1997). Human caveolin 1 AND 2 are closely-linked genes mapping on chromosome. *Molecular Biology of the Cell* 8, 1203–1203.
- 7) Ikonen, E., Scheiffele, P., **Fra, A.M.**, Parton, R.G., and Simons, K. (1996). Role of VIP21-caveolin oligomeric complex in protein and lipid sorting in MDCK cells. *Molecular Biology of the Cell* 7, 1599–1599.

Brescia, 5th May 2019


