BIOGRAPHICAL SKETCH

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NAME: **MINGOZZI, Federico**

POSITION TITLE: **Research Director 2, INSERM (France Institute of Health and Medical Research)**

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

INSTITUTION AND LOCATION	DEGREE *(if applicable)*	Completion Date MM/YYYY	FIELD OF STUDY
University of Ferrara, Italy	**B.S.**	**06/98**	**Molecular Biology**
University of Ferrara, Italy	**Ph.D.**	**04/04**	**Biochemistry and Molecular Biology**
Children's Hospital of Philadelphia, PA, USA	**Post-Doc**	**06/06**	**Immunology/Gene Transfer**
Drexel University, PA, USA	**M.S.**	**12/06**	**Business Administration**

A. Personal Statement

Most of my career in research has been devoted to the understanding of the interactions of adeno-associated virus (AAV) vectors with the immune system.
During my undergraduate and graduate studies, I focused on the molecular and biochemical characterization of coagulation factor variants and their role in thrombotic and hemorrhagic disorders. As a postdoctoral fellow, I studied the mechanisms of immunological tolerance to coagulation factor IX induced by liver-directed gene transfer. This work showed for the first time that hepatic expression of an antigen elicits tolerance, rather than immunity, to the expressed antigen (1). After my postdoc, my research focus shifted to the study of immune responses directed against the AAV capsid antigen. These studies initiated with the observation that AAV vector administration in humans results in capsid-specific CD8+ T cell expansion and, potentially, clearance of AAV-transduced cells (2-6). Findings from these studies contributed to the design of gene transfer studies in which the vector was co-administered with immunosuppression, resulting in long-term transgene expression. In parallel to the study of immune responses in gene transfer, I have been closely involved in translational gene therapy studies for inherited and acquired diseases, including hemophilia A and B, RPE65 deficiency, lysosomal storage diseases, etc.
The work on immune responses in viral gene transfer continues in my current position, together with a research program focused on the preclinical and clinical development of AAV vector-based liver directed gene therapies for the treatment inherited diseases.

References:
1. Mingozzi F, Liu YL, Dobrzynski E, et al. Induction of immune tolerance to coagulation factor IX antigen by in vivo hepatic gene transfer. J Clin Invest. 2003;111:1347-1356.
2. Manno CS, Pierce GF, Arruda VR, et al. Successful transduction of liver in hemophilia by AAV-Factor IX and limitations imposed by the host immune response. Nature Medicine. 2006;12:342-347.
3. Mingozzi F, Maus MV, Hui DJ, et al. CD8(+) T-cell responses to adeno-associated virus capsid in humans. Nature Medicine. 2007;13:419-422.
4. Mingozzi F, Meulenberg JJ, Hui DJ, et al. AAV-1-mediated gene transfer to skeletal muscle in humans results in dose-dependent activation of capsid-specific T cells. Blood. 2009;114:2077-2086.
5. Nathwani AC, Tuddenham EG, Rangarajan S, et al. Adenovirus-associated virus vector-mediated gene transfer in hemophilia B. New England Journal of Medicine. 2011;365:2357-2365.
6. Nathwani AC, Reiss U, Tuddenham E, et al. Long Term Safety and Efficacy of a Liver-Directed Adeno-Associated Viral Vector Encoding Human FIX in Severe Hemophilia B Patients. New England Journal of Medicine. 2014. 371(21):1994-2004.

B. Positions and Honors

Postgraduate Training and Fellowship Appointments

2008 Patient Oriented Research Training, University of Pennsylvania, Philadelphia, PA
2005 Basic training in Immunology, American Association of Immunologists, Philadelphia, PA
2004-06 Research Associate, Hematology, The Children's Hospital of Philadelphia, Philadelphia, PA
2000-02 Research Fellow, Hematology, The Children's Hospital of Philadelphia, Philadelphia, PA
2000 Certificate Degree in Scientific Communication, University of Milan, Milan, Italy.

Faculty Appointments

2016- Director or Research Level 2, INSERM, France
2013- Associate Professor, University Pierre and Marie Curie - Paris 6, Paris, France
2011- Adjunct Professor, Universitat Autonoma de Barcelona, Barcelona, Spain
2011- International PhD Program Faculty Member, University of Ferrara, Ferrara, Italy

Non-Academic Appointments

2013- Team Leader, Immunology and Liver Gene Transfer Unit, Genethon, Evry, France
2006-13 Director of Translational Research, Center for Cellular and Molecular Therapeutics, The Children's Hospital of Philadelphia, USA

Specialty Certifications

2014 Accreditation to supervise research (HDR), University Pierre and Marie Curie, France
1999 Italian Board of Biology, Italy

Awards, Honors and Membership in Honorary Societies

2014 Grifols Martin Villar Hemostasis Basic Research Award
2013 Bayer Hemophilia, Early Career Investigator Award
2010 American Association of Pharmaceutical Scientists, Innovation in Biotechnology Awards
2006 Young Investigator Award, European Society of Gene and Cell Therapy
2005 Beta Gamma Sigma, Honors Society
2002 Travel Award, American Society of Hematology

Memberships in Professional and Scientific Societies

Scientific Societies:
2004-pres. American Society of Gene and Cell Therapy:
- Committee on Cell and Gene Therapy of Genetic and Metabolic Diseases, 2012-2017
- Chair of the Cell and Gene Therapy of Genetic and Metabolic Diseases, 2015-2016
- Committee on Immune Responses to Cell and Gene Therapy, 2014-2017

2014-pres. French Society of Gene and Cell Therapy:
- Executive Board Member

2007-pres. European Society of Gene and Cell Therapy

Scientific advisory board, meeting organizer:

2015 Organizing Committee, Workshop "Targeting liver disease at the DNA level", Venice, Italy,
2009 Organizing Committee, Workshop on immune responses to gene therapy vectors. Clinigene European Network of Excellence, Paris, France

Editorial positions:

2017- Cellular Immunology: Special topic editor
2016- Frontiers in Medicine, Associate Editor
2015- Human Gene Therapy, Editorial Board
2014- PlosONE, Academic Editor
2013-14 Frontiers in Immunology: Editor, Special Topic on immune responses to AAV vectors

C. Contribution to Science

1. In my early work as undergraduate and graduate student focused on basic aspects of coagulation disorders. In particular in these studies I contributed to identify variants of clotting factor genes associated with hemorrhagic or thrombotic disorders.
    a. Lunghi B, Castoldi E, **Mingozzi F**, et al. A novel factor V null mutation detected in a thrombophilic patient with pseudo-homozygous APC resistance and in an asymptomatic unrelated subject. **Blood**. 1998;92:1463-1464.
    b. **Mingozzi F**, Legnani C, Lunghi B, et al. A FV multiallelic marker detects genetic components of APC resistance contributing to venous thromboembolism in FV Leiden carriers. **Thromb Haemost**. 2003;89:983-989.
2. During my postdoc I contributed to lay the fundaments for the development of gene transfer strategies targeting the liver, showing that it is possible to induce immunological tolerance to an antigen by liver-directed gene transfer with AAV vectors.
    a. **Mingozzi F**, Liu YL, Dobrzynski E, et al. Induction of immune tolerance to coagulation factor IX antigen by in vivo hepatic gene transfer. **J Clin Invest**. 2003;111:1347-1356.
    b. Dobrzynski E, **Mingozzi F**, Liu YL, et al. Induction of antigen-specific CD4+ T-cell anergy and deletion by in vivo viral gene transfer. **Blood**. 2004;104:969-977.
    c. **Mingozzi F**, Hasbrouck NC, Basner-Tschakarjan E, et al. Modulation of tolerance to the transgene product in a nonhuman primate model of AAV-mediated gene transfer to liver. **Blood**. 2007;110:2334-2341.
3. Perhaps my most important contributions to the field of gene therapy come from my studies on the immune responses directed against the AAV capsid antigen.
    a. Manno CS, Pierce GF, Arruda VR, et al. Successful transduction of liver in hemophilia by AAV-Factor IX and limitations imposed by the host immune response. **Nature Medicine**. 2006;12:342-347.
    b. **Mingozzi F**, Maus MV, Hui DJ, et al. CD8(+) T-cell responses to adeno-associated virus capsid in humans. **Nature Medicine**. 2007;13:419-422.
    c. **Mingozzi F**, Meulenberg JJ, Hui DJ, et al. AAV-1-mediated gene transfer to skeletal muscle in humans results in dose-dependent activation of capsid-specific T cells. **Blood**. 2009;114:2077-2086.
    d. Nathwani AC, Tuddenham EG, Rangarajan S, et al. Adenovirus-associated virus vector-mediated gene transfer in hemophilia B. **New England Journal of Medicine**. 2011;365:2357-2365.
4. In my career, I contributed to the development and clinical translation of gene therapies for a number of disorders.
    a. Maguire AM, Simonelli F, Pierce EA, et al. Safety and efficacy of gene transfer for Leber's congenital amaurosis. **New England Journal of Medicine**. 2008;358:2240-2248.
    b. Amado D*, **Mingozzi F***, Hui D, et al. Safety and efficacy of subretinal readministration of a viral vector in large animals to treat congenital blindness. **Science Translational Medicine**. 2010;2:21ra16. *co-authors.
    c. Bennett J, Ashtari M, Wellman J, et al. AAV2 Gene therapy readministration in three adults with congenital blindness. **Science Translational Medicine**. 2012;4:120ra115.
    d. A. Nathwani, U. Reiss, E. Tuddenham, et al. Long Term Safety and Efficacy of a Liver-Directed Adeno-Associated Viral Vector Encoding Human FIX in Severe Hemophilia B Patients. **New England Journal of Medicine**. 2014. 371:1994-2004.
    e. Bennett JE, Wellman J, Marshall KA, et al. AAV2 Gene Therapy Contralateral Eye Administration in Childhood Onset Blindness due to RPE65 Mutations: Results of a Follow-on Phase 1/2 Study. **Lancet**. 2016, 388:661-72.
    f. Ronzitti G, Bortolussi G, van Dijk R, et al. A translationally optimized AAV-UGT1A1 vector drives safe and long-lasting correction of Crigler-Najjar syndrome. **Molecular Therapy Methods and Clinical Development**. 2016;3:16049.

Complete List of Published Work in MyBibliography:
https://www.ncbi.nlm.nih.gov/sites/myncbi/1nOIqW3WCcGkH/bibliography/49477827/public/?sort=date&direction=ascending

D. Research Support

Ongoing:

EU-FP7 ERC Co-G 617432 MoMAAV, Mingozzi (PI), 7/2014-6/2019
Role: Principal Investigator

EU-FP7 Marie Curie CIG 333628 NosMod, Mingozzi (PI), 5/2013-4/2017
Role: Principal Investigator

EU-H2020 Marie Curie IF 658712 GLYCODIS3, Mingozzi (PI), 1/2016-12/2017
Role: Principal Investigator (mentor)

EU-H2020 667751 MYOCURE, Chuah (PI), 1/2016-12/2019
Role: Co-Investigator - Partner in the consortium

EU-eRARE SMART-Haemocare, Lenting (PI), 3/2016-2/2019
Role: Co-Investigator - Partner in the consortium