BIOGRAPHICAL SKETCH
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NAME: Banfi, Sandro

POSITION TITLE: Associate Investigator, TIGEM; Associate Professor of Medical Genetics, University of Campania "Luigi Vanvitelli", Naples, Italy

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
"Federico II" University Medical School, Napoli, Italy	M.D.	07/1989	Medicine
"Federico II" University Medical School, Napoli, Italy	Residency	05/1993	Neurology

A. Personal Statement

The elucidation of the molecular basis of inherited disorders has always been the primary goal of my research activities. I was trained as an MD and started my scientific career, during the positional cloning era, by working in the field of genetics of neurodegenerative disorders. When I became an independent investigator, I gradually shifted the topic of my research to the elucidation of the molecular basis of another group of neural disorders, namely inherited retinal diseases. To achieve the latter goal, I developed a specific expertise in the exploitation of publicly available bioinformatics resources coupled with functional genomics and gene functional approaches. This integrated strategy allowed me to identify and characterize genes, of high relevance for eye development and function and potentially involved in disease pathogenesis. In the past fifteen years, I have been focusing my research efforts on the study of the functional role of microRNAs in retinal function, both in physiological and pathological conditions. In the latter respect, I recently reported the first example of a microRNA (miR-204) with a pathogenic role in retinal dystrophy in human patients. I believe that my longstanding expertise in medical genetics, functional genomics and gene functional studies applied to the study of microRNA biology make me well suited to carry out the proposed research finalized to the evaluation of the putative therapeutic role of miR-181a/b in Inherited Retinal Diseases.

B. Positions and Honors

Positions and Employment

09/91-12/94 Postdoctoral Fellow, Department of Pediatrics, Baylor College of Medicine, Houston, TX, USA.
1995-2000 Researcher, Telethon Institute of Genetics and Medicine (TIGEM), Milan, Italy.
2000- Associate investigator, Telethon Institute of Genetics and Medicine (TIGEM), Naples, Italy.
2011-2012 Assistant Professor, Medical Genetics, Second University of Naples (SUN), Naples, Italy.
2012- Associate Professor, Medical Genetics, Department of Biochemistry, Biophysics and General Pathology, Second University of Naples (SUN), Naples, Italy.

Other Experience and Professional Memberships

2005- Coordinator, TIGEM-Open University PhD program in Human Genetics.
1992- Member, American Society of Human Genetics (ASHG)
2000- Member, Association for Research in Vision and Ophthalmology (ARVO)
1996- Member, European Society of Human Genetics (ESHG)

2006- Board of Scientific Advisors, Retina Italia

Honors

1990 Recipient of a Residency Fellowship, Federico II University, Naples, Italy.
2009 "Board of Director Awards", Foundation Fighting Blindness, USA.
2017 Visionary of the Quarter, European Vision Institute (http://www.vision-research.eu/index.php?id=1097)

C. Contribution to Science

1. My field of interest in the early stages of my scientific career was the study of the molecular basis of inherited ataxias and of other neurodegenerative conditions. The main outcome of this work was the elucidation of the molecular mechanisms underlying the pathogenesis of the autosomal dominant Spino-Cerebellar Ataxia type I (SCA1). We found that this disease was due to the expansion of a poly-glutamine tract in the *SCA1* gene that encodes for the Ataxin 1 protein. This was the first evidence that a dynamic mutation caused an inherited ataxia. I was deeply involved as postdoctoral fellow in the identification and characterization of the SCA1 gene and mutation as well as in the identification of its murine ortholog.

a. **Banfi S**, Chung MY, Kwiatkowski TJ, Jr., Ranum LP, McCall AE, Chinault AC, Orr HT and Zoghbi HY. Mapping and cloning of the critical region for the spinocerebellar ataxia type 1 gene (SCA1) in a yeast artificial chromosome contig spanning 1.2 Mb. *Genomics* **18**, 627-35 (1993).
b. Orr HT, Chung MY, **Banfi S,** Kwiatkowski TJ, Jr., Servadio A, Beaudet AL, McCall AE, Duvick LA, Ranum LP and Zoghbi HY. Expansion of an unstable trinucleotide CAG repeat in spinocerebellar ataxia type 1. Nat Genet 4, 221-6 (1993).
c. **Banfi S**, Servadio A, Chung MY, Kwiatkowski TJ, Jr., McCall AE, Duvick LA, Shen Y, Roth EJ, Orr HT and Zoghbi HY. Identification and characterization of the gene causing type 1 spinocerebellar ataxia. Nat Genet 7, 513-20 (1994).
d. **Banfi S**, Servadio A, Chung M, Capozzoli F, Duvick LA, Elde R, Zoghbi HY and Orr HT. Cloning and developmental expression analysis of the murine homolog of the spinocerebellar ataxia type 1 gene (Sca1). Hum Mol Genet 5, 33-40 (1996).

2. As soon as I became an independent researcher, I started a new research line aimed at an effective data mining of publicly available bioinformatic resources and databases. In particular, I developed approaches that, by taking advantage of either cross-species sequence comparison or careful analysis of genome sequencing data, led to the identification of a large number of genes (both coding and non-coding) of high biological interest. Some of the latter, particularly those associated with ocular function, were also functionally characterized by *in vivo* studies. I served as the primary investigator or co-investigator in most of these studies.

a. **Banfi S,** Borsani G, Rossi E, Bernard L, Guffanti A, Rubboli F, Marchitiello A, Giglio S, Coluccia E, Zollo M, Zuffardi O and Ballabio A. Identification and mapping of human cDNAs homologous to Drosophila mutant genes through EST database searching. Nat Genet 13, 167-74 (1996).
b. Barbieri AM, Lupo G, Bulfone A, Andreazzoli M, Mariani M, Fougerousse F, Consalez GG, Borsani G, Beckmann JS, Barsacchi G, Ballabio A and **Banfi S**. A homeobox gene, vax2, controls the patterning of the eye dorsoventral axis. Proc Natl Acad Sci U S A 96, 10729-34 (1999).
c. Barbieri AM, Broccoli V, Bovolenta P, Alfano G, Marchitiello A, Mocchetti C, Crippa L, Bulfone A, Marigo V, Ballabio A and **Banfi S**. Vax2 inactivation in mouse determines alteration of the eye dorsal-ventral axis, misrouting of the optic fibres and eye coloboma. Development 129, 805-13 (2002).
d. Alfano G, Vitiello C, Caccioppoli C, Caramico T, Carola A, Szego MJ, McInnes RR, Auricchio A and **Banfi S**. Natural antisense transcripts associated with genes involved in eye development. Hum Mol Genet 14, 913-23 (2005).

3. More recently, I became interested in the study of the functional role of microRNAs both in normal and in pathological condition, with a stronger focus on the eye. By taking again advantage of a rational exploitation of public datasets, such as transcriptome data, our group developed new algorithms to predict microRNA targets and biological functions. Moreover, we performed systematic gene expression studies that led to the generation of the most comprehensive atlas of microRNA expression in the eye to date. All of the above resources constitute valuable tools for the microRNA research community to gain preliminary insight into the potential role of this class of small non-coding RNAs in many biological processes.

a. Karali M, Peluso I, Marigo V, **Banfi S**. Identification and characterization of microRNAs expressed in the mouse eye. Invest Ophthalmol Vis Sci., 48(2): 509-15 (2007).

b. Gennarino VA, Sardiello M, Avellino R, Meola N, Maselli V, Anand S, Cutillo L, Ballabio A, **Banfi S**. MicroRNA target prediction by expression analysis of host genes. Genome Res. 2009 Mar;19(3):481-90. Epub 2008 Dec 16.

c. Karali M, Peluso I, Gennarino VA, Bilio M, Verde R, Lago G, Dollé P and **Banfi S**. miRNeye: a microRNA expression atlas of the mouse eye. BMC Genomics. 2010 Dec 20;11:715.

d. Gennarino VA, D'Angelo G, Dharmalingam G, Fernandez S, Russolillo G, Sanges R, Mutarelli M, Belcastro V, Ballabio A, Verde P, Sardiello M and **Banfi S**. Identification of microRNA-regulated gene networks by expression analysis of target genes. Genome Res. 2012 Jun;22(6):1163-72. Epub 2012 Feb 24.

e. Karali M, Persico M, Mutarelli M, Carissimo A, Pizzo M, Marwah V, Ambrosio C, Pinelli M, Carrella D, Ferrari S, Ponzin D, Nigro V, Di Bernardo D, **Banfi S**. High-resolution analysis of the human retina miRNome reveals isomiR variations and novel microRNAs. Nucleic Acids Res. 2016 Feb 29;44(4):1525-40.

4. One additional outcome of the above-mentioned work was the functional characterization of microRNAs with a relevant role in eye function, namely miR-204 and miR-181a/b. By *in vivo* studies we gained insight into the role of these microRNAs in many aspects of ocular development and function.

a. Conte I, Carrella S, Avellino R, Karali M, Marco-Ferreres R, Bovolenta P, **Banfi S**. miR-204 is required for lens and retinal development via Meis2 targeting. Proc Natl Acad Sci U S A. 2010 Aug 31;107(35):15491-6.

b. Conte I, Merella S, Garcia Manteiga, JM, Migliore C, Lazarevic D, Carrella S, Avellino R, Marco-Ferreres R, Emmett W, Sanges R, Bockett N, Davidson NP, Meroni G, van Heel D, Bovolenta P, Stupka E, **Banfi S**. The combination of transcriptomics and informatics identifies pathways targeted by miR-204 during neurogenesis and axon guidance. Nucleic Acids Res. 2014;42(12):7793-806.

c. Carrella S, D'Agostino Y, Barbato S, Huber-Reggi SP, Salierno FG, Manfredi A, Neuhauss SCF, **Banfi S***, Conte I*. miR-181a/b control the assembly of visual circuitry by regulating retinal axon specification and growth. Dev Neurobiol. 2015 Nov;75(11):1252-67. *co-corresponding authors.

5. My strong interest in the study of the molecular mechanisms of eye development and function brought me to undertake studies aimed at unraveling the genetic basis of inherited eye diseases in vast and clinically well-characterized collections of patients. Thanks to a fruitful collaboration with the Ophthalmology clinic at the Second University of Naples and with the European Retinal Disease Consortium (ERDC, https://www.erdc.info) my group has played so far the most relevant role in the determination of the genetic epidemiology of inherited retinal disorders in the Italian population and significantly contributed to the identification of novel genes for inherited retinal diseases, including the first example of a microRNA, namely miR-204. The results of the above studies were instrumental also for the application of the first gene therapy-based clinical trial on a genetic retinal disease.

a. Simonelli F, Ziviello C, Testa F, Rossi S, Fazzi E, Bianchi PE, Fossarello M, Signorini S, Bertone C, Galantuomo S, Brancati F, Valente EM, Ciccodicola A, Rinaldi E, Auricchio A, **Banfi S**. Clinical and molecular

genetics of Leber's congenital amaurosis (LCA): a multicenter study of Italian patients. Invest Ophthalmol Vis Sci., 48(9): 4284-90 (2007).

b. Maguire AM, Simonelli F, Pierce EA, Pugh EN Jr, Mingozzi F, Bennicelli J, **Banfi S**, Marshall KA, Testa F, Surace EM, Rossi S, Lyubarsky A, Arruda VA, Konkle B, Stone E, Sun J, Jacobs J, Dell'Osso L, Hertle R, Ma J, Redmond TM, Zhu-X, Hauck B, Zelenaia O, Shindler KS, Maguire MG, Fraser Wright J, Volpe NJ, Wellman McDonnell J, Auricchio A, High KA, Bennett J. Vision in a Safety Study of Gene Transfer for Leber Congenital Amaurosis. N Engl J Med. 2008 May 22; 358(21):2240-8.

c. Conte I, Hadfield KD, Barbato S, Carrella S, Pizzo M, Bhat RS, Carissimo A, Karali M, Porter LF, Urquhart J, Hateley S, O'Sullivan J, Manson F, Neuhauss SCF, **Banfi S***, and Black GCM*. MiR-204 is responsible for inherited retinal dystrophy associated with ocular coloboma. PNAS, 2015 2015 Jun 23;112(25):E3236-45.. *co-corresponding authors

d. Testa F, Filippelli M, Brunetti-Pierri R, Di Fruscio G, Di Iorio V, Pizzo M, Torella A, Barillari MR, Nigro V, Brunetti-Pierri N, Simonelli F, and **Banfi S**. Mutations in the *PCYT1A* gene are responsible for isolated forms of retinal dystrophy. Eur J Hum Genet. 2017 May;25(5):651-655.

e. Van de Sompele S, Smith C, Karali M, Corton M, Van Schil K, Peelman F, Cherry T, Rosseel T, Verdin H, Derolez J, Van Laethem T, Khan KN, McKibbin M, Toomes C, Ali M, Torella A, Testa F, Jimenez B, Simonelli F, De Zaeytijd J, Van den Ende J, Leroy BP, Coppieters F, Ayuso C, Inglehearn CF, **Banfi S***, De Baere E*. *co-corresponding authors. Biallelic sequence and structural variants in RAX2 are a novel cause for autosomal recessive inherited retinal disease. Genet Med. 2018 Oct 31. [Epub ahead of print]

Complete List of Published Work can be found at: https://scholar.google.com/citations?hl=en&user=2mSMwYYAAAAJ&view_op=list_works&pagesize=100

D. Research Support

a) Ongoing Research Support

-Foundation Fighting Blindness (FFB) Banfi (PI) 1/6/2019-30/5/2022
AAV-Sponge-mediated modulation of microRNA-181a/b: a potential therapeutic approach for Inherited Retinal Disease. Role: PI

-European Union H2020-MSCA-ITN-2018 De Baere (coordinator) 1/10/2018-30/9/2022
European Training Network to Diagnose, Understand and Treat Stargardt Disease, a Frequent Inherited Blinding Disorder. Role: Partner

b) Completed Research Support

-Telethon Foundation Banfi (PI) 1/1/2017-31/12/2018
Systematic search for microRNAs that play a role in photoreceptor degeneration. Role: PI

-European Union FP7-PEOPLE-2012-ITN Inglehearn (coordinator) 11/2012-11/2016
EyeTN - Beyond the Genome; training the next generation of ophthalmic researchers.
Role: Partner

- Fondazione Roma Banfi (coordinator) 1/11/2015-31/07/2019
Retinitis Pigmentosa: an integrated application of novel strategies towards diagnosis and treatment
Role: PI