Curriculum vitae Andrés F. Muro

PERSONAL DATA

Name/Surname:	**Andrés Fernando MURO**
Date and place of birth:	Buenos Aires (Argentina), November 15th, 1964
Nationality:	Argentinian/Italian
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Financial interests disclosure: I have no financial interests to disclose

EDUCATION AND TRAINING

1982−1988:	Master of Sciences in Molecular Biology, University of Buenos Aires, School of Sciences.
1988−1992:	Doctor in Biology (PhD., Biology), University of Buenos Aires, School of Sciences.
1992-1995:	ICGEB, UNIDO post doctoral fellowship, ICGEB, Trieste, Italy
1996-2004:	Staff Scientist Position at the Molecular Pathology Group, ICGEB, Trieste, Italy
2005-present:	Head of the Mouse Molecular Genetics Group, ICGEB, Trieste, Italy

Languages: Spanish (native), English (spoken and written), Italian (spoken and written)

EMPLOYMENT AND RESEARCH EXPERIENCE

Professional employment

1987-1988:	Undergraduate student at the School of Sciences, University of Buenos Aires, Argentina, Dept. of Biological Chemistry (Prof. M.L. Cantore and S. Passeron).
1988-1992:	Graduate Student Fellowship, Consejo Nacional de Investigaciones Científicas y Técnicas (CONICET), Argentina, to work at the INGEBI ("Instituto de Ingeniería Genética y Biología Molecular", Genetic Engineering and Molecular Biology Institute), Buenos Aires, Argentina (Supervisor: Prof. Alberto R. Kornblihtt).
1989-1990:	Teaching Instructor of the Department of Molecular Genetics and Biotechnology, School of Sciences, University of Buenos Aires
1990-1992:	Chief Teaching Instructor of the Course of Genetic Engineering, Department of Molecular Genetics and Biotechnology, School of Sciences, University of Buenos Aires and INGEBI, Buenos Aires, Argentina.
1992-1994:	ICGEB-UNIDO post-doctoral fellowship, Molecular Pathology Group of the ICGEB, Trieste, Italy (Supervisor: Prof. Francisco Baralle).
1995-2004:	Staff Scientist Position at the Molecular Pathology Group of the ICGEB, Trieste, Italy (Prof. Francisco Baralle).
2005-present:	Group Leader of the Mouse Molecule Genetics Group at the International Centre of Genetic Engineering and Biotechnology (ICGEB), Trieste, Italy.

ACADEMIC AND SCIENTIFIC ACTIVITIES

Student supervision
PhD Thesis directed: Twelve (Open University, London, UK, 7; SISSA, Trieste, 1; Scuola Normale Superiore di Pisa, 1; Trieste University, 2; University of Trento, 1)
Graduate Thesis directed: Ten (Trieste University, 7; Bologna University, 2; University of Valencia, 1)

Current Editorial positions:
2017-present: Member of the Editorial Board as a Review Editor of the journal "Frontiers Genetics and Molecular Biosciences – RNA".
2021-present: Member of the Editorial Board as a Review Editor of Frontiers in Molecular Medicine, Gene and Virotherapy

Membership of Scientific Societies
2014-Present: Member of the American Society of Gene and Cell Therapy (**ASGCT, USA**)
2016-present: Member of the European Society of Gene and Cell Therapy (**ESGCT, EU**)
2025 Member of the Italian Society of Gene and Cell Therapy (**SITGEC**)

Membership of Academic Societies
2019-Present: Academic Member of the Latin American Academy of Sciences (**Academia de Ciencias de América Latina, ACAL**)

RESEARCH ACTIVITY

Present research activity:
The main research interest focuses on the study of the functions of genes related to human diseases, using genetically engineered mouse models, and possible therapeutic approaches, ranging from pharmacological therapies, to phototherapy, *in vivo* and *in vitro* gene therapy, gene targeting and gene editing.
Research activity is supported through grants from public and private agencies, including Telethon (Italy), Genethon (France), Beneficentia Stiftung (Lichtenstein), AFM-Telethon (France), the local Region Government, and the European Commission (H2020), as well as through collaborations with companies (Bayer, Germany; Selecta Biosciences, US; LogicBio, US).

1) Crigler-Najjar Syndrome (CNSI) and neonatal hyperbilirubinemia: We are interested in determining the molecular mechanisms and genetic determinants involved in bilirubin neurotoxicity, in particular in neonatal jaundice and babies with CNSI, and in the possible therapeutic approaches to improve the condition of patients. We have generated a mouse model of hyperbilirubinemia by mutating the endogenous UGT1A gene. This model closely resembles the major clinical features occurring in babies with CNSI. We are studying the mechanism of disease and therapeutic approaches based in AAV-mediated gene therapy, different pharmacological treatments, and gene editing *in vivo*.

2) Gilbert's syndrome: it has been reported that subjects with the Gilbert's syndrome (GS), who have heterogeneous mild elevated UCB levels because of genetic mutations in the Ugt1a gene, show a lower risk of developing T2D and T2D-related outcomes, OB, and MetS as well as atherosclerosis/ischemic CVD. The prevalence of GS subjects is not negligible, since it accounts for about 4% to 16% of the general population, depending on the ethnicity. We are studying the molecular mechanism of protection exerted by mild elevated UCB levels since they can reveal molecular mechanisms of disease progression in the general population.

3) AAV-mediated liver gene therapy for ornithine transcarbamylase deficiency (OTCD):

a. **Infantile OTCD form:** develop a liver-specific AAV-mediated non-integrative medical product for a gene therapy treatment of the infantile form (2 years-old and older patients) of OTCD, the most common urea cycle disease, to be used in a clinical trial in patients.
b. **Neonatal severe OTC form:** this OTCD form is lethal, with 50% of patients dying before 1 year. We are developing a combined strategy to treat this very severe form using a KO mouse model of OTCD

4) Fabry disease: We are interested in setting up a novel therapeutic protocol for Fabry disease, in order to develop a more efficient and less expensive therapeutic alternative. The strategy is based in the application of in-vivo gene targeting of the GLA cDNA into the albumin locus of hepatocytes, without the use of artificial nucleases to increase safety. In this way, we expect that the liver will be converted into a

"bio-factory" that will produce high levels of circulating GLA that will be captured by the target organs, as it now occurs with the ERT approach.

Patents filed:

2014 – European Patent Office - Treatment of Crigler-Najjar syndrome – Patent No. 14305622.4 - 1410

2015 – WIPO - Treatment of Hyperbilirubinemia – International Publication Number: WO 2015/162302 A3 – Abstract: The invention relates to a nucleic acid sequence useful in the treatment of hyperbilirubinemia, in particular in the treatment of Crigler-Najjar syndrome. More particularly, the nucleic acid sequence of the present invention is a codon-optimized UGT1A1 coding sequence.

2020 – Methods and composition of OTC constructs and vectors – US2020/0038462 A1

2024 - Human alpha galactosidase A coding sequence for the treatment of Fabry disease. PCT/EP2024/055793

List of 10 selected publications (a complete list of publications is available at http://orcid.org/0000-0002-9628-0494).

Number of Publications: ninety-three (fifty-four-nine as first or last/corresponding author); H-Index (Scopus)=36

1. **Muro, A.F.**, Marro, M.L., Gajovic, S., Porro, F., Luzzatto, L. and Baralle, F.E., *Mild spherocytic hereditary elliptocytosis and altered levels of alpha- and gamma-adducins in beta-adducin-deficient mice.* **Blood**, 2000. **95**(12): p. 3978-85.

2. **Muro, A.F.**, Chauhan, A.K., Gajovic, S., Iaconcig, A., Porro, F., Stanta, G. and Baralle, F.E., *Regulated splicing of the fibronectin EDA exon is essential for proper skin wound healing and normal lifespan.* **J Cell Biol**, 2003. **162**(1): p. 149-60.

3. White, E.S., Baralle, F.E. and **Muro, A.F.**, *New insights into form and function of fibronectin splice variants.* **J Pathol**, 2008. **216**(1): p. 1-14.

4. Bortolussi, G., Zentilin, L., Baj, G., Giraudi, P., Bellarosa, C., Giacca, M., Tiribelli, C. and **Muro, A.F.**, *Rescue of bilirubin-induced neonatal lethality in a mouse model of Crigler-Najjar syndrome type I by AAV9-mediated gene transfer.* **FASEB J**, **2012**. **26**(3): p. 1052-63.

5. Porro, F., Bortolussi, G., Barzel, A., De Caneva, A., Iaconcig, A., Vodret, S., Zentilin, L., Kay, M.A. and **Muro, A.F.**, *Promoterless gene targeting without nucleases rescues lethality of a Crigler-Najjar syndrome mouse model.* **EMBO Molecular Medicine**, 2017. **9**(10): p. 1346-1355.

6. De Caneva, A., Porro, F., Bortolussi, G., Sola, R., Lisjak, M., Barzel, A., Giacca, M., Kay, M.A., Vlahoviček, K., Zentilin, L. and **Muro, A.F.**, *Coupling AAV-mediated promoterless gene targeting to SaCas9 nuclease to efficiently correct liver metabolic diseases.* **JCI Insight**, 2019. **4**(15).

7. De Sabbata, G., Boisgerault, F., Guarnaccia, C., Iaconcig, A., Bortolussi, G., Collaud, F., Ronzitti, G., Sola, M.S., Vidal, P., Rouillon, J., Charles, S., Nicastro, E., D'Antiga, L., Ilyinskii, P., Mingozzi, F., Kishimoto, T.K. and **Muro, A.F.**,

Long-term correction of ornithine transcarbamylase deficiency in Spf-Ash mice with a translationally optimized AAV vector. **Molecular Therapy - Methods & Clinical Development**, 2021. **20**: p. 169-180.

8. Tsuji, S., Stephens, C.J., Bortolussi, G., Zhang, F., Baj, G., Jang, H., de Alencastro, G., **Muro, A.F.**, Pekrun, K. and Kay, M.A., *Fludarabine increases nuclease-free AAV- and CRISPR/Cas9-mediated homologous recombination in mice.* **Nature Biotechnology**, 2022, Aug;40(8):1285-1294.

9. D'Antiga L, Beuers U, Ronzitti G, Brunetti-Pierri N, Baumann U, Di Giorgio A, Aronson S, Hubert A, Romano R, Junge N, Bosma P, Bortolussi G, **Muro AF**, Soumoudronga RF, Veron P, Collaud F, Knuchel-Legendre N, Labrune P, Mingozzi F. Gene Therapy in Patients with the Crigler-Najjar Syndrome. N Engl J Med. 2023 Aug 17;389(7):620-631

10. Lisjak M, Iaconcig A, Guarnaccia C, Vicidomini A, Moretti L, Collaud F, Ronzitti G, Zentilin L, and **Muro AF**. Lethality rescue and long-term amelioration of a citrullinemia type I mouse model by neonatal gene-targeting combined to SaCRISPR-Cas9. *Molecular therapy Methods & clinical development.* 2023;31:101103.