CV date	25/04/2020

Part A. PERSONAL INFORMATION

First and Family name	LUIS MENÉNDEZ ARIAS		
Social Security, Passport, ID number	02526089E	Age	58
Researcher codes	WoS Researcher ID *(*)*	G-2436-2016	
	SCOPUS Author ID*(*)*	7004203204	
	Open Researcher and Contributor ID (ORCID) **	0000-0002-1251-6640	

(*) At least one of these is mandatory
(**) Mandatory

A.1. Current position

Name of University/Institution	CONSEJO SUPERIOR DE INVESTIGACIONES CIENTÍFICAS			
Department	CENTRO DE BIOLOGÍA MOLECULAR "SEVERO OCHOA"			
Address and Country	c/ Nicolás Cabrera, 1; Campus de Cantoblanco; 28049 Madrid			
Phone number	911964494	E-mail	lmenendez@cbm.csic.es	
Current position	CSIC Research Professor		From	21/04/2009
Key words	HIV, retrovirus, reverse transcriptases, antivirals, drug resistance			

A.2. Education

Ph.D.	University	Year
Ph.D. Biological Sciences	Complutense - Madrid	1989

A.3. JCR articles, h Index, thesis supervised…

5 approved 6-yr research periods ("sexenios", last year evaluated: 2015).
Number of Ph.D. Thesis supervised and defended: **8** (**5** in the last 10 years; **1** in progress)
Author or coauthor of **120** articles listed in PubMed (**74** in the first quartile of their discipline).
Since 2009: **51** articles (**34** in first quartile)
Web of Knowledge information: **h index = 34** (as of April 21, 2020).
Nº total citations: **3.692** (without autocitations: 3.091); 190 (average per year, last 5 years)
Research Gate information: RG factor: 41'05

Part B. CV SUMMARY *(max. 3500 characters, including spaces)*

Luis Menéndez Arias is a Research Professor of the Consejo Superior de Investigaciones Científicas (Spanish National Research Council) and Group Leader at the Centro de Biología Molecular "Severo Ochoa" (CBMSO) in Madrid, where he has been working since March 1994. He studied biology at the Complutense University in Madrid, Spain, where he obtained his Ph.D. He was then trained as a protein chemist working on the elucidation of the amino acid sequence of the major allergen of mustard seeds and the determination of its major antigenic sites. In September 1990, he moved to the Basic Research Program of the Frederick Cancer Research and Development Center (Frederick, MD, USA) where he conducted studies on the biochemical properties of retroviral proteases and their implications in virus maturation and antiviral therapy.

In 1994 Luis returned to Spain to join Dr. Esteban Domingo's lab at the CBMSO where he started to work on the human immunodeficiency virus type 1 (HIV-1) reverse transcriptase (RT), in an effort to understand the molecular basis of its fidelity and nucleotide specificity. Since then, and as an independent scientist his research has been devoted to studying structure-activity relationships in retroviral RTs, elucidating mechanisms of HIV-1 resistance to antiretroviral drugs, and understanding HIV replication fitness.

Dr. Menéndez Arias and his collaborators identified Tyr^{115} in HIV-1 RT as a steric gate in the active site of the viral polymerase, critical for the discrimination between dNTPs and rNTPs. They also found that Tyr^{115} has an influential role in the fidelity of DNA synthesis of HIV-1 RT. Dr. Menéndez-Arias' group has also designed and obtained engineered RTs with increased fidelity and/or thermal stability, currently commercialized for biotechnological

applications (Scriptools™ and SunScript™, distributed by Biotools B&M Labs and 4Basebio, respectively). In the field of antiretroviral drug resistance, his lab has made important contributions to our understanding of the molecular basis of resistance to nucleoside analogue RT inhibitors (AZT and others) and particularly, on how insertions and deletions found in the RT of virus isolated from heavily-treated patients contribute to the resistant phenotype.

Dr. Menéndez Arias has been a member of the steering committee of the CBMSO (2008-2014) and served as Director of its Department of Virology and Microbiology (2011-2014). He is author or co-author of more than 100 peer-reviewed research papers, most of them related to retroviruses and antiretroviral therapy. He is Academic Editor of *PLoS ONE*, and member of the Editorial Boards of *Antimicrobial Agents and Chemotherapy, Antiviral Research*, *Antiviral Therapy*, *Journal of Biological Chemistry, Virus Research* and *Viruses*. In addition, he served as guest editor or co-editor of special issues of *Virus Research* ('Retroviral reverse transcription', 2008; and 'Viral polymerases', 2017), *Viruses* ('Retroviral enzymes', 2010) and *Current Opinion in Virology* ('Antivirals and drug resistance', 2014). In March 2013, Dr. Menéndez-Arias was an invited fellow of the Japan Society for the Promotion of Science (2013) and of the School of Pharmaceutical Sciences (Shandong University, Jinan, China) (2019). In February 2016 he delivered a keynote lecture in the opening session of the International Conference on Translational Biotechnology, organized by the Motilal Nehru National Institute of Technology in Allahabad (India).

Part C. RELEVANT MERITS

C.1. Publications (selection of 120 listed in PubMed)

Selected research articles (out of 29 published between 2013 and 2020)

1.- Álvarez, M., Barrioluengo, V., Afonso-Lehmann, R. & Menéndez-Arias, L. (2013) Altered error specificity of RNase H-deficient HIV-1 reverse transcriptases during DNA-dependent DNA synthesis. *Nucleic Acids Res*. **41**, 4601-4612.

2.- Matamoros, T., Barrioluengo, V., Abia, D. & Menéndez-Arias, L. (2013) Major groove binding track residues of the connection subdomain of human immunodeficiency virus type 1 reverse transcriptase enhance cDNA synthesis at high temperatures. *Biochemistry* **52**, 9318-9328.

3.- Álvarez, M. & Menéndez-Arias, L. (2014) Temperature effects on the fidelity of a thermostable HIV-1 reverse transcriptase. *FEBS J*. **281**, 342-351.

4.- Betancor, G., Nevot, M., Mendieta, J., Gómez-Puertas, P., Martínez, M.A. & Menéndez-Arias, L. (2014) Molecular basis of the association of H208Y and thymidine analogue resistance mutations M41L, L210W and T215Y in the HIV-1 reverse transcriptase of treated patients. *Antiviral Res*. **106**, 42-52.

5.- Pauls, E., Ruiz, A., Badia, R., Permanyer, M., Gubern, A., Riveira-Muñoz, E., Torres-Torronteras, J., Álvarez, M., Mothe, B., Brander, C., Crespo, M., Menéndez-Arias, L., Clotet, B., Keppler, O.T., Martí, R., Posas, F., Ballana, E. & Esté, J.A. (2014) Cell cycle control and HIV-1 susceptibility are linked by CDK6-dependent CDK2 phosphorylation of SAMHD1 in myeloid and lymphoid cells. *J. Immunol*. **193**, 1988-1997.

6.- Betancor, G., Álvarez, M., Marcelli, B., Andrés, C., Martínez, M.A. & Menéndez-Arias, L. (2015) Effects of HIV-1 reverse transcriptase connection subdomain mutations on polypurine tract removal and initiation of (+)-strand DNA synthesis. *Nucleic Acids Res*. **43**, 2259-2270.

7.- Corona, A., Meleddu, R., Esposito, F., Distinto, S., Bianco, G., Masaoka, T., Maccioni, E., Menéndez-Arias, L., Alcaro, S., Le Grice, S.F.J. & Tramontano, E. (2016) Ribonuclease H/DNA polymerase HIV-1 reverse transcriptase dual inhibitor: mechanistic studies on the allosteric mode of action of isatin-based compound RMNC6. *PLoS ONE* **11**, e0147225.

8.- Pacheco, B., Menéndez-Arias, L. & Sodroski, J. (2016) Characterization of two distinct early post-entry blocks to HIV-1 in common marmoset lymphocytes. *Sci. Rep*. **6**, 37489.

9.- Álvarez, M., Sebastián-Martín, A., García-Marquina, G. & Menéndez-Arias, L. (2017) Fidelity of classwide-resistant HIV-2 reverse transcriptase and differential contribution of K65R to the accuracy of HIV-1 and HIV-2 reverse transcriptases. *Sci. Rep.* **7**, 44384.

10.- Badia, R., Pujantell, M., Torres-Torronteras, J., Menéndez-Arias, L., Martí, R., Ruzo, A., Pauls, E., Clotet, B., Ballana, E., Esté, J.A. & Riveira-Muñoz, E. (2017) SAMHD1 is active in cycling cells permissive to HIV-1 infection. *Antiviral Res*. **142**, 123-135.

11.- Sebastián-Martín, A., Barrioluengo, V. & Menéndez-Arias, L. (2018) Transcriptional inaccuracy threshold attenuates differences in RNA-dependent DNA synthesis fidelity between retroviral reverse transcriptases. *Sci. Rep*. **8**, 627.

12.- Álvarez, M., Nevot, M., Mendieta, J., Martínez, M.A. & Menéndez-Arias, L. (2018) Amino acid residues in HIV-2 reverse transcriptase that restrict the development of nucleoside analogue resistance through the excision pathway. *J. Biol. Chem*. **293**, 2247-2259.

13.- Sun, L., Gao, P., Dong, G., Zhang, X., Cheng, X., Ding, X., Wang, X., Daelemans, D., De Clercq, E., Pannecouque, C.*, Menéndez-Arias, L.*, Zhan, P.* & Liu, X.* (2018) 5-Hydroxypyrido[2,3-b]pyrazin-6(5H)-one derivatives as novel dual inhibitors of HIV-1 reverse transcriptase-associated ribonuclease H and integrase. *Eur. J. Med. Chem*. **155**, 714-724. *(Co-corresponding authors).

14.- Luczkowiak, J., Matamoros, T. & Menéndez-Arias, L. (2018) Template-primer binding affinity and RNase H cleavage specificity contribute to the strand transfer efficiency of HIV-1 reverse transcriptase. *J. Biol. Chem*. **293**, 13351-13363.

15.- Martín-Alonso, S., Alvarez, M., Nevot, M., Martinez, M. A. & Menéndez-Arias, L. (2020) Defective strand-displacement DNA synthesis due to accumulation of thymidine analogue resistance mutations in HIV-2 reverse transcriptase. *ACS Infect. Dis.* doi:10.1021/acsinfecdis.9b00512.

Selected reviews (8 reviews, 3 book chapters and 1 meeting report, period 2013 - 2020)

1.- Menéndez-Arias, L., Álvarez, M. & Pacheco, B. (2014) Nucleoside/nucleotide analog inhibitors of hepatitis B virus polymerase: mechanism of action and resistance. *Curr. Opin. Virol*. **8**, 1-9.

2.- Menéndez-Arias, L., Sebastián-Martín, A. & Álvarez, M. (2017) Viral reverse transcriptases. *Virus Res*. **234**, 153-176.

3.- Tramontano, E., Corona, A. & Menéndez-Arias, L. (2019) Ribonuclease H, an unexploited target for antiviral intervention against HIV and hepatitis B virus. *Antiviral Res*. **171**, 104613; https://doi.org/10.1016/j.antiviral.2019.104613

C.2. Research projects and grants (last 5 years)

In progress

Ref.: **BIO2016-76716-R**. L. Menéndez-Arias (PI). 12/30/16-12/31/20. Ministry of Economy, Industry and Competitiveness, Spain. Improving HIV reverse transcriptases for bio-technological applications: Engineering strand transfer and non-templated nucleotide addition activities. Funding: 160930 euros (+ funding for 4 years for a pre-doctoral student stipend)

Ref.: **COOPA20299**. L. Menéndez-Arias (PI). 04/01/19-12/31/20. CSIC. Resistance to reverse transcriptase inhibitors in HIV variants circulating in the North of Colombia: mutations and involved mechanisms. Funding: 22000 euros.

Completed (since 2014)

Ref.: **BIO2013-48788-C2-1-R**. L. Menéndez-Arias (PI). 01/01/14-12/31/16. Ministry of Economy and Competitiveness, Spain. Fidelity of viral polymerases copying RNA templates: Mechanistic insights into the molecular basis of antiviral drug resistance. Funding: 130,000 €

Ref.: **332623** (HIVMARMOD). L. Menéndez-Arias (supervisor). 01/01/13-12/31/15. European Union, FP7 Program, Marie Curie Action (FP7-PEOPLE-2012-CIG). Innate intracellular blocks to HIV-1 in New World monkeys. Funding: 75,000 €

Ref.: **BIO2010-15542**. L. Menéndez-Arias (PI). 10/01/11-06/30/14. Ministry of Science and Innovation, Spain. Engineered HIV-1 group O RT variants with increased stability, nucleic acid affinity and fidelity of DNA synthesis: Exploring the effects of mutations in the connection subdomain and the RNase H domain of the RT. Funding: 169,400 €

All projects have been executed in the CBMSO

C.3. Contracts

1.- Agreement with **Biotools Biotechnol. and Medical Laboratories S.L.** for the exploitation of "Expression and purification systems for HIV-1 group O reverse transcriptases", approved by CSIC, 16 February 2009 (10 years), and "HIV-1 group O reverse transcriptase variant with mutations that increase its fidelity and thermostability: K65R/V75I RT", renewed on May 2016.

2.- Patent License Agreement entre Agencia Estatal Consejo Superior de Investigaciones Científicas and **Expedeon Inc.** (patent application ES201330705). Madrid, July 22nd, 2014. Sygnis commercializes our RTs since 2015, as **SunScript™ RNaseH+** and **RNaseH-**.

C.4. Patents [3, one under exploitation]

Inventors: L. Menéndez, T. Matamoros, D. Abia, V. Barrioluengo. Title: "HIV-1 group O reverse transcriptases, active at high temperatures". C.S.I.C. No: 201330705 (Spain). Submission date: 05/17/13. Published on November 20th, 2014 [WO 2014184409 (A1)]. Awarded on Sept 29th, 2015 (Oficina Española de Patentes y Marcas, pub. no.: 2525135; Patent title: January 25th, 2016). Patent awarded in the U.S.: US 9,428,738 B2, Date: Aug. 30, 2016. Awarded in China with no. 80037516, Feb. 17, 2016, and in Japan (no. 2016525878), in May 8, 2017.

C.5. Supervised Ph.D. Thesis (since 2009)

Mónica Kisic Aguirre, 2010. Universidad Autónoma de Madrid (*cum laude*)
Verónica Barrioluengo Fernández, 2013. Universidad Autónoma de Madrid (*cum laude*)
Gilberto J. Betancor Quintana, 2013. Univ. Autónoma Madrid (*cum laude*, Faculty Prize)
César Garriga Fuentes, 2014. Universidad Rey Juan Carlos, Alcorcón (Madrid) (*cum laude*)
Alba Sebastián Martín, 2019. Universidad Autónoma de Madrid (*cum laude*)

C.6, C.7… (e. g., Institutional responsibilities, memberships of scientific societies…)

FIRST PRIZE for best academic record in Biology in Spain (academic yr 1983/1984). Premio Extraordinario de Licenciatura, Fac. Biology, Univ. Complutense, Madrid (1986). Premio Extraordinario de Doctorado, Fac. Biology, Univ. Complutense, Madrid (1990).

2006-2010: Member of the Editorial Board of *Current HIV Research* (Bentham Publishers).

2008-present: Member of the Editorial Board of *Viruses* (MDPI, Basel, Switzerland).

2011-present: Member of the Global Virus Network (www.gvn.org), representing CBMSO.

2011-present: Member of the Editorial Board/Academic Editor of *PLoS ONE*, and member of the Editorial Board of *Antiviral Therapy* (Int. Medical Press).

2012-present: Member of the Editorial Boards of *Antiviral Research* and *Virus Research* (Elsevier) and *World Journal of Translational Medicine* (Baishideng Pub).

2013: Invitation fellowship (short-term) from the Japan Society for the Promotion of Science (February 24th, 2013 to March 10th, 2013).

2013: Tohoku Medical Society Lecture Medal, Faculty of Medicine, Tohoku University, Sendai, Japan, March 4th, 2013.

2016: Keynote speaker at the International Conference on Translational Biotechnology, Motilal Nehru National Institute of Technology, Allahabad, India, February 4, 2016.

July 2016-Sept. 2021: Member of the Editorial Board of *Journal of Biological Chemistry* (American Society for Biochemistry and Molecular Biology, Rockville, Maryland, USA).

Jan 2017-Dec 2022: Member of the Editorial Board of *Antimicrobial Agents and Chemotherapy* (American Society for Microbiology, USA).

Sept. 2019: Invited scholar of the School of Pharmaceutical Sciences, Shandong University, Jinan, China (August 30th, 2019 to September 10th, 2019).

October 2017, 2018, 2019: Coordinator (with Dr. Cecilio López-Galíndez) Course: A1. Introduction to virus biology (Master in Virology, Universidad Complutense de Madrid, academic years 2017/18, 2018/19 and 2019/20), 6 ECTS credits (45 hours; 22 lecturers).