

Part A. Personal Information

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|-------------|------------|
| DATE | 09.09.2021 |
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| | | |
|--------------------------------------|--------------------------------------------|---------------------|
| Surname(s) | Martinez Gil | |
| Forename | Ana | |
| Social Security, Passport, ID number | 00688492-X | |
| Sex | Female | |
| Age | 60 | |
| Researcher codes | WoS Researcher ID (*) | L-6414-2014 |
| | SCOPUS Author ID(*) | 74040254547 |
| | Open Researcher and Contributor ID (ORCID) | 0000-0002-2707-8110 |

(*) At least one of these is mandatory

A.1. Current position

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|------------------------------------|----------------------------------------------------------------------------------------------------------------|-----------------------------------------|
| Post/Professional Category | Research Professor | |
| UNESCO Code | 2390.01 | |
| Key Words | Pharmaceutical Chemistry, Medicinal chemistry, Biological Chemistry, Drug design, anti-neurodegenerative drugs | |
| Name of the University/Institution | Consejo Superior de Investigaciones Científicas (CSIC) | |
| | Department/Centre | Centro Investigaciones Biológicas (CIB) |
| | Unit | White Biotechnology |
| | Full Address | Ramiro de Maeztu 9, 28040 Madrid |
| | Email Address | ana.martinez@csic.es |
| | Phone Number | +34 918 37 31 12 |
| Start date | 21.4.2009 (1.3.1990 as tenured scientist) | |

A.2. Education (title, institution, date)

| Year | University | Degree | Title |
|------|----------------------|--------|-----------------------|
| 1984 | Complutense (Madrid) | Bs, Ms | Organic Chemistry |
| 1987 | Complutense (Madrid) | PhD | Medicinal Chemistry |
| 2005 | Navarra-IESE | Ms | Bussiness Development |

A.3. Indicators of Quality in Scientific Production (See the instructions)

Six positive sexenios (first 1985-90, last 2015-20). One positive technological sexenio (2000-09)
 Thesis supervised (since 2011): 6 (V. Palomo 2012, I. García-Salado 2014, A.M. García 2015, J. Zaldivar 2018, C. Roca 2018, E. Rojas 2020, L. Martinez 2021). Currently 6 thesis on going (forecast defenses: R. Benitez and I. Maestro 2021, V. Nozal 2022, C. Tosat 2023 and E. Madruga and E. Caballero 2024)

Total number of citations: 6717 (WoS)/ 7003 (Scopus) (2010 to 2020: 5047 citations Scopus)

Average number of citations during the last five years (2016-2020): 570 citations/year

Total number of publications (2010-2020): 120 (95% in Q1 medicinal chemistry, drug discovery, pharmacy&pharmacol, biochemistry, neurosciences, multidisciplinary)

h-index: 48 (WoS) h-index: 49 (Scopus)

Part B. Free Summary of CV (Max. of 3.500 characters, including spaces)

My expertise and research interests are based on drug discovery and medicinal chemistry fields. Since 1995 my goals were focused on neurodegenerative disorders, leading numerous research projects on the medicinal chemistry and rational drug design of new drugs for Alzheimer's (AD) and Parkinson's (PD) diseases, multiple sclerosis (MS) and amyotrophic lateral sclerosis (ALS). The main areas of my research involve cholinesterase, protein kinase and phosphodiesterase inhibitors. More recently, I am also involved in the discovery of inhibitors of protein-protein interaction (PPIs), mitophagy modulators and anti-SARS-CoV-2 inhibitors.

Technology transfer is a constant in my professional career. In summer 2000, some of my results were worldwide licensed to NeuroPharma, being engaged with the company as external researcher. From February 2002 to 2008, I joined to NeuroPharma as R&D Director where I have provided strategic, leadership management and guidance in R&D activities from the drug

discovery to the final proof of concept in different animal models. In these six years, two research projects based on molecules from my own laboratory reached clinical trials as disease modifying drugs for AD.

As NeuroPharma's R&D Director, I designed, equipped and supervised more than 2.000 m² of research laboratories of molecular biology, assay development, medicinal chemistry, natural products isolation, spectroscopic and analytical techniques, pharmaceutical technology and pharmacology with more than 50 scientists on staff. In these years, two of my compounds reached clinical trial: NP-12, tideglusib, a ATP non-competitive GSK-3 inhibitor, and NP-61, a dual binding site AChEI and potent β -amyloid modulator, as disease modifying drugs for AD. Today, tideglusib has been acquired by Autism Therapeutics, now AMO Pharma, with the goal to develop it for the treatment of rare diseases. Currently, clinical studies are ongoing in Canada, USA and UK, for fragile x and myotonic dystrophy with successful interim analysis.

Since February 2008, I come back to my academic position in the CSIC, firstly in the Medicinal Chemistry Institute (IQM-CSIC) and since April 2014 in the Biological Research Center (CIB-CSIC). In these years I lead different projects focused in the development of small molecules for the treatment of PD, ALS, MS, retinitis pigmentosa, fragile X and since March 2020 for the treatment of COVID-19.

In 2010, we licensed some of our new drugs to the Spanish biotech ARACLON with the aim to reach the clinic for PD therapy. Funding by different public-private projects, we have performed all the tasks to fill the IMPD that is pending of AEMPS approval to start phase I studies. Furthermore, an innovative treatment for multiple sclerosis discover in my group has been the basis of ANKAR PHARMA. I am one of the founders and currently the CSO of this spin-off that acquired patent rights from the CSIC to develop the compounds until clinical trials. Recently, I am the coordinator of a solid network biomedicine project funded by Madrid Community will allow me to develop new drugs for ALS. Finally, my laboratory is CIBERNED member and one of the only five validated chemistry sites of EU-OPENSREEN, the European infrastructure platform for biological chemistry and drug screening.

I am mentor of 12 PhD (6 more ongoing), more than 40 Master thesis and many postdoctoral trainings and ERASMUS placements. I am also member of several editorial boards of different international journals (Curr Med Chem, Mini Rev Med Chem, Recent Patents CNS) and book collections (RSC Drug Discovery Serie). Moreover, I act as reviewer in different calls and programs, being member of the Med1 pannel (Pharmaceutical and Medical Sciences) of FWO (Flemish research agency) during 6 years (2014-2019), expert of the European Commission (EX2006C132745) and reviewer of ANEP, AEI, international agencies (France, Austria, Portugal, UK and Italy) and private research associations (Wellcome trust, Alzheimer Association, AFM, Weston Brain Institute, etc.)

Part C. Relevant accomplishments

C.1. Publications (among more than 270)

1. V. Nozal, A. Garcia-Rubia, C. Perez, E. Perez-Cuevas, C. Tosat-Bribian, F. Bartolome, D. Ramirez, E. Carro, V. Palomo, * **A. Martinez*** From Kinase Inhibitors to Multitarget Ligands as Powerful Drug Leads for Alzheimer's Disease using Protein-Templated Synthesis. *Angew Chem Int Eng Ed* 2021, <https://doi.org/10.1002/anie.202106295> D1 IF 13.52
2. C. Gil,* T. Ginex, I. Maestro, V. Nozal, L. Barrado-Gil, M.A. Cuesta-Geijo, J. Urquiza, D. Ramirez, C. Alonso, N. E. Campillo, **A. Martinez***. COVID19: Drug targets and potential treatments. *J Med Chem* 63, 12359–12386 (2020) D1 IF 6.23 no. citations: 106
3. Loreto Martínez-González, Carmen Rodríguez-Cueto, Diego Cabezudo, Fernando Bartolomé, Pol Andrés-Benito, Isidro Ferrer, Carmen Gil, Ángeles Martín-Requero, Javier Fernández-Ruiz, **Ana Martínez,*** Eva de Lago*. Motor neuron preservation of in vivo TDP-43 phosphorylation by protein CK-1d kinase inhibitor treatment. *Sci Rep.* 10: 4449 (2020) Q1 IF: 4.57 no. citations: 8
4. A. Gandini, M. Bartolini, D. Tedesco, L. Martinez-Gonzalez, C. Roca, N.E. Campillo, J. Zaldivar-Diez, C. Perez, G. Zuccheri, A. Miti, A. Feoli, S. Castellano, S. Petralla, B. Monti, M. Rossi, F. Moda, G. Legname, **A. Martinez***, M.L. Bolognesi*. Tau-Centric Multitarget Approach for Alzheimer's Disease: Development of First-in-Class Dual Glycogen Synthase Kinase 3 β and Tau-Aggregation Inhibitors. *J Med Chem.* 61, 7640-7656 (2018) D1 IF 6.23 no. citations: 44
5. V. Palomo, DI Perez, C Roca, C Anderson, N Rodríguez-Muela, C Perez, JA Morales-Garcia, JA Reyes, NE Campillo, AM Perez-Castillo, LL Rubin, L Timchenko, C Gil, **A Martinez***.

Subtly Modulating Glycogen Synthase Kinase 3 β : Allosteric Inhibitor Development and Their Potential for the Treatment of Chronic Diseases. *J Med Chem.* 60, 4983-5001 (2017) D1 IF 6.23 no. citations: 31

6. F Prati, A de Simone, P Bisignano, A Armirotti, M Summa, D Pizzirani, R Scarpelli, V Andrisano, A Perez-Castillo, B Monti, F Massenzio, L Polito, M Racchi, A D Favia, G Bottegoni, **A Martinez**,* ML Bolognesi,* A Cavalli.* Multitarget drug discovery for Alzheimer's disease; triazinones as the first dual BACE1/GSK-3 fragment hits *Angew Chem Int Ed Engl.* 54, 1578-1582 (2015) D1 IF 11.68 no. citations: 82

7. IG Salado, M Redondo, ML Bello, C Perez, NF Liachko, BC Kraemer, L Miguel, M Lecourtois, C Gil, **A Martinez**,* DI Perez.* Protein kinase CK-1 inhibitors as new potential drugs for amyotrophic lateral sclerosis. *J Med Chem.* 57, 2755-2772 (2014) D1 IF: 6.23 no. citations: 53

8. V. Palomo, D. I. Perez, C. Perez, J. A. Morales-Garcia, I. Soteras, S. Alonso-Gil, A. Encinas, A. Castro, N. E. Campillo, A. Perez-Castillo, C. Gil, **A. Martinez**.* 5-Imino-1,2,4-thiadiazoles: First Small Molecules as substrate competitive inhibitors of Glycogen Synthase Kinase 3. *J. Med. Chem.*, 55, 1645-1661 (2012) D1 IF: 6.23 no. citations: 50

9. V. Palomo, I. Soteras, D.I. Perez, C. Perez, C. Gil, NE. Campillo, **A. Martinez**.* Exploring the binding sites of Glycogen Synthase Kinase 3. Identification and characterization of allosteric modulation cavities. *J. Med. Chem.*, 54, 8461-8470 (2011) D1 IF: 6.23 no. citations: 60

10. D.I. Perez, V. Palomo, C. Perez, C. Gil, P. Dansk, FJ. Luque, S. Conde, **A. Martinez*** Switching reversibility to irreversibility in GSK-3 inhibitors: Clues for specific design of new compounds. *J. Med. Chem.*, 54, 4042-4056 (2011) D1 IF: 6.23 n.citas: 49

C.2. Research Projects and Grants (among more than 60)

1. HR21-00931 Drugs4ALS:Targeting TDP-43 with protein kinase inhibitors: a effective and measurable therapy for ALS. Fundación La Caixa. 11/2021-10/2024. Grant: 500.000 € PI. AM

2. PID2019-105600RB-I00. Modulación del envejecimiento y la neurodegeneración por moléculas pequeñas inhibitoras de proteína quinasa. AEI. 06/2020-06/2023. Grant: 130.000 € PI. AM

3. B2017/BMD-3813. ELA-MADRID: Diseño y desarrollo de fármacos innovadores para el tratamiento de la esclerosis lateral amiotrofica. Comunidad Madrid. Programa Biomedicina 2017. 1/2018-12/2021. Grant: 767.395 € Coordinator PI. AM

4. CB18/05/00040. Investigación clínica en esclerosis lateral amiotrofica. CIBERNED, ISCiii 1/2019-12/2020. Grant: 90.000 € PI. AM

5. MSCA-ITN-ETN-765912. DRIVE: Driving next generation autophagy researchers towards translation. EU Commission H2020. 11/2017-10/2021. Grant: 3.890.064 €. PI: F.Reggiore (CSIC-PI: AM Grant CSIC:247.872 €)

6. H2020-INFRADEV-2018-1 (GA 823893): EU-OPENSREEN-DRIVE: Ensuring long-term sustainability of excellence in chemical biology within Europe and beyond. EU Commission H2020-INFRADEV-2018-2020. 2/2019-1/2023. Grant: 4.999.563 €. PI: P. Gribbon (CSIC-PI: AM Grant CSIC: 136.043 €)

7. SAF2016-76693-R "Modulación de proteínas quinasas y BACE/1 con moléculas pequeñas de diseño multidiana: una nueva aproximación para la prevención y tratamiento de las enfermedades cognitivas". MINECO Retos-Sociedad Program. 12/2016-12/2019. Grant: 172.000 € PI: AM.

8. SAF2015-72325-EXP "El ojo como ventana diagnóstica del cerebro". MINECO EXPLORA program. 04/2017-03/2018 Grant: 60.000 € PI: AM.

9. RTC-2015-3439-1 Desarrollo de un fármaco innovador para la enfermedad de Parkinson. Seguridad clínica y nuevas terapias con S14. MINECO Retos-Colaboración program. 04/2015-12/2018. Grant: 193.292 € PI: AM.

10. IPT-2012-0762-300000 Desarrollo de terapias innovadoras para la enfermedad de Parkinson. MINECO INNPACTO program. 07/2012-12/2015. Grant: 128.663 € PI: AM.

11. ADDF-20121102 Evaluation of cognition and hippocampal neurogenesis after oral administration of a phosphodiesterase 7 inhibitor in an Alzheimer disease mice mode". ADDF. 01-2013/12- 2013 Grant: 150.00 \$ PI: AM.

C.3. Contracts

1. Title: "The eye as brain window". AEDEM (Multiple sclerosis patient's association). PI: AM (CIB-CSIC). 1/2018-6/2018. Funding 49.000 €.

2. Title: "Allosteric GSK-3 modulators development". AMO Pharma. PI: AM (CIB-CSIC). 1/2016-12/2018. Funding 170.000 €.

3. Title: "Eficacia en modelos animales de la enfermedad de Parkinson del compuesto S14". ARACLON Biotech. PI: AM (IQM-CSIC). 5/2011-5/2013. Funding: 90.000 €.

- Title: "Descubrimiento de fármacos neurogénicos con potencial neuroreparador en la enfermedad de Parkinson". ARACLON Biotech. PI: AM (IQM-CSIC). 3/2009-2/2011. Funding: 50.000 €.
- Title: "Inhibidores de quinasas para enfermedades neurodegenerativas". NOSCIRA S.A. PI: AM (IQM-CSIC). 10/2008-09/2011. Funding: 48.000 €.
- Title: "Descubrimiento y desarrollo de fármacos eficaces para la esclerosis lateral amiotrófica". Fundación MEDINA. PI: AM (IQM-CSIC). 7/2009-12/2011. Funding: 100.000 €.

C.4. Patents and other IPR (among more than 40 patent applications)

- Gil, C.; Martínez, A.; García, A. M.; Pérez, D.I. ES2544519(B1): Quinazolininas S-Sustituidas y sus aplicaciones terapéuticas para el tratamiento de enfermedades mediadas por PDE7. Priority countries: ES, USA (US9796687 (B2)), EU, JP, AU. Priority date: 22/05/2015. Owner: CSIC. Exploiting by: ARACLON BIOTECH.
- Martínez, A.; Gil, C.; Palomo, V.; Pérez, D. I.; Pérez, C.; Pérez-Castillo, A.; Loza, M. I.; Cadavid, M. I.; Brea, J. ES2360783(B1) "5-imino substituted 1,2,4-thiadiazoles useful in the treatment of neurodegenerative diseases". Priority Countries: AU (AU2010302536(B2)), EU (EP2484670(B1)), USA (US9604947(B2)). Priority date: 02.10.2009. Owner: CSIC. Exploiting by: ANKAR PHARMA.
- Martínez, A.; Gil, C.; Palomo, V.; Pérez, C.; Pérez, D. I. ES2402503(B1): GSK-3 Allosteric modulators. Priority countries: ES, USA (US9193688 (B2)), EU (EP2769720 (B1)), AU (AU2012314283(B2)). Priority date: 30.09.2011. Owner: CSIC Exploiting by: AUTISM THERAPUTICS
- Martínez, A.; Gil, C.; Pérez, C.; Pérez-Castillo, A.; Morales, J.; Redondo, M.; Sanz, M. ES2353093(B1): "Use of quinazoline derivatives and their pharmaceutical compositions in the treatment of neurodegenerative diseases". Priority countries: ES, USA (US9192610 (B2)), EU (EP2433637 (B1)), AU (AU2010251044(B2)), JP (JP5563068(B2)) Priority date: 20.05.2009. Owner: CSIC. Exploiting by: ARACLON BIOTECH
- Martínez, A.; Medina, M.; Alonso, M.; Fuertes, A.; Navarro, ML.; Pérez-Puerto, MJ.; Castro, A.; Martín-Aparicio, E. EP20050380176: "GSK-3 Inhibitors" Priority Countries: AU (AU2006278829(B2)), CN (CN101257900(B)), JP (JP5484726(B2)), RU (RU2449998(C2)), USA (US8686042(B2)), ZA (ZA200800983(B)). Priority date: 29/07/2005. Owner: NOSCIRA Exploiting by: AUTISM THERAPUTICS
- Martínez, A.; Dorronsoro, I.; Alonso, M.; Panizo, G.; Fuertes, A.; Pérez-Puerto, MJ.; Medina, M. EP1586319(B1): "Thiadiazolidindiones as GSK-3 inhibitors". Priority countries: AU (AU2005230392(B2)), CN (CN1946398(B)), JP (JP4995076(B2)), MA (MA28515(B1)), NO (NO332751(B1)), RS (RS51340(B)), RU (RU2379300(C2)), TW (TWI352084(B)), USA (US7531561(B2)) Priority date: 4.05.2004 Owner: NOSCIRA Exploiting by: AUTISM THERAPUTICS
- Founder of ANKAR-PHARMA (www.ankarpharma.com), February 2014

C.5 Dissemination

- Book Title: "El Parkinson". Author: A. Martínez, C. Gil. Editorial: La Catarata-CSIC. Madrid 2015. ISBN: 978-84-00-09918-3.
- Book Title: "El Alzheimer". Author: A. Martínez. Editorial: La Catarata-CSIC. Madrid 2009. ISBN: 978-84-00-08818-7
- Lecture: ¿Qué sabemos del Alzheimer?. CIUDAD-CIENCIA (CSIC) program. Cities: Plasencia, 16 Abril 2015; Vila-Seca (Tarragona), 27 Septiembre 2013; Valdepeñas (Ciudad Real), 11 Abril 2013; Tárrega (Lérida), 24 Mayo 2012.
- Lecture: ¿Qué sabemos del Parkinson?. CIUDAD-CIENCIA (CSIC) program. Cities: Valdepeñas (Ciudad Real), 12 Diciembre 2015; Barbastro (Huesca), 20 Noviembre 2015
- Lecture: ¿Qué sabemos del Alzheimer? ¿Hemos avanzado?. QUE SABEMOS DE? Program (CSIC). Cities: Lanzarote, 22 Mayo 2016; Fuerteventura, 24 Mayo 2016; Sevilla, 15 Noviembre 2016; Santiago Compostela, 26 Noviembre 2016; Zaragoza 15 Noviembre 2017; Huesca, 16 Noviembre 2017; Pamplona, 25 Noviembre 2017; Logroño, 30 Noviembre 2017.
- Lecture: ¿Qué sabemos del Parkinson? ¿Hemos avanzado?. QUE SABEMOS DE? Program (CSIC). Cities: Barbastro, Noviembre 2016; Valdepeñas, Abril 2018; Madrid, septiembre 2020 .

C.6 Awards

- 2021: Prize to the best scientific research program in ALS. Fundació Luzón
2018: Annual Scientific Prize from the Royal Spanish Pharmacy Academy (RANF)
2015: Madrid+d award to the best patent.
1989: Almirall-SEQT award for young researchers
1988: Caja Madrid award for PhD Thesis
1987: Extraordinary University award to PhD
1985: SEQT award for young researchers in medicinal chemistry