

**Part A. PERSONAL INFORMATION**

**CV date** 2-2-2023

First and Family name	M. CARMEN MÉNDEZ FERNÁNDEZ		
Social Security, Passport, ID number	10580460T	Age	66
Researcher codes	Open Researcher and Contributor ID (ORCID**)	<a href="https://orcid.org/0000-0003-2729-841X">https://orcid.org/0000-0003-2729-841X</a>	
	SCOPUS Author ID (*)	7004302596	
	WoS Researcher ID (*)	ABE-5745-2020	

(\*) Optional

(\*\*) Mandatory

**A.1. Current position**

Name of University/Institution	UNIVERSITY OF OVIEDO		
Department	FUNCTIONAL BIOLOGY (MICROBIOLOGY)		
Address and Country	FACULTY OF HEALTH SCIENCES. JULIÁN CLAVERÍA		
Phone number	985103558	E-mail	<a href="mailto:cmendezf@uniovi.es">cmendezf@uniovi.es</a>
Current position	FULL PROFESSOR IN MICROBIOLOGY	From	2-12-2011
Key words	Streptomyces, combinatorial biosynthesis, metabolic engineering, antibiotic, antitumor, biosynthesis pathways, biosynthesis gene clusters, genome mining		

**A.2. Education**

PhD, Licensed, Graduate	University	Year
Licensed in Biological Sciences	University of Oviedo	1979
PhD in Biology	University of Oviedo	1984

**A.3. General indicators of quality of scientific production (see instructions)**

- ✓ **7 research six-terms (sexenios), 6 actives** (last one obtained 31<sup>st</sup> of December 2022)
- ✓ **9.425 total citations** (SCOPUS, 7<sup>th</sup> of September 2023)
- ✓ **488 average citations last five years** (from 2018) (SCOPUS, 7<sup>th</sup> of September 2023)
- ✓ **h-index: 56** (SCOPUS, 7<sup>th</sup> of September 2023)
- ✓ **8 Doctoral Thesis defended** (from 1<sup>st</sup> of January 2010), **1 ongoing (28 in total)**
- ✓ **59 publications** from 1<sup>st</sup> of January 2011 (**192 in total**)
- ✓ **2 patents filled** from 1<sup>st</sup> of January 2011 (**17 in total**)
- ✓ **8 research projects as PI** from 1<sup>st</sup> of January of 2011

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

She is licensed in Biological Sciences (1979) and doctor in Biology (1984) by the University of Oviedo. After a postdoctoral stay (1984-86) at the John Innes Institute (Norwich, UK), she returned to the University of Oviedo where she obtained a permanent position as an Associate Professor (1988), and later on as a Full Professor (2011) in Microbiology. She is the coordinator of a university research group named "Biosíntesis de compuestos bioactivos por microorganismos (BIOMIC)". Her group has a strong expertise in identification and characterization of biosynthesis gene clusters involved in the biosynthesis of bioactive compounds (antibiotic, antitumor, immunosuppressor) in *Streptomyces*; in the application of combinatorial biosynthesis approaches to generate novel bioactive compounds; in using metabolic engineering strategies to improve production yields; in increasing/activating expression of cryptic gene clusters; and in identification and purification of new compounds. The research group has created a platform of genetic tools to modify the glycosylation profiles of bioactive compounds, which has been used to generate novel glycosylated derivatives of several antitumor compounds (mithramycin, elloramycin, rebeccamycin, among others). Some of these compounds have shown higher activity and/or lower toxicity than their parental compounds and have been patented and licensed to Entrechem S.L. (Oviedo), a spin-off

company of which she was a co-founder. She is coinventor of **17 patents**, 13 of which are international and have been licensed to and/or are used by several companies (Hoescht Marion Roussel, Biotica Technology Ltd., Asturpharma S. A., PharmaMar S. A., Entrechem S. L.). She has been supervisor of **24 Doctoral Thesis** (8 in the last ten years) and she is now supervising 1. She is author of **192 publications** (59 in the last ten years), including **14 book chapters** and **173 reviews and original articles** in international journals from JCR. From those, more than **106** are in journals at **the first quartile** (Q1) of its area, being **42** in journals at the **first decile** (D1). In the last ten years she has been continuously PI of research projects financed by the Spanish Ministry (MICINN; MINECO), including two International research projects in collaboration with other EU research groups. Also, she has been PI in projects financed by the University of Oviedo. Her research interest is focused in mining *Streptomyces* genomes looking for unknown biosynthesis gene clusters potentially encoding new bioactive compounds with unusual chemical characteristics, and in the identification and characterization of uncommon biosynthesis steps that take place along the pathways for bioactive compounds, whose genes/enzymes have potential application in the generation of novel compounds.

## Part C. RELEVANT MERITS (sorted by typology)

### C.1. Publications (see instructions)

- Ye S, Molloy B, Pérez-Victoria I, Montero I, Braña AF, Olano C, Arca S, Martín J, Reyes F, Salas JA, Méndez C. Uncovering the Cryptic Gene Cluster *ahb* for 3-amino-4-hydroxybenzoate Derived Ahbamycins, by Searching SARP Regulator Encoding Genes in the *Streptomyces argillaceus* Genome (2023). *Int J Mol Sci.* 2023, 24(9): 8197. doi: 10.3390/ijms24098197. **FI. 5,6.**
- Becerril A, Pérez-Victoria I, Martín JM, Reyes F, Salas JA, Méndez C. (2022). Biosynthesis of Largimycins in *Streptomyces argillaceus* Involves Transient  $\beta$ -Alkylation and Cryptic Halogenation Steps Unprecedented in the Leinamycin Family. *ACS Chem Biol*17(8):2320-2331. doi: 10.1021/acschembio.2c00416. **FI. 4,634.**
- Ye, S., Ballin, G., Pérez-Victoria, I., Braña, A.F., Martín, J., Reyes, F., Salas, J.A. and Méndez, C. (2022). Combinatorial biosynthesis yields novel hybrid argimycin P alkaloids with diverse scaffolds in *Streptomyces argillaceus*. *Microbial Biotechnology.* doi: 10.1111/1751-7915.14167. **FI. 6,575**
- Becerril, A.; Perez-Victoria, I.; Ye, S.; Brana, A.F; Martin, J. ; Reyes, F.; Salas, J.A; **Mendez, C.** (2020). Discovery of Cryptic Largimycins in *Streptomyces* Reveals Novel Biosynthetic Avenues Enriching the Structural Diversity of the Leinamycin Family. *ACS Chemical Biology* 15 (6): 1541-1553. **F. I. 4,434**
- Botas A, Eitel M, Schwarz PN, Buchmann A, Costales P, Núñez LE, Cortés J, Morís F, Krawiec M, Wolański M, Gust B, Rodriguez M, Fischer WN, Jandeleit B, Zakrzewska-Czerwińska J, Wohlleben W, Stegmann E, Koch P, **Méndez C**, Gross H. (2021). Genetic Engineering in Combination with Semi-Synthesis Leads to a New Route for Gram-Scale Production of the Immunosuppressive Natural Product Brasilicardin A. *Angew Chem Int Ed Engl.* 60(24):13536-13541. **F. I. 15.336**
- Zabala, D; Song, LJ; Dashti, Y; Challis, GL; Salas, J; **Méndez, C** (2020). Heterologous reconstitution of the biosynthesis pathway for 4-demethyl-premithramycinone, the aglycon of antitumor polyketide mithramycin. **Microbial Cell Factories** 19(1): 111. **F.I. 4,187**
- Becerril, A., Perez-Victoria, I., Ye, S., Braña, A. F., Martin, J., Reyes, F., Salas, J. A., **Méndez, C.** (2020). Discovery of Cryptic Largimycins in *Streptomyces* Reveals Novel Biosynthetic Avenues Enriching the Structural Diversity of the Leinamycin Family. **ACS Chemical Biology** 15 (6): 1541-1553. **F. I. 4,434**
- Becerril, A., S. Álvarez, A. F. Braña, S. Díaz, R. I. Santamaría, J. A. Salas and **C. Méndez** (2018). Uncovering production of specialized metabolites by *Streptomyces argillaceus* : activation of cryptic biosynthesis gene clusters using nutritional and genetic approaches. **PLoS One** 13(5) :e0198145. **F. I. 2,766**
- Ye, S., A. F. Braña, J. González-Sabín, F. Morís, C. Olano, J. A. Salas and **C. Méndez.** (2018). New insights into the biosynthesis pathway of polyketide alkaloid argimycins P in *Streptomyces argillaceus*. **Frontiers in Microbiology** 9, 252. **F.I. 4,019**

- Ye, S., B. Molloy, A. F. Braña, D. Zabala, C. Olano, J. Cortés, F. Morís, J. A. Salas, **C. Méndez**. (2017). Identification by genome mining of a type I polyketide gene cluster from *Streptomyces argillaceus* involved in the biosynthesis of pyridine and piperidine alkaloids argimycins P. **Frontiers in Microbiology** 8:194. **F.I. 4.076**
- Medema et al. (**Méndez, C.** 104/154). (2015). Minimum Information about a Biosynthetic Gene cluster. **Nature Chemical Biology**, 11: 625-631. **FI 12.709**
- Zabala, D., A. F. Braña, A. B. Flórez, J. A. Salas, and **C. Méndez**. (2013). Engineering precursor metabolite pools for increasing production of antitumor mithramycins in *Streptomyces argillaceus*. **Metabolic Engineering** 20: 187–197. **FI 8.258**
- Núñez, L. E., S. E. Nybo, J. Gonzalez-Sabin, M. Pérez, N. Menéndez, A. F. Braña, M. He, F. Morís, J. A. Salas, J. Rohr and **C. Méndez**. (2012). A novel mithramycin analogue with high antitumor activity and less toxicity generated by combinatorial biosynthesis. **Journal of Medicinal Chemistry** 55: 5813-5825. **FI 5.614**
- García, B., J. González-Sabín, N. Menéndez, A. F. Braña, L. E. Núñez, F. Morís, J. A. Salas, and **C. Méndez** (2011). The chromomycin CmmA acetyltransferase: a membrane-bound enzyme as a tool for increasing structural diversity of the antitumour mithramycin. **Microbial Biotechnology** 4 (2): 226-38. doi: 10.1111/j.1751-7915.2010.00229.x . **FI 2.534**
- Olano, C., **C. Méndez** and J. A. Salas (2010). Post-PKS tailoring steps in natural product-producing actinomycetes from the perspective of combinatorial biosynthesis. **Natural Products Report**. 27:571-616. **FI 9.202**

## C.2. Research projects

- PID2020-113062RB-I00. Streptomyces como fuente de compuestos bioactivos y de actividades enzimáticas nuevas. Entidad financiadora: Agencia Estatal de Investigación. **Investigador Principal. M. Carmen Méndez Fernández**. 1/9/2021-31/08/2024. Financiación recibida: 211.750 €. Participación: IP. Concedido
- PAPI-20-GR-2010-0019. Biosíntesis de Compuestos Bioactivos por Microorganismos. Entidad financiadora: Universidad de Oviedo (UO-Acciones Complementarias de la U.O.). **Investigador Principal. M. Carmen Méndez Fernández**. 1/1/2020-31/12/2020. Financiación recibida: 4.200 €. Participación: IP. Concedido
- BIO2017-82462-R. Identificación y caracterización de agrupamientos de genes de biosíntesis de compuestos derivados de hidroxibenzoatos y aminobenzoatos, en *Streptomyces*. Entidad financiadora: Ministerio de Ciencia, Innovación y Universidades. **Investigador Principal. M. Carmen Méndez** . 1/1/2018-31/12/2020 (extensión aceptada hasta 30-6-2020). Financiación recibida: 217.800 €. Participación: IP. Concedido
- PCIN-014-066. Next Generation Immunosuppressants: Brasilicardin synthesized by *Nocardia* spp. Entidad financiadora: MINECO (Acciones de Programación Conjunta Internacional 2014). 1/3/2015-28/2/2018. **Investigador principal: M. Carmen Méndez Fernández**. Financiación recibida: 150.000 €. Participación: IP. Concedido
- BIO2014-56752-R. Activación y caracterización de rutas de biosíntesis de compuestos bioactivos en *Streptomyces*. Entidad financiadora: MINECO (Programa Estatal de Investigación, Desarrollo e Innovación orientada a los Retos de la Sociedad). 1/1/2015 – 31/12/2017. **Investigador Principal: M. Carmen Méndez Fernández**. Financiación recibida: 217.800,00 €. Participación: IP. Concedido
- BIO2011-25398. Secuenciación del genoma de *Streptomyces argillaceus*, productor del antitumoral mitramicina, e identificación de genes reguladores de biosíntesis. Entidad financiadora: MICINN (subprograma de Proyectos de Investigación Fundamental No orientada). 1/1/2012-31/12/2014. **Investigador Principal: M. Carmen Méndez Fernández**. Financiación recibida: 187.550 €. Participación: IP. Concedido
- PIM2010EEI-00752. Genome mining for drug discovery: activation of silent biosynthetic gene clusters. Entidad financiadora: MICINN (Programa Nacional de Internacionalización de la I+D. Subprograma Proyectos Internacionales). 1/3/2011-31/12/2014. **Investigador Principal: M. Carmen Méndez Fernández**. Financiación recibida: 158.000 €. Participación: IP. Concedido
- BIO2008-00269. Regulación y canalización de precursores metabólicos en la biosíntesis del antitumoral mitramicina por *Streptomyces argillaceus*. Entidad financiadora: MICINN (Subprograma de Proyectos de Investigación Fundamental no orientada). 1/1/2009-31/12/2011. **Investigador Principal: M. Carmen Méndez Fernández**. Financiación recibida: 215.000 €. Participación: IP. Concedido

### C.3. Contracts, technological or transfer merits

- Aplicación de la Ingeniería Genética a la mejora de la biosíntesis de un producto natural bioactivo sintetizado por *Streptomyces*. Ventu Biotech S.L. (CN-11-025). 2011-2012. Investigador Principal: J.A. Salas

### C.4. Patents

- Suhui Ye Huang, Brian Molloy Galiana, Alfredo Fernández Braña, Jesús Cortés Bargalló, Francisco Moría Varas, José A. Salas Fernández y **M. Carmen Méndez Fernández**. Compuestos alcaloides argimicinas producidas por *Streptomyces argillaceus* y sus usos. Solicitud patente española: P201500825. Fecha de solicitud: 18-11-2015. Patente española ES 2602255 (A1). Entidad titular: Universidad de Oviedo.
- García Llorente, I. , N. Miguel Vior, C. A. Sialer Guerrero, J. González. Sabín, A. Fernández Braña, **C. Méndez Fernández**, J. A. Salas Fernández y F. Morís Varas. Derivados de colismicina. Solicitud patente española: P201130010. Patente internacional WO2012093192 (A1) Fecha de solicitud: 5 enero 2011. Entidad titular: Universidad de Oviedo/ Entrechem S. L. Empresa co-titular y explotadora: Entrechem S. L.
- Olano, C., Gómez, C., Braña, A. F., **Méndez, C.**, Salas, J. A. Procedimiento para aislar genes implicados en la biosíntesis de estreptolidigina, moléculas de ADN, manipulación genética de la ruta y sus usos. Patente española: ES2334755 (B2). Fecha concesión: 14-10-2010. Patente Internacional: WO2011/012761 (A3). Fecha solicitud: 29-7-2010. Número solicitud: PCT/ES2010/070528. Fecha de prioridad: 30-7-2009. Entidad titular: Universidad de Oviedo. Empresa que la está explotando: Entrechem S.L.
- Pérez Salas, A., C. Sánchez, A. F. Braña, **C. Méndez**, J. A. Salas y F. Morís. Indolocarbazoles glicosilados, su procedimiento de obtención y sus usos. Patente Española: ES 2326459 (B1). Fecha concesión: 13-5-2010. Patente Europea: EP2277885 (A1). Fecha solicitud: 6-4-2009. Patente Americana: US 2011/0136753 (A1). Fecha solicitud: 6-4-2009. Fecha de prioridad: 8-4-2008. Entidad titular: Universidad de Oviedo/Entrechem S.L. Empresa que la está explotando: Entrechem S.L.
- **Méndez, C.**, F. Lombó, A. F. Braña y J. A. Salas. Derivados de Oviedomicina, su procedimiento de obtención y sus usos. Patente Española: ES2331397 (B1). Fecha de la concesión: 23-9-2010. Patente Internacional: WO2009/118443 (A1). Fecha solicitud: 26-3-2009. Fecha de prioridad: 28-3-2008. Entidad titular: Universidad de Oviedo. Empresa que la está explotando: Entrechem S.L.

### C.5. Training activities

The PI has been supervisor of 27 Doctoral Thesis (5 of which have received a PhD with distinction). Most of them have a duration of 4 years and at least they have originated one publication in an international journal (4 publications/Thesis as an average), and in many cases one or more patents. Most of the doctors have spent some time as postdocs in European or American research groups, and some of them are working in foreign and Spanish companies. Moreover, the PI has been supervisor of 6 Master Thesis and 20 Research Seminars.