

**Part A. PERSONAL INFORMATION**

CV date 23/09/2024

First and Family name	ALVARO GUTIERREZ UZQUIZA		
ID number	71273618E	Age	43
Researcher codes	ORCID**	0000-0002-0446-4131	
	WoS Researcher ID (*)	E-4073-2012	
	WEB:	<a href="https://gutierrezuzquiza.com/">https://gutierrezuzquiza.com/</a>	

(\*) Optional (\*\*) Mandatory

**A.1. Current position**

Name of University/Institution	Complutense University of Madrid		
Department	Biochemistry and Molecular Biology		
Address and Country	Plaza Ramon y Cajal s/n 28040 Madrid SPAIN		
Phone number	681003839	E-mail	<a href="mailto:alguuz@ucm.es">alguuz@ucm.es</a>
Current position	Associate professor	From	08/03/2023
Key words	CRISPR, CANCER, METASTASIS, PROSTATE		

**A.2. Education**

PhD, Licensed, Graduate	University	Year
Biochemistry and Molecular Biology	Complutense University of Madrid	2009
Specialization program (posgrade)	Bioinformatics/University UOC	2013
Grade	Biological Science/University of Salamanca	2002

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

Publications: 32 (88% Q1; 12% D1.)

H-Index: 17

Total citations: 1286

Thesis supervised: (2) Sara Manzano Figueroa (2021) and Maria Rodrigo Faus (ongoing)

Master Supervised: (4) S. García, A. Vicente, N Alonso, M. Fernandez

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

I have always been inclined to pursuing research in human health. Since the early steps of my career, I committed myself to study cancer-signaling pathways and devoted my career to work on understanding the molecular basis of the diseases. I have worked in close contact with world-renowned experts in cellular signaling, genetics, cancer and metastasis to get a comprehensive view of the main steps that govern biology of the cancer cells. Including names like: Dr. Hakon Hakonarson (CHOP, Philadelphia, USA), Dr. Julio Aguirre-Ghiso (Mount Sinai Hospital, NY, USA) or Dr. Marcelo Kazanietz (PostDoc supervisor, Upenn, Philadelphia, USA).

After defending my doctoral dissertation on MAPK and cellular stress supervised by Dra. A. Porras I moved to Dr. Kazanietz's lab at the Dept. of Pharmacology at the University of Pennsylvania at Philadelphia, USA. I was soon awarded with a Cancer Award granted by the Department of Defense of USA, where I contributed as the Principal Investigator: "Role of PKCs in tumorigenesis and metastasis". I continued my research on the cancer field in the Department of Cancer Biology at the University of Pennsylvania, one of the top Cancer Biology departments in the world, where I learned the great advantage of the identification of key genes using unbiased high throughout based approaches.

The nature of the research I have performed over the years and my expertise were the main factors that led to my hiring in 2016 as a Research Scientist at the Center for Applied Genomics (CAG), the largest pediatric biorepository in the world at the Children's Hospital of Philadelphia. At CAG, my research was focused on the identification and characterization of pathogenic variants to develop new therapeutic strategies. To that end, I developed state-of-the-art molecular biology technologies including CRISPR/Cas9 for designing and developing mammalian cellular models. The bulk of this work led to the development of new therapeutic approaches for 2 rare and untreatable disease currently being used in patients (Published in Nat Medicine or Nat comm). In addition, my position in a laboratory with a strong

computational biology expertise has also allowed me to gain insight into the statistical, informatics, and analytical approaches used in the high-throughput genomics conducted in the lab.

After these 8 years working in first class laboratories at USA, I moved to Spain where **I am currently applying my expertise in “hard-core” signaling and cancer using CRISPR/Cas9 libraries to unravel new therapeutic targets in prostate metastasis.** I have been awarded with the highly competitive “Programa de atracción de talento 2017” from Autonomous government of Madrid. In addition, my research has been funded in “convocatoria RETOS 2020” (PID2020-117650RA-I00). **The laboratory that I currently lead** (1 PhD student, 1 technician and one master student) focuses on the development of CRISPR technology and molecular techniques together with bioinformatics to identify new therapeutic targets and increase our knowledge on the mechanisms and pathways involved in the metastatic cancer. This work has been recently published, as senior author (Cell Death & Dis, Sci Report, Intern Jour of Cancer). Additional information -> <https://gutierrezuzquiza.com/>

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

- **Granted with a PROYECTO CONSOLIDA from Agencia Española de Investigación :** Development of CRISPR/Cas9 tools for characterization of prognosis biomarkers and therapeutic targets in metastatic prostate cancer (CHIMPC)
- **Granted with a PROYECTO RETOS from Spanish Ministry of Science** to identify novel genes essential for prostate cancer metastasis using CRISPR libraries.
- **Program of “atracción de talento 2017” from Autonomous government of Madrid** to identify novel genes essential for prostate cancer metastasis using CRISPR libraries.
- **Development of new therapeutic approaches and its uses in patients with Lymphangiomatosis and Hereditary Angiopathy (HCCAA).** Published in Nat Comm and Nature Medicine.
- **Development of a patent for the identification of new therapies in angiopathies**
- **Prostate Cancer Award** from the Department of Defense to conduct a study on the role of PKCs kinases in tumorigenesis and metastasis and on the molecular mechanisms that underlie the bone tropism of prostate cancer.
- **EMBO Fellowship award:** collaborative studies on C3G/p38 $\alpha$  in chronic myeloid leukemia, dormancy, and tumor dissemination in the laboratory of Dr. Julio Aguirre-Ghiso, PhD (Mount Sinai School of Medicine, New York, USA)

#### **C.1. Publications** (Selected)

1. Ahmad R, Barcellini A, Baumann K, Benje M, Bender T, Bragado P, Charalampopoulou A, Chowdhury R, Davis AJ, Ebner DK, Eley J, Kloeber JA, Mutter RW, Friedrich T, Gutierrez-Uzquiza A. Particle Beam Radiobiology Status and Challenges: A PTCOG Radiobiology Subcommittee Report. *Int J Part Ther.* 2024 Aug 8;13:100626. doi: 10.1016/j.ijpt.2024.100626. eCollection 2024 Sep.
2. García-Sáez J, Figueroa-Fuentes M, González-Corrales C, Roncero C, Lazcanoiturburu N, Gutiérrez-Uzquiza Á. Uncovering a Novel Functional Interaction Between Adult Hepatic Progenitor Cells, Inflammation and EGFR Signaling During Bile Acids-Induced Injury. *Int J Biol Sci.* 2024 Apr 8;20(7):2339-2355. doi: 10.7150/ijbs.90645. 2024.
3. Rodrigo-Faus M, Mendiburu-Eliçabe M, Huiqui Q, Lopez A, Musteanu M, Reyes Palomares A, Hakonarson H, Porras A, Bragado P, Gutierrez-Uzquiza A\*. “CRISPR-Cas9 screening in metastatic prostate cancer cell lines identifies PRMT7 as an essential gene for prostate cancer metastasis”. *Cancer Letter.* 2024 Apr 28;588:216776. doi: 10.1016/j.canlet.2024.216776. (18/19) (Q1) (IF: 9,4). **(last and corresponding).**
4. Leire Recalde-Percaz, Patricia Jauregui, Anna López-Plana, Patricia Fernández-Nogueira, Minerva Iniesta-González, Sara Manzano, Raul Alonso, Aleix Noguera-Castells, Nuria Moragas, Cristina Baquero, Maria Rodrigo-Faus, Nerea Palao, Erica Dalla, Francesc Xavier Aviles-Jurado, Isabel Vilaseca, Mercedes Camacho, Xavier Leon-Vintro, Gemma Fuster, Jordi Alcaraz, Julio Aguirre-Ghiso, Pere Gascón, **Álvaro Gutierrez-Uzquiza**, Almudena Porras, Neus Carbo, Paloma Bragado.” Neuropilin-2 upregulation by stromal. “TGF $\beta$ 1 induces lung disseminated tumour cells dormancy escape and promotes

- metastasis outgrowth". Researchsquare repository. [https://assets.researchsquare.com/files/rs-1956933/v1\\_covered.pdf?c=1660597215](https://assets.researchsquare.com/files/rs-1956933/v1_covered.pdf?c=1660597215)
5. Palao N, Sequera C, Cuesta ÁM, Baquero C, Bragado P, **Gutierrez-Uzquiza A**, Sánchez A, Guerrero C, Porras A."C3G down-regulation enhances pro-migratory and stemness properties of oval cells by promoting an epithelial-mesenchymal-like process". *Int J Biol Sci.* 2022 Sep 25;18(15):5873-5884. Doi: 10.7150/ijbs.73192. eCollection 2022.
  6. L Martin-Morales, S Manzano, M Rodrigo, AVicente Barrueco, V Lorca, P Bragado, A Porras, T Caldes, P Garre, and **A Gutierrez-Uzquiza**. "Germline gain-of-function MMP11 variant results in an aggressive form of colorectal cancer". *International Journal of Cancer.* (2022) (10/10) (Q1) (IF: 7,3). **(last and corresponding)**.
  7. España S, Sánchez-Parcerisa D, Bragado P, **Gutiérrez-Uzquiza Á**, et al. "In vivo production of fluorine-18 in a chicken egg tumor model of breast cancer for proton therapy range verification". *Scientific Report* (2021).(9/9.m IF: 3.9)
  8. N Palao, C Sequera, A M Cuesta, C Baquero, P Bragado, **A Gutierrez-Uzquiza**, et al. "C3G down-regulation enhances pro-migratory and stemness properties of oval cells by promoting an epithelial-mesenchymal-like process". *International Journal of Biological Sciences.* 2021. (Q1) (6/9. IF: 5,5).
  9. S. Manzano, **A. Gutierrez-Uzquiza** et al. "C3G Protein, a New Player in Glioblastoma". *Int. Jour. Of Molecular Science.* (2021) (2/6) (Q1) (IF: 5,9)
  10. F Fernández-Nogueira G Fuster **A Gutierrez-Uzquiza**, et al. "Cancer-Associated Fibroblasts in Breast Cancer Treatment Response and Metastasis" *Cancers* (2021) (3/6) (Q1) (IF: 6,6).
  11. S. Garcia-Garcia, M. Rodrigo-Faus, N. Fonseca, S. Manzano, Balázs Györffy, A. Ocaña, P. Bragado, A. Porras and **A. Gutierrez-Uzquiza\***. "HGK promotes metastatic dissemination in prostate cancer". *Scientific Report* (2021). **(last and corresponding)**. (9/9.m IF: 3.9)
  12. España S, Sanchez-Parcerisa D. Ibñez P, Sanchez-Tembleque V, Udias JM, Onecha V, **Gutierrez-Uzquiza A**, et al. "Direct proton range verification using oxygen-18 enriched water as a contrast agent". *Radiation Physics and Chemistry.* Volume 182, May 2021,
  13. Pancione M, Cerulo L, Remo A, Giordano G, **Gutierrez-Uzquiza A**, "Centrosome Dynamics and Its Role in Inflammatory Response and Metastatic Process". *Biomolecules.* 2021
  14. S. Manzano, **A. Gutierrez-Uzquiza+**, P.Bragado, et al. "C3G down-regulation induces the acquisition of a mesenchymal phenotype that enhances aggressiveness of glioblastoma cells". *Cell Death & disease* (2020). **Senior author.** (2/11. IF:6.2).
  15. **Gutierrez-Uzquiza A\***, March ME\*, Snorraddottir AO, Matsuoka LS, Balvis NF, Gestsson T, Nguyen K, Sleiman PMA, Kao C, Isaksson HJ, Bragason BT, Olafsson E, Palsdottir A, Hakonarson H. NAC blocks Cystatin C amyloid complex aggregation in a cell system and in skin of HCCAA patients. *Nature Communicatons.* 2021 Mar 23 (1/14. IF: 12. 1).
  16. A. Mazal, JA Vera Sanchez, D.Sanchez-Parcerisa, JM Udias, SEspaña, V. Sanchez-Tembleque, LM Fraile, P. Bragado, **A. Gutierrez-Uzquiza** et al. "Biological and mechanical synergies to deal with proton therapy pitfalls: minibeam, FLASH, arcs and gantryless room". *Front. Oncol. - Radiation Oncology.* (2020). Accepted (9/19. IF:4.8)
  17. Sequera C, Bragado P, Manzano S, Arechederra M, Richelme S, **Gutiérrez-Uzquiza A**, , et al. C3G Is Upregulated in Hepatocarcinoma, Contributing to Tumor Growth and Progression and to HGF/MET Pathway Activation. *Cancers* (2020) Aug 14. (6/10. IF: 6. 1)
  18. Dong Li, Michael E. March, **A. Gutierrez-Uzquiza**, Charly Kao, Christoph Seiler, et al. "ARAF recurrent mutation causes central conducting lymphatic anomaly treatable with a MEK inhibitor". *Nature Medicine.* (2019) Jul 25. (3/23. IF: 34)
  19. Zhou N, **Gutierrez-Uzquiza A**, Zheng XY, Chang R, Vogl DT, Garfall AL, Bernabei L, Saraf A, et al. "RUNX proteins desensitize multiple myeloma to lenalidomide via protecting IKZFs from degradation". *Leukemia.* (2019) Feb 13 (2/13. IF:10)
  20. Li D, Wenger TL, Seiler C, March ME, **Gutierrez-Uzquiza A**, Kao C, Bhoj E, et al. "Pathogenic variant in EPHB4 results in central conducting lymphatic anomaly". *Hum Mol Genet.* (2018) Jun 14. (5/24. IF:4.5)
  21. Priego, Arechederra, Sequera, Bragado, Vázquez-Carballo, **A. Gutierrez-Uzquiza**, Martín-Granado, et al as. "C3G knock-down enhances migration and invasion by

- increasing Rap1-mediated p38 $\alpha$  activation, while it impairs tumor growth through p38 $\alpha$ -independent mechanisms.” **Oncotarget** (2016) Jun;7. (6/11. IF:5.1)
22. **Gutierrez-Uzquiza A**, Lopez-Haber C, Jernigan DL, et al. “PKC $\epsilon$  Is an Essential Mediator of Prostate Cancer Bone Metastasis”. **Mol Cancer Res.** (2015) Sep;13 (selected as "Molecular Cancer Research HIGHLIGHTS"). (1/5 IF:4.5)
23. Wang H, **Gutierrez-Uzquiza A**, Garg R, Barrio-Real L, Abera MB, Lopez-Haber C, Rosembli C, Lu H, Abba M, Kazanietz M). “Transcriptional regulation of oncogenic protein kinase C $\epsilon$  (PKC $\epsilon$ ) by STAT1 and Sp1 proteins”. **J Biol Chem.** Jul 2014. (5/10. IF:4.5)
24. **Gutierrez-Uzquiza A.**, L. Zubeldia-Brenner, L. Barrio-Real, H.Wang, M.G. Kazanietz, F. Coluccio Leskow. “ $\beta$ 3-Chimaerin, a novel member of the chimaerin Rac-GAP family”. **Molecular Biology reports.** January 2014. (1/5. IF: 2.1)
25. **Gutierrez-Uzquiza A.**, Colon-Gonzalez F., Leonard T. A., Canagarajah B. J., et al. “Coordinated activation of the rac-gap  $\beta$ 2-chimaerin by an atypical proline-rich domain and diacylglycerol”. **Nature Communication.** 2013 (1/8. IF:10,8)
26. Wertheimer E., **Gutierrez-Uzquiza A.**, Rosembli C., Lopez-Haber C., Sosa M.S., Kazanietz M.G. “Rac signaling in breast cancer: a tale of GEFs and GAPs.” **Cell Signaling.** 2012. Feb;24(2):353-62. (2/6 IF: 4.3)

## C.2. Research projects

### Principal Investigator:

1- Title: "**Development of CRISPR/Cas9 tools for characterization of prognosis biomarkers and therapeutic targets in metastatic prostate cancer (CHIMPC)**".

Sponsor Agency: Agenica Española de investigación. Period of award: 2024 - 2026

Host Institution: Universidad Complutense de Madrid.

PI: Álvaro Gutiérrez Uzquiza. Funding:160.000€

1- Title: "**Using CRISPR/Cas9 technology to identify new biomarkers in metastatic prostate cancer (CRISPCAN)**". (REF: PID2020-117650RA-I00).

Sponsor Agency: Ministerio de Ciencia e innovación. Period of award: 1/9/2021 - 1/9/2024

Host Institution: Universidad Complutense de Madrid.

PI: Álvaro Gutiérrez Uzquiza. Funding:157.000€

2- Title: **Genome-scale screening to identify and validate novel genes essential for prostate cancer metastasis. (2021-5A/BMD-20956).**

Host Institution: Complutense University of Madrid Period of award: 13/05/2022 - 13/05/2023

PI: Álvaro Gutiérrez Uzquiza Funding:30.000€

3-Title: **Genome-scale screening to identify and validate novel genes essential for prostate cancer metastasis. (2017-T1/BMD5468)**

Sponsor Agency: Autonomous government of Madrid-Complutense University of Madrid

Host Institution: Complutense University of Madrid Period of award: 19/02/2018 - 19/02/2023

PI: Álvaro Gutiérrez Uzquiza Funding:227.000€

4-Title: **Postdoctoral Prostate Cancer award**

Sponsor Agency: DEPARTMENT OF DEFENSE (USA)

Host Institution: Universidad De Pennsylvania. Philadelphia (USA)--Period of award: 01/06/2011 - 01/06/2013

PI: ALVARO GUTIÉRREZ UZQUIZA Funding:\$120.000

### Other roles:

5- Title: “Comprendiendo la radioterapia flash con dispositivos de tejido-en-chip y resonancia magnética mejorada con hiperpolarización. FLASOHOnCHIP” (PLEC2022-009256). Plan estatal de investigación científica, técnica y de innovación 2021-2023. Plan de recuperación, transformación y resiliencia.

Host Institution: *Universidad Complutense de Madrid. Period of award: 01/11/2023-01/07/2027. PI: Irene Marco Rius (Role in Grant:Co-research)*

6- *Title: ADVANCED STRATEGIES AND NEW APPROACHES FOR PROTON-THERAPY (P2022/BMD-7434)Actividades de I+D entre grupos de investigación de la Comunidad de Madrid en tecnologías y en biomedicina*

Host Institution: *Universidad Complutense de Madrid. Period of award: 01/11/2023-01/07/2027. PI: Luis Mario Fraile (Role in Grant:Co-research)*

7-*Título: “Radiobiología de la protonterapia a tasas flash estudiada en un modelo de cáncer de pulmón”. Convocatoria 2021 Proyectos de I+D+i – RTI (PID2021-124094OA-I00)*

Host Institution: *Universidad Complutense de Madrid. Period of award: 01/09/2022-31/08/2025. PI: Daniel Sánchez Parcerisa (Role in Grant:Co-research)*

*Investigador Principal: Daniel Sánchez Parcerisa*

8-*Title: Descodificación epigenética de la inmunidad a malaria. ref. PR65/19-22460*

Sponsor Agency: *Comunidad Autonoma de Madrid.*

Host Institution: *Universidad Complutense de Madrid. Periodo f award: 01/07/2020-30/06/2022. PI: Armando Reyes Palomares (Role in Grant:Co-research)*

9-*Title: The Future of Genomics Medicine in Patient Care: Contributions from CHOP*

Sponsor Agency: *National Institute of Health NIH (USA)*

Host Institution: *The Children’s Hospital of Philadelphia. (USA). Period of award: 01/09/2015-01/09/2019. PI: Hakon Hakonarson (Role in Grant: Research Associate)*

10-*Title: SPECIFICITY OF THE UBIQUITIN SYSTEM IN LYMPHOID MALIGNANCIES*

Sponsor Agency: *NATIONAL CANCER INSTITUTE. (USA). R00CA166181*

Host Institution: *Universidad De Pennsylvania. Filadelfia (USA). Period of award: 01/01/2014-01/12/2016. PI: Luca Busino (Role in Grant: Research Associate)*

11-*Title: ERBB RECEPTOR SIGNALING VIA SMALL G-PROTEINS IN BREAST CANCER*

Sponsor agency: *NATIONAL CANCER INSTITUTE (USA)*

Host Institution: *Universidad De Pennsylvania. Filadelfia (USA). Period of award: 01/04/2010-01/06/2014. PI: Marcelo Kazanietz (Role in Grant: Postdoctoral Researcher)*

12-*Title: PROSTATE CARCINOGENESIS AND PKC SIGNALING*

Sponsor agency: *NATIONAL CANCER INSTITUTE (EE.UU)*

Host Institution: *Universidad De Pennsylvania. Philadelphia (USA). Period of award: 01/04/2010-01/04/2011. PI: Marcelo Kazanietz (Role in Grant: Postdoctoral Researcher)*

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

**Research contract (article 83): 2020 & 2022 UCM-Arctic Therapeutics Company.**

“Identification of new treatment for diseases. UCM researchers: Alvaro Gutierrez Uzquiza (Principal investigator), Paloma Bragado. Arctic therapeutic CEO: Ivor Hakonarson

### **C.4. Patents**

Compositions and Methods for the Treatment of Hereditary Cystatin C Amyloid Angiopathy (HCCAA) and Other Neurodegenerative Disorders. Authors: Hakon Hakonarson, **Alvaro Gutierrez Uzquiza**; Michael March. # Cystatin C CHOP 0989 US Provisional 62/555,496 3460-P06517US00. Country: United States of America. Date 07/09/2018

### **C.5 HONORS AND AWARDS**

- **Biochem. Journal Outstanding Poster Award.** FASEB-confer. Signaling in cancer (2012)
- **PhD Thesis Award “Abilio Rodríguez Paredes”** (2009)
- **EMBO Fellowship.** Mount Sinai School of Medicine. New York. USA (2008-2009)

**C.6 Education:** Assistant professor of Biochemistry and Molecular Biology at Pharmacy school (Universidad Complutense de Madrid)

**C.7 Memberships of scientific societies:** AACR//ASHG//SEBBM//ASEICA