

## CURRICULUM VITAE ABREVIADO (CVA)

### Part A. PERSONAL INFORMATION

First name	Clara		
Family name	Álvarez	Villamarín	
Gender (*)	F	Completion date (dd/mm/yyyy)	31/01/2023
Scientific name		Alvarez, CV or Alvarez, Clara	
e-mail	<a href="mailto:clara.alvarez@usc.es">clara.alvarez@usc.es</a>	URL Web:	
		<a href="https://www.usc.es/cimus/en/research/research-groups/neoplasia-endocrine-differentiation">https://www.usc.es/cimus/en/research/research-groups/neoplasia-endocrine-differentiation</a>	
Open Researcher and Contributor ID (ORCID) (*)		0000-0003-1500-4058	

#### A.1. Current position

Position	Professor, M.D. Ph.D. Head (PI) of Neoplasia and Endocrine Differentiation		
Initial date	01/07/2020—01/01/2012		
	Universidade de Santiago de Compostela (USC)		
Department/Center	Physiology	Centro de Investigación en Medicina Molecular y Enfermedades Crónicas (CIMUS)	
Country	Spain	Teleph. number	+34881815483
Key words	Thyroid, Pituitary, Cancer, Acromegaly, Stem cells, TGFb, RET		

#### A.2. Previous positions (research activity interruptions, indicate total months)

Period	Position/Institution/Country/Interruption cause
07/01/1997-30/06/2020	Associated Professor / Univ de Santiago de Compostela
01/09/1994-06/01/1997	Profesor Propio/ Universidade de Vigo
04/03/1993-31/08/1994	Postdoc. DIBIT. Hosp San Raffaele. Univ Vita Salute Milan
01/09/1991-03/03/1993	Postdoc. Institut für Molekularbiologie & Tumorforschund. Marburg (Germany)

#### A.3. Education

PhD, Licensed, Graduate	University/Country	Year
Licenciada Medicina y Cirugía (M. D.)	Universidad de Santiago de Compostela (USC)	1989
Doctor en Medicina (Ph. D.)	Universidad de Santiago de Compostela (USC)	1992

### Part B. CV SUMMARY (max. 5000 characters, including spaces)

My research activity is focused on Endocrinology, special emphasis on studies related to thyroid and pituitary gland. Most studies are centred in the physiological mechanisms involved in cancer cell proliferation and normal cellular turnover, and their implications in the development of different physiological and pathological processes.

**The Group.** We are a transdisciplinary group which includes basic researchers (technicians, doctoral students and postdoc), and clinicians including surgeons (MN Blanco incorporated to replace retired F. Barreiro), pathologist (J Cameselle-Teijeiro, world expert on thyroid pathology) and endocrinologists (I Bernabéu).

**Publications.** During the last 18 years, as PI, our work in the most well defined endocrinology cellular models (human primary cultures from surgical surplus of patients' surgery; mouse and rat in vivo models of endocrine diseases such as hypothyroidism; endocrine stem cells) has been published in journals such as EMBO J, Clin Can Res, Oncogene, Annals Oncol, J Clin Endocrinol Metab, Endocrine Rel Cancer or Endocrinology. Our models have also led from collaborations with groups working in related research like hypothalamic/peripheral regulation of energy balance, to our recent role in the European consortium for nano-encapsulated insulin for oral administration, leading to publications like Cell Metab, Nature Comm, J Control



Release, Trends Mol Med, Mol Metab or FASEB J. As a whole, see <https://scholar.google.es/citations?user=IJRXsUAAAAJ&hl=es>, my total number of publications is 72 (59 being Q1 and 30 of these are D1). Total number of citations are 3346 and my H number is 31. During the period 2012-22 my total number of publications was 40 (Q1=25; D1=16) and acted as principal/corresponding author in 16

**Congress.** Our research activity has aroused the interest of a large number of audiences having given lectures by invitation as the most relevant endocrine forums. I was invited speaker in more than 40 international workshops/symposia/ congress. Among others, at International Thyroid Congress (ITC, worldwide), European Congress Endocrinology (ECE), American Endocrine Soc (ENDO) and the Eur Thyroid Assoc. (ETA). and ENEA (European), etc. Of note, my recent Plenary Lecture at the European Congress of Endocrinology (2021).

**Funding.** Funded by projects of the Spanish “Plan Nacional”, by companies (Novartis) and foundations (Pfizer), and until recently by a project of MRC-UK in which I was Co-PI with M Korbonits (Queen Mary Univ of London).

**Training and Mentorship.** 14 Ph.D students and 11 TFM's were trained in my Group. Among the former, several are independent researchers (Assoc Prof USC, IMDEA-Madrid, or Heads of Technological facilities —Confocal Microscopy, Proteomics), some are doing long postdocs (Dana Farber Cancer Center in harvard, CBMSO in Madrid), and some are working as clinicians (Santiago, Valladolid) or in private pharma/biomed sector (Madrid, Ferrol). In addition, I teach Endocrinology and Signal Transduction to >450 Medicine (1<sup>st</sup>, 2<sup>nd</sup> year), 250 Pharmacy, 50 Biotechnology graduate students; and Cancer Epidemiology to 30 Master degree students.

**International Recognition.** Besides invited lectures (above), I have organized international scientific activities: in addition to be the Chair of the European Thyroid Association (ETA) Meeting in 2014 in Santiago (>1000 participants), I was appointed (2017-2021) “*Focus Area Lead in Basic Thyroidology*” of the European Society of Endocrinology (ESE), elected member from 2018-2022 of the ETA Exec Com (POC of annual congress), and elected from 2018-on Secretary of the Thyroid Cancer Group (TCG), a powerful sub-group within ETA. I am also a member of the experts group “*European Alliance for Personalised Medicine*” (EAPM), organized at the behest of the European Parliament, to identify initiatives to improve molecular diagnostics, and management, of thyroid cancer (Horgan D et al, Healthcare 10, 2022). I also serve as panel member of the European Research Council for Consolidator Grants LS4 2015-

**Outreach activities.** I am strongly committed to bring biomedical research closer to patients and society. As examples during the last 5 years my participation in: **a)** disseminating our research in mass media, newspapers, radio and television interviews with Spanish, European and SouthAmerican media; **b)** the use of social networks (like Twitter, Instagram, Facebook); **c)** participation with ASEICA in “CONÓCELAS” program, specially focused in ESO/high school; **d)** participation in the “Open doors days in CIMUS”, where we receive the visit of the lay public and talk about our research in a comprehensive way, or organize learning activities (e.g. our successful “Pathology index activity: Ki67, mitotic index —differences between adenomas and carcinomas), as well as in programmed visits by high schools; **e)** I also engage in activities like “a pint of science”, which is organized by researchers of our institute in different places of the city every year.

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

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

From 2012 to now, I published 40 papers as (see Alvarez CV, or Alvarez,Clara in PubMed). In addition to the ones listed below, as co-author I have published in journals such as: Cell Metabolism (IF 27,2) Nat Comm (IF: 12.3), Trends in Mol Med (IF: 9-45), three in J.Control Rel (IF: 7.9), FASEB J (IF: 5,7), Mol Met (IF 6,79), J Clin End Metab (IF: 6.3), Am J Surg Path (IF 6,3), Endocr Rel Cancer (IF: 5,2), Endocrinology (IF: 4.7), etc.

I would like to highlight the 10 most relevant ones to this project, including one under consideration:

#### **\*Corresponding author**

Rodrigues JS, Chenlo M, Bravo S, Perez-Romero S, Suarez-Fariña M, Sobrino T, Sanz R, Blanco Freire N, Nogueiras R, Lopez M, Fugazzola L, Cameselle-Teijeiro JM, **Alvarez CV\***. PIAS2b dsRNAi repression kills by mitotic catastrophe anaplastic thyroid and non-thyroid carcinomas, but not normal thyroid or differentiated carcinomas. **Nature Commun** (under second revision 2023).

1.-Garcia-Rendueles AR, Chenlo M, Oroz-Gonjar F, Solomou A, Mistry A, Barry S, Gaston-Massuet C, Garcia-Lavandeira M, Perez-Romero S, Suarez-Fariña M, Pradilla-Dieste A, Dieguez C, Mehlen P, Korbonits M, **Alvarez CV\***. RET signalling provides tumorigenic mechanism and tissue specificity for AIP-related somatotrophinomas. **Oncogene**. 2021 Nov;40(45):6354-6368. Impact Factor: 8,3. Q1/D1.

2.-Chenlo M, Aliyev E, Rodrigues JS, Vieiro-Balo P, Blanco Freire MN, Cameselle-Teijeiro JM, **Alvarez CV\***. Sequential Colocalization of ERα, PR, and AR Hormone Receptors Using Confocal Microscopy Enables New Insights into Normal Breast and Prostate Tissue and Cancers. **Cancers** (Basel). 2020 Nov 30;12(12):3591. Impact factor: 6,63. Q1.

3.-Pradilla Dieste A, Chenlo M, Perez-Romero S, Garcia-Rendueles ÁR, Suarez-Fariña M, Garcia-Lavandeira M, Bernabeu I, Cameselle-Teijeiro JM, **Alvarez CV\***. GFRα 1-2-3-4 co-receptors for RET are co-expressed in Pituitary Stem Cells but individually retained in some Adenopituitary Cells. **Front Endocrinol** (Lausanne). 2020.;11:631. Impact Factor: 5,5. Q1.

4.-Chenlo M, Rodriguez-Gomez Ia, Serramito R, Garcia-Rendueles Ar, Villar- Taibo R, Fernandez-Rodriguez E, Perez-Romero S, Suarez-Fariña M, Garcia- Allut A, Cabezas-Agricola JM, Rodriguez-Garcia J, Lear PV, Alvarez-San Martin RM, Alvarez-Escola C, \*Bernabeu I, **Alvarez CV\***. Unmasking a new prognostic marker and therapeutic target from the GDNF-RET/PIT1/p14ARF/p53 pathway in acromegaly. **EBioMedicine**. 2019 May;43:537-552. Impact Factor: 6,68.,Q1/D1

5.-Capdevila J, Mayor R, Mancuso FF, Iglesias C, Caratù G, Matos I, Zafón C, Hernando J, Petit A, Nuciforo P, Cameselle-Teijeiro JM, **Alvarez CV**, Recio JA, Tabernero J, Matias-Guiu X, Vivancos A, Seoane J. Early evolutionary divergence between papillary and anaplastic thyroid cancers. **Ann Oncol**. 2018 Jun 1;29(6):1454-1460. Impact Factor: 11.19, Q1/D1

6.-Garcia-Rendueles AR, Rodrigues JS, Garcia-Rendueles MER., Suarez Fariña M, Perez-Romero S, Bernabeu I, Rodriguez-Garcia J, Fugazzola L, Sakai T, Liu F, Cameselle-Teijeiro J, Bravo SB., **Alvarez CV\***. Rewiring of the apoptotic TGF-β-SMAD/NFκB pathway through an oncogenic function of p27 in human papillary thyroid cancer (PTC). **Oncogene**. 2017. 36(5):652-666. Impact Factor: 6,85. Q1/D1

7.-García M, Barrio R, García-Lavandeira M, Escudero A, Díaz-Rodríguez E, Gorbenko Del Blanco D, Fernández A, De Rijke Yb, Vallespín E, Nevado J, Matre V, Hinkle PM, Hokken-Koelega ACS, De Miguel MP, Cameselle-Teijeiro JM, Nistal M, **Alvarez CV\***, Moreno JC\*. The syndrome of central hypothyroidism and macroorchidism: IGSF1 controls TRHR and FSHB expression by differential modulation of pituitary TGFβ and Activin pathways. **Sci Rep**. 2017 Mar 6;7:42937. Impact Factor: 5.228. Q1/D1.

8.-Bravo SB#, Garcia-Rendueles MER#, Garcia-Rendueles AR, Rodrigues JS, Perez-Romero S, Garcia-Lavandeira M, Suarez-Fariña M, Barreiro F, Czarnocka B, Senra A, Lareu MV, Rodriguez-Garcia J, Cameselle-Teijeiro J, **Alvarez CV\***. Humanized medium (h7H) allows long-term primary follicular thyroid cultures from human normal thyroid, benign neoplasm and cancer. 2013. **J Clin Endocrinol Metab**. Jun;98(6):2431-41.Impact Factor: 6,43. Q1/D1.

9.-Garcia-Lavandeira M, Saez C, Diaz-Rodriguez E, Perez-Romero S, Senra A, Dieguez C, Japon MA, **Alvarez CV\***. Craniopharyngiomas express embryonic stem cell markers (SOX2, OCT4, KLF4 and SOX9) as pituitary stem cells but do not co-express RET/GFRA3 receptors. 2012. **J Clin Endocrinol Metab**. Jan;97(1):E80-87.Impact Factor: 6,5. Q1/D1

10.-Diaz-Rodriguez E, Garcia-Lavandeira M, Perez-Romero S, Senra A, Cañibano C, Palmero I, Borrelo MG, Dieguez C, **Alvarez CV\***. Direct promoter induction of p19Arf by Pit-1 explains the dependence receptor RET/Pit-1/p53 induced apoptosis in the pituitary somatotroph cells. 2012. **Oncogene**. Jun 7;31(23):2824-2835 doi: 10.1038/onc.2011.458. Impact Factor: 7,414; Q1/D1

## C.2. Congress/Workshops Invited presentations exclusively.

During my career, I have been invited to 88 talks in scientific events: 44 international (22 in the last ten years) and 44 national (28 in the last ten years). Selected ones:

-**Alvarez CV**. European Thyroid Association. New treatment for Anaplastic Thyroid Cancer inducing mitotic catastrophe. Milan. (Accepted invitation: 03-07/09/2023)

-**Alvarez CV**. European Society Endocrinology. Advances in pituitary research (Plenary Lecture)" Virtual with >750 connected vivo attendants worldwide (2021)

**-Alvarez CV.** "Pituitary cell turnover: balance between adult stem cell recruitment and cell death of endocrine secretory cells". FASEB Meeting. Steamboatstream (Denver, USA). 2017.

**-Alvarez CV.** European Task Force in Endocrine Cancer (ETEC). Advances in molecular understanding of thyroid cancer. Munich. 2016

**-Alvarez CV.** The GPS niche of stem cells in the pituitary. 15th International world Congress of Endocrinology and 14th Eur Cong of End. Florence. 2012.

### **C.3. Research projects and grants as "Principal Investigator"**

**National Public Competitive Calls: Financing Agencies: MEC, MINECO, MICINN, AEI:**

1. Reference: [MEC BFU2010-16652](#). Duration: [1/1/2011–31/12/2013](#). Amount: [€170.000](#). Title: [Mecanismos fisiopatológicos implicados en la proliferación de las células foliculares tiroideas humanas](#).
2. Reference: [BFU2013-46109-R](#). Duration: [1/01/2014–31/12/2016](#). Amount: [€200.000](#). Title: [Mecanismos fisiológicos de recambio y proliferación, benigna y maligna, de las células foliculares tiroideas humanas](#)
3. Reference: [BFU2016-76973-R](#). Duration: [30/12/2016 – 29/12/2019](#). Amount: [€254.100](#). Title: [Implicaciones fisiopatológicas de los mecanismos de recambio y proliferación, benigna y maligna, de las células foliculares tiroideas humanas y de glándulas endocrinas](#).
4. Reference: [PIID2019-110437RB-100](#). Duration: [1/06/2020–30/05/2023](#). Amount: [€274.670](#). Title: [Mecanismos de proliferación y recambio celular de células endocrinas normales y cancerosas de la tiroides y la hipófisis](#).
5. Ref: [PDC2021-121621-I00](#). Duration: [1/12/2021-30/11/2023](#). Amount: [129.950€](#) Title: [Ensayo pre-clínico para PIAS2b-dsRNAi](#).

**European Public Competitive Calls**

6. Reference: [MRC/MR/M018539/1-010550 QM](#). Duration: [1/09/2015-30/09/2019](#). Amount: [TOTAL :£309548,4 \(EUR 425964,497\)](#) PI, UK: [MK:£181759,4 \(EUR 250116,141\)](#); Co-PI, SPAIN: [CVA :£127789 \(EUR 175848,356\)](#). Title: [The effect of AIP Mutations on the apoptotic RET pathway in Pituitary Adenomas](#) Funding agency: [MEDICAL RESEARCH COUNCIL MRC \(UK\)](#). PI: [MARTA KORBONITS \(UK\)](#). Co-PI: [CLARA ALVAREZ \(Spain\)](#).

**Non-profit Endocrinology Foundations Private Projects. PI Clara Alvarez**

7. Reference: [EUROPEAN PROJECT EUROPEAN THYROID ASSOCIATION \(ETA\) FOUNDATION](#) Duration: [1/03/2016 – 31/03/2018](#). Amount: [€37.5000](#). Title: [Thyroid Cancer and Rare diseases in Thyroid as cause of Congenital Hypothyroidism](#). Funding agency: [Fundación European Thyroid Association \(ETA\)](#)

### **C.4. Contracts, technological or transfer merits**

#### **C.4.1. Contracts & Industry Supported Projects**

1. Reference: [PROYECT IC2 PFIZER ACROMEGALY](#). Duration: [1/06/2013–30/06/2015](#). Amount: [€20.000](#). Financing agency: [FUNDACIÓN PFIZER EUROPE](#). Title: [Study of RET-dependent apoptosis pathway and interactions RET / AIP in somatotrophs cells of pituitary tumours secreting GH or ACTH and in non-functioning pituitary tumours: correlation with clinical and biochemical characteristics, and response to treatments](#). PI: [IGNACIO BERNABEU](#). Co- PI: [CLARA ALVAREZ](#).
2. Reference: [PROYECTO NOVARTIS-FUNDACIÓN FSEEN](#). Duration: [1/01/2012–31/12/2014](#). Amount (Euros): [€15.000 EUR](#). Financing agency: [NOVARTIS-FSEEN](#). Title: [REMAH \(Registro Molecular y análisis de Adenomas Hipofisarios; 6 nodos\)](#).. PI (NODO 6 Básico): [CLARA V ALVAREZ](#); PI (NODO 6 Clínico): [IGNACIO BERNABEU](#).

#### **C.4.2. Patents**

1. European Patent Office (EPO) Application NoJ / Patent [No. 19382211 .1 – 1118](#) Date of Filing: [26.03.2019](#). Title: [Prognostic Markers, Therapeutic Target and Treatment for Acromegaly](#). Investigators: [I Bernabeu \(50%\)+CV Alvarez \(50%\)](#); Institutions: [USC+SERGAS](#)
2. Oficina Española de Patentes y Marcas (OEPM). Patent sol: [P201930743](#), Extendida y en revisión en Europa (EPO) y USA (USPTO) [WO2021028610 A1](#) Date of Filing: [13/08/2019](#). Title: [Compuestos y métodos para el tratamiento del cáncer](#). Investigators: [JS Rodrigues \(33%\)+JM Cameselle Teijeiro \(33%\)+ CV Alvarez. \(34%\)](#). Institutions: [USC+ SERGAS](#).