CVA Date	03.12.2021

Part A. PERSONAL INFORMATION

First name	José Ignacio		
Family name	Casal Alvarez		
Gender (*)	Male	Birth date	06/05/1958
ID number	10581499G		
e-mail	icasal@cib.csic.es	URL Web	
Open Researcher and Contributor ID (ORCID) (*)		0000-0003-1085-2840	

A.1. Current position

Position	Scientific Investigator OPIs		
Initial date	2008		
Institution	Consejo Superior de Investigaciones Científicas-Centro de Investigaciones Biológicas Margarita Salas		
Department/Center	Molecular Biomedicine		
Country	Spain	Teleph.	91837112
Keywords	Colorectal Cancer, Molecular Oncology, Metastasis, Proteomics		

A.2. Previous positions (research activity interuptions, art. 14.2.b))

Period	Position/Institution/Country/Interruption cause
2001-2008	Director of the Biotechnology Programme CNIO (Spain)
1987-1997/1997-2001	Project leader/ Research Director INGENASA (Spain)
1985-1986	Postdoctoral fellow. Massachusetts Institute of Technology (USA)
1980-1984	Doctoral Thesis. CBM-CSIC. Spain

A.3. Education

PhD, Licensed, Graduate	University/Country	Year
Ciencias Químicas/Bioquímica	Complutense de Madrid	1980
Doctor en Ciencias	Autónoma de Madrid	1985

A.4. General quality indicators of scientific production

Research sections that have been accredited: Six research six-year terms + 1 Technology transfer
Total citations: 9319
Total articles in Q1: 117
H Index: 59 (Google Scholar)

Part B. CV Summary

For almost 20 years I investigated the development of new diagnostic methods and vaccines in animal viruses, first at the CBM (CSIC), then at MIT (USA) and later as Research Director at the biotechnology company INGENASA. This research resulted in a high number of European projects, publications, patents and products. In 2001, I joined the CNIO as Director of the Biotechnology Program, starting new lines of research in colorectal cancer that included the development of recombinant antibodies and biomarker discovery. In 2006, I promoted the creation of the technology-based company Protein Alternatives SL, which is still active today. In October 2008, I moved to the CIB Margarita Salas (CSIC) as principal investigator (PI) of the laboratory of "Mechanisms of cancer metastasis". In the last 14 years, I have consolidated a solid experience in in the identification and development of new therapeutic targets for colorectal cancer. Our group has identified a large number of proteins relevant in metastatic progression. We have thoroughly characterized the functionality of many of these proteins including cadherin 17 (CDH17), IL13Rα2, PAUF/ZG16B and SOSTDC1 in CRC metastasis (see selected publications). Indeed, our group has developed new therapeutic strategies based on these targets. Therapeutic antibodies against the RGD motif of cadherin 17 and the binding motif of IL13/IL13Rα2 as well as peptides derived from IL13Rα2 have been developed and patented. These patents have been licensed or are in the licensing process. Currently, our main lines of research are focused on: 1) the in-depth characterization of novel metastatic mediators, 2) characterization of epithelial plasticity, stemness and drug resistance and 3) metabolic reprogramming in colorectal cancer metastasis, using a multidisciplinary approach. To support this cancer research, I have been uninterruptedly funded by the National Plan since 2003, the AECC (2011-2015), the Community of Madrid and the Areces Foundation (2017-2019), among others. The PI has been a member of the Spanish proteomic platform ProteoRed. Our technological transfer activities have been also funded by different national and international Programs as well as by R&D research contracts with several companies. Doctoral theses supervised in the last 10 years: 5 (3 more in progress), 4

JAE-Intro (CSIC), 5 TFMs and 5 TFGs plus two contracts of the CAM "Garantia Juvenil" (predoc+assistant).

Part C. MOST RELEVANT MERITS

C.1. Selected Publications (2012-2021)

Jaen M,Bartolomé R. Aizpurua C, Martin-Regalado A,Imabud JI and **JI.Casal** [2021] Inhibition of Liver Metastasis in Colorectal Cancer by Targeting IL-13/IL13Rα2 Binding Site with Specific Monoclonal Antibodies. **Cancers** (Basel). 13(7):1731.

Bartolomé RA, Robles J, Martin-Regalado A, Pintado-Berninches L, Burdiel M, Jaén M, Aizpurúa C, Imbaud JI and **JI Casal**. [2021] CDH6-activated αIIbβ3 crosstalks with α2β1 to trigger cellular adhesion and invasion in metastatic ovarian and renal cancers**. Mol Oncol**. 15(7):1849-1865.

Bartolomé RA, Pintado-Berninches L, Jaén M, de los Ríos V, Imbaud JI and **JI Casal.** [2020] SOSTDC1 promotes invasion and liver metastasis in colorectal cancer via interaction with ALCAM/CD166. **Oncogene**. 39, 6085-6098.

Bartolomé RA, Martín-Regalado Á, Jaén M, Zannikou M, Zhang P, de Los Ríos V, Balyasnikova IV, **Casal JI.** [2020] Protein Tyrosine Phosphatase-1B Inhibition Disrupts IL13Rα2-Promoted Invasion and Metastasis in Cancer Cells. **Cancers** (Basel). 12(2).

Escudero-Paniagua B, Bartolome R, Rodriguez S, de los Rios V, Pintado L, Jaén M, Lafarga M, Fernandez-Aceñero MJ and **JI Casal** [2020] PAUF/ZG16B promotes colorectal cancer progression through alterations of the mitotic functions and the Wnt/β-catenin pathway. **Carcinogenesis**. 41(2), 203-213.

Bartolomé RA, Jaén M, and **Casal JI** [2018] An IL13Rα2 peptide exhibits therapeutic activity in metastatic colorectal cancer. **Br J Cancer**. 119, 940-9

Casal JI and Bartolomé RA [2018]. RGD cadherins and α2β1 integrin in cancer metastasis: A dangerous liaison. **BBA Reviews on Cancer**. 1869, 321-332

Torres, S., García-Palmero, I., Marín-Vicente, C., Bartolomé, R.A., Calviño, E., Fernández-Aceñero, M.J., **Casal, J.I**. [2018]. Proteomic Characterization of Transcription and Splicing Factors Associated with a Metastatic Phenotype in Colorectal Cancer. **J Proteome Res**. 17:252-264.

Bartolomé RA, Aizpurua C, Jaén M, Torres S, Calviño E, Imbaud JI and **Casal JI** [2018] Monoclonal antibodies directed against cadherin RGD exhibit therapeutic activity against melanoma and colorectal cancer metàstasis. **Clin Cancer Res**. 24, 433-44.

Torres S, I Garcia-Palmero, RA Bartolomé, MJ Fernandez-Aceñero, E Molina, E Calviño, MF Segura and **JI Casal** [2017] Combined miRNA profiling and proteomics demonstrates that different miRNAs target a common set of proteins to promote colorectal cancer metástasis**. J. Pathol** 242, 39-51

de Barrios O, B Győrffy, MJ Fernández-Aceñero, E Sánchez-Tilló**,** L. Sanchez-Moral, L. Siles, A. Esteve-Arenys, G. Rouge, **JI Casal,** DS Darling, A Castells and A Postigo (2017) ZEB1-induced tumorigenesis requires senescence inhibtion via activation of DKK1/mutant p53/Mdm2/CtBP and repression of macroH2A1. **Gut**. 66, 666-682

Alba-Castellón L, Olivera-Salguero R, Mestre-Farrera A, Pena R, Herrera M, Bonilla F, **Casal JI**, Baulida J, Pena C, Garcia de Herreros A. [2016] Snail1-dependent activation of cancer-associated fibroblast controls epithelial tumor cell invasion and metastasis. **Cancer Res**. 76, 6205-17

García-Palmero I, S Torres, RA Bartolomé, A Peláez-García, MJ Larriba, M Lopez-Lucendo, C Peña, B Escudero-Paniagua, A Muñoz and **JI Casal** (2016). Twist1-induced activation of human fibroblasts promotes matrix stiffness by upregulating palladin and collagen α1(VI). **Oncogene.** I2016 Oct 6;35(40):5224-5236.

Torres S, I Garcia-Palmero, M Herrera, RA Bartolomé, MJ Fernandez-Aceñero, G Padilla, A Peláez-García, C Peña, M Lopez-Lucendo, A Garcia de Herreros, F Bonilla**, JI Casal** [2015] LOXL2 is highly expressed in cancer-associated fibroblasts and associates to poor colorectal cancer outcome. **Clin Cancer Res**. 21 (21):4892-902.

Bartolomé RA, I García-Palmero, S Torres, M López-Lucendo, IV Balyasnikova and **JI Casal** [2015] IL-13 receptor α2 signaling requires a scaffold protein, FAM120A, to activate FAK and PI3K pathways in colon cancer metastasis. **Cancer Res**. 75(12), 2434-44

Peláez-García A, Barderas R, Batlle R, Viñas-Castells R, Bartolomé RA, Torres S, Mendes M, Lopez-Lucendo M, Mazzolini R, Bonilla F, García de Herreros A, **Casal JI** [2014] A proteomic analysis reveals that Snail regulates the expression of the nuclear orphan receptor Nr2f6 and IL-17 to inhibit adipocyte differentiation. **Mol Cell Proteomics**. 14(2), 303-15.

Bartolomé RA., Barderas R, Torres S, Fernandez-Aceñero MJ, Mendes M, García-Foncillas J, Lopez-Lucendo M, **Casal JI** [2014] Cadherin-17 interacts with α2β1 integrin to regulate cell proliferation and adhesion in colorectal cancer cells causing liver metastasis. **Oncogene** 33, 1658-69

Torres S, RA Bartolomé, M Mendes, R Barderas, MJ Fernandez-Aceñero, A Peláez-García, C Peña, M Lopez-Lucendo, R Villar-Vázquez, A Garcia de Herreros, F Bonilla, **Casal JI** [2013] Proteome profiling of cancer-associated fibroblasts identifies novel proinflammatory signatures and prognostic markers for colorectal cancer. **Clin Cancer Res**. 19, 6006-19

Barderas R., Marta Mendes, Sofia Torres, Ruben A. Bartolome, Maria Lopez-Lucendo, Roi Villar-Vazquez, Alberto Pelaez, Eduardo Fuente, Felix Bonilla, and **JI Casal** [2013] In-depth characterization of the secretome of colorectal cancer metastatic cells identifies key proteins in cell adhesion, migration and invasion. **Mol Cell Proteomics**. 12(6), M112.022848

Barderas R, Bartolomé RA, Fernandez-Aceñero MJ, Torres S, **Casal JI**. [2012] High Expression of IL-13 Receptor α2 in Colorectal Cancer Is Associated with Invasion, Liver Metastasis, and Poor Prognosis. **Cancer Res**. 72, 2780-90

C2. Congresses

Casal JI. Novel therapeutic agents for the treatment of liver metastasis. Liver Metastasis Network Research Meeting 2019. Valencia. Invited Speaker.

Casal JI. Proteomic strategies for cáncer research: Applications in cáncer diagnosis and therapy. Mendel University. Brno. Czech Republic. 2019. Invited Seminar

Casal JI. Key proteins in liver colonization in colorectal cancer and other tumors. IPBLN. Granada. Spain. 2017. Invited seminar.

Casal JI. Proteomic characterization of new transcription factors associated with a more invasive phenotype in colorectal cancer. 6th Congress of the Spanish Proteomics Society. Cadiz. Spain 2016. Invited presentation.

Casal JI. MicroRNAs upregulated in colorectal cancer metastasis target multiple overlapping proteins. XIV HUPO World Congress. Vancouver (Canada). 2015. Oral presentation.

Casal JI. Molecular insights in colon cancer metastasis. HUPO 13th Annual World Congress. Madrid (Spain). 2014. Keynote speaker

C.3. Selected Grants

Ayudas para la realización de doctorados industriales en la Comunidad de Madrid.
Entidad financiadora: V PRICYT (2016-2020) Comunidad de Madrid, IND2019/BMD-17153
Duración, desde: 1.01.2020 hasta: 31.12.2022
Financiación: 90.000 €

Targeting RGD cadherins, α2β1 integrin and interleukin 13 receptor α2 (IL13Rα2) for cancer metastasis therapy (Therabodies). Proyecto RETOS 2018. MCIU RTI2018-095055-B-100
Duración, desde: 1.01.2019 hasta: 31.12.2021
Financiación: 121.000 €

Plataforma de proteomica, genotipado y líneas celulares (PRB3).ISCIII. FIS. PT17/0019/0008
Entidades participantes: Red de laboratorios proteómica (entre otros CIB-CSIC)
Duración, desde: 01.01.2018 hasta: 31.12.2020
Financiación: 123.750 €

Desarrollo de nuevas dianas para inmunoterapia en la metástasis tumoral. Fundación Areces
Duracion: 2017-2020
Financiación: 109.000 €

Mecanismos de progresión y metástasis en cáncer colorrectal y otros tumores. Implicaciones en pronóstico y terapia. Proyectos RETOS 2015. MINECO. BIO2015-66489-R (2016-2018)
Financiación: 242.000 €

Validation studies on new diagnostic and therapeutic targets for colorectal cancer using different proteomic strategies. Plan Nacional MINECO. BIO2012-31023 (2013-2015)
Financiación: 210.600 €

Transcriptoma, proteoma e interactoma en el tejido epitelial y estromal del colon humano y sus alteraciones patológicas. Comunidad de Madrid. S2011/BMD-2344/ Colomics2 (2012-2015)
Entidades Participantes: A Muñoz (IIB), F. Bonilla (H. Puerta de Hierro), JI Casal (CIB), J Gonzalez-Sancho (UAM), F. Rojo (F. Jimenez Díaz) y A. Carrato (H. Ramón y Cajal)
Financiación CIB: 129.488 €
Coordinador general: Alberto Muñoz

Análisis del papel del estroma en el crecimiento e invasión de carcinomas de colon: identificación, caracterización y potencial clínico de marcadores de la activación estromal. Asociación Española Contra el Cáncer (2011-2015)
Entidades participantes: Hospital Universitario Puerta de Hierro. IMIM. CIB-CSIC

Financiación: 356.047 €
Dr Felix Bonilla (Coordinador). Dr.Ignacio Casal (IP en CIB)

C.4. Technology transfer activities and patents

R&D contracts

Optimization of IL13Rα2 peptide sequences for improved theraputic capacity
Financing company: Panford Investment (Canada)
Duration: 1.09.2021-30.06.2022
PI: Dr.Ignacio Casal CIB: 61.750 euros

Desarrollo de anticuerpos terapéuticos para el tratamiento de metástasis tumorales en diversos tipos de cáncer –METABODIES. Proyecto RETOS 2017. MCIU. RTC-2017-6260-1
Entidades participantes: Protein Alternatives SL and Centro de Investigaciones Biológicas
Duración, desde: 1.07.2018 hasta: 30.10.2021
Financiación Dr.Ignacio Casal CIB: 188.378,20 €

Development of a novel blood-based diagnostic test for colorectal cancer
Investigador principal: Juan Ignacio Imbaud. PROALT SL
Entidad financiadora: UE Horizon 2020. SME instrument phase 2 Grant agreement No: 666540
Duración: 1/8/2015-31/07/2018
Financiación recibida (en euros): Subcontratación CIB 175.000 €

COLONTEST: Diseño y puesta a punto de kits para el diagnóstico del cáncer de colon en sangre basados en plataformas multiplex. Proyectos Retos-Colaboracion. MINECO. RTC-2014-1518-1 (2014-2016)
Entidades Participantes: Protein Alternatives SL., CSIC, Azurebio SL, IDIBAPS
Financiación CIB: 43.710 €
Coordinador: Protein Alternatives SL

PATENTS

Antibody and use thereof for the treatment of cancer. J. Ignacio Casal, Marta Jaen and Ruben A. Bartolomé. Application EP21382266.1. Priority date: 31/03/2021. TITULAR: CSIC

Methods and compositions for the treatment of Il13Rα2-overexpressing cancers. **J.Ignacio Casal** y Ruben A. Bartolomé. USA Patent Aplication # 63/121,790. Priority date: 04/12/2020. TITULAR: CSIC

IL13Ralpha2 peptide and its uses. **J.Ignacio Casal** y Ruben A. Bartolomé. Patent #: EP17382737.9. Priority date: 03/11/2017. ENTIDAD TITULAR: CSIC

Agents binding specifically to human cadherin-17, human cadherin-5, human cadherin-6 and/or human cadherin-20, and methods and uses thereof. **J.Ignacio Casal** y Ruben A. Bartolomé. Patent #: PCT/EP2015/058527. Priority date: 30/04/2015. TITULAR: CSIC. License agreement: Protein Alternatives SL

Método de diagnóstico/pronóstico del cáncer colorrectal basado en la detección en suero de anticuerpos frente a autoantígenos tumorales. Ingrid Babel, Rodrigo Barderas y **J.Ignacio Casal. Patent #:** P201030708. Priority date: 13/05/2010. TITULAR: CSIC. License agreement: Protein Alternatives SL

C5. Present and past scientific management and coordination activities
Miembro de la Junta Directiva de la Sociedad Española de Proteómica (2009-2019)
Adjunto del Área de Medicina Clínica de la ANEP (2011)
Director del Departamento de Medicina Celular y Molecular del CIB (2011-12)
Miembro del Comité de Dirección y Científico del CNIO (2001-8)
Director del Programa de Biotecnología del CNIO (2001-8)
Miembro del Comité Científico de ASEBIO (1998-2001)
Miembro de la Junta directiva de la Sociedad Española de Biotecnología (97-2002)
Director del Departamento de Investigación de INGENASA (1997-2001)

C6. Peer review activities, Editorial Boards
Senior Editor **BMC Cancer**
Editorial Board **Int J. Mol. Sci**