CURRICULUM VITAE ABREVIADO (CVA)

Part A. PERSONAL INFORMATION

First name	Alfredo		
Family name	Berzal Herranz		
Gender (*)	Male	Birth date (dd/mm/yyyy)	
Social Security, Passport, ID number			
e-mail	aberzalh@ipb.csic.es	URL Web: www.ipb.csic.es	
Open Researcher and Contributor ID (ORCID) (*)		0000-0003-3722-7973	

(*) Mandatory

A.1. Current position

Position	Research Scientist		
Initial date	June 15, 2005		
Institution	CSIC		
Department/Center	Molecular Biology	IPBLN	
Country	Spain	Teleph. number	958181648
Key words	RNA; Aptamers; ribozymes; Viral RNA genomes; HCV, Flavivirus		

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

Period	Position/Institution/Country/Interruption cause
1993-2005	Tenured Scientist/IPBLN-CSIC/Spain
1993-1993 (6 months)	Postdoctoral Researcher/CIB-CSIC/Spain
1990-1993	Postdoctoral Researcher/University of Vermont/USA
1990-1990 (3 months)	Postdoctoral Researcher/Uppsala University/Sweden
1985-1990	PhD student//CIB-CSIC/Spain

A.3. Education

PhD, Licensed, Graduate	University/Country	Year
Graduated in Biological Sciences	Complutense de Madrid (UCM)/Spain	1986
PhD in Biological Sciences	Autónoma de Madrid (UAM)/Spain	1990

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

1990 PhD (CIB-CSIC; supervisor: Ramón Díaz Orejas) Mechanism of action of the natural antisense RNA CopA of the E. coli R1 plasmid. 1990-93 Post-Doc (University of Vermont, US; John M Burke group) Characterization of the mechanism of action of natural catalytic RNAs (hairpin and group I ribozymes). May-Dec 1993, Post-Doc (CIB-CSIC) Resistance to tobamovirus (RNA virus) in plants. Since Dec 1993 Independent researcher at IPBLN-CSIC. Responsible of the “Biological Activity of RNA”. Research Group. PI of 20 research grants, financed by international, national or regional agencies, and foundations.

2003-2016 Coordinator of the National RNA Network "RNA: Structure, Function and Biomedical and Biotechnological Applications".

Supervisor of 7 PhD Thesis; 8 Master Thesis (+1 in development); 10 Degree Thesis

IP or participant in seven research contracts with private companies or Public entities. Author of 6 patents.

The scientific interest throughout my career has been the knowledge of the biological function of RNA molecules and the exploration of its potential biomedical applications. Studying and characterizing natural non-coding RNAs (ncRNAs) in different biological processes (antisense RNAs, ribozymes, miRNAs and functional domains of RNA genomes), as well as artificial RNAs designed from natural domains or completely de novo. Always with

a double meaning: basic research characterizing the function and mechanisms of action of natural RNA molecules and structural domains; and applied exploring the potential of these molecules and RNA in general, as molecular tools and targets for suppression or modulation of gene expression or as antiviral agents.
Milestones. -The characterization of the antisense CopA was a pioneering work in Spain. To my knowledge, it was the first biochemical and functional characterization of a natural bacterial non-coding RNA (an antisense RNA) in Spain.
- Development of a powerful and experimental method, an ***In vitro* selection** strategy that allowed quickly determining the requirements of sequence and structure of the hairpin ribozyme and its substrate. The achievement of this objective was a milestone in my career, a pioneering work in the development of *in vitro* molecular selection techniques that allow the analysis of very complex populations of nucleic acids, and identify RNAs or DNAs with unsuspected activities. They have been extensively used for obtaining aptamers (this application is named SELEX). -Another important milestone was the demonstration for the first time that **a natural catalytic RNA can catalyze the synthesis of an RNA molecule** of at least equal size to that of the catalyst in a template-dependent manner. I was pioneer in Spain for ribozymes and *in vitro* selection technologies of great and scientific potential.
-Since 2005 we follow a new line of research focused on the functional characterization of viral genomic functional RNA domains taking HCV and HIV as models. A key achievement has been the identification and characterization of **the first long-distance RNA-RNA interaction between the two ends of the HCV genome**. This interaction involves two essential highly conserved functional RNA domains and is responsible and sufficient for the circularization of the viral genome in the absence of proteins. Currently, we have extended our studies to flaviviruses. Another important aspect to which we dedicate the activity of the group is the design and characterization of aptamers as molecular tools for interfering with genomic RNA domains. The most important achievement in this research line was the **isolation of a 16 nt-long RNA aptamer, which targets de Poly A element of the HIV genome and leads to >85% inhibition of viral particle production**. This is the smallest aptamer ever described. This molecule has been patented in Spain, Europe and US. Our main objective of our current research is the identification and structural/functional characterization of viral genomic RNA domains of flaviviruses, and their role in the essential viral processes, exploring their potential as antiviral targets. We have demonstrated the functional implication of defined structural elements of the genomic 3' UTR of WNV in the viral translation. Further **we have shown the existence of a cap-independent translation initiation in WNV, which is dependent on the 3' UTR**. We are also interested in the development of innovative antiviral therapeutic strategies based on RNA molecules or nucleic acids analogs targeting these essential structural elements. We have disseminated our results to the general society participating in numerous outreach activities.
R&D management experience Since Nov. 2005 to March 2014 director of the IPBLN. April 1997 to Nov 2005 Vice-Director of the IPBLN.

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

C.1. Publications (The most relevant to the proposal in recent years; *Corresponding author)

- Ramos-Lorente, S.E.; Berzal-Herranz, B.; Romero-López, C. and **Berzal-Herranz, A.*** (2024). Recruitment of the 40S ribosomal subunit by the West Nile virus 3' UTR promotes the cross-talk between the viral genomic ends for translation regulation. *Virus Res* **343** (199340): 1-18.
- Romero-López, C.; Roda-Herreros, M.; Berzal-Herranz, B.; Ramos-Lorente, S.E. and **Berzal-Herranz, A.*** 2023. Inter- and intramolecular RNA–RNA interactions modulate the regulation of translation mediated by the 3' UTR in West Nile virus. Int. J. Mol. Sci. 24: 1-18.
- **Berzal-Herranz, A.***; Berzal-Herranz, B.; Ramos-Lorente, S.E. and Romero-López, C.* 2022. The genomic 3' UTR of flaviviruses is a translation initiation enhancer. Int. J. Mol. Sci. 23: 1-15.
- Ramos-Lorente, S.E.; Romero-López, C.* and **Berzal-Herranz, A.*** 2021. Information Encoded by the Flavivirus Genomes beyond the Nucleotide Sequence. Int. J. Mol. Sci. 22: 1-18.
- Romero-López C*; Ríos-Marco, P; Berzal-Herranz, B. and **Berzal-Herranz, A.*** 2018. The HCV genome domains 5BSL3.1 and 5BSL3.3 act as managers of translation. Sci. Rep. 8, 1-12.

- Romero-López C*; Barroso-delJesus, A. and **Berzal-Herranz, A.*** 2017. The chaperone-like activity of conserved RNA elements in the hepatitis C virus regulates genome dimerization. Sci. Rep. 7: 1-15.
- Sánchez-Luque, F.J.; Stich, M.; Manrubia, S; Briones, C. and **Berzal-Herranz, A.*** 2014. Efficient HIV-1 inhibition by a 16 nt-long RNA aptamer designed by combining in vitro selection and in silico optimization strategies. Sci. Rep. 4: 1-10.
- Romero-López C*, Barroso-delJesus, A.; García-Sacristan, A.; Briones, C. and **Berzal-Herranz, A.*** 2014. End-to end cross-talk within the Hepatitis C virus genome mediates the conformational switch of the 3'X-tail region. Nucleic Acids Res. 42: 567-582.
- Marton, S.; Romero-López, C. and **Berzal-Herranz, A.*** 2013. RNA aptamer-mediated interference of HCV replication by targeting the CRE-5BSL3.2 domain. J. Viral Hepatitis 20: 103-112
- Romero-López C*; Barroso-delJesus, A.; García-Sacristan, A.; Briones, C. and **Berzal-Herranz, A.*** 2012. The folding of the hepatitis C virus internal ribosome entry site depends on the 3'-end of the viral genome. Nucleic Acids Res. 40: 11697-11713.
- Romero-López, C.; Berzal-Herranz, B.; Gómez, J. and **Berzal-Herranz, A.*** 2012. An engineered inhibitor RNA that efficiently interferes with hepatitis C virus translation and replication. Antiviral Res. 94: 131-138.
- Romero-López, C* and **Berzal-Herranz, A.*** 2012. The functional RNA domain 5BSL3.2 within the NS5B coding sequence influences hepatitis C virus IRES-mediated translation. Cell. Mol. Life Sci. 69: 103-113.
- Romero-López, C. and **Berzal-Herranz, A.*** 2009. A long-range RNA-RNA interaction between the 5' end 3' ends of the HCV genome. RNA 15: 1740-1752.

C.2. Congress, Presenting author

- Genetic information encoded in viral RNA structural units. CONFERENCIA INVITADA. **Berzal Herranz, A.**; Romero-López, C.*; Ramos-Lorente, S.E. and Berzal-Herranz, B. October/2023. Baeza, Spain
- Function of viral genomic structural RNA elements and their potential as antiviral target. ORAL. **Berzal-Herranz, A**; Romero-López, C; Ramos-Lorente, S.E and Berzal-Herranz. 6th International Conference on Nucleic Acids: Research and Therapeutics. 27/1/2023 On line.
- The encoding of genetic information in RNA structures. CONFERENCIA INVITADA. **Berzal-Herranz, A.** 1st LIFEHUB.CSIC Origins & Synthesis of life. 7-9/3/2022, Madrid.
- RNA Aptamers: Descifrando la información que codifican los genomas virales RNA en forma de dominios estructurales CONFERENCIA INVITADA. **Berzal-Herranz, A.** 1er Encuentro Red Iberoamericana de Aptámeros (REDIBA). 10-11/11/2021. On-line
- RNA Aptamers: The 3'UTR of WNV genome is an excellent target for antiviral drugs. CONFERENCIA INVITADA. 7th Intemational Electronic Conference on Medicinal Chemistry. Sara E. Ramos-Lorente; Berzal-Herranz, B.; Jiménez-Sánchez,A.; Romero-López, C. and **Berzal-Herranz, A.**. November 2020 On-line.
- Potential of the aptamers to fill therapeutic gaps to fight RNA viruses. COMUNICACIÓN ORAL. **Berzal Herranz, A.** 12th Internacional Virology Summit & 8th World Congress on Control and Prevention of HIV/AIDS (Eurovirology 2020). 24/6/2020. On-line
- RNA Aptamers: Drugs of the future. ORAL, KEYNOTE PRESENTATION. **Berzal Herranz, A.** 5th ECMC. November 2019 On-line.
- Targeting the other genetic information coded by the viral RNA genomes. ORAL, KEYNOTE PRESENTATION. **Berzal Herranz, A.** 4th Intemational Electronic Conference on Medicinal Chemistry. 1-30/11/2018. On-line.
- Deciphering the information coded by the functional RNA domains of the hepatitis C virus genome. ORAL KEYNOTE PRESENTATION. **Berzal Herranz, A.** 10th Internacional Virology Summit & 4th Influenza & Zoonotic Diseases. 2-14/6/2018 Vienna. Austria
- New frontiers in the investigation of structural functional RNA domains in viral genomes. Understanding the hepatitis C virus (HCV). CONFERENCIA INVITADA. **Berzal Herranz, A.** and Romero-López, C. Internacional World-Conference on Bioinformatics and Biomedical Engineering. 7-9/4/2015 Granada, Spain.

C.3. Research projects

- PID2019-104018RB-I00. Implicaciones funcionales e interacciones RNA/RNA en genomas de flavivirus. AEI-Ministerio de Ciencia e Innovación. IP **Berzal-Herranz A.** (CSIC; June 2020-May 2023).

- BFU2015-64359-P. Estructura/función de dominios RNA conservados en el genoma del virus de la hepatitis C (HCV). MINECO.IP **Berzal-Herranz A.** (CSIC; Jan. 2016-Jun 2019).
- CVI-7430Estudio del fenómeno de circularización del RNA genómico del virus de la hepatitis C y su potencial uso como diana terapéutica. Junta de Andalucia, IP **Berzal-Herranz A.** (CSIC; Feb. 2013-Oct.2016).
- BFU2012-31213. Aptámeros RNA. Herramientas moleculares para la caracterización funcional del dominio genómico CRE del virus de la hepatitis C. MINECO, IP **Berzal-Herranz A.** (CSIC; Jan. 2016-Jun 2019).
- CTS-5077 Identificación y optimización de RNAs que interfieren específicamente la replicación del VHC. RNA como base para el desarrollo de herramientas antivirales. Junta de Andalucia, IP **Berzal-Herranz A.** (CSIC; Feb. 2010-Oct.2013).
- BFU2009-08137. Caracterización de motivos RNA funcionales de estructura conservada en genomas RNA. Uso de aptámeros RNA como herramientas moleculares. MICINN. IP **Berzal-Herranz A.** (CSIC; Jan. 2010-Dic.2013), 217.800 €.
- BFU2006-2008Ribozimas y aptámeros. Analisis funcional y bioquímica de RNAS inhibidores de la actividad biológica del IRES del VHC. MEC. IP **Berzal-Herranz A.** (CSIC; Oct. 2006-Sep.2009), 217.437 €.
- 36472/05. Estrategias de selección de moléculas de rna como herramientas moleculares para el estudio de la actividad biológica de dominios funcionales del genoma viral, e identificación de nuevas dianas terapéuticas. FIPSE. IP **Berzal-Herranz A.** (CSIC; Nov. 2005-Nov.2008), 82.162 €.
- HTECH.LG 961134 Alpha 1-interferon gene as model for selection of hairpin ribozymes. NATO linkage grant. Coordinador and IP **Berzal-Herranz A.** (CSIC; Dic 1996-Dic 1998). 682.000 Belgium Francs; Countries: Spain, Bulgaria.
- CIPA-CT94-0142. Specific gene suppression mediated by catalytic RNA: comparative analysis of different types of ribozymes and application strategies. European Union. Copernicus Program. Coordinator and IP **Berzal-Herranz A.** (CSIC; Dic 1994-Dic 1997) 250.000 ECU. Countries Spain, Greece, Bulgaria, Estonia and Lithuania

C.4. Contracts, technological or transfer merits

- **Alfredo Berzal Herranz**, Carlos Briones Llorente, Francisco José Sánchez Luque, Susanna Cuevas Manrubia, Michael Stich. P201231819. Moléculas inhibidoras del virus de la inmunodeficiencia humana tipo 1 (VIH-1), procedimiento de obtención y sus aplicaciones. PCT/ES2013/070809, WO2014080061 (internacional), EP13857023.9 (european), US Pat No. 9,938,532 (USA). 23/11/2012 Spain.
- **Alfredo Berzal Herranz** y José Antonio Reyes Darias. P201031026. Método y Kit para la Detección de la Activación de Interferón y la Respuesta Inflamatoria Independiente de Interferón. 28/11/2012 Spain.
- Alicia Barroso del Jesus, Pablo Menéndez Buján, Gema Lucena Aguilar, **Alfredo Berzal Herranz** y Cristina Romero López. P200800957. Promotor Específico de Células Troncales. PCT/ES09/070091. 4/4/2008 Spain.
- Cristina Romero López, Alicia Barroso del Jesus, Elena Puerta Fernández y **Alfredo Berzal Herranz**. ES200702203DIV. Moléculas para la inhibición específica del Virus Causante de la Hepatitis Tipo C, y sus Aplicaciones. PCT/ES2005/070034. 3/8/2007 Spain.
- Cristina Romero López, Alicia Barroso del Jesus, Elena Puerta Fernández y **Alfredo Berzal Herranz**. ES200400734. Secuencia de RNA, Construcción de RNA y DNA, y Composición Farmacéutica Inhibidoras de la Proliferación del Virus Causante de la Hepatitis Tipo C (VHC), y sus Aplicaciones. 25/3/2004 Spain
- Relevancia de Proteasas Extracelulares Durante la Progresión Tumoral. Fundación Progreso y Salud. IP **Berzal-Herranz A**. (CSIC; Sep. 2009-March 2013). 46.200,00 €.- Desarrollo de nuevas terapias basadas en Ciclodextrinas para combatir la tripanosomiasis africana. FIBAO. IP **Berzal-Herranz A**. (CSIC; Jan. 2009- Dic 2013). 30.000,00 €.
- Actividad del Retroelemento Line-1 en Células Stem Somáticas: Impacto y Mosaicismo Genómico. Fundación Progreso y Salud. IP **Berzal-Herranz A**. (CSIC; Jan. 2009-Dic 2012).
- Desarrollo kit Diagnóstico Genético Basado en Tecnología Array Bac. Genycell Biotech España SL. IP **Berzal-Herranz A**. (CSIC; Jan. 2009-Jan 2010). 20.000 €
- Identificación y Caracterización de miRNAs en los Procesos de Diferenciación de Líneas Celulares Embrionarias Murinas y Humanas. Fundación Progreso y Salud. IP **Berzal-Herranz A**. (CSIC; March 2007-Dic 2008). 36.941,28 €.