**CURRICULUM VITAE ABREVIADO (CVA)**

## Part A. PERSONAL INFORMATION

| | | | |
|---|---|---|---|
| First name | Analia | | |
| Family name | Bortolozzi Biassoni | | |
| Gender (*) | Female | Birth date (dd/mm/yyyy) | 27/06/1969 |
| ID number | 47593943C | | |
| e-mail | analia.bortolozzi@iibb.csic.es | URL Web https://www.iibb.csic.es/es/research/54 | |
| Open Researcher and Contributor ID (ORCID) (*) | | 0000-0002-2069-9192 | |

### A.1. Current position

| | | | |
|---|---|---|---|
| Position | Tenured Scientific, A1 | | |
| Initial date | 01/08/2018 | | |
| Institution | Agencia Estatal Consejo Superior de Investigaciones Científicas (CSIC) | | |
| Department/Center | Neuroscience and Experimental Therapeutics (IIBB – CSIC) | | |
| Country | Spain | Teleph. number | 93-3638313 |
| Key words | Depression, Parkinson's disease, Brain circuits, Animal models, Oligonucleotides therapies, Molecular neuropharmacology | | |

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

| Period | Position/Institution/Country/Interruption cause |
|---|---|
| 2022 - | Group leader (R4-IIBB-CSIC), Intitut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS), Spain |
| 2019 - | Principal investigator group G02 , CIBERSAM |
| 2013 - 2018 | Associate Researcher, IDIBAPS, Spain (65 months) |
| 2010 - 2013 | Research Excellence I3 accreditation, IDIBAPS, Spain (36 months) |
| 2004 - 2010 | Researcher Ramón y Cajal, IDIBAPS, Spain (72 months, 3 maternity leaves) |
| 2000 - 2004 | Post-doctoral Researcher, Intitut d'Investigacions Biomèdiques de Barcelona (IIBB-CSIC), Spain (48 months) |
| 1999 - 2000 | Post-doctoral Researcher, Instituto de Química y Fisicoquímica Biológicas (UBA-CONICET), Buenos Aires, Argentina (12 months) |
| 1998 -1999 | PhD student, Instituto de Investigaciones Biológicas Clemente Estable, Montevideo, Uruguay (15 months) |
| 1994 - 1998 | PhD student, Instituto de Farmacología y Toxicología (UNR, CONICET), Rosario, Argentina (54 months) |

### A.3. Education

| PhD, Licensed, Graduate | University/Country | Year |
|---|---|---|
| PhD Homologation | Spain | 2004 |
| Pharmacy Homologation | Spain | 2004 |
| PhD Pharmacy | Universidad Nacional de Rosario (UNR) Argentina | 1999 |
| Pharmacy | Universidad Nacional de Rosario (UNR), Argentina | 1992 |

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

Dr. A. Bortolozzi is tenured research scientist at IIBB-CSIC, principal investigator of G02 group at the Center for Biomedical Research in Mental Health Network (CIBERSAM - ISCIII), and group leader of the Systems Neuropharmacology, IDIBAPS. After obtaining the PhD grade (UNR, Argentina, 1999), I moved to the IIBB-CSIC, Spain, where I carried out a postdoctoral stay under the direction of Prof. F. Artigas. During this period (2000-2004), I acquired a solid expertise on the molecular neuropharmacology of monoamine systems. Later, as a Ramón y Cajal researcher (2004-2009), I extended my studies on the regulation of the prefrontal cortex - monoaminergic circuit involved in neuropsychiatric disorders such as depression and schizophrenia. One of the main contributions was to demonstrate the differential co-localization of serotonin receptors (5-HT1A and 5-HT2A) in pyramidal and GABAergic neurons in different

layers of the rat/mouse prefrontal cortex and their functional role as a target of action of antidepressant/antipsychotic drugs. These studies resulted in several publications in high-impact journals (Cerebral Cortex, J Neurosci, Neuropsychopharmacol), with a remarkable number of cumulative citations. In fact, I am the fourth most cited author in Cerebral Cortex (2004) for these contributions. After obtaining the I3 accreditation (2010), I managed to stabilize as an associate researcher (R3) at IDIBAPS. Since then, my projects have received uninterrupted funding from public agencies (Cibersam, ISCIII, Mineco), international foundations (Brain and Behavior Foundation, MJFox Foundation), and private sectors (nLife Therapeutics, Merck SD, miCure Therapeutics). This period marked a turning point in my research career and allowed me to lead my own research group. In recent years, the Systems Neuropharmacology group that I lead is a translational research group focused on the study of brain circuits and synaptic processes involved in the pathophysiology and treatment of depression and Parkinson's disease. The team employs innovative technologies ranging from molecular studies and connectivity analysis (e.g., in vivo electrophysiology and microdialysis, as well as recently implementation of optogenetic tools) to neuroimaging (fMRI) and behavioral assessment in animal models, providing detailed insights into the functioning of brain circuits at different levels of complexity. The laboratory has extensive experience in the neuropharmacology of monoaminergic circuits and is engaged to developing next-generation therapeutics for brain disorders, including antisense oligonucleotides (ASO, siRNA, miRNA) to address cell type-specific targeting. The main goal of our research is to identify novel molecular targets for potential therapeutic intervention and biomarkers for early detection or response to treatment. In addition, our team maintain a commitment to the training of human resources; I have supervised five PhD students at the University of Barcelona (2 more ongoing) and 3 postdoctoral positions (Margarita Salas, Ibero-American agreements), as well as several master students and other students/technical assistants (Internship agreements with University of Cagliari and University of Edinburgh). I am a member of different Editorial Boards of scientific journals. I have published more than 69 articles (Q1/D1 journals) and some book chapters, with cumulative citations: 4995 times (h:29-WOS; h:34-Google Scholar). I am among the 1,500 researchers in the ranking of the top 5,000 women scientists doing research in Spanish organizations. I am co-inventor of three patents for brain oligo delivery. I have three six-year research periods (CNEAI), and received several awards including: Pfizer Foundation Basic Research Award-2012, CSIC Researcher Award-2013, ECNP Neuropsychopharmacol Junior-2015, CIBER Outstanding Researcher-2019, and International Society for Serotonin Research Award-2020.

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

**C.1. Publications** (some relevant publications linked to this proposal, *corresponding author)

Bortolozzi A: https://pubmed.ncbi.nlm.nih.gov/?term=bortolozzi+a&sort=date

1. Miquel-Rio L, Alarcón-Arís D, Torres-López M, Cóppola-Segovia V, Pavia-Collado R, Paz V, Ruiz-Bronchal E, Campa L, Casal C, Montefeltro A, Vila M, Artigas F, Revilla R, **Bortolozzi A***. Human α-synuclein overexpression in mouse serotonin neurons triggers a depressive-like phenotype. Rescue by oligonucleotide therapy. **Transl Psychiatry** 2022, 12:79, IF: 7.989, Q1.

2. Pavia-Collado R, Rodríguez-Aller R, Alarcón-Arís D, Miquel-Rio L, Ruiz-Bronchal E, Paz V, Campa L, Galofré M, Sgambato V, **Bortolozzi A***. Up and down γ-synuclein transcription in dopamine neurons translates into changes in dopamine neurotransmission and behavioral performance in mice. **Int J Mol Sci.** 2022, 23:1807, IF: 6.208, Q1.

3. **Bortolozzi A***, Manashirov S, Chen A, Artigas F. Oligonucleotides as therapeutic tools for brain disorders: Focus on major depressive disorder and Parkinson's disease. **Pharmacol Therapeutics** 2021, 227:107873, IF: 13.40, D1.

4. Alarcón-Arís D, Pavia-Collado R, Miquel-Rio L, Coppola-Segovia V, Ferrés-Coy A, Ruiz-Bronchal E, Galofré M, Paz V, Campa L, Revilla R, Montefeltro A, Kordower JH, Vila M, Artigas F, **Bortolozzi A***. Anti-α-synuclein ASO delivered to monoamine neurons prevents α-synuclein accumulation in a Parkinson's disease-like mouse model and in monkeys. **EBioMedicine** 2020, 59:102944. IF: 8.143, Q1.

5. Fullana N, Ruiz-Bronchal E, Ferrés-Coy A, Artigas F, **Bortolozzi A***. Regionally-selective knockdown of astroglial glutamate transporters in infralimbic cortex induces a depressive phenotype in mice. **Glia** 2019, 67:1122-1137. IF: 5.984, Q1.

6. Fullana N, Ferrés-Coy A, Ortega JE, Ruiz-Bronchal E, Paz V, Meana JJ, Artigas F, **Bortolozzi A*.** Selective knockdown of TASK3 potassium channel in monoamine neurons: a new therapeutic approach in depression. **Mol Neurobiol** 2019, 56:3038-3052. JIF: 5.59, Q1.
7. Alarcón-Arís D, Recasens A, Galofré M, Carballo-Carbajal I, Zacchi N, Ruiz-Bronchal E, Pavia-Collado R, Chica R, Ferrés-Coy A, Santos M, Revilla R, Montefeltro A, Fariñas I, Artigas F, Vila M*, **Bortolozzi A***. Selective α-Synuclein Knockdown in Monoamine Neurons by Intranasal Oligonucleotide Delivery: Potential Therapy to Parkinson's disease. **Mol Therapy** 2018, 26:550-567. IF: 8.402, D1.
8. Ferrés-Coy A, Galofré M, Pilar-Cuéllar F, Vidal R, Paz V, Ruiz-Bronchal E, Campa L, Pazos A, Caso JR, Leza JC, Alvarado G, Montefeltro A, Valdizán EM, Artigas F, **Bortolozzi A***. Therapeutic antidepressant potential of a conjugated siRNA silencing the serotonin transporter after intranasal administration. **Mol Psychiatry** 2016, 21:328-338. IF: 13,204, D1. COVER

Outstanding collaborative articles (period 2018-2022)

9. Haddad-Tóvolli R, Ramírez S, Muñoz-Moreno E, Milà-Guasch M, Miquel-Rio L, Pozo M, Chivite I, Altirriba J, Obri A, Gómez-Valadés AG, Toledo M, Eyre E, **Bortolozzi A**, Valjent E, Soria G, Claret M. Food craving-like episodes during pregnancy are mediated by accumbal dopaminergic circuits. **Nat Metab** 2022, 4:424-434, IF: 19.95, D1
10. Calero M, Moleiro LH, Sayd A, Dorca Y, Miquel-Rio L, Paz V, Robledo-Montaña J, López-Martínez E, Enciso E, Acción F, Herráez-Aguilar D, Hellweg T, Sánchez L, **Bortolozzi A**, Leza JC, García-Bueno B, and Monroy F. Lipid nanoparticles for oligonucleotide delivery into brain border-associated macrophages to silence neuroinflammation-related genes. **Front Mol Biosci** 2022; 9: 887678. IF: 6.113, Q1.
11. Duperrier S, **Bortolozzi A**, Sgambato V. Increased expression of Alpha-, Beta- and Gamma-synucleins in brainstem regions of a non-human primate model of Parkinson's disease. **Int J Mol Sci** 2022; 23, 8586. IF: 6.208, Q1.
12. Carballo-Carbajal I, Laguna I, Romero-Giménez J, Bové J, Torra A, Cuadros T, Parent A, Rodríguez-Galván B, Martinez-Vicente M, Ballabio A, Hasegawa T, **Bortolozzi A**, Gelpi E, Vila M. Brain tyrosinase overexpression implicates age-dependent intracellular neuromelanin accumulation in humanized rats triggers Parkinson's disease pathology. **Nat Commun** 2019, 10:973. IF:12.121, D1
13. Perez-Villalba A, Sirerol-Piquer MS, Belenguer G, Soriano-Cantón R, Muñoz-Manchado AB, Villadiego J, Alarcón-Arís D, Soria FN, Dehay B, Bezard E, Vila M, **Bortolozzi A**, Toledo-Aral JJ, Pérez-Sánchez F, Fariñas I. Synaptic regulator α-synuclein in dopaminergic fibers is essentially required for the maintenance of subependymal neural stem cells. **J Neurosci** 2018, 38:814-825. IF: 6.074, Q1.

### C.2. Congress

Over 60 invited communications/seminars in international congresses, meetings and national/ international training courses, and more than 400 poster presentations. Some of the most relevant (period 2018-2022, oral presentations): 11$^{th}$ FENS Congress, Berlin, Germany, 2018; 18$^{th}$ SENC Congress, Santiago de Compostela, Spain, 2019; 17$^{th}$ Annual Meeting of the Oligonucleotide Therapeutics Society, 2021 (online); Invited Professor in the postgraduate course "Neurochemical transmission systems and their implications in pathologies of the Central Nervous System", Montevideo, Uruguay, 2021 (online); Invited speaker in 34$^{th}$ ECNP Congress, Lisboa, Portugal, 2021; Invited Professor in Institute of Cognitive Science Marc Jeannerod UMR 5229 CNRS & Université de Lyon, France, 2021; Invited speaker in Oligonucleotide and Peptide Therapeutics, TIDES, Boston, USA, 2022 (online); Invited speaker in Precision Medicine Forum, Santander, Spain, 2022; Invited speaker in Prodromal Parkinson Symposium organized by MJF Foundation, Barcelona, Spain, 2022.

### C.3. Research projects

PI of several competitive projects since 2009. During period 2018-2022, I have achieved funding worth **€1.6mio as PI**.

1- New therapeutic strategies for the treatment of synucleinopathies. RTC-2014-2812-1, Ministerio de Economía y Competitividad, FEDER (2014-2018), **PI: A Bortolozzi**. Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS). €402.259

2- Synucleinopathies and inhibitory oligonucleotides: role of alpha and gamma-synucleins in the regulation of cognitive function. SAF2016-75797-R, Ministerio de Economía y Competitividad, FEDER (2016-2019), **PI: A Bortolozzi**. Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS). €157.300

3- Characterization study of alpha-synuclein modulation in transgenic mice. Research Agreement between IDIBAPS and Fundación Pública Andaluza Progreso y Salud (2017-2018), **PI: A Bortolozzi**. (IDIBAPS). €150.000
4- Validation of endoplasmic reticulum pathways as a novel target to restore alpha-synuclein protein homeostasis. Implication in Parkinson's disease. 2018201077, Vicepresidencia de Investigación Científico y Técnica (VYCIT), Programa I3 (2018-2019), **PI: A Bortolozzi**. Instituto de Investigaciones Biomédicas de Barcelona (IIBB-CSIC). €5.000
5- Connection between endoplasmic reticulum stress and alpha-synucleinopathy in brain disorders PID2019-105136RB-I00 (2020-2023), Ministerio de Ciencia e Innovación, FEDER, **PI: A Bortolozzi**. Instituto de Investigaciones Biomédicas de Barcelona (IIBB-CSIC). €166.980
6- Gliotransmitters and cannabinoid receptors at the hub of cognitive and synaptic plasticity impairments in Huntington's disease. 30/C/2020, FundacióLaMaratódeTV3 (2020-2023). Coordinating PI: S Ginés. **PI of work-packages**: G. Perea (Instituto Cajal - CSIC), M. Guzmán (Universidad Complutense) y **A. Bortolozzi** (IIBB – CSIC). €320.000
7- Depression and its treatment: Role of miRNAs in the anterior cingulate cortex, as peripheral biomarkers, and their targeted modulation by nano-tools as a promising antidepressant therapy. FundacióLaMaratódeTV3 (2023-2025). **Coordinating PI: A Bortolozzi**. PI of work-packages: C. Fornaguera (Universitat Ramon Llull Fundació), FJ de Diego Adeliño (IIB Sant Pau). €380.9000
8- In vivo assessment of the potential of human helical peptides to treat Parkinson's Disease. Generalitat de Catalunya (2022-2023). Coordinating PI: S Ventura (UAB), **PI of work-packages: A Bortolozzi** (IIBB – CSIC). €50.000
9- Consolidated Research Group – Trastorns Biplars I Depressius. Generalitat de Catalunya (2021SGR-01358), Coordinating PI: E. Vieta (IDIBAPS), Role: **A. Bortolozzi**, IDIBAPS leader researcher. €60.000

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

PI of contracts with industry and private sector since 2011. During the period 2018-2022, I have had several contracts as PI with biotech companies reaching a funding value of **€600k**.
1- Characterization of the in vivo efficacy of chemically modified oligonucleotide (ASO/siRNA) molecules to silence α-synuclein expression in mouse brain, as well as the in vivo efficacy of chemically targeted mRNA molecules to neurons for the production of GFP or CAS9 proteins in mouse brain. Research Agreement between Institut d'Investigacions Biomèdiques August Pi i Sunyer (IDIBAPS) and nLife Therapeutics S.L. (2017-2018), **PI: A Bortolozzi**. €60.000
2- In vivo evaluation of efficacy of proprietary conjugated miRNA. Research Agreement between Consejo Superior de Investigaciones Científicas (CSIC) and miCure Therapeutics Ltd. (2019-2021), **PI: A Bortolozzi**. €197.336.
3- 5$^{th}$ Addendum: In vivo evaluation of efficacy of proprietary conjugated miRNA. Research Agreement between CSIC and miCure Therapeutics Ltd. **PI: A Bortolozzi**. 2021-2022: 86.500€.
4- 6$^{th}$ Addendum: In vivo evaluation of efficacy of proprietary conjugated miRNA. Research Agreement between CSIC and miCure Therapeutics Ltd. PI: **A Bortolozzi**. 2022-2023: €257.088

Patents

1. Title: Compositions and methods for selective delivery of oligonucleotide molecules to specific neuron types. PCT/EP2011/056270. International filling date: 19/04/2011. Publication number: WO/2011/131693. Applicant: nLife Therapeutics, S.L. Inventors: AP Montefeltro, G Alvarado, **A Bortolozzi,** F Artigas, M Vila
2. Title: Compositions and Methods for the Treatment of Parkinson Disease by the Selective Delivery of Oligonucleotide Molecules to Specific Neuron Types. PCT/EP2013/072410 International filling date: 25/10/2013. Publication number: WO/2014/064257. Applicant: Nlife Therapeutics. Inventors: MC Carmona, AP Montefeltro, G Alvarado, **A Bortolozzi,** F Artigas, M Vila
3. Title: Compositions and methods for selective delivery of oligonucleotide molecules to cell types. PCT/EP2013/072411. International filling date: 25/10/2013. Publication number: WO/2014/064258. Applicant: Nlife Therapeutics. Inventors: MC Carmona, A Montefeltro, G Alvarado, **A Bortolozzi**, R Revilla