PhD position in Structural Virology.
Project Title and reference: **Unveiling the molecular bases of RNA virus replication PID2023-148560NB-I00.**
Contact: Núria Verdaguer nvmcri@ibmb.csic.es

The Viruses and large biological complexes group at IBMB-CSIC (https://ibmb.csic.es/en/department-of-structural-and-molecular-biology/virus-large-biological-complexes/), is looking for highly motivated PhD students, interested in understanding the structural bases of the replication of RNA viruses, with international projection and important biomedical implications.

We offer a 4-year pre-doctoral contract, starting on January 2025, associated to our recently granted project: "Unveiling the molecular bases of RNA virus replication". In the framework of this project, we will study the structure and function of different multicomponent complexes involved in replication of two important pathogens: Menglà virus (MLAV), a recently discovered filovirus, considered a new potential human pathogen, and the Coronavirus SARS-CoV-2.

The project will take place at the Structural and Molecular Biology Department (DSMB) of the Institute of Molecular Biology of Barcelona of the Spanish Research Council (IBMB-CSIC). The IBMB is located at the Barcelona Science Park (PCB), which provides an excellent scientific and technological framework. It belongs to the Barcelona Knowledge Campus (BKC), a campus of international excellence that includes the University of Barcelona (UB) and the Polytechnic University of Catalonia (UPC), which also brings the IBMB in close connection with the academic world. In addition, one of the two only synchrotron facilities of Southern Europe, the synchrotron ALBA, is located in the outskirts of Barcelona and provides a unique nearby infrastructure for X-ray data collection, with direct and frequent access for the DSMB members. The PI of this proposal is also an active member of the Joint Electron Microscopy Center at Alba (JEMCA), as scientific coordinator of the cryo-TEM platform (https://www.cells.es/en/instrumentation/em01-cryo-tem).

Available methodologies include: (1) Cloning, expression and purification of proteins, RNAs, multiprotein complexes and protein-RNA complexes. The group uses of both bacterial and eukaryotic expression systems to produce significant amounts of soluble proteins from viruses for structural studies. Recombinant Baculovirus (rBV) and/or Vaccinia virus (rVV) expression systems are used to successfully produce soluble amounts of large and difficult viral proteins. Multiple protein co-expression strategies are also available in the group in order to purify specific pre-assembled complexes. (2) Structural Biology techniques, mainly X-ray crystallography and cryo-EM, sometimes combined by SAXS and other biophysical techniques.

Candidates must have a Master degree in Biology, Biochemistry, Biotechnology, or related disciplines in life sciences, practical experience in molecular biology techniques and good English communication skills.

Applicants are requested to send an e-mail to nvmcri@ibmb.csic.es with a CV and a motivation letter.

A summary of the lab training plan and a short CV of the PI, with a list of recent publications, are included in the following pages

PhD Training

The project provides an optimal interdisciplinary setting for training at the PhD level. It includes applications to specific health problems and has a strong component of interaction with research groups of other especialities covering the full spectrum of Molecular, Cellular and Structural Biology, Virology, Biochemistry and Biophysiscs.

Verdaguer's lab has a long-term tradition in the accomplishment of Ph.D. thesis. The team has a specific training program intended to provide PhD students with the required tools to become independent researchers with soft skills such as: (i) training in biosafety and good laboratory practices; (ii) assignment of specific objectives, to allow students to independently perform experiments, analyze the data, write papers and present the results; (iii) participation in specialized training courses on structural biology and biophysics; vi) traveling to other laboratories, experts in complementary disciplines (e.g. Molecular and Cellular Virology) to complement the students' training; and (iv) contribution to national and international scientific conferences.

In addition, the IBMB-CSIC has a Ph. D. Office that is aimed at facilitating the scientific and administrative life of our Ph. D. students, create a good work environment, promote scientific and social events and provide guidance during the development of their Ph. D. Thesis (https://ibmb.csic.es/en/researchers-training-programs/).

CV summary of the PI

Núria Verdaguer is a CSIC Research Professor and leader of the Virus and Large Biological Complexes at IBMB. PhD in Biological Sciences by the Technical University of Catalonia, UPC (1991). Assistant professor at UPC (1992-95). Visiting researcher at Oxford University, UK (1995). 1996-2001 Research associate in Ignacio Fita's group (Dept. Structural Biology, IBMB) and visiting researcher at Purdue University, USA (1999). Verdaguer got a position as CSIC Científico Titular in 2002 and started the Structural Virology research group. In 2009, she got promoted to CSIC Research Professor.
Her research focuses on the structure-function relationships of proteins and multicomponent complexes directly involved in pathological processes. In particular, viral proteins and protein-complexes involved in RNA replication, viral particles and large macromolecular assemblies, like the eukaryotic vault ribonucleoprotein particle. She has authored 108 indexed publications (e.g. Nat Struct Mol Biol, Proc Natl Acad Sci USA, EMBO J, Cell Stem Cell, Sci Adv), and has 100 macromolecular structures deposited with the Protein Data Bank.
Highlights of Verdaguer's research include: i) The structural characterization of the early steps of human rhinovirus infection, including the first high resolution X-ray structures of a human minor group rhinovirus bound to its cellular receptor protein and the first X-ray structures of the virus trapped in the process of RNA uncoating; ii) Structural and functional studies of protein priming and nucleotide incorporation by viral the RNA-dependent RNA polymerases, addressing important questions related with regulation of viral replication and fidelity ; iii) The characterization of non-canonical RNA-dependent RNA polymerases of Birnavirus and Permutatetraviruses, revealing unexpected evolutionary relationships between RdRPs encoded by distant RNA virus groups; iv) The supramolecular arrangement of ZIKV NS5 and its involvement in ZIKV associated neurodevelopmental disease; v) The first structure and mechanism of action of the NS5 Methyltransferase (MTase) from the emerging flavivirus Usutu virus (USUV), in complex with natural ligands and with the universal inhibitor sinefungin; vi) The discovery of the dual role of the 3B1 protein of the picornavirus FMDV in the replication complex: as protein primer and as an essential component to recruit the RNA polymerase 3Dpol to membranes; and, vii) The helical arrangement of the nucleoprotein C-terminal domain of

Mengla virus and its participation in the control of inclusion bodies formation during viral replication.
She has been Principal Investigator of more that 20 national and international research projects and supervised 11 PhD theses and 6 postdocs.
Verdaguer has also contributed to scientific management at the IBMB as head of the Department of Structural Biology 2010-2012, Deputy Director (2014-2016), Scientific Director of the Structural Biology Unit, Maria de Maeztu Unit of Excellente (SBU-IBMB-CSIC; 2015-2019) and Director of the IBMB (July 2018-July 2022).
In 2008 Verdaguer was elected member of the European Molecular Biology Organization (EMBO), and in February 2023 she has been appointed as a member of the "Real Academia Española de Ciencias".

Selected publications

Ferrer-Orta C, Vázquez-Monteagudo S, Ferrero DS, Martínez-González B, Perales C, Domingo E, **Verdaguer N**. Point mutations at specific sites of the nsp12-nsp8 interface dramatically affect the RNA polymerization activity of SARS-CoV-2. *Proc Natl Acad Sci U S A*. 2024 Jul 16; 121(29): e2317977121. doi: 10.1073/pnas.2317977121.

Ferrero DS, Tomás Gilabert O, **Verdaguer N**. Structural insights on the nucleoprotein C-terminal domain of Měnglà virus *Microbiol Spectr* 2023 11:e02373-23. doi: 10.1128/spectrum.02373-23.

Ferrer-Orta C, Ferrero DS, **Verdaguer N**. Dual role of the foot-and-mouth disease virus 3B1 protein in the replication complex: As protein primer and as an essential component to recruit 3Dpol to membranes. *PLoS Pathog*. 2023 May 1;19(5):e1011373. doi: 10.1371/journal.ppat.1011373.

Guerra P, González-Alamos M, Llauró A, Casañas A, Querol-Audí J, de Pablo PJ, **Verdaguer N**. Symmetry disruption commits vault particles to disassembly. *Sci Adv*. 2022 Feb 11;8(6):eabj7795. doi: 10.1126/sciadv.abj7795.

Ferrero DS, Albentosa-González L, Mas A, **Verdaguer N**. Structure and function of the NS5 methyltransferase domain from Usutu virus. *Antiviral Res*. 2022 Dec;208:105460. doi: 10.1016/j.antiviral.2022.105460.

Saade M, Ferrero DS, Blanco-Ameijeiras J, Gonzalez-Gobartt E, Flores-Mendez M, Ruiz-Arroyo VM, Martínez-Sáez E, Ramón Y Cajal S, Akizu N, **Verdaguer N**, Martí E. Multimerization of Zika Virus-NS5 Causes Ciliopathy and Forces Premature Neurogenesis. *Cell Stem Cell*. 2020 Dec 3;27(6):920-936.e8. doi: 10.1016/j.stem.2020.10.002.
Highlighted in Nature Rev Microbiol https://www.nature.com/articles/s41579-020-00481-9

Ferrero DS, Ruiz-Arroyo VM, Soler N, Usón I, Guarné A, **Verdaguer N**. Supramolecular arrangement of the full-length Zika virus NS5. *PLoS Pathog*. 2019 Apr 5;15(4):e1007656.