

## Part A. PERSONAL INFORMATION

|             |               |  |  |
|-------------|---------------|--|--|
| First name  | José Félix    |  |  |
| Family name | Prado Velasco |  |  |

(\*) *Mandatory*

### A.1. Current position

|                   |                                                               |           |           |
|-------------------|---------------------------------------------------------------|-----------|-----------|
| Position          | Scientist Researcher CSIC                                     |           |           |
| Initial date      | 23/05/2023                                                    |           |           |
| Institution       | CSIC (from 14/07/2006)                                        |           |           |
| Department/Center | Genome Biology/ CABIMER                                       |           |           |
| Country           | Spain                                                         | Telephone | 954468210 |
| Key words         | DNA repair/ replication/ recombination/ chromatin/ cell cycle |           |           |

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

| Period    | Position/Institution/Country/Interruption cause         |
|-----------|---------------------------------------------------------|
| 1991-1996 | PhD / Sevilla University (FPI fellowship)               |
| 1996-2000 | Postdoc / Marburg University /Germany (EMBO fellowship) |
| 2000-2006 | Postdoc / Sevilla University (Ramón y Cajal contract)   |

### A.3. Education

| PhD, Licensed, Graduate  | University/Country | Year |
|--------------------------|--------------------|------|
| Degree in Biology        | Sevilla University | 1991 |
| PhD in Molecular Biology | Sevilla University | 1996 |

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

**Scientific contributions.** The main objective of my scientific career has been to understand the mechanisms that maintain genome integrity. My work has been focused in two major research lines: 1) **Mechanisms of Homologous Recombination (HR)** and 2) **Roles of chromatin in genome integrity**. The major achievements of my work during my PhD and Postdoc were the finding of transcription as a potential source of HR-mediated genetic instability (EMBO J 1997), in particular as a consequence of transcription/replication collisions (EMBO J 2005), the regulatory role of nucleosome positioning in transcription (JBC 2002), and the importance of nucleosome assembly in preventing unscheduled HR (EMBO R 2004; MCB 2005). The major contributions of my research as **Principal investigator** can be summarized in the following points:

1. Cell-cycle regulation of HR during DNA damage tolerance (DDT), which in contrast to double-strand break (DSB) repair is coupled to replication and regulated in a spatiotemporal manner (EMBO J. 2013). This led to the hypothesis that replicative and repair functions need to be separated to prevent the recombinogenic processing of damaged replication forks (BioEssays 2014). This study generated tools to follow the recombinational repair of DNA lesions during DDT (Method Mol Biol 2021).

2. The description for the first time of non-recombinogenic functions for the core HR proteins Rad51 and Rad52 in translesion synthesis (TLS) (EMBO R 2021), pointing to the hypothesis that these factors operate as a molecular switch to choose the DDT mechanism (reviewed in Genes 2021).

3. The description of non-canonical roles for the MCM helicase in genome integrity through physical and dynamic interactions with Rad51 and Rad52 to facilitate fork assistance through non-recombinogenic functions (Cell R 2021). This work has allowed us to propose the existence of a specialized compartment to assist stressed replication forks (reviewed in FEBS J 2023). Second, it interacts with the ribonucleotide reductase complex to regulate the dynamic of DNA repair centers (PloS Genetics 2024).
4. The critical role of replication-coupled chromatin assembly for HR during DDT (Cell R 2023), replication fork stability (EMBO R 2009; PLoS Genetics 2011), chromosome segregation and cohesin distribution (NAR 2014; Epigenetics and Chromatin 2019) and transcription elongation and splicing (PNAS 2015). These studies also revealed the importance of controlling the levels of histones to protect telomeres by HR during senescence (PLoS Genetics 2018; 2019) and the existence of mechanisms to restore defects in chromatin assembly (Scientific Rep 2023).
5. The role of the chromatin remodeller SWR in the generation of HR-mediated genetic instability and transcriptional defects in the absence of its substrate the histone variant H2A.Z (PLoS One 2009; **cited in the seminal text book “Epigenetics”, Edt. By David Allis**), revealing the pathogenic effects of unscheduled chromatin processing.
6. The mechanisms by which cells respond to broken replication forks (PLoS Genetics 2025).

These studies, funded by national and regional grants, and published in internationally prestigious journals, have allowed to build a research group with a reputed national and international experience in the field of genetic instability, as exemplified by invited reviews and seminars and successful collaborations with national and international researchers (Dr. Reyes, Seville; Dr. San Segundo, Salamanca; Dr. Ulrich, Germany; Dr. Luke, Germany; Dr. Heyer, USA, Dr. Vertegaal, Payses Bajos...).

Currently, I am **Director of the Genome Biology Department in CABIMER** from 2025 and **Manager of the Molecular and Cellular Biology subarea (BIO area) of the Spanish Research Agency (AEI)** from 2023. I have participated as member of different committees for the evaluation of national and international grants (ANEP; I-LINC, CSIC, CDA, Human Frontier Science Program; PICT, Argentina; ANR, France; Wellcome Trust, England; US-Israel BS,...), researchers (CSIC, Ramón y Cajal, Juan de la Cierva) and national and international thesis (30), and I have worked as reviewer for prestigious journals (Science, Science Advances, NCOMMS, EMBO J, ...). In addition, I have been in charge of the Model Organism Unit in CABIMER for 15 years, **coordinator of the national network “Chromosome dynamics and stability” (2016-2019)**, formed by 13 prestigious investigators, and **coordinator of the group “Gene expression and genome dynamics” from SEBBM (2013-2016)**. Finally, I have participated in different Master programs from Seville and Salamanca Universities and I have been invited to national and international conferences.

**Contributions to young researchers.** I have directed **8 thesis (plus 2 in progress), 7 Master and 2 TFG**, and trained several students in the frame of different programs (JAE-Intro, Garantía Juvenil,...). PhDs from my group are now working either in the Academy or Pharmaceutic industry.

**Contributions to society.** I have focused my work to basic research, which is in itself a major objective in science with unpredictable benefits for human being and society. I have collaborated with CABIMER in disseminating the importance of research through seminars to school students.

## Part C. RELEVANT MERITS

### C.1. Selected Publications

For a complete list of papers please go to ORCID (0000-0001-9805-782X) or Scopus (7007066781).

1. Ana Amiama-Roig, Marta Barrientos-Moreno, Esther Cruz, Luz M. López-Ruiz, Román González-Prieto, Gabriel Ríos-Orelogio & **Félix Prado (AC; Autor de correspondencia)**. A Rfa1-MN-based system reveals new factors involved in the rescue of broken replication forks. **PLoS Genetics** (2025) 21(4): e1011405 Clave: A
2. Aurora Yáñez-Vélchez, Antonia M. romero, Marta Barrientos-Moreno, Esther Cruz, Román González-Prieto, Sushma Sharma, Alfred C.O. Vertegaal and **Félix Prado (AC; Autor de correspondencia)**. Physical interactions between specifically regulated subpopulations of the MCM and RNR complexes prevent genetic instability. **PLoS Genetics** (2024) 20(5): e1011148 Clave: A
3. Cristina González-Garrido and **Félix Prado (AC)**. Parental histone distribution and location of the replication obstacle at nascent strands control homologous recombination. **Cell Rep.** (2023) 42: 112174 Clave: A
4. María J. Cabello-Lobato, Cristina González-Garrido, María I. Cano-Linares and **Félix Prado (AC)**. Physical interactions between MCM and Rad51 facilitate replication fork lesion bypass and ssDNA gap filling through non-recombinogenic functions. **Cell Rep.** (2021) 36: 109440 Clave: A
5. María I. Cano-Linares, Aurora Yáñez-Vilches, Néstor García-Rodríguez, Marta Barrientos-Moreno, Román González-Prieto, Pedro San-Segundo, Helle D. Ulrich and **Félix Prado (AC)**. Non-recombinogenic role for Rad52, Rad51 and Rad57 in translesion synthesis. **EMBO Rep.** (2021) 22: e50410 Clave: A
6. Macarena Morillo-Huesca, Marina Murillo-Pineda, Marta Barrientos-Moreno, Elena Gómez-Marín, Marta Clemente-Ruiz and **Félix Prado (AC)**. Actin and nuclear envelope components influence ectopic recombination in the absence of Swr1. **Genetics** (2019) 213:819-834 Clave: A
7. Douglas Maya-Miles, Eloisa Andújar, Monica Pérez-Alegre and **Félix Prado (AC)**. Crosstalk between chromatin structure, cohesion activity and transcription. **Epigenetics & Chromatin** (2019) 12:47 Clave: A
8. Marta Barrientos-Moreno, Marina Murillo Pineda, Ana M. Muñoz-Cabello and **Félix Prado (AC)**. Histone depletion prevents telomere fusions in pre-senescent cells. **PLoS Genetics** (2018) 14:e1007407 Clave: A
9. Silvia Jimeno-Gonzalez, Laura Payán, Ana M. Muñoz-Cabello, Macarena Guijo, Gabriel Gutierrez, **Félix Prado** and José C. Reyes (AC). Chromatin structure regulates RNA polymerase II elongation rate and co-transcriptional pre-mRNA splicing. **PNAS** (2015) 112:14840-14845 Clave: A
10. Marina Murillo-Pineda, María J. Cabello-Lobato, Marta Clemente-Ruiz, Fernando Monje-Casas and **Félix Prado (AC)**. Defective histone supply causes condensin-dependent chromatin alterations, SAC activation and chromosome decatenation impairment. **Nucleic Acid Research** (2014) 42:12469-12482 Clave: A
11. Román Gonzalez-Prieto, Ana Muñoz-Cabello, María J. Cabello-Lobato and **Félix Prado (AC)**. Rad51 replication fork recruitment is required for DNA damage tolerance. **EMBO J** (2013) 32: 1307-1321 Clave: A
12. Marta Clemente-Ruiz, Román Gonzalez-Prieto and **Félix Prado**. Histone H3K56 acetylation, CAF1 and Rtt106 coordinate nucleosome assembly and stability of advancing replication forks. **PLoS Genetics** (2011) 7: e1002376 Clave: A
13. Macarena Morillo-Huesca, Marta Clemente-Ruiz, Eloísa Andujar and **Félix Prado**. In the Absence of H2A.Z the SWR1 Histone Replacement Complex Causes Genetic Instability and Genome-Wide Transcription Missregulation. **PloS One** (2010) 5: e12143 Clave: A
14. Marta Clemente and **Félix Prado (AC)**. Chromatin assembly controls replication fork stability. **EMBO Rep** (2009) 10: 790-796 Clave: A

## C.2. Selected Congresses

- 19 International Congresses and 9 National Congresses

1. **Félix Prado**. 2<sup>nd</sup> International Symposium Cell Division and Genome Dynamics. Salamanca, Spain. October 27-28, 2022. Invited speaker
2. **Félix Prado**. The 2022 IMB/SFB 1361 Conference “Restore, Reorganise, Repurpose: The many faces of DNA repair” Mainz, Germany. September 20-23, 2022. Invited speaker
3. **Félix Prado**. 1<sup>st</sup> CABIMER international workshop “Trends in genome integrity & chromosome dynamics”. Seville, Spain. February 19, 2020. Invited speaker

4. María J. Cabello-Lobato, María I. Cano-Linares, Román González-Prieto and **Félix Prado**. EMBO Conference. Atenas, Grecia. October 2-6, 2017. Poster
5. Murillo M, Clemente-Ruiz M, Monje-Casas F, and **Prado F**. “26<sup>th</sup> International Conference on Yeast Genetics and Molecular Biology”. Yeast (ISSN 0749-503X). Franckfurt, Germany. 29 August-3 September 2013. Selected talk
6. **Meeting organization:** “SEBBM” meetings (Gene expression regulation and genome dynamics workshop) at Cordoba (2013), Granada (2014), Valencia (2015) and Salamanca (2016). “Chromodyst” meetings at Santiago de Compostela (2016), Cáceres (2017) and Alcalá de Henares (2019).

### C.3. Selected Research projects

1. Mecanismos de respuesta a estrés replicativo por bloqueo y rotura de las horquillas de replicación (PID2024-156544NB-I00). **Investigador principal (IP): Félix Prado**. Ministerio de Ciencia, Innovación y Universidades. 01/09/2025-31/08/2028; 325000 euros
2. Mecanismos de asistencia a horquillas de replicación (PID2021-127486NB-I00). **Investigador principal (IP): Félix Prado**. Ministerio de Ciencia e Innovación. 01/09/2022-31/08/2025; 217800 euros
3. Papel del reciclaje de histonas parentales en la integridad genómica (PY20\_00750). **IP: Félix Prado**. Consejería de Conocimiento, investigación y Universidad de la Junta de Andalucía. 01/09/2021-30/06/2023; 95000 euros
4. Estudio del papel de la helicasa MCM en la respuesta a daños en el ADN (PGC2018-099182-B-I00). **IP: Félix Prado**. Ministerio de Ciencia, Innovación y Universidades. 01/01/2019 -31/12/2021; 179927 euros
5. Dinámica de la cromatina asociada a la replicación y estabilidad genómica (BFU2015-63698-P). **IP: Félix Prado**. Ministerio de Economía y Competitividad. 01/01/2016-31-12-2018; 237166 euros
6. Dinámica y estabilidad Cromosómica (BFU2015-69142-REDT). **Coordinador e IP: Félix Prado**. Ministerio de Economía y Competitividad. 01/12/2015-30/11/2017; 47000 euros
7. Efecto de la reducción de los niveles de histonas en la estabilidad genética, el envejecimiento celular, y la entrada en senescencia (P12-CTS-2270). **IP: Félix Prado**. Junta de Andalucía “Proyectos de Excelencia”. 01/01/2014-31-12-2016; 162850 euros
8. Mecanismos y regulación por ciclo celular de la respuesta a daños replicativos en el ADN (BFU2012-38171). **IP: Félix Prado**. Ministerio de Economía y Competitividad. 01/01/2013-31-12-2015; 173160 euros
9. Papel de la dinámica de la cromatina en la integridad genómica y la progresión del ciclo celular (BFU2009-09036). **IP: Félix Prado**. Entidad financiadora: Ministerio de Ciencia e Innovación. Duración: 01/01/2010-31-12-2012; 187550 euros
10. Papel de la cromatina en la acumulación y reparación de daños en el DNA. (BFU2006-08336/BMC). **IP: Félix Prado**. Ministerio de Educación y Ciencia. 01/01/2007-31/12/2009. 151250 euros.