

# Juan Pablo Unfried, Ph.D

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# CURRENT POSITION

Sept. 2021-Post-doctoral ResearcherpresentWeizmann Institute of Science, Rehovot, Israel.

# EDUCATION

| 2021 | Diploma in Management and Business Creation in Biological Sciences<br>European Center for Business and Innovation of Navarra (CEIN) and University of Navarre,<br>Pamplona, Navarre  |
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| 2019 | International Ph.D. <i>cum laude</i> , Biomedical Research (December 2019)<br><b>University of Navarre</b> , Pamplona, Navarre<br>Dissertation: Identification and Functional Analysis of Long Non-Coding RNAs in<br>Hepatocellular Carcinoma. |
| 2015 | M.Sc. <i>honors</i> , Biomedical Research<br><b>University of Navarre</b> , Pamplona, Navarre  |
| 2014 | B.Sc. Microbiology and Clinical Chemistry<br><b>University of Costa Rica</b> , San José, Costa Rica  |

## **GRANTS AND AWARDS**

| 2021-2024 | Azrieli International Postdoctoral Fellowship<br>Azrieli Foundation   |
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| 2021-2023 | <b>Excellence Fellowship Program for International Postdoctoral Researchers</b><br>Council for Higher Education & Israel Academy of Sciences & Humanities |
| 2021-2023 | EMBO Postdoctoral Fellowship<br>European Molecular Biology Organization   |
| 2019      | International Ph.D. Travel Award<br>Asociación de Amigos, University of Navarre   |
| 2015-2019 | ADA Pre-doctoral Fellowship<br>Asociación de Amigos, University of Navarre  |
| 2014-2015 | Incentive Program for Dissertations in Science<br>Faculty of Science, University of Navarre   |

## RESEARCH EXPERIENCE

# 2019-2021 Postdoctoral Research; Supervisor: Dr. Puri Fortes

#### Center for Applied Medical Research, University of Navarre

Project: Study of the mechanism of action of a Long <u>Non-coding RNA Induced in HC</u>C with an <u>Oncogenic role in Ligation Efficiency</u> (NIHCOLE) (Unfried *et al.; Can Res.* 2021)

- Characterized the functional interaction of NIHCOLE in complex with components of the Non-Homologous End-joining (NHEJ) machinery of DNA damage repair.
- Validated a novel function for a lncRNA in promoting the ligation efficiency of doublestranded breaks.
- Worked with collaborators to study the cryo-EM structure of NHEJ components with NIHCOLE and validated its role in ligation efficiency using single-molecule analyses.

April-August Predoctoral Visiting Student; Supervisors: Dr. Susan Lees-Miller and Dr. Gareth Williams

2019 Arnie Charbonneau Cancer Institute, University of Calgary

Project: Characterization of the interaction of lncRNA NIHCOLE with the NHEJ machinery of DNA damage repair.

- Performed RNA-protein interaction analyses to determine the ability of NIHCOLE to support higher-order complexes with the main components of the NHEJ machinery.
- Validated a defect in DNA repair of NIHCOLE-depleted HCC cells using yH2AX immunofluorescence, the comet assay, and DNA damage reporter assays.

2014-2019 M.Sc. and Ph.D. student; Supervisor: Dr. Puri Fortes

#### Center for Applied Medical Research, University of Navarre

Project: Identification of novel lncRNAs deregulated in HCC and mechanistic interrogation of their oncogenic functions.

- Used big data analysis to extract cancer-deregulated lncRNAs and their normal tissue of preferential expression. We proposed to consider the "transcript donor-tissue" to anticipate adverse effects of lncRNA-based therapies (Unfried *et al.; Can Res.* 2019)
- Generated a list of lncRNA candidates and performed gain- and loss-of-function analyses to select the most promising candidates for therapeutic targeting.
- Characterized the phenotypical changes of lncRNA knockdown and performed transcriptomic and proteomic analyses to identify their functional targets.

2012-2014 Undergraduate Student; Supervisor: Dr. Eugenia Corrales-Aguilar

Research Center for Tropical Diseases, University of Costa Rica

Project: Development of a multiplex PCR to detect the circulating Dengue virus serotypes in serum samples during the 2013 outbreak in Costa Rica.

#### SUPERVISOR EXPERIENCE

- 2021-present Co-supervisor of Ph.D. student in Biomedical Research
- 2019-2020 Co-supervisor of M.Sc. student in Biomedical Research
- 2015-2019 Teaching assistant for Biochemistry and Medicine undergraduate students
- 2015-2019 Project supervisor of summer practice for Biochemistry undergraduate students
- 2010-2014 Teaching assistant to undergraduate students for the courses of Analytical and Quantitative Chemistry, and General and Clinical Virology.

# PARTICIPATION IN R&D PROJECTS FUNDED THROUGH COMPETITIVE CALLS

| 2013 - 2015 | <ul><li>Project: Identification and characterization of non-coding RNAs for the treatment of liver diseases.</li><li>Funding Agency: Ministry of Science and Technology. Spain.</li><li>P.I.: Dr. Puri Fortes.</li></ul>  |
|-------------|---|
| 2014 - 2016 | Project: Whole-genome analysis of the DNA (hydroxy)methylome and transcriptome in<br>multiple myeloma.<br>Funding Agency: La Marató de TV3 Foundation. Spain<br>P.I.: Dr. Ignacio Martín Subero   |
| 2015 - 2017 | <ul> <li>Project: Development of therapeutic compounds to block long non-coding RNAs implicated in liver cirrhosis and hepatocarcinoma.</li> <li>Funding Agency: Government of Navarre 33/2015. Spain</li> <li>P.I.: Dr. Victoriano Segura Ruiz</li> </ul>          |
| 2017 – 2019 | <ul><li>Project: Therapeutic Development based on the identification, analysis, and inhibition of non-coding genes implicated in the progression of HCC.</li><li>Funding Agency: Ministry of Science and Technology. Spain.</li><li>P.I.: Dr. Puri Fortes</li></ul> |
| 2019 - 2021 | <ul><li>Project: Analysis of long non-coding RNAs related to survival that allow the growth of hepatocellular carcinoma (THOR).</li><li>Funding Agency: Ministry of Economic Affairs and Digital Transformation. Spain</li><li>P.I.: Dr. Puri Fortes</li></ul>      |
| 2019 – 2021 | Project: <b>COST DARTER. Delivery of antisense RNA Therapeutics.</b><br>Funding Agency: European Union<br>P.I.: Dr. Virginia Arechavala   |
| 2019 – 2022 | Project: <b>COSTINC. International nucleome consortium.</b><br>Funding Agency: European Union<br>P.I.: Dr. Marc Martí   |
| 2020 – 2022 | Project: <b>RNA Life.</b><br>Funding Agency: Ministry of Science and Innovation. Research Networks. Spain<br>P.I.: Dr. Jose E. Perez Ortin  |
| 2020 – 2022 | Project: <b>From donated testis transcripts to novel anticancer therapies.</b><br>Funding Agency: Spanish Association Against Cancer (AECC). Spain<br>P.I.: Dr. Puri Fortes   |
| 2021 - 2025 | Project: <b>BLANCA (Breast and Liver ANti-Cancer Antigens).</b><br>Funding Agency: Government of Navarre<br>P.I.: Dr. Puri Fortes   |

# PRESENTATIONS

Invited

- 1. Spanish National Cancer Research Center CNIO, Madrid, Spain: "NIHCOLE, a long non-coding RNA involved in ligation efficiency of NHEJ DNA damage repair" February 2021.
- 2. Keystone Symposia. Non-Coding RNAs: Biology and Applications. **"LncRNA NIHCOLE promotes DNA damage repair in hepatocellular carcinoma cells"** May 2021.
- 3. Keystone Symposia. Hepatobiliary Cancers: Pathobiology and Translational Advances. **"LncRNA NIHCOLE** is involved in DNA damage repair of liver cancer cells" March 2021.
- 4. Spanish RNA Society Meeting, Seville, Spain: "NIHCOLE, a long non-coding RNA involved in ligation efficiency of NHEJ DNA damage repair" September 2020.
- 5. University of Calgary BMB Advance, Banff, Canada: **"LncRNAs with oncogenic potential in hepatocellular carcinoma identified by big data analysis"** May 2019.
- 6. International University of Andalusia, Baeza, Spain: "LncRNAs as potential therapeutic targets for hepatocellular carcinoma" October 2018.
- 7. Spanish RNA Society Meeting, Madrid, Spain: "HCV infection upregulates EGOT, a PKR-induced lncRNA that favors viral replication by regulating the antiviral response" June 2016.

# Posters

- 1. Fusion Conference. Genome Regulation through RNA Conference. Cancún, México. **"LncRNA FOSIL regulates the induction dynamics of FOS"** J.P. Unfried & Ulitsky, I. 2024.
- 2. Gordon Conference. Genome Architecture in Cell Fate and Disease. California, USA. **"LncRNA FOSIL regulates the induction dynamics of FOS"** J.P. Unfried & Ulitsky, I. 2023.
- 3. RNA Society. 26th Annual Meeting of the RNA Society. Online. **"LncRNA NIHCOLE promotes DNA damage repair in hepatocellular carcinoma cells"** J.P. Unfried; *et al.* 2021.
- 4. International Liver Cancer Association ILCA. ILCA virtual meeting 2020. **"Healthy testis expresses long non-coding RNAs upregulated in cancer"** J.P. Unfried; *et al.* 2020.
- 5. European Cooperation in Science and Technology COST. Delivery of Antisense RNA Therapies, Bilbao, Spain: **"ASOs targeting lncRNA NICO5 inhibit proliferation of hepatocellular carcinoma cells"** J.P. Unfried; *et al.* 2019.
- 6. Keystone Symposia. Long Non-coding RNAs: From Molecular Mechanism to Functional Genetics, Vancouver, Canada: **"Healthy testis expresses long non-coding RNAs upregulated in cancer"** J.P. Unfried; *et al.* 2019.
- 7. American Association for Cancer Research AACR Annual Meeting. Chicago, USA: **"Big data analysis allows the identification of long non-coding RNAs with therapeutic potential against hepatocellular carcinoma"** J.P. Unfried; *et al.* 2018.
- 8. American Association for the Study of Liver Diseases AASLD. AASLD The Liver Meeting. Washington, USA: **"Identification of long non-coding RNAs as therapeutic targets for hepatocellular carcinoma"** J.P. Unfried; *et al.* 2017.
- Barcelona Conference on Epigenetics and Cancer 2016 Beyond Cancer Genomes. Barcelona, Spain: "Long non-coding RNAs induced in hepatocellular carcinoma are involved in the proliferation of HCC cell lines" J.P. Unfried; et al. 2016.
- 10. Center for Genomic Regulation CRG. RNA Biology in Cancer and other Diseases. Barcelona, Spain: **"Several long non-coding RNAs induced in hepatocellular carcinoma are upregulated in liver cirrhosis"** J.P. Unfried; *et al.* 2016.

#### LIST OF PUBLICATIONS

#### **Research articles**

- 1. <u>Unfried, J. P.</u> *et al.* Long noncoding RNA NIHCOLE promotes ligation efficiency of DNA double-strand breaks in hepatocellular carcinoma. *Cancer Res.* 81(19):4910-4925 (2021).
- 2. <u>Unfried, J. P.</u> *et al.* **Identification of coding and long noncoding RNAs differentially expressed in tumors and preferentially expressed in healthy tissues.** *Cancer Res.* 79(20):5167-5180 (2019)

#### Collaborations

- 3. Recalde, M., Gárate-Rascón, M., Herranz, J. M., Elizalde, M., Azkona, M., <u>Unfried, J. P. et al.</u> DNA Methylation Regulates a Set of Long Non-Coding RNAs Compromising Hepatic Identity during Hepatocarcinogenesis. *Cancers (Basel).* 14(9):2048 (2022).
- 4. Barriocanal, M., Prats-Mari, L., Razquin, N., Prior, C., <u>Unfried</u>, J.P. *et al.* **ISR8/IRF1-AS1 Is Relevant for IFNα** and NF-κB Responses. *Front. Immunol.* 13:829335. (2022).
- 5. Garitano-Trojaola, A., José-Enériz, E. S., Ezponda, T., <u>Unfried, J. P. et al.</u> Deregulation of linc-PINT in acute lymphoblastic leukemia is implicated in abnormal proliferation of leukemic cells. *Oncotarget* 9(16):12842-12852 (2018).
- 6. Carnero, E., Barriocanal, M., Prior. C., <u>Unfried, J. P.</u> *et al.* Long noncoding RNA EGOT negatively affects the antiviral response and favors HCV replication. *EMBO Rep.* 17, 1013–1028 (2016).
- 7. Weber, N. D. Goñi-Salaverri, A., Rodríguez, J. A., <u>Unfried, J. P. et al.</u> Large-scale silane bead-based SARS-CoV-2 testing of a nursing home in Spain identifies a viral reservoir during lockdown period. *medRxiv* 2021.02.08.21251358 (2021).

## Commissioned publications

- 8. <u>Unfried, J. P.</u> & Ulitsky, I. Substoichiometric action of long noncoding RNAs. *Nat. Cell. Biol.* 24(5):608-615 (2022). PERSPECTIVE
- 9. <u>Unfried, J. P.</u>, Sangro, P., Prats-Mari, L., Sangro, B. & Fortes, P. **The Landscape of IncRNAs in Hepatocellular Carcinoma: A Translational Perspective.** *Cancers.* 13, 2651 (2021). REVIEW
- 10. Suarez, B., Prats-Mari, L., <u>Unfried, J. P.</u> & Fortes, P. LncRNAs in the Type I Interferon Antiviral Response. *Int. J. Mol. Sci.* 21, 6447 (2020). REVIEW
- 11. <u>Unfried, J. P.</u> & Fortes, P. LncRNAs in HCV Infection and HCV-Related Liver Disease. *Int. J. Mol. Sci.* 21, 2255 (2020). REVIEW
- 12. <u>Unfried</u>, J. P. & Fortes, P. **SMIM30**, a tiny protein with a big role in liver cancer. *J. Hepatol.* 73(5):1010-1012 (2020). EDITORIAL
- 13. <u>Unfried, J. P.</u> & Fortes, P. Looking for hints to mark functional Lincs. *Non-coding RNA Investig.* 1, 17–17 (2017). EDITORIAL

#### PROFESSIONAL COLLABORATION AND AFFILIATIONS

- Reviewer for the journals: Nature Cell Biology, Nature Cardiovascular Research, Science Advances, Hepatology, Molecular Cell, Cell Reports, Nucleic Acids Research.
- Member of American Association for Cancer Research (AACR)

2018-present 2020-present

- Member of RNA Society

## REFERENCES

#### Prof. Igor Ulitsky. Principal Investigator

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#### Dr. Puri Fortes. Principal Investigator.

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#### Dr. Oscar Llorca. Principal Investigator.

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#### Prof. Susan P. Lees-Miller. Principal Investigator.

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