# BRIEF CURRICULUM VITAE

Jan 2025

## A. PERSONAL INFORMATION

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|---|---|---|---|
| First and Family name | JOAQUIM ROCA | | |
| Passport, ID number | 35026021B | Birth | Barcelona 10/11/1960 |
| Contributor ID (ORCID) | 0000-0003-1462-954X | SCOPUS Author ID: 7101624422 | |

### A.1. Current position

| | | |
|---|---|---|
| University/Institution | CSIC (Spanish Research Council) | |
| Department | IBMB (Molecular Biology Institute of Barcelona) | |
| Address and Country | Baldiri Reixac 4-12, 08028 Barcelona, Spain | |
| Phone number | (34) 934020117 | E-mail: <joaquim.roca@ibmb.csic.es> <j.roca@csic.es> |
| Current position | Group Leader (IBMB)<br>Full Professor (CSIC) | From: 01/01/1997<br>From: 30/05/2008 |
| UNESCO codes | 241500 (Molecular Biology) 240699 (Biophysics) | |
| Key Words | DNA Topology - DNA Supercoiling - DNA Knotting - Chromosome - Chromatin - Nucleosome - Topoisomerase - Cohesin - Condensin | |

### A.2. Education

| Degree (Title) | University | Year |
|---|---|---|
| Medicine (MD) | University of Barcelona (UB) | 1983 |
| Molecular & Structural Biology (Ms) | Polytechnic University of Catalonia (UPC) | 1985 |
| Medicine (PhD) | University of Barcelona (UB) | 1988 |

## B. RESEARCH TRACK

**Doctoral training**:

1984-1988 Molecular Genetics Lab. Barcelona Medical School. UB.
1985-1986 Chemical Engineering of Macromolecules. UPC.
1987-1988 Assistant Professor of Human Physiology. Barcelona Medical School. UB.

**Post-Doctoral training**:

1988-1992 Research Fellow. Dep of Biochemistry. Harvard University
1993-1996 Research Associate. Dep of Biochemistry. Harvard University

**Tenure positions**:

1996-2005 Staff Scientist. Spanish Research Council (CSIC) Barcelona
2005-2008 Senior Staff Scientist. Molecular Biology Institute of Barcelona (IBMB-CSIC)
2008- present Full Professor. Molecular Biology Institute of Barcelona (IBMB-CSIC)

## B. Indicators of Quality in Scientific Production

- University of Barcelona Extraordinary Award (1989) for his Doctoral Thesis studies
- JCR publications as first or corresponding author: 53 (most in D1) Theses directed: 12
- Ranked within the world's top 2% most influential scientists (Standford University 2021).
- Maria de Maeztu Excellence Award (2015) as guarantor of the Structrural Biology Unit of IBMB

Research interest: DNA topology, its regulation and its biological implications.

Main scientific accomplishments:

- An earlier and main contribution of my research has been deciphering the mechanism of DNA transport of type-II topoisomerases (Cell 1992, PNAS 1994, Cell 1994, TiBS 1995, PNAS 1996, JBC 2004, NAR 2009), currently depicted in the textbooks.

- My additional studies on eukaryotic topoisomerase II clarified its DNA transport preferences and how this essential enzyme can simplify DNA topology to below equilibrium values (JBC 1993, GenCells 1996, JMB 2001, GenCells 2002, JMB 2004, NAR 2014).

- My lab has pioneered the research on the interplay of topoisomerase activities with chromatin structure (EMBO 1989, JBC 2001, JBC 2002, EMBO 2006, EMBO 2010, NAR 2012, NAR 2013, EMBO 2014). These studies produced two relevant findings: (i) that topoisomerase II is the main relaxase of nucleosomal DNA; and (ii) that unbalanced relaxation of (+) and (-) supercoils by topoisomerase II produces a prevalence of (-) supercoiled DNA in eukaryotic chromatin.

- By measuring how protein-DNA interactions alter the DNA topology, my lab described the molecular architecture of point centromeres (Cell Rep 2015), in which DNA follows a right-handed instead of a left-handed path. With a similar approach, we determined that native nucleosomes restrain a DNA linking number difference of about -1.26 (Nature com 2018). This value solved the "linking number paradox of nucleosomal DNA", which had puzzled scientists over decades.

- My lab has pioneered the analysis of in vivo DNA knots using high-resolution 2D electrophoresis (NAR 2001, NAR 2019a). As knots are a footprint of the 3D path of DNA, we used this principle to infer DNA folding in viruses (PNAS 2002, PNAS 2005) and in eukaryotic chromatin (NAR 2018, NAR 2019b). These studies highlighted the occurrence of DNA knots as an unexpected yet common actor able to restrict chromatin configuration and genome transactions.

- By exploiting DNA topology analyses, my lab made two seminal contributions to the field of SMC complexes. We unravelled a new role of condensin in minimizing intracellular DNA entanglements (EMBO 2021, BioEssays 2022) and how condensin made DNA translocation steps during the process of DNA loop extrusion (EMBO 2023).

- Finally, my lab has introduced to the scientific community the new field of "Topolomics". We conducted the first analysis of psoralen:DNA photo-binding to map supercoiled DNA regions *in vivo* (NAR 2010, EMBO 2010), a method now broadly accepted and used. More recently, we have developed "topo-seq", a novel procedure to inspect the topology of large libraries of DNA circles in a single gel electrophoresis. We used topo-seq to conduct the first genome-wide analysis of the DNA topology constrained by nucleosomes (Nature com 2024).

Part C. SELECTED Publications *(only first or last Author in D1 Journals)*:

- Nucleosomal DNA has topological memory. Segura; Diaz-Ingelmo, Martínez-García, Ayats-Fraile, Nikolaou; Roca* **Nature Com** (2024)
- Condensin pinches a short negatively supercoiled DNA loop during each round of ATP usage. Martínez-García, Dyson, Segura, Gutierrez-Escribano, Aragón, and Roca* **EMBO J** -e111913 (2023)
- Condensin minimizes topoisomerase II-mediated entanglements of DNA in vivo. Dyson, Segura, Martínez-García, Valdés, and Roca*. **EMBO J** - e105393 (2021)
- Transcriptional supercoiling boosts topoisomerase II-mediated knotting of intracellular DNA. Valdés, Coronel, Martínez-García, Segura, Dyson, Díaz-Ingelmo, Micheletti, and Roca* **Nucleic Acids Res**. 47:6946-6955 (2019)
- Quantitative disclosure of DNA knot chirality by high-resolution 2D-gel electrophoresis Valdés, Martínez-García, Segura, Dyson, Díaz-Ingelmo and Roca* **Nucleic Acids Res**. 47:e29 (2019)
- Intracellular nucleosomes constrain a DNA linking number difference of -1.26 that reconciles the Lk paradox. Segura, Joshi, Díaz-Ingelmo, Valdés, Dyson, Martínez-García and Roca* **Nature Com** 28:3989 (2018)
- DNA knots occur in intracellular chromatin. Valdes, Segura, Dyson, Martinez-Garcia and Roca* **Nucleic Acids Res** 46, 650-660 (2018)
- DNA Topology and Global Architecture of Point Centromeres. Diaz-Ingelmo, Martinez-Garcia, Segura, Valdes and Roca* **Cell Reports** 13, 667-677 (2015)
- Topoisomerase II minimizes DNA entanglements by proofreading DNA topology after DNA strand passage. Martinez-Garcia, Fernandez, Diaz-Ingelmo, Rodriguez-Campos, Manichanh and Roca* **Nucleic Acids Res** *42*, 1821-1830 (2014)
- Chromatin regulates DNA torsional energy via topoisomerase II-mediated relaxation of positive supercoils. Fernandez, Diaz-Ingelmo, Martinez-Garcia and Roca* **EMBO J** *33*, 1492-1501 (2014)
- Topoisomerase II regulates yeast genes with singular chromatin architectures. Nikolaou, Bermudez, Manichanh, Garcia-Martinez, Guigo, Perez-Ortin and Roca* **Nucleic Acids Res**. 41, 9243-9256 (2013)
- Topoisomerase II is required for the production of long Pol II gene transcripts in yeast. Joshi, Piña and Roca* **Nucleic Acids Res** *40*, 7907-7915 (2012)
- Positional dependence of transcriptional inhibition by DNA torsional stress in yeast chromosomes. Joshi, Pina and Roca* **EMBO J** *29*, 740-748 (2010)
- Topoisomerase II, not topoisomerase I, is the proficient relaxase of nucleosomal DNA. Salceda, Fernandez and Roca* **EMBO J** *25*, 2575-2583 (2006)
- DNA knots reveal a chiral organization of DNA in phage capsids. Arsuaga, Vazquez, McGuirk, Trigueros, Sumners and Roca* **PNAS** USA *102*, 9165-9169 (2005)
- Knotting probability of DNA molecules confined in restricted volumes: DNA knotting in phage capsids. Arsuaga, Vazquez, Trigueros, Sumners and Roca* **PNAS** USA *99*, 5373-5377 (2002)
- DNA transport by a type II topoisomerase: direct evidence for a two-gate mechanism. Roca, Berger, Harrison and Wang. **PNAS** USA *93*, 4057-4062 (1996)
- DNA transport by a type II DNA topoisomerase: evidence in favor of a two-gate mechanism. Roca and Wang. **Cell** *77*, 609-616 (1994).
- Antitumor bisdioxopiperazines inhibit yeast DNA topoisomerase II by trapping the enzyme in the form of a closed protein clamp. Roca, Ishida, Berger, Andoh, and Wang. **PNAS** USA *91*, 1781-1785 (1994)
- The capture of a DNA double helix by an ATP-dependent protein clamp: a key step in DNA transport by type II DNA topoisomerases. Roca and Wang. **Cell** *71*, 833-840 (1992)
- DNA topoisomerase II activity in nonreplicating, transcriptionally inactive, chicken late spermatids. Roca and Mezquita. **EMBO J** *8*, 1855-1860 (1989).

Methods developed

- A method for genome-wide analysis of DNA helical tension by means of psoralen-DNA photobinding. Bermudez, Garcia-Martinez, Perez-Ortin and Roca* Nucleic Acids Res *38*, e182 (2010)
- Two-dimensional gel electrophoresis of DNA topoisomers. Roca* Methods Mol Biol *582*, 27-37 (2009)
- Production of highly knotted DNA by means of cosmid circularization inside phage capsids. Trigueros and Roca* BMC Biotechnol *7*, 94 (2007)
- Novel display of knotted DNA molecules by two-dimensional gel electrophoresis. Trigueros, Arsuaga, Vazquez, Sumners, and Roca* Nucleic Acids Res *29*, E67-67. (2001).
- A hit-and-run system for targeted genetic manipulations in yeast. Roca, Gartenberg, Oshima, and Wang Nucleic Acids Res *20*, 4671-4672 (1992)

Reviews

- Keeping intracellular DNA untangled: A new role for condensin? Roca* et al. BioEssays, 44, 1, (2022)
- In silico, in vitro and in vivo imageries of type II topoisomerases. Roca* Phys Life Rev *18*, 147-149 (2016)
- Transcriptional inhibition by DNA torsional stress. Roca* Transcription *2*, 82-85 (2011)
- The torsional state of DNA within the chromosome. Roca* Chromosoma *120*, 323-334 (2011)
- Topoisomerase II: a fitted mechanism for chromatin landscape. Roca* Nucleic Acids Res *37*, 721-730 (2009)
- The mechanisms of DNA topoisomerases. Roca* Trends Biochem Sci *20*, 156-160 (1995)

## D. Research projects and funding as Principal Investigator in the last ten years

- DNA Topology, regulation & Biological Implications (2012-2015) BFU2011-23851 310.970 €
- Unit of Excellence Maria de Maeztu (2016-2019) MDM 2014-0435 2.000.000 €
- DNA Topology, regulation & Biological Implications (2016-2019) BFU2015-67007-P 355.740 €
- Unit of Excellence Maria de Maeztu. Extra-CSIC (20120-2021) 20202CEX003 281.250 €
- DNA Topology, regulation & Biological Implications (2020-2024) PID2019-109482GB 350.900 €
- DNA Topology, regulation & Biological Implications (2025-2028) PID2023-146602NB 375.000 €

## E. Institutional responsibilities

2002-2006: Chairman of the Molecular and Cellular Biology Department of IBMB
2006-2010: Deputy Director of the IBMB
2012-2022: Member of the CSIC Advisory Committee for Biology and Biomedicine.
2022-current: Chairman of the Structural and Molecular Biology Department of IBMB