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## BIOGRAPHICAL SKETCH

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NAME: Marina Mapelli

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POSITION TITLE: Senior Group Leader

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EDUCATION/TRAINING (*Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.*)

| INSTITUTION AND LOCATION                                                   | DEGREE                                                             | Completion Date | FIELD OF STUDY                            |
|----------------------------------------------------------------------------|--------------------------------------------------------------------|-----------------|-------------------------------------------|
| University of Milan, Milan (It)                                            | Degree in Physics,<br><i>summa cum laude</i>                       | 10/1995         | Biophysics                                |
| European Molecular Biology Laboratory<br>EMBL, Heidelberg and Hamburg (De) | PhD in Crystallography<br>from the Birkbeck<br>College London (Uk) | 12/2001         | Structural Biology                        |
| European Institute of Oncology, Milan<br>(It)                              | Postdoctoral training                                              | 12/2004         | Structural Biology<br>of mitotic proteins |

### A. Personal Statement

I am currently a Senior Group Leader at the Department of Experimental Oncology of the European Institute of Oncology, Milan (Italy), faculty member of SEMM (European PhD School of Molecular Medicine), and adjunct professor at the University of Milan (Italy). Interest in my laboratory focus on the understanding of the mechanisms connecting asymmetric cell divisions to self-renewal and cell-fate determination in epithelial stem cells under physiological and oncological conditions. More recently, we dedicated substantial efforts in exploring the mechanistic of stem cell-niche communications, with a focus on Wnt-dependent niches. To address these biological questions, we use an integrative structural biology approach combining X-ray crystallography, cryo-Electron Microscopy, biochemistry, proteomics, genomics, stem cell and organoid biology. Over the years, my group has deciphered the atomic structure and the cellular function of macromolecular assemblies coordinating division orientation and asymmetry in vertebrate epithelia, providing a comprehensive picture of the molecular mechanisms coupling the mitotic spindle to polarity cues and tissue homeostasis. We are now studying the molecular principles of new layers of  $\beta$ -catenin dependent Wnt gene transcription associated to self-renewal.

I serve as *ad hoc* reviewer on several peer-reviewed journals and European funding agencies. I am part of the editorial board of *FEBS Letters*, and I served as moderator for the EU Horizon-2020 funded program iNext-Discovery. I have trained over 20 PhD and postdoctoral scientists.

- Palmerini V., Monzani S., Laurichesse Q., Loudhaief R., Mari S., Cecatiello V., Olieric V., Pasqualato S., Colombani J., Andersen D., **Mapelli M.** (2021) Drosophila TNFRs Grindelwald and Wengen bind Eiger with different affinities and promote distinct cellular functions. **Nat. Comm.** April 6. doi: 10.1038/s41467-021-22080-9. PMCID
- Pirovano L., Culurgioni S., Carminati M., Alfieri A., Monzani S., Cecatiello V., Gaddoni C., Rizzelli F., Foadi J., Pasqualato S., **Mapelli M.** (2019) Hexameric NuMA:LGN structures promote multivalent interactions required for planar epithelial divisions. **Nat. Comm.** 10, doi:10.1038/s41467-019-09999-w
- Culurgioni S., Mari S., Bonetti P., Gallini S., Bonetto G., Brennich M., Round A., Nicassio F., **Mapelli M.** (2018) Insc:LGN tetramers promote asymmetric divisions of mammary stem cells. **Nat. Comm.** 9, doi: 10.1038/s41467-018-03343-4.
- Carminati M., Gallini S., Pirovano L., Alfieri A., Bisi S. and **Mapelli M.** (2016) Concomitant binding of Afadin to LGN and F-actin directs planar spindle orientation. **Nat. Struct. Mol. Biol.**, 23,155-63. doi: 10.1038/nsmb.3152.

## B. Positions, Scientific Appointments, and Honors

### Positions

- 2016 – pres. Tenured Group Leader, European Institute Oncology, Milan (It)  
2009 – 2015 Tenure-track Group Leader, European Institute Oncology, Milan (Italy)  
2005 – 2008 Staff Scientist, Institute of Oncology, Milan (Italy)

### Scientific Appointment

- 2022 – 2032 MIUR (Ministry of Schools, University and Research) Habilitation for Full Professor of Biochemistry, Molecular Biology. Habilitation for Associate Professor of Applied Biology.  
2020 – 2024 Moderator for the EU Horizon-2020 funded program for infrastructure iNext-Discovery  
2016 – 2021 MIUR (Ministry of Schools, University and Research) Habilitation for Full Professor in Biochemistry.  
2016 – 2019 Member of the User Panel of the Horizon-2020 EU program for infrastructures iNext.  
2014 – 2020 Representative for Structural Biology at User Organization Committee of the European Synchrotron Radiation Facility ESRF, Grenoble (Fr).  
2011- 2016 Italian Coordinator of the EU Program BioStruct-X (FP7/2007-2013).  
2011- 2014 Coordinator of the Italian Block Allocation Group to the European Synchrotron Radiation Facility ESRF, Grenoble (Fr).  
2007 - 2010 Scientific supervisor of the Crystallization Facility, Cogentech, Milan (It).

### Honors

- 2022 Elected EMBO member

### Professional Memberships

- 2020 – pres. Italian Association of Crystallography (AIC) – steering committee

### Editorial Board Member

FEBS Letters

### Teaching

- 2022 – pres. Adjunct Professor at the OMICS Master Course, University of Milan (It)  
2013 – pres. Organizer of the Biochemistry Course at the European School of Molecular Medicine (SEMM), Milan (It)  
2009 – pres. Organizer of the Structural Biology Course at the SEMM School, Milan (It)  
2009 – 2018 Lecturer at the course of Cell Biology of the SEMM School, Milan (It)  
2014 Lecturer at the PhD program of the Istituto di Candiolo, Torino (It)  
2012 Lecturer at the course *Mitosis: Experimental approaches and model systems* CNR Roma (It)  
2009 – pres. Direct supervisor of 10 post-doctoral fellows, 11 PhD students, 3 technicians, and 5 undergraduate students (graduated with highest marks) working in my laboratory at the European Institute of Oncology.  
2009 – pres. Co-supervisor and internal examiner for the Molecular Oncology program of the SEMM School, Milan (It), PhD examiner for the Ecole Normale Supérieure, Paris (Fr), King's College London, (Uk) ESRF-University of Grenoble (Fr), University of Geneva, University of Bologna, University of Padova, University of Pavia, University of Rome La Sapienza and the CNR.

**Ad hoc Reviewer** for peer-reviewed journals including Nature Chemical Biology, Nature Cell Biology, EMBO, EMBO Rep; Nature Communications, Journal of Cell Biology, eLife, Journal of Biological Chemistry, NAR, Journal of Molecular Biology, Acta Crystallographica D, Scientific Reports, International Journal of Molecular Sciences, Eur. J. Med Chem.

**Grant Reviewer** for ERC European Research Council; MRC Career Developmental panel (Uk); the Hungarian Scientific Research found OTKA (Hu); US-Israel Binational Science Foundation (II); French National Cancer Institute INCa (Fr), UKRI (Uk)

**Tenure Evaluation** for Okinawa Institute of Technology (J), Program evaluation for the MRL Laboratory of Molecular Biology LMB (Uk).

#### **Invited presentations (2022 – 2024)**

26-30.8.2024 Organizer of a microsymposium at the European Crystallographic Meeting ECM, Padova (It)  
19-26.8.2024 Invited speaker at the FEBS/EMBO Course *Molecular mechanisms in signal transduction and cancer*, Spetses (Gr)  
26-27.6.2024 Invited speaker at the AIRC Symposium, Milan (It)  
10-13.6.2024 Invited speaker at the iNEXT-Discovery Meeting, Brno (Ce)  
27.05.2024 Invited seminar at the University of Pavia (It)  
21.05.2024 Invited seminar at the University of Lausanne, UniL (Ch)  
14-16.5.2024 Invited speaker at the PhD Symposium, University of Patras (Gr)  
8.05.2024 Invited seminar at the University of Southampton (Uk)  
19.04.2024 Invited seminar at the CRG, Barcelona (Es)  
6.03.2024 Invited seminar at the University of Piemonte Orientale, Novara (It)  
14.12.2023 Invited seminar at the Curie Institute, Paris (Fr)  
29.10.2023 Invited speaker at the *Cellular Dynamics and Chemical Biology* Conference, Hefei (Cn)  
21.10.2023 Invited seminar at the Collaborative Research Center on *Mechanisms and Functions of Wnt Signaling*, University of Heidelberg – DKFZ (De).  
23.09.23 Seminar at the ABCD Congress Association of Cell Biology and Differentiation, Paestum (It)  
5-6.5.2023 Organizer of the meeting of the Italian Association of Crystallography (AIC) – BMM section  
11.04.2023 Invited seminar at the Meeting Chinese Society for Cell Biology, Suzhou (Cn); (virtual)  
25.11.2022 Invited seminar at the Human Technopole, Milan (It)  
26.10.2022 Invited seminar at the EMBO Member Meeting, Heidelberg (De)  
19.10.2022 Invited seminar at the i3S, Porto (Pt)  
12-09.2022 Keynote speaker at the Congress of the Italian Association of Crystallography, Trieste (It)  
23-25.5.2022 Organizer of the Italian Association for Crystallography meeting, section BMM, Fiesole (It)  
07.04.2022 Invited seminar at the Karolinska Institute, Stockholm (Se)

#### **C. Contributions to Science**

1. Our laboratory was the first one to dissect the mechanistic basis for oriented asymmetric divisions of epithelial cells, and to determine the architecture of apical complexes instructing asymmetry. The pathway relies on the stem-cell specific protein Inscuteable, which is recruited at the apical site of polarized epithelial stem cells and promotes the localized cortical targeting of dynein-based microtubule motors. Biochemical and structural studies combined with analysis in murine mammary stem cells (MaSCs) uncovered the molecular event for asymmetry and revealed that Insc is lost in p53-deficient MaSCs which over-proliferate by symmetric divisions.

a. Culurgioni S., Alfieri A., Pendolino V., Laddomada F. and **Mapelli M.** (2011) Inscuteable and NuMA proteins bind competitively to Leu-Gly-Asn repeat-enriched protein (LGN) during asymmetric cell divisions. **P.N.A.S.**, 108, 20998-1003.

b. Culurgioni S., **Mapelli M.** (2013) Going vertical: functional role and working principles of the protein Inscuteable in Asymmetric Cell Divisions. **Cellular and Molecular Life Sciences**, 70, 4039-46.

c. Santoro A, Vlachou T, Carminati M, Pelicci PG, **Mapelli M.** (2016) Molecular mechanisms of asymmetric divisions in mammary stem cells. **EMBO Rep.**, 17, 1700-1720.

d. Culurgioni S., Mari S., Bonetti P., Gallini S., Bonetto G., Brennich M., Round A., Nicassio F., **Mapelli M.** (2018) Insc:LGN tetramers promote asymmetric divisions of mammary stem cells. **Nat. Comm.** 9, doi: 10.1038/s41467-018-03343-4.

2. Our laboratory characterized the architecture and the functional principles of dynein-based microtubule motors executing oriented cell divisions. Additionally, we identified the adherens-junction protein Afadin as the molecular connection between actomyosin cortex and microtubule motors.
  - a. Carminati M., Gallini S., Pirovano L., Alfieri A., Bisi S. and **Mapelli M.** (2016) Concomitant binding of Afadin to LGN and F-actin directs planar spindle orientation. **Nat. Struct. Mol. Biol.**, 23,155-63. doi: 10.1038/nsmb.3152.
  - b. Gallini S., Carminati M., De Mattia F., Pirovano L., Martini E., Oldani A., Asteriti I.A., Guarguaglini G, **Mapelli M.** (2016) NuMA phosphorylation orchestrates spindle orientation. *Current Biol.*, doi: 10.1016/j.cub.2015.12.051
  - c. Pirovano L, Culurgioni S, Carminati M, Alfieri A, Monzani S, Cecatiello V, Gaddoni C, Rizzelli F, Foadi J, Pasqualato S, Mapelli M (2019) Hexameric NuMA:LGN structures promote multivalent interactions required for planar epithelial divisions. **Nat. Comm.** 10, doi:10.1038/s41467-019-09999-w
  - d. Renna C, Rizzelli F, Carminati M, Gaddoni C, Pirovano L, Cecatiello V, Pasqualato S, **Mapelli M.** (2020) Organizational principles of the NuMA-Dynein interaction interface and implications for mitotic spindle functions. **Structure** May 11, doi: 10.1016/j.str.2020.04.017.
  - e. Rizzelli F, Malabarba MG, Sigismund S, **Mapelli M.** (2020) The crosstalk between microtubules, actin and membranes shapes cell division. **Open Biology** 10, 190341. doi: 10.1098/rsob.190314
  - f. Polverino F., Naso F.D., Asteriti I.A., Palmerini V., Singh D., Valente D., Bird A.W., Rosa A., **Mapelli M.\***, Guarguaglini G.\* (2021) The Aurora-A/TPX2 Axis Directs Spindle Orientation in Adherent Human Cells by Regulating NuMA and Microtubule Stability. **Curr. Biol.** 31(3). doi: 10.1016/j.cub.2020.10.096.
  - g. Lechler T. and **Mapelli M.** (2021) Spindle positioning and its impact on vertebrate tissue architecture and cell fate. **Nat. Rev. Mol. Cell Biol.** doi: 10.1038/s41580-021-00384-4.
  - h. Eli S, Castagna R, **Mapelli M\***, Parisini E\* (2022) Recent Approaches to the Identification of Novel Microtubule-Targeting Agents. **Front Mol Biosci.** doi: 10.3389/fmolb.2022.841777
  - i. Donà F, Eli S, **Mapelli M.** (2022) Insights into mechanisms of oriented division from studies in 3D cellular models. **Front Cell Dev Biol.** doi: 10.3389/fcell.2022.847801.
3. We contributed to the structural and functional characterization of the newly identified Drosophila TNF Receptor Grindelwald able to couple loss of epithelial polarity to neoplastic overproliferation.
  - a. Andersen D.S., Colombani J., Palmerini V., Chakrabandhu K., Röthlisberger M., Toggweiler J., Basler K., **Mapelli M.**, Hueber A., and Léopold P. (2015) The Drosophila TNF receptor Grindelwald couples loss of cell polarity with neoplastic growth. (2015) **Nature**, 522, 482
  - b. Palmerini V., Monzani S., Laurichesse Q., Loudhaief R., Mari S., Cecatiello V., Olieric V., Pasqualato S., Colombani J., Andersen D., **Mapelli M.** (2021) Drosophila TNFRs Grindelwald and Wengen bind Eiger with different affinities and promote distinct cellular functions. **Nat. Comm.** April 6. doi: 10.1038/s41467-021-22080-9.

#### Complete list of published work in my bibliography

<https://pubmed.ncbi.nlm.nih.gov/?term=marina+mapelli&sort=date>