

## Curriculum Vitae Thierry Lepage 08/2024

### Personal information

name Thierry Lepage  
date of birth Born in Calvi (France) 23rd of June 1962  
civil status unmarried , with 2 children

### Current position

Group leader at the IBV, UMR7277 CNRS 06108 Nice  
Research Director (DR1)  
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<https://orcid.org/0000-0003-2889-5064>

### Education

1993 **Permanent position CNRS** Marine Station of Villefranche-sur-Mer  
1985-1991 **PhD in life Sciences** under the supervision of Dr Christian Gache  
University of Nice/Marine Station of Villefranche sur Mer.  
1984: **DEA (equiv. B.A) of Molecular Genetics** University of Nice (mention Bien, major de promotion).  
1984-1985 : **"DEA" Microbiology Pasteur Institute** (mention Très Bien)  
Virology course at the Pasteur Institute Paris.

### Postdoctoral experience

1994-1995 post doc in the laboratory of **Susan Parkhurst**: Fred Hutchinson Cancer Research Center Seattle:  
Role of PKA in the **hedgehog-signaling pathway** in *Drosophila*.  
1995-1997 post doc in the laboratory of **David Kimelman** University of Washington. Research on zebrafish developmental genetics. Characterization of the structure and expression of **pitx2**. Isolation of the **nacre** mutant (Microphthalmia).

### Research experience

from 1997-Nov 2013: group leader at the CNRS (UMR 7009) Marine Station of Villefranche.  
Research focused on developmental genetics of the sea urchin and zebrafish. Dissection of the gene regulatory networks controlling morphogenesis and specification of the primordial axes of polarity.  
Since Nov 2013: group leader at the iBV-Université Côte d'Azur.

### RESEARCH GRANTS

#### current

2021-2024 ARC (Projet ARC) 50 K€

#### completed

|   |        |
|---|--------|
| 2018-2021 label Equipe FRM  | 370 K€ |
| 2017-2019 ARC (subvention fixe)   | 50 K€  |
| 2014-2018 ANR blanche (TL coordinator) « Echinodal »  | 270 K€ |
| 2012-2014 ARC subvention fixe   | 50 K€  |
| 2008-2012 ANR blanche (TL coordinator) « DV network »   | 250 K€ |
| 2008-2010 Prix Coup d'élan pour la Recherche Fondation Bettencourt<br>75% of the budget dedicated for renovating the old lab located in the marine station) | 250 K€ |
| 2007-2009 ARC subvention fixe   | 50 K€  |
| 2005-2007 ARC subvention fixe   | 50 K€  |
| 2005-2008 ANR blanche (TL coordinator) « sea urchin »   | 150 K€ |
| 2003-2006 Subvention ACI Biologie du développement (coordinator)  | 100 K€ |
| 2002-2004 ARC Subvention fixe   | 50 K€  |
| ARC Regional Equipment  | 50 K€  |

### Honors and Awards, Fellowships

2008 **Prize "Coup d'Élan pour la Recherche "** from the **Bettencourt Foundation**  
2009 **Prize Tregouboff in Marine Biology** from the French Academy of Sciences  
1995 Postdoctoral Fellowship **Human Frontiers Science Program**  
1994 Fellowship for the **Embryology Course of Woods Hole**  
1993 Postdoctoral Fellowship Medical Research Foundation (FRM)  
1992 Fellowship Cancer Research Foundation (ARC)

**Teaching activities:** As a group leader at the marine station of Villefranche-sur-mer, I was involved in a course on Developmental biology of marine organisms with plenary lectures and experimental work and oral presentations at the end of the course. Since 1998 and every year, I also taught a course in developmental biology of vertebrates (signalling pathways regulating germ layer formation, D/V axis formation and neural induction, as well as a course on development of the sea urchin embryo (UE17 in master at the University of Nice(6-8h / year). In addition I gave plenary lectures at the EPFL of Lausanne, at the DanStem, university Copenhagen, at the University of Strasbourg, at the University of Lyon, at the University of Toulouse.

#### **Training and dissemination of scientific culture:**

Director of 9 PhDs (100%): Morgane Poulain, Véronique Duboc, François Lapraz, Eric Röttinger, Flavien Mekpoh, Nathalie Bessodes, Magali Quirin, Emmanuel Haillot, Praveen Viswanathan.  
Two of these students (E.Röttinger and F. Lapraz) successively won the prize for the best doctoral thesis of the ED85 doctoral school. I also directly supervised sixteen Master2, ten Master1 and dozens of technician or bachelor's / summer interns. My team regularly hosts interns from middle and high-school and takes part in the Fête de la Science, MEDITES and in DECLIC programs (capitaine dé clic en 2023 lycée St Barthélémy)) that promote and popularize modern understanding of fundamental research, Developmental Biology, molecular Biology and evolutionary biology. We regularly contribute to textbooks such as "Developmental Biology" Scott Gilbert (cf tenth edition p225 and 229 that illustrate the functions of Nodal and FGF signalling during sea urchin development). In 2019, we have hosted (for one week), a young talented photographer from the national school of photography of Arles

**Mentoring:** Almost all my former students obtained a position in science: F. Lapraz has obtained a permanent position at the University of Nice as researcher engineer (laboratory of S. Noselli) and N. Bessodes has obtained a job in a private scientific company. One of my former students (E. Röttinger) obtained the prestigious ATIPE grant from the CNRS and is now group leader at the IRCAN Institute in Nice, working on regeneration in Cnidarians, while V. Duboc supervises the cytogenetics platform at C3M Nice.

**postdocs:** I supervised the work and trained 6 postdocs (Ryan Range, Alexandra Saudemont, Emmanuel Haillot, Noémie de Croze, Julie Hanotel, Dolores Molina). One of them, R. Range, is PI in the United States at the University of Mississippi and uses the sea urchin as a model system. Two other postdocs (A. Saudemont and N. de Croze) are permanent scientists in private biotechnology firms (Loreal) or on technical platforms. My last postdoc, M. D. Molina, obtained a position as an associate researcher in Spain after applying to the CNRS in 2018.

#### **Collective responsibilities and research management**

2006: member of the collective responsible for annotating the genome of the sea urchin *S. purpuratus* 2002-2016 Member of a network of excellence "Marine Genomics Europe" (MGE). <http://www.marinegenomics>  
2010-today: **Coordinator of a European consortium** for sequencing the genome of *P. lividus*  
2008-2012 Member of the committee "LABEX" UPMC and the ESFRI and "(EMBRIC)" project  
2017- 2023 Co-coordinator of the bioinformatics platform of the IBV  
2010- 2014 Member of the board of the French Society for Developmental Biology (SFBD).  
2004-2017 Member of 18 evaluation committees for doctoral theses.  
2004-2019 Regular member of the master's jury of the UPMC and UNSA/UCA.  
2004-2014 Member of 3 selection committees of MCF (Nice, Paris (UPMC), Toulouse)  
2004-2013 Member of the selection committee of group leaders at UMR7009.  
2013-2019 Member of the selection committee of group leaders at the IBV.  
2006-2012 Member for 6 years of the ARC CN3 scientific committee.  
2006-2017 Tenure assessor (Assistant Professor positions in the United States and Korea.

**Grant review:** regular reviewer for the ANR, BBSRC, NSF, NSERC, Wellcome trust, Israel Science Foundation, Einstein Foundation.

**Reviewer:** regular reviewer for Dev, Dev Biol, Nature, Dev Cell, Evol Dev, PLOS Genetics, MOD, F1000 etc..

**Invitations to International Conferences:** invited as speaker in a plenary session in 21 International conference (Zebrafish Development and Genetics (1997), Xenopus Conference (1998), Jacques Monod Conferences (1998 and 2012). SFDB (2005, 2008, 2014) and Joint meeting of the French and Japanese societies for DB (2008), Joint meeting of the Spanish and English societies for DB (2008); Invited as a speaker at the meeting "Origins of the vertebrate body plan". April 16 - 20, 2007 organized by Pr Mike Levine, the Center for Integrative genomics CIG, Moorea. *Dorsal ventral axis formation during sea urchin development*. Invited at International conferences on sea urchin (2005, 2007, 2008, 2012, 2014 2015,

2017, 2019, 2021).

Regularly invited to give seminars to internationally (EPFL Lausanne, Danstern Copenhagen) and nationally renowned Universities (Toulouse, Strasbourg, Marseille, Lyon).

**Organization of Conferences:** Member of the organizing committee of the sea urchin XXIV meeting in 2017 (150 scientists).

## Publications

since 1998 (postdoc) 34 research articles, 5 reviews, **h index:32 total of 5857 citations (average of 183 citations /article).**

**Original work from the lab** (Thierry Lepage first or last author)

Nature (1x), Developmental Cell (2x), Cell Genomics 1x), EMBO (1x) PLOS Biology (3x), PLOS Genetics (3x), Nature Communications (2x), Development (10x), Developmental Biology (5x ) Journal of Biochemistry (1x), Current Opinion in Genetics and Development (1x), Current Topics in Developmental Biology (1x),

**Work in collaboration :** Development (4x) Developmental Biology (2x), Science (1x), EMBO (1x) reviews: ), Current Opinion in Genetics and Development (1x), Current Topics in Developmental Biology (1x), Journal of Proteomics (1x).

**Field of expertise:** Sea urchin development, D/V Axis and germ layer formation, Left-right asymmetry, Wnt and TGF-beta signaling, Nodal, Univin, and BMP signaling, Lateral factors involved in axis formation and symmetry breaking, TGF-beta agonists and antagonists, FGF signaling, Epithelial mesenchymal transition, ERK MAP kinase signaling, Kinase Suppressor of Ras signaling, Transcriptomics, ATAC\_Seq, Gene regulatory analysis, Cis regulatory analysis.

Our group is interested in fundamental questions of developmental Biology such as how are the axes of polarity and the germ layers of the embryo specified and how are morphogens gradients formed, shaped and interpreted to generate the extraordinary diversity of patterns of gene expression. Our main model is the sea urchin embryo, which is phylogenetically related to vertebrates and offers many advantages for the functional analysis of genes and signals that constitute **the gene regulatory networks that orchestrate early development**. Our research is focused on a family of morphogens that represents one of the most prominent and versatile family: **the TGF-beta superfamily**. One of our main achievements is the mid-scale **dissection of the Gene Regulatory Network** that is deployed by the TGF beta Nodal and that controls patterning along the dorsal-ventral axis of the embryo. We have shown the crucial roles played by Nodal, Univin/Vg1 and BMP2/4 in specification of the ventral and dorsal regions. We showed that the long-range organizing activity of Nodal is assured by **BMP2/4, which is synthesized in the ventral ectoderm, then translocated** to the opposite side of the embryo. We identified a number of direct and indirect targets of these ligands in all three germ layers and dissected **conserved circuits involved in mouth formation, skeletogenesis, ectoderm patterning, neural induction and in patterning of the mesoderm and in the autoregulation of BMP signalling**. Altogether, our results suggest that the ventral ectoderm of the sea urchin embryo shares fundamental properties with the **Spemann organizer of vertebrates**, strongly suggesting that the evolutionary origin of this signalling center can be traced back to the ancestor of deuterostomes. We are continuing to dissect this GRN using a combination of mid-scale functional analyses and genome-scale screens such as **RNA-seq**. We try to unravel the roles of **maternal factors** such as the **Inhibin-like TGF beta Panda** which acts as a maternal determinant of the D/V axis in establishment of the Nodal gradient. We dissect the mechanism by which Nodal and BMP2/4 work, to understand **how this gradient is interpreted** and try to decipher the **molecular basis of the antagonism between the Nodal and BMP2/4 pathways**. Another focus of our research is the analysis of the mechanisms regulating determination of **left-right polarity** in the sea urchin embryo. We identified a **nodal expressing left-right organizer in archenteron** of the gastrula. We showed that formation of this centre and subsequent positioning of the rudiment requires a combination of **inhibitory signals from the Notch pathway and inductive signals from the FGF, and BMP pathways**. We are trying to identify the nature of the event that breaks the symmetry of the embryo. In parallel, we are analyzing morphogenesis and patterning of the mesoderm. We uncovered the crucial role played by the MAP kinase **ERK in the epithelial mesenchymal transition** of the skeletogenic precursors that build the skeleton of the larva and in the GRN controlling specification of these mesodermal cells. Recently, using functional genomics approaches, we identified a novel and constitutively active member of the **Kinase Suppressor of RAS family** of RAF activators as the signal responsible for the cell-autonomous RAS-independent activation of this pathway at the vegetal pole of the embryo. We are now trying to dissect the relative contributions of the RAS independent and RAS -dependent mechanisms of ERK activation.

Thierry Lepage was recipient of the Bettencourt prize "**Coup d'élan pour la Recherche** (2007) (<https://www.fondationbs.org/notre-communaute/laureats-et-projets/thierry-lepage>) and of the Prix Tregouboff de l'Académie des Sciences (2009)