Patrick Laurent
FNRS, ULB-UNI Research Associate

+32472495688; +32 2 555 41 27 patrick.laurent@ulb.be Born on 01/07/1976
C. elegans Team Principal Investigator.
ULB Neuroscience Institute, ULB, Campus Erasme,808 route de Lennik, 1070 Brussels, BE
https://celegans.ulb.ac.be/wordpress/

PERSONAL STATEMENT

My group focuses its research on neuronal cell biology and on neuron circuit function in the simple multicellular organism *C. elegans*. My group established in 2014, we acquired and developed all the necessary material and protocols to manipulate *C. elegans*, generate mutants and transgenics, analyze neuronal cell biology, and neuronal and circuit functions through optogenetic, pharmacological and behavioural assays.

EDUCATION TRAINING

2014 to date: Research associate, FNRS, Laboratoire de neurophysiologie, Bruxelles, ULB
- Ageing of the neurons and glial cells, circuits and behavior.
- Neuropeptide cell biology and peptidergic communication.

2007-2014: Post- doctoral position, MRC-LMB, Cambridge (with *M. De Bono*)
- Neuropeptide biogenesis, trafficking and secretion.
- Genetic and neurobiology of oxygen responses.

2004-2006: Post-doctoral position, IRIBHN, Bruxelles (With *M. Parmentier* and *G. Vassart*) , ULB
- Immune and striatal functions of an orphan GPCR: GIR/GPR83.
- Developmental function of an orphan GPCR: LGR4.

1998-2004: PhD, IRIBHN, Bruxelles (With *M. Parmentier*) ULB
- Neuropeptide/ GPCR characterization.
- Generation of two knockout mice for neuropeptides GPCR (GPR10 and GIR/GPR83).
- Endocrine, nociceptive and rewarding function in GPR10-knockout mice.

1994-1998: Master of Science, UMons, Mons (*With A. Alexandre*) UMH
- Functions of focal adhesions in mouse preimplantation embryo

CURRENT TEAM MEMBERS

Patrick Laurent	Principal Investigator
Adria Sanfeliu	PhD student (UNI 2017, FRIA 2018-2022)
Michiho Onizuka	PhD Student (FRIA 2018-2022)
Katerina Stratigi	PhD student (FRIA 2016-2021)
Jose Badziak	PhD student (2020-2024)
Teresa Lobo	Master Student (2020-2021)
Laetitia Cuvelier	Lab technician ¼ time (2020-2021)

FORMER MENTORING

Post Docs: Ramiro Lorenzo (2017-2018, now in CONICET, Argentica); Celine Martineau (2016-2019, now in J. Ewbank lab); Stephanie Grimbert (2016-2017, now in A. Piekny Lab).
PhD Thesis co-supervision: Ferdinand Ngale Njume (IBMM, ULB, 2016-2020), Abdulkadir ABAKIR (FRIA 2014-2015, finished his PhD with *A. Ruzov*); Zoltan Soltesz (MRC 2010-2015, Post-Doc with *J. Chin* lab).
Master thesis: Teresa Lobo (2021), Claire Vanbeleghem (2020), Sheima Ali Mansour (2019), Leonore Bleret (2018), Annissa Termataj (2018), David de la Marca (2017, Works in GSK), Cedric Vanaudenhove (2016), Muriel Laurent (2014; PhD with *A de Kerchoove*, ULB), Baptiste Libé (2012; PhD with *C. Petit* (Pasteur); post Doc with *P. Vanderhaegen* (ULB)), Ingrid Chama (2012; PhD with *O. Toumine* (IINS); CR INSERM Bordeaux).

PROFESSIONAL MEMBERSHIPS:

Deputy director of the ULB Institute for Neuroscience (UNI), Founding Member of the COST action GeNiE, Member of Federation of European Neuroscience Societies (FENS), the Belgian Society for neuroscience (BSN), Involved in HCERES evaluation committee (The High Council for Evaluation of Research and Higher Education-France), Allumni of the Darwin College, Cambridge.

FELLOWSHIPS, GRANTS, HONORS AND AWARDS:

1998	FRIA Ph.D. fellow, FNRS
2002	Televie Ph.D. fellow, FNRS
2003	Fondation Van Buuren
2004	Fondation reine Elizabeth, Postdoctoral fellow
2005	European Community, Postdoctoral fellow
2007	Darwin College research fellow
2007	Fondation Wienner-Anspach Postdoctoral fellow
2008	EMBO Postdoctoral fellow
2010	MRC-career development Postdoctoral fellow
2012	MRC centenary award
2013	FNRS- Ulysse Grant
2014	Research Associate FNRS
2015	FNRS Equipment Grant
2016	Fondation Defay
2016	Cephaly Prize (BBC)
2018	FNRS CDR
2019	ULB FER

MAIN CONTRIBUTIONS TO SCIENCE

Peptidergic antiopioid systems in mouse.

- *The prolactin-releasing peptide (PrRP) antagonizes the opioid system through its receptor GPR10.* ***Laurent P****, Becker JA* et al. M.* ***Nature neuroscience*** *(2005) * for co-authorship.*
- *RF9, a potent and selective neuropeptide FF receptor antagonist, prevents opioid-induced tolerance associated with hyperalgesia. Simonin F et al.* ***PNAS.*** *2006*

The prolonged use of opiate drugs induces the development of tolerance and dependence. In addition to adaptation of the signaling pathway at the cellular level, a growing contribution of the plasticity of neuronal networks has been recognized. We identified the PrRP-GPR10 system as a new peptidergic system opposing the effects of the opioid system (a system that can be called an "antiopioid system"). NPFF receptors are part of a second established antiopioid system. The RF9 antagonist of these receptors represents a useful therapeutic agent for improving the efficacy of opioids in chronic pain treatment.

Tubular tissue development in mouse.

- *Defective postnatal development of the male reproductive tract in LGR4 knockout mice. Mendive F*,* ***Laurent P****, et al.* ***Developmental Biology*** *(2006). * for co-authorship*

The molecular and cellular basis of epithelial tubular elongation and branching is actively studied. We established that the G protein-coupled receptor LGR4 plays an important role in epithelial-mesenchymal interactions required for the postnatal remodeling of the epididymis. R-spondins were shown later to act through LGR4 to regulate the development and differentiation of many other epithelial tubular tissues. The phenotypes of human patients recapitulated our observations in the mouse.

Oxygen sensing genes, neurons and circuits in *C. elegans.*

- *Persson A et al. Natural variation in a neural globin tunes oxygen sensing in wild C. elegans.* ***Nature*** *(2009)*
- *Bretscher AJ et al. Temperature, oxygen, and salt-sensing neurons in C. elegans are carbon dioxide sensors that control avoidance behavior.* ***Neuron*** *(2011)*
- *Busch KE*,* ***Laurent P*** *, et al. Tonic signaling from O_2 sensors sets neural circuit activity and behavioral state.* ***Nature Neuroscience*** *(2012).*
- *Chen C et al. IL-17 is a neuromodulator of Caenorhabditis elegans sensory responses.* ***Nature*** *(2017)*

Previous work identified the soluble Guanylate cyclases GCY-35 & GCY-36 as the molecular sensors for high O_2 concentrations (>7%O_2). We identified a hexa-coordinated neuroglobin, GLB-5, as a new sensor for high O_2 concentrations. Calcium imaging revealed that the O_2 sensory neurons displayed positive, tonic and graded responses to increasing O_2 concentrations, and confirmed the role of GLB-5 in this response. Most sensory neurons adapt to their cues. How the few non-adapting neurons, e.g. pain neurons maintain their activity over long period of time is poorly understood. We explored the genetic basis for the tonic cGMP and calcium responses activities in the O_2-sensory neurons. Using a combination of behavior, genetics and optogenetics, our results clarify the molecular mechanisms allowing the generation and maintenance of these long-term activities.

- ***Laurent P****, Soltesz Z*, et al. Decoding a neural circuit controlling global animal state in C. elegans.* ***e-Life*** *(2015).*
- *Rabinowitch I et al. Neuropeptide-Driven Cross-Modal Plasticity following Sensory Loss in C. elegans.* ***Plos Biol*** *(2016).*

We showed that activity-dependent neuropeptide signaling secreted from the touch circuit leads to cross-modal plastic changes in the chemosensory circuit, enhancing its sensory performance when the touch circuit is less functional. In addition to such cross-modal communication, neuropeptides contribute to establish global states in response to threats or opportunities: they are able to coordinate changes in physiology and neurochemistry. We showed that the sensory neurons monitoring of the ambient oxygen control a cascade of responses across multiple layers of interneurons to switch the global state of the nematode *C. elegans*: it reprogram behavior and gene expression to enable escape from the surface exposure and prepare the animal to the physiological challenge.

Neuropeptide Cell biology

- ***Laurent P** et al. Genetic dissection of neuropeptide cell biology at high and low activity in a defined sensory neuron. **PNAS** (2018).*

The previous works highlighted the importance of the neuropeptidergic signalling in the nervous system. However, the organelle mediating the peptidergic signaling, namely the Dense Core Vesicles (DCVs), remain relatively unexplored in neurons. *C. elegans* had greatly contributed to the genetic understanding of the Synaptic Vesicle biology and offered similar advantages to explore DCVs biology. We identified a set of genes involved in the biogenesis, the maturation and the trafficking of the DCVs and neuropeptide secretion. We suggest that DCV biogenesis involve the fusion between immature granules synthesized de novo via the conventional secretory pathway and recycling endosomal compartments. Our recent results suggest DCV secretion and biogenesis are coupled via this proposed recycling route, possibly in conjunction with calcium.

Phenotypic ageing of C. elegans

- *Martineau CNM et al. Multidimensional phenotyping predicts lifespan and quantifies health in C. elegans. **Plos Comp Biol**. (2020).*

Despite their simplicity, the *C. elegans* neuronal circuits shape complex behaviors. We still knew little about the circuit and behavioral change induced by ageing. As a first step, we described in much detail these age-related behavioral changes and used them to quantify the health decline of the animals. I consider this as a future readout for sub-circuit rejuvenation.

A molecular atlas of C. elegans nervous system

- Lorenzo R et al. Combining single-cell RNA-sequencing with a molecular atlas unveils new markers for *C. elegans* neuron classes. **Nucleic Acid Research** (2020).

Building on recent Single-cell RNA-sequencing data and on a molecular atlas describing the expression pattern of ~800 genes at the single cell resolution, we obtained partial expression profiles for 76 neuron classes of the ~100 anatomically defined neuron classes of *C. elegans*. We expanded the list of neurons amenable to genetic manipulations by specific promoters described the maturation of some neuron classes and predicted a number of neuron fate regulators.

Ciliary extracellular vesicles are released from C. elegans neurons

- *Razauti A et al Ectosome uptake by glia sculpts* Caenorhabditis elegans *sensory cilia. BioRxiv : https://doi.org/10.1101/2021.02.14.430969. In revision in **eLife***

We describe the production of Extracellular Vesicles (EVs) by most ciliated sensory neurons. Outward budding of EVs (ectosomes) is observed at the tip of sensory cilia and produce EV that are externally released. Ectosomes are also produced by the cilia base that are captured by the associated glia. Cargo accumulation at cilia tip or cilia base in cilia trafficking mutant lead to apical or basal release, respectively. Our result suggest EVs production is part of safeguard mechanisms to avoid local accumulations of membrane proteins within cilia (in revision in eLife).

PUBLICATIONS

1. Razzauti, A., **Laurent, P.** (2021). Ectocytosis prevents accumulation of ciliary cargo in *C. elegans* sensory neurons. eLife (accepted, sept 2021).
2. Martineau, C., Brown, A. E. X., & **Laurent, P.** (2020). Multidimensional phenotyping predicts lifespan and quantifies health in Caenorhabditis elegans. PLoS computational biology, 16(7), e1008002.

doi:10.1371/journal.pcbi.1008002
https://dipot.ulb.ac.be/dspace/bitstream/2013/316007/1/doi_299651.pdf

3. Lorenzo, R., Onizuka, M., Defrance, M., & **Laurent, P**. (2020). Combining single-cell RNAsequencing with a molecular atlas unveils new markers for Caenorhabditis elegans neuron classes. Nucleic acids research. doi:10.1093/nar/gkaa486
https://dipot.ulb.ac.be/dspace/bitstream/2013/316017/1/doi_299661.pdf

4. **Laurent, P.,** Ch'ng, Q., Jospin, M. J. M., Chen, C. C. C., Lorenzo, R., & de Bono, M. (2018). Genetic dissection of neuropeptide cell biology at high and low activity in a defined sensory neuron. Proceedings of the National Academy of Sciences of the United States of America. doi:10.1073/pnas.1714610115
https://dipot.ulb.ac.be/dspace/bitstream/2013/273245/3/doi_256872.pdf

5. Chen, C. C. C., Itakura, E., Nelson, G. M., Sheng, M., **Laurent, P.,** Fenk, L. L., Butcher, R. A., Hegde, R. S., & de Bono, M. (2017). IL-17 is a neuromodulator of Caenorhabditis elegans sensory responses. Nature (London), 542(7639), 43-48. doi:10.1038/nature20818
https://dipot.ulb.ac.be/dspace/bitstream/2013/266553/4/PMC5503128.pdf

6. Abakir, A., Wheldon, L. L., Johnson, A. A., **Laurent, P.**, & Ruzov, A. (2016). Detection of modified forms of cytosine using sensitive immunohistochemistry. Journal of Visualized Experiments, 2016(114), e54416. doi:10.3791/54416 https://dipot.ulb.ac.be/dspace/bitstream/2013/237747/3/doi_221374.pdf

7. Rabinowitch, I., **Laurent, P.,** Zhao, B., Walker, D., Beets, I., Schoofs, L., Bai, J., Schafer, W. R., & Treinin, M. (2016). Neuropeptide-Driven Cross-Modal Plasticity following sensory loss in Caenorhabditis elegans. PLoS biology, 14(1), e1002348. doi:10.1371/ journal.pbio.1002348
https://dipot.ulb.ac.be/dspace/bitstream/2013/225983/4/doi_209610.pdf

8. **Laurent, P.**, Soltesz, Z., Nelson, G. M., Chen, C. C. C., Arellano-Carbajal, F., Levy, E., & de Bono, M. (2015). Decoding a neural circuit controlling global animal state in C. elegans. eLife, 4. doi:10.7554/eLife.04241 * shared 1st authors.
https://dipot.ulb.ac.be/dspace/bitstream/2013/225441/4/doi_209068.pdf

9. Busch, K. E.*, **Laurent, P.*,** Soltesz, Z., Murphy, R. J., Faivre, O., Hedwig, B., Thomas, M., Smith, H. L., & de Bono, M. (2012). Tonic signaling from O# sensors sets neural circuit activity and behavioral state. Nature neuroscience, 15(4), 581-591. doi:10.1038/nn.3061 * shared 1st authors.
https://dipot.ulb.ac.be/dspace/bitstream/2013/160906/4/PMC3564487.pdf

10. Bretscher, A. J., Kodama-Namba, E., Busch, K. E., Murphy, R. J., Soltesz, Z., **Laurent,P.**, & de Bono, M. (2011). Temperature, oxygen, and salt-sensing neurons in C. elegans are carbon dioxide sensors that control avoidance behavior. Neuron, 69(6), 1099-1113. doi:10.1016/j.neuron.2011.02.023
https://dipot.ulb.ac.be/dspace/bitstream/2013/225434/4/doi_209061.pdf

11. Lambot, M.-A., Mendive, F., **Laurent, P.**, Van Schoore, G., Noël, J. C., Vanderhaeghen, P., & Vassart, G. (2009). Three-dimensional reconstruction of efferent ducts in wild-type and Lgr4 knock-out mice. The Anatomical Record, 292(4), 595-603. doi:10.1002/ar.20883
https://dipot.ulb.ac.be/dspace/bitstream/2013/51785/3/51785.pdf

12. Persson, A., Gross, E., **Laurent, P.**, Busch, K. E., Bretes, H., & de Bono, M. (2009). Natural variation in a neural globin tunes oxygen sensing in wild Caenorhabditis elegans. Nature, 458, 1030-1033.

13. Mendive, F., **Laurent, P.**, Van Schoore, G., Skarnes, W., Pochet, R., & Vassart, G. (2006). Defective postnatal development of the male reproductive tract in LGR4 knockout mice. Developmental biology, 290(2), 421-434. doi:10.1016/j.ydbio.2005.11.043
https://dipot.ulb.ac.be/dspace/bitstream/2013/52402/1/Dev_Biol_2006.pdf

14. Simonin, F., Schmitt, M., Laulin, J.-P., Laboureyras, E., Jhamandas, J. H., MacTavish, D., Matifas, A., Mollereau, C., **Laurent, P.**, Parmentier, M., Kieffer, B. L., Bourguignon, J.-J., & Simonnet, G. (2006). RF9, a potent and selective neuropeptide FF receptor antagonist, prevents opioid-induced tolerance associated with hyperalgesia. Proceedings of the National Academy of Sciences of the United States of America, 103(2), 466-471. doi:10.1073/pnas.0502090103
https://dipot.ulb.ac.be/dspace/bitstream/2013/52318/4/PMC1326150.pdf

15. **Laurent, P.***, Becker, J.*, Valverde, O., Ledent, C., de Kerchove d'Exaerde, A., Schiffmann, S. N., Maldonado, R., Vassart, G., & Parmentier, M. (2005). The prolactin-releasing peptide antagonizes the opioid system through its receptor GPR10. Nature neuroscience, 8(12), 1735-1741. doi:10.1038/nn1585. * shared 1st authors.
https://dipot.ulb.ac.be/dspace/bitstream/2013/50711/1/NatureNeuro2005PrPPr.pdf