**Profile/CV H. Llewelyn (Llew) Roderick B.Sc., Ph.D.**

**Current Position:** Professor (Hoogleraar) in the Laboratory of Experimental Cardiology, Department of Cardiovascular Sciences, KULeuven, Leuven, Belgium. Tel:+3216377150. E-mail: Llewelyn.roderick@kuleuven.be

**Professional career:**

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| 2016-current | Affiliated Investigator, K.G. Jebsen Center for Cardiac Research, University of Oslo, Oslo, Norway. |
| 2014-current | Professor (BOF-ZAP, tenured), Laboratory of Experimental Cardiology, Department of Cardiovascular Sciences, KULeuven |
| 2014-current | Affiliated Lecturer, Department of Pharmacology, University of Cambridge. |
| 2010-2014 | Group leader with Tenure, Babraham Institute, Cambridge, UK. |
| 2005-2012 | Royal Society University Research Fellow, Department of Pharmacology, University of Cambridge, Cambridge, UK |
| 2004-2010 | Group Leader (Tenure track), Babraham Institute, Cambridge, UK. |

**Training:**

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| 2001-2004 | Postdoctoral Research, M. D. Bootman and Sir M. J. Berridge FRS, Babraham Institute, Cambridge, UK. |
| 1997-2001 | Postdoctoral Research, P. Camacho, Dept. Physiology, University of Texas Health Science Center, San Antonio, Texas. |

**Education:**

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| 1993-97 | Ph.D., supervised by D. H. Llewellyn and A. K. Campbell, Dept. Medical Biochemistry, University of Cardiff, Cardiff, UK. |
| 1989-92 | B.Sc., Zoology and Genetics (Jt Hons). Dept. Pure and Applied Biology, UWCC, Cardiff, UK. |

**Research Themes:**

Physiological and underlying epigenome/transcriptome changes associated with and controlling cardiomyocyte function during health, disease and ageing. Our research spans from fundamental aspects of molecular cardiology to preclinical translational research. We collaborate widely within KULeuven with clinicians in the Department of Cardiology and outside with leading researchers and clinicians in Europe, the US and Australia.

**This research is divided between:**

1. *Defining the contribution of the epigenome to determining the differentiated state of adult cardiac myocytes and in the remodeling of the heart in response to physiological and pathological stressors including during maturation and following MI, aortic stenosis and normal ageing.* Through these analysis, we aim to identify strategies that can be employed to reverse the deleterious functional remodelling associated with disease and ageing. These strategies will target reactivation of cell cycle activity to improve regeneration of damaged tissue and suppression of disease-associated gene transcription programmes. To these ends, we employ next generation sequencing including single cell sequencing, genome wide epigenomic analysis, genetic and surgical models of cardiac disease, and human tissue.

2. *Delineating the contribution of $Ca^{2+}$ signalling to disease-associated structural, functional and physiological remodelling of cardiac myocytes.* A particular interest is in the dual roles of $Ca^{2+}$ signaling microdomains regulated by $IP_3$ in disease and ageing-associated remodelling of excitation contraction coupling and activation of hypertrophic gene transcription. Specifically, we investigate how specificity is encoded by a given $Ca^{2+}$ signal. To these ends, we perform combined

cellular electrophysiology and $Ca^{2+}$ imaging approaches, employ genetically encoded $Ca^{2+}$ indicators, tissue preparations, large (pig) and small mammal models of disease, human cell/tissue analysis, iPS derived cardiomyocytes/tissues and super resolution imaging. In collaboration, these wet lab approaches are combined with mathematical modelling, which reveals additional mechanistic insights into $Ca^{2+}$-dependent processes.

**Publications:** 105 peer reviewed articles and reviews, 9 book chapters, 18600 citations and h index 50. https://scholar.google.be/citations?user=zaoRw14AAAAJ&hl=en.

Key publications:


1. Jin, X., A. Meletiou, J. Chung, A. Tilunaite, K. Demydenko, E. Dries, R.D. Puertas, M. Amoni, A. Tomar, G. Gilbert, P. Claus, C. Soeller, V. Rajagopal, K. Sipido, and **H.L. Roderick**. 2023. InsP3R-RyR channel crosstalk augments sarcoplasmic reticulum Ca2+ release and arrhythmogenic activity in post-MI pig cardiomyocytes. *J Mol Cell Cardiol*. 179:47–59. doi:10.1016/j.yjmcc.2023.03.015.
2. Amoni, M., D. Vermoortele, S. Ekhteraei-Tousi, R.D. Puertas, G. Gilbert, M. Youness, B. Thienpont, R. Willems, **H.L. Roderick***, P. Claus*, and K.R. Sipido*. 2023. Heterogeneity of Repolarization and Cell-Cell Variability of Cardiomyocyte Remodeling Within the Myocardial Infarction Border Zone Contribute to Arrhythmia Susceptibility. *Circulation Arrhythmia Electrophysiol*. 16:e011677. doi:10.1161/circep.122.011677.* co Senior Author.
3. Chung, J., A. Tilūnaitė, D. Ladd, H. Hunt, C. Soeller, E.J. Crampin, S.T. Johnston, **H.L. Roderick***, and V. Rajagopal*. (2023). IP3R activity increases propensity of RyR-mediated sparks by elevating dyadic [$Ca^{2+}$]. *Math Biosci*. 355:108923. doi:10.1016/j.mbs.2022.108923. Co-senior author.
4. Vervliet, T., R. Duelen, A. Pradhan, R.L. Rovere, **H.L. Roderick**, and M. Sampaolesi. 2022. Cardiomyocyte differentiation from human induced pluripotent stem cells is delayed following knockout of Bcl-2. *J Cell Sci*. 136. doi:10.1242/jcs.260216.
5. Jin, X., M. Amoni, G. Gilbert, E. Dries, R.D. Puertas, A. Tomar, C.K. Nagaraju, A. Pradhan, D.I. Yule, T. Martens, R. Menten, P.V. Berghe, F. Rega, K. Sipido, and **H.L. Roderick**. (2022). InsP3R–RyR Ca2+ channel crosstalk facilitates arrhythmias in the failing human ventricle. *Basic Res Cardiol*. 117:60. doi:10.1007/s00395-022-00967-y.
6. Demydenko, K., S. Ekhteraei-Tousi, and **H.L. Roderick**. (2022). Inositol 1,4,5-trisphosphate receptors in cardiomyocyte physiology and disease. Philosophical Transactions Royal Soc B. 377:20210319. doi:10.1098/rstb.2021.0319.
7. Demydenko, K., K.R. Sipido, and **H.L. Roderick**. 2021. Ca2+ release via InsP3Rs enhances RyR recruitment during Ca2+ transients by increasing dyadic [Ca2+] in cardiomyocytes. J Cell Sci. 134: doi:10.1242/jcs.258671.
8. Puertas, R.D., R. Arora, S. Rome, B. Asatryan, **H.L. Roderick***, and P. Chevalier. 2021. Epigenetics in atrial fibrillation: a reappraisal. *Heart Rhythm*. doi:10.1016/j.hrthm.2021.01.007. co-senior Author.
9. Robinson EL, Alkass K, Bergmann O, Maguire JJ, **Roderick HL***, Davenport AP. 2020. Genes encoding ACE2, TMPRSS2 and related proteins mediating SARS-CoV-2 viral entry are upregulated with age in human cardiomyocytes. J Mol Cell Cardiol. 147:88-91. doi: 10.1016/j.yjmcc.2020.08.009. *co-senior author
10. Dries, E., M. Amoni, B. Vandenberk, D.M. Johnson, G. Gilbert, C.K. Nagaraju, R.D. Puertas, M. Abdesselem, D.J. Santiago, **H.L. Roderick**, P. Claus, R. Willems, and K.R. Sipido. 2020. Altered adrenergic response in myocytes bordering a chronic myocardial infarction underlies in vivo triggered activity and repolarization instability. The Journal of Physiology. JP278839. doi:10.1113/jp278839.
11. Gilbert, G., K. Demydenko, E. Dries, R.D. Puertas, X. Jin, K. Sipido, and **H.L. Roderick**. 2019. Calcium Signaling in Cardiomyocyte Function. *Cold Spring Harb Perspect Biol* doi:10.1101/cshperspect.a035428
12. Nagaraju, C.K., E.L. Robinson, M. Abdesselem, S. Trenson, E. Dries, G. Gilbert, S. Janssens, J. Van Cleemput, F. Rega, B. Meyns, **H.L. Roderick**, R.B. Driesen, and K.R. Sipido. 2019.

Myofibroblast Phenotype and Reversibility of Fibrosis in Patients With End-Stage Heart Failure. *J Am Coll Cardiol.* 73:2267–2282. doi:10.1016/j.jacc.2019.02.049.
13. Archer, C.R., E.L. Robinson, F.M. Drawnel, and **H.L. Roderick**. 2017. Endothelin-1 promotes hypertrophic remodelling of cardiac myocytes by activating sustained signalling and transcription downstream of endothelin type A receptors. *Cell Signal*. 36:240–254.
14. Thienpont, B., J.M. Aronsen, E.L. Robinson, H. Okkenhaug, E. Loche, A. Ferrini, P. Brien, K. Alkass, A. Tomasso, A. Agrawal, O. Bergmann, I. Sjaastad, W. Reik, and **H.L. Roderick**. 2017. The H3K9 dimethyltransferases EHMT1/2 protect against pathological cardiac hypertrophy. *J Clin Invest*. 127:335–348. doi:10.1172/JCI88353.
15. Drawnel, F.M., Wachten, D., Molkentin, J.D., Maillet, M., Aronsen, J.M., Swift F, Sjaastad, I., Liu, N., Catalucci, D., Mikoshiba, K., Hisatsune, C., Okkenhaug, H., Andrews, S.R., Bootman, M.D., **Roderick, H.L**. (2012) Mutual antagonism between IP3RII and miRNA-133a regulates calcium signals and cardiac hypertrophy. *J Cell Biol*. 199:783–798. Editorial Highlight 'In this Issue' and Cover Image.
16. Harzheim, D., Movassagh, M., Foo, R.S., Ritter, O., Tashfeen, A., Conway, S.J., Bootman, M.D. and **Roderick, H.L**. (2009) Increased InsP3Rs in the junctional sarcoplasmic reticulum augment Ca2+ transients and arrhythmias associated with cardiac hypertrophy. *Proc Natl Acad Sci U S A*, 106, 11406-11411. (Highlighted in Physiology)
17. Higazi, D.R., Fearnley, C.J., Drawnel, F.M., Talasila, A., Corps, E.M., Ritter, O., McDonald, F., Mikoshiba, K., Bootman, M.D. and **Roderick, H.L**. (2009) Endothelin-1-stimulated InsP3-induced Ca2+ release is a nexus for hypertrophic signaling in cardiac myocytes. *Mol Cell*, 33, 472-482. Editor's Choice Science Signalling.
18. Berridge, M.J., Bootman, M.D. and **Roderick, H.L.** (2003) Calcium signalling: dynamics, homeostasis and remodelling. *Nat Rev Mol Cell Biol*, 4, 517-529.

## Funding:

- The Roderick lab receives funding from the Flemish Research Funds (FWO), KULeuven (Internal, C1 and Global PhD studentships, Interuniversity funding (iBOF)) and from the KGJebsen Center for Cardiac Research (KGJ-CCR), Oslo, Norway.

## Awards and Recognition:

- Odysseus Award from the Flemish Research Funds (FWO), Belgium (2014-2019). Award to recruit top foreign researchers to Flemish Universities.
- Royal Society University Research Fellowship, The Royal Society, UK (2004-2012). This award of salary and working money is considered one of the most prestigious fellowships in the UK awarded across all scientific disciplines.
- In the last 5 years, HLR has been invited to speak at high level conferences including the ESC Congress, the Frontiers in Cardiovascular Biology of the ESC (proposed a session), ISHR European Section, Australian Physiological Society meeting, Gordon Conferences on Cardiac regulatory mechanisms on Cardiovascular Epigenetics and on Excitation Contraction Coupling.

## Departmental/Institutional Responsibilities:

HLR was an 'observer' on the Departmental board 2016-2020 and is a member of the current board. He contributed to writing of the current and previous Departmental 4 year Plans.

Teaching: At KULeuven, HLR contributed to the establishment of a new course on cardiovascular sciences taught through the medium of English to the medical students (Engels OPO cardiovascular diseases) and proposed and is coordinator of a new Bachelor course on Epigenetics, which will also be given in a modified form in the new medical student curriculum. At University of Cambridge, HLR lectures on cardiac calcium signalling in the Pharmacology course and contributes to practical sessions to the medical and veterinary students.

## Societies, Memberships:

- President of the Belgian Working Group of Basic Research in Cardiology (BWG-BRC) of the Belgian Society of Cardiology.
- Nucleus member and secretary of the European Society of Cardiology Working Group on Cardiac Electrophysiology.
- Member of the ISHR, the Physiological Society, the European Calcium Society and Belgian Society of Physiology and Pharmacology.

**Service (other):**

HLR is an editorial advisory board member of the Journal of Cardiovascular Research, JMCC plus, the Journal of Clinical Epigenetics and Frontiers in Oncology. He is a frequent reviewer for these as well other general and field-specific journals. HLR reviews grants for European Research Council (ERC; Junior, Senior and Advanced), the MRC, Wellcome Trust, BBSRC and BHF in the UK, ANR in France, Telethon in Italy and as well as organisations from other European countries.