ESC
Council
Cardiovascular Genomics

Elections to Council Nucleus and Nominating committee 2024-2026

Motivation letter: Why are you interested in joining the Council Nucleus or Nominating committee (250 words max)?

I believe I am in an excellent position to continue to contribute to the Council as a Nucleus member.

I am a current Nucleus member (2022-2024), have participated in the writing of 3 statements, will contribute to further 2 and to the organization of Cardiogenomics 2024.

I am an Inherited Cardiovascular Disease Consultant Cardiologist at St. Bartholomew's Hospital, London and Associate Professor at University College London.

Other past and present roles included Chairman of the Portuguese Working Group of Myocardial Diseases and member of the executive committee of the Portuguese Registry of Hypertrophic Cardiomyopathy; I led the analysis of the registry genetic data. I was an active contributor to the ESC EORP registry and have published an ancillary analysis. I am cardiology lead of the North Thames Hub of the NHS Genomics Service.

Throughout my career, I have built strong collaborations with fundamental science groups across a range of disciplines.

I have extensive expertise on the application and interpretation of genomics and have published novel insights regarding associations with outcome, non-coding variation and new genes. High impact publications as first and senior author focused on deep-intronic splice variants in HCM (Circulation Genomics), novel causal genes including *ALPK3* (EHJ), maximal wall thickness GWAS (Circulation Genomics), deep-phenotyping mutation carriers (Circulation and JACC).

Novel insights are allowing the direct application of genetics to risk stratification and driving therapeutic innovation. My experience aligns perfectly with the Council's mission of integrating genetics into routine practice and promoting knowledge, education and research in this field.

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Dr. Luís da Rocha Lopes, MD, PhD, FESC

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Education / Qualifications

Dates	Universities		Degree
10/1995 to 10/2001	University of Lisbon- Faculty of Medicine	Medicine	MD
04/2011 to 02/2015	University College London	Cardiovascular Science-	PhD

Professional History

Dates (month/year) From	To	Name of organisation and position held.
10/2022		Institute of Cardiovascular Science, University College London – Associate Professor (honorary)
02/2023		Cardiovascular Centre, Faculty of Medicine, University of Lisbon – Associate Professor (honorary)
09/2016		Barts Heart Centre, Barts Health NHS Trust – Consultant Cardiologist - Inherited Cardiovascular Disease Unit and Cardiac MRI Unit
08/2016	10/2022	Institute of Cardiovascular Science, University College London – Honorary Clinical Senior Lecturer
08/2015	02/2023	Cardiovascular Centre, Faculty of Medicine, University of Lisbon – Assistant Professor
02/2009	9/2016	Hospital Garcia de Orta, Almada, Portugal - Cardiologist
05/2004	7/2015	Cardiovascular Centre, Faculty of Medicine, University of Lisbon – Clinical Lecturer
05/2011	09/2013	Heart Hospital/UCLH – Clinical Research Fellow
01/2004	02/2009	Hospital Garcia de Orta, Almada, Portugal – Cardiology Resident
01/2002	12/2003	Hospital Garcia de Orta, Almada, Portugal –General Intern (equivalent to SHO)

Other Appointments and Affiliations

- Cardiology Specialty Lead, North Thames Genomic Laboratory Hub, London
- Nucleus Member of the Board of the European Society of Cardiology (ESC) Council on Cardiovascular Genomics (2022-2024)
- Fellow of the European Society of Cardiology (FESC)
- Member of the ESC Working Group on Myocardial and Pericardial Diseases
- Past Chairman (2013-2017) of the Portuguese Society of Cardiology Working Group on Myocardial and Pericardial Diseases
- Member of the European Association of Cardiovascular Imaging of the ESC

Grants

- Apr 2023-Apr 2026: Ischaemia in apical hypertrophic cardiomyopathy: clinical significance and potential therapeutic target – BHF Clinical Research Training Fellowship (Co-PI, secondary supervisor): £320,980
- July 2023-July 2025: Deep structural changes in Hypertrophic Cardiomyopathy, from mutation to hypertrophy- BMS project grant (PI): £180,000

- Jan 2023-Jan 2025: Novel human stem cell-based models of genetic cardiomyopathy as a platform for disease modelling and therapeutic development NHMRC 2022 MRFF (Co-I): £395,394
- Feb 2022-Feb 2024: Deep structural changes in Hypertrophic Cardiomyopathy – BHF Clinical Research Training Fellowship (Co-PI): £215,178
- Nov 2020-present: Investigating the causes of mutation-negative hypertrophic cardiomyopathy: Role of cryptic RNA mis-splicing in myosin binding protein C (MYBPC3) (Co-I) - BHF Project Grant - PG/20/10170 : £221,111
- Oct 2019 – Present: First Study of myocardial perfusion in hypertrophic cardiomyopathy patients and relatives using exercise stress cardiac magnetic resonance (PI) - UCL/UCLH BRC NIHR : £37,500
- Oct 2019 – Oct 2023: MRC Clinical Academic Research Fellowship: Discovering the causes of genotype-negative HCM (PI) - Medical Research Council/NIHR : £301,913
- Feb 2019-Sep 2023: Evaluating myocardial ischaemia to improve the care of hypertrophy cardiomyopathy patients and relatives (PI) - Barts Charity : £38,500
- Feb 2018-Feb 2020: Discovering novel genes in cardiomyopathy (Co-PI) - BRC Cardiovascular Diseases Theme – Small Grant Funding - UCL/UCLH NIHR : £21,887
- 2013-2014: The Heart Hospital Charitable Grant - New genetic determinants of disease phenotype in hypertrophic cardiomyopathy
- 2010-2013: Calouste Gulbenkian Foundation Advanced Medical Education (Doctoral Programme) -PhD Scholarship - 3 years stipend and tuition fees

Academic Supervision: PhD primary supervisor or co-supervisor: 4 current students, 1 past student as primary supervisor (completed PhD April 2024); 1 past student secondary supervisor (completed PhD 2022). Examiner of final PhD vivas; **Masters Degrees:** 1 current student; 6 past students.

Reviewer activity: I am a reviewer for high impact journals in the field including Circulation, Circulation Genomics and Precision Medicine, Circulation Heart Failure, European Heart Journal, JACC, JACC Imaging, European Heart Journal Cardiovascular Imaging. I am an abstract reviewer for the ESC Congress. I am a reviewer of grant proposals for the British Heart Foundation (BHF), Heart Research UK and UKRI Medical Research Council.

Academic career summary:

During my PhD (University College London (UCL) 2015), using a pioneer large-scale next-generation sequencing study in hypertrophic cardiomyopathy (HCM), I demonstrated novel genotype-outcome associations, the contribution of copy number variants, and co-developed an *insilico* pathogenicity prediction tool. Since my appointment as an honorary senior lecturer 2016 and then associate professor, I have been investigating the contribution of non-coding variation to cardiomyopathies and conducted a whole-exome-sequencing (WES) project in >1500 patients for new gene discovery. This resulted in high impact papers in Circulation, JACC, Circulation Genomics and Precision Medicine and European Heart Journal. Examples include previously unknown high prevalence of deep-intronic MYBPC3 splice variants, detecting causal mitochondrial DNA variants with WES, and the description of *ALPK3* as an autosomal dominant HCM gene. I am also leading research projects in cardiac magnetic resonance. For arrhythmogenic cardiomyopathy (AC), resulting in a characteristic fibrosis pattern description, now widely used by peers. In HCM mutation carriers, I have described for the first-time perfusion defects in carriers without hypertrophy. I have led a study on perfusion, disarray and ECGimaging in carriers and overt HCM; data has been presented in young investigator and best abstract sessions and the study was published in Circulation (July 2023, senior-last author) and JACC (Feb 2024, joint first author). My active involvement in a study using machine learning to analyse big imaging data from UK Biobank has led to the most recent description of HCM prevalence, published in JAMA Cardiology (first-author). I am leading on a project leveraging these data for redefining the genetic architecture of HCM via a genome wide association study (GWAS). I am coinvestigator in large international collaborative studies focusing on new gene discoveries, gene-first approaches and genotype-phenotype associations, resulting in publications in JACC, Circulation, Circulation Heart Failure, European Heart Journal, European Journal of Heart Failure. I had a very active role as coinvestigator of the ESC EuroObservational Research Program (EORP) registry in cardiomyopathies.

I have made significant contributions to teaching and education at both undergraduate and postgraduate level. I am involved in undergraduate teaching for medical students and in postgraduate masters courses including the UCL Cardiovascular Science MSc and the Cardiovascular Imaging MSc at University of Lisbon. I regularly teach and lecture at postgraduate meetings (e.g. at Royal Society of Medicine), national and international congresses, courses and events, mainly on Cardiovascular Genomics. I have authored education materials with international reach including three chapters on reference cardiology textbooks ("ESC Textbook on Cardiovascular Medicine" and "Hurst's The Heart"). I have been an external examiner of final theses vivas in the UK and overseas. I have successfully co-supervised a PhD student at the NOVA University of Lisbon (finished July 2022) and was primary supervisor of one UCL PhD student (who secured a BHF CTRF grant and finished April 2024) and I am currently secondary supervisor of another four (including

two funded with a BHF project grant). I have also successfully supervised MSc students as primary supervisor; the majority of theses were published.
I am a peer reviewer for Medical Research Council, Heart Research UK and BHF grant schemes and have extensively reviewed for high impact journals in my field and for the European society of Cardiology. Throughout the last 5 years, I have developed close links with research groups across faculties, including the MRC Centre for Neuromuscular Disease (mitochondrial causes of cardiomyopathy), Structural and Molecular biology (in silico prediction of variant pathogenicity), Children Cardiovascular Disease (RAS-Mapk variants). I have also built ongoing research collaborations with colleagues at other Universities including King's College London (Z-disc genes), Institute of Molecular Medicine - University of Lisbon (stem cell modelling) and Queen Mary University of London (machine learning and UK Biobank). All resulted in productive research and publications. The work described above, where I have been dissecting the causes of previously genotype-elusive patients, has generated a very high interest by peers, including an editorial and highlight, citations in review papers, and media attention.
My research has direct impact on clinical practice, with the results of genetic studies described above continuously providing diagnostic results to patients and families in the last 10 years. The clinical translation has been immediate; the new genetic mechanisms described increased the yield of genetic testing in clinical practice. I have been invited to consultancy roles by pharmaceutical companies, machine learning developers and gene testing companies.
In earlier career stages, I was chair of the Portuguese Working Group on Myocardial and Pericardial Diseases 2013-2017. I was an invited reviewer of the Spanish Society of Cardiology recommendations on genetic testing and ESC Guidelines of Pericardial Disease. I was appointed in 2022 as clinical lead for cardiology for the NHS Genomic Service North East Thames Genomic Laboratory Hub; this allows me to shape testing indications and relevant pathways regionally and nationally. I was elected in July 2022 for the nucleus of the ESC Council on Cardiovascular Genomics, which will provide further opportunities to contribute to the development of International guidance and education in the field.
I have been awarded an MRC-NIHR Clinical Academic Research Partnership (Oct 2019-Oct 2023) and an NIHR Development and Skills Enhancement (DSE) award in 2023.

List of selected publications:

1. Joy G, **Lopes LR (joint first author)**, (…), Moon JC, Orini M, Captur G. Electrophysiological Characterization of Subclinical and Overt Hypertrophic Cardiomyopathy by Magnetic Resonance Imaging-Guided Electrocardiography. J Am Coll Cardiol. 2024 Mar 19;83(11):1042-1055. doi: 10.1016/j.jacc.2024.01.006.

2. Joy G, Kelly CI, Webber M, Pierce I, Teh I, McGrath L, Velazquez P, Hughes RK, Kotwal H, Das A.....**Lopes LR**. Microstructural and microvascular phenotype of sarcomere mutation carriers and overt hypertrophic cardiomyopathy. Circulation. 2023. doi: 10.1161/CIRCULATIONAHA.123.063835.

3. Garcia Brás P, Rosa SA, Cardoso I, Branco LM, Galrinho A, Gonçalves AV, Thomas B, Viegas JM, Fiarresga A, Branco G, Pereira R, Selas M, Silva F, Cruz I, Baquero L, Ferreira RC, **Lopes LR**. Microvascular Dysfunction Is Associated With Impaired Myocardial Work in Obstructive and Nonobstructive Hypertrophic Cardiomyopathy: A Multimodality Study. J Am Heart Assoc. 2023 Apr 18;12(8):e028857. doi: 10.1161/JAHA.122.028857.

4. Hughes RK, Augusto JB, Knott K, Davies R, Shiwani H, Seraphim A, Malcolmson JW, Khoury S, Joy G, Mohiddin S, **Lopes LR**, McKenna WJ, Kellman P, Xue H, Tome M, Sharma S, Captur G, Moon JC. Apical Ischemia Is a Universal Feature of Apical Hypertrophic Cardiomyopathy. Circ Cardiovasc Imaging. 2023 Mar;16(3):e014907. doi: 10.1161/CIRCIMAGING.122.014907. Epub 2023 Mar 21. PMID: 36943913

5. Joy G, Moon JC, **Lopes LR**. Detection of subclinical hypertrophic cardiomyopathy. Nat Rev Cardiol. 2023 Jun;20(6):369-370. doi: 10.1038/s41569-023-00853-7. PMID: 36869094

6. Aung N, **Lopes LR (joint first author)**, van Duijvenboden S, Harper AR, Goel A, Grace C, Ho CY, Weintraub WS, Kramer CM, Neubauer S, Watkins HC, Petersen SE, Munroe PB. Genome-Wide Analysis of Left Ventricular Maximum Wall Thickness in the UK Biobank Cohort Reveals a Shared Genetic Background With Hypertrophic Cardiomyopathy. Circ Genom Precis Med. 2023 Feb;16(1):e003716. doi: 10.1161/CIRCGEN.122.003716. Epub 2023 Jan 4. PMID: 36598836

7. Savvatis K, Vissing CR, Klouvi L, Florian A, Rahman M, Béhin A, Fayssoil A, Masingue M, Stojkovic T, Bécane HM, Berber N, Mochel F, Duboc D, Fontaine B, Krett B, Stalens C, Lejeune J, Pitceathly RDS,

Lopes L, Saadi M, Gossios T, Procaccio V, Spinazzi M, Tard C, De Groote P, Dhaenens CM, Douillard C, Echaniz-Laguna A, Quinlivan R, Hanna MG, Yilmaz A, Vissing J, Laforêt P, Elliott P, Wahbi K. Cardiac Outcomes in Adults With Mitochondrial Diseases. J Am Coll Cardiol. 2022 Oct 11;80(15):1421-1430. doi: 10.1016/j.jacc.2022.08.716.

8. de Frutos F, Ochoa JP, Navarro-Peñalver M, Baas A, Bjerre JV, Zorio E, Méndez I, Lorca R, Verdonschot JAJ, García-Granja PE, Bilinska Z, Fatkin D, Fuentes-Cañamero ME, García-Pinilla JM, García-Álvarez MI, Girolami F, Barriales-Villa R, Díez-López C, **Lopes LR**, Wahbi K, García-Álvarez A, Rodríguez-Sánchez I, Rekondo-Olaetxea J, Rodríguez-Palomares JF, Gallego-Delgado M, Meder B, Kubanek M, Hansen FG, Restrepo-Córdoba MA, Palomino-Doza J, Ruiz-Guerrero L, Sarquella-Brugada G, Perez-Perez AJ, Bermúdez-Jiménez FJ, Ripoll-Vera T, Rasmussen TB, Jansen M, Sabater-Molina M, Elliot PM, Garcia-Pavia P; European Genetic Cardiomyopathies Initiative Investigators. Natural History of MYH7-Related Dilated Cardiomyopathy. J Am Coll Cardiol. 2022 Oct 11;80(15):1447-1461. doi: 10.1016/j.jacc.2022.07.023. Epub 2022 Aug 22. PMID: 36007715

9. Protonotarios A, Bariani R, Cappelletto C, Pavlou M, García-García A, Cipriani A, Protonotarios I, Rivas A, Wittenberg R, Graziosi M, Xylouri Z, Larrañaga-Moreira JM, de Luca A, Celeghin R, Pilichou K, Bakalakos A, **Lopes LR**, Savvatis K, Stolfo D, Dal Ferro M, Merlo M, Basso C, Freire JL, Rodriguez-Palomares JF, Kubo T, Ripoll-Vera T, Barriales-Villa R, Antoniades L, Mogensen J, Garcia-Pavia P, Wahbi K, Biagini E, Anastasakis A, Tsatsopoulou A, Zorio E, Gimeno JR, Garcia-Pinilla JM, Syrris P, Sinagra G, Bauce B, Elliott PM. Importance of genotype for risk stratification in arrhythmogenic right ventricular cardiomyopathy using the 2019 ARVC risk calculator. Eur Heart J. 2022 Aug 21;43(32):3053-3067. doi: 10.1093/eurheartj/ehac235. PMID: 35766183

10. Shah RA, Asatryan B, Sharaf Dabbagh G, Aung N, Khanji MY, **Lopes LR**, van Duijvenboden S, Holmes A, Muser D, Landstrom AP, Lee AM, Arora P, Semsarian C, Somers VK, Owens AT, Munroe PB, Petersen SE, Chahal CAA; Genotype-First Approach Investigators. Frequency, Penetrance, and Variable Expressivity of Dilated Cardiomyopathy-Associated Putative Pathogenic Gene Variants in UK Biobank Participants. Circulation. 2022 Jul 12;146(2):110-124. doi: 10.1161/CIRCULATIONAHA.121.058143. Epub 2022 Jun 16. PMID: 35708014

11. **Lopes LR**, Losi MA, Sheikh N, Laroche C, Charron P, Gimeno J, Kaski JP, Maggioni AP, Tavazzi L, Arbustini E, Brito D, Celutkiene J, Hagege A, Linhart A, Mogensen J, Garcia-Pinilla JM, Ripoll-Vera T, Seggewiss H, Villacorta E, Caforio A, Elliott PM; Cardiomyopathy Registry Investigators Group. Association between common cardiovascular risk factors and clinical phenotype in patients with hypertrophic cardiomyopathy from the European Society of Cardiology (ESC) EurObservational Research Programme (EORP) Cardiomyopathy/Myocarditis registry. Eur Heart J Qual Care Clin Outcomes. 2022 Dec 13;9(1):42-53. doi: 10.1093/ehjqcco/qcac006. PMID: 35138368

12. Hughes RK, Camaioni C, Augusto JB, Knott K, Quinn E, Captur G, Seraphim A, Joy G, Syrris P, Elliott PM, Mohiddin S, Kellman P, Xue H, **Lopes LR (joint last-senior author)**, Moon JC. Myocardial Perfusion Defects in Hypertrophic Cardiomyopathy Mutation Carriers. J Am Heart Assoc. 2021 Aug 3;10(15):e020227. doi: 10.1161/JAHA.120.020227. Epub 2021 Jul 27. PMID: 34310159

13. **Lopes LR** et al . Alpha-protein kinase 3 (ALPK3)-truncating variants are a cause of autosomal dominant hypertrophic cardiomyopathy. European Heart Journal, ehab424, https://doi.org/10.1093/eurheartj/ehab424. Published: 15 July 2021

14. **Lopes, L. R.**, Murphy, D., Bugiardini, E., Salem, R., Jager, J., Futema, M., . . . Elliott, P. M. (2021). Iterative Reanalysis of Hypertrophic Cardiomyopathy Exome Data Reveals Causative Pathogenic Mitochondrial DNA Variants.. Circulation: Genomic and Precision Medicine. doi:10.1161/CIRCGEN.121.003388

15. **Lopes, L. R.**, Aung, N., van Duijvenboden, S., Munroe, P. B., Elliott, P. M., & Petersen, S. E. (2021). Prevalence of Hypertrophic Cardiomyopathy in the UK Biobank Population.. JAMA Cardiol. doi:10.1001/jamacardio.2021.0689

16. Augusto, J. B., Davies, R. H., Bhuva, A. N., Knott, K. D., Seraphim, A., Alfarih, M., …**Lopes LR** . . Moon, J. C. (2020). Diagnosis and risk stratification in hypertrophic cardiomyopathy using machine learning wall thickness measurement: a comparison with human test-retest performance. The Lancet Digital Health. doi:10.1016/s2589-7500(20)30267-3

17. Protonotarios A, Brodehl A, Asimaki A, Jager J, Quinn E, Stanasiuk C, Ratnavadivel S, Futema M, Akhtar MM, Gossios TD, Ashworth M, Savvatis K, Walhorn V, Anselmetti D, Elliott PM, Syrris P, Milting H, **Lopes LR**. The novel desmin variant p.Leu115Ile is associated with a unique form of biventricular Arrhythmogenic Cardiomyopathy. Can J Cardiol. 2020 Dec 5:S0828-282X(20)31136-3. doi: 10.1016/j.cjca.2020.11.017. Online ahead of print.

18. Lorenzini M, Norrish G, Field E, Ochoa JP, Cicerchia M, Akhtar MM, Syrris P, **Lopes LR**, Kaski JP, Elliott PM. Penetrance of Hypertrophic Cardiomyopathy in Sarcomere Protein Mutation Carriers. J Am Coll Cardiol. 2020 Aug 4;76(5):550-559.

19. Lopez-Sainz A, Dominguez F, **Lopes LR**, Ochoa JP, Barriales-Villa R, Climent V, Linschoten M, Tiron C, Chiriatti C, Marques N, Rasmussen TB, Espinosa MÁ, Beinart R, Quarta G, Cesar S, Field E, Garcia-Pinilla JM, Bilinska Z, Muir AR, Roberts AM, Santas E, Zorio E, Peña-Peña ML, Navarro M, Fernandez A, Palomino-Doza J, Azevedo O, Lorenzini M, García-Álvarez MI, Bento D, Jensen MK, Méndez I, Pezzoli L, Sarquella-Brugada G, Campuzano O, Gonzalez-Lopez E, Mogensen J, Kaski JP, Arad M, Brugada R, Asselbergs FW, Monserrat L, Olivotto I, Elliott PM, Garcia-Pavia P; European Genetic Cardiomyopathies Initiative Investigators. Clinical Features and Natural History of PRKAG2 Variant Cardiac Glycogenosis. J Am Coll Cardiol. 2020 Jul 14;76(2):186-197.

20. **Lopes LR**, Barbosa P, Torrado M, Quinn E, Merino A, Ochoa JP, Jager J, Futema M, Carmo-Fonseca M, Monserrat L, Syrris P, Elliott PM. Cryptic Splice-Altering Variants in MYBPC3 Are a Prevalent Cause of Hypertrophic Cardiomyopathy. Circ Genom Precis Med. 2020 Jun;13(3):e002905.

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22. **Lopes LR**, Futema M, Akhtar MM…Elliot PM, Prevalence of TTR variants detected by whole-exome sequencing in hypertrophic cardiomyopathy, Amyloid 2019 Dec;26(4):243-247

23. Augusto JB (…) **Lopes LR**. Dilated cardiomyopathy and arrhythmogenic left ventricular cardiomyopathy: a comprehensive genotype-imaging phenotype study. European Heart Journal Cardiovascular Imaging 2019 Jul 16 pii: jez188

24. Al-Numair NS, **Lopes L**, (…), Martin AC. The structural effects of mutations can aid in differential phenotype prediction of beta-myosin heavy chain (Myosin-7) missense variants. Bioinformatics. 2016 Oct 1;32(19):2947-55.

25. **Lopes LR**, Syrris P, Guttmann OP, O'Mahony C, Tang HC, Dalageorgou C, Jenkins S, Hubank M, Monserrat L, McKenna WJ, Plagnol V, Elliott PM. Novel genotype-phenotype associations demonstrated by high-throughput sequencing in patients with hypertrophic cardiomyopathy. Heart. 2015 Feb 15;101(4):294-301.

26. Captur G, **Lopes LR**, (…), Moon JC. Abnormal cardiac formation in hypertrophic cardiomyopathy: fractal analysis of trabeculae and preclinical gene expression. Circulation Cardiovasc Genet. 2014 Jun;7(3):241-8.

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