BIOGRAPHICAL SKETCH STEPHANE HEYMANS

NAME Heymans, Stephane	POSITION TITLE Professor of Cardiomyopathies		
Born, 14 November 1970 in Brussels			
INSTITUTION AND LOCATION	DEGREE *(if applicable)*	YEAR(s)	FIELD OF STUDY
Leuven University, Belgium Leuven University, Belgium Maastricht University Medical Centre, Netherland	MD PhD Cardiologist Professor	1995 2000 2003 2011	Medicine PhD Heart Failure Cardiomyopathies

Current international appointments.

- Professor of Inflammation and Matrix Biology, University of Leuven, Belgium. (2010-)
- Vice-Chair of the Study Group of Myocarditis of the the Heart Failure Association of the European Society of Cardiology.
- Scientific advisory Board, CNIC Spanish National Cardiovascular Research Centre Madrid, Spain (2020-)
- Scientific advisory board, INSERM, Paris, PARCC U970, France (2020-)

- Cardiologist and Research Scientist since 2003 focusing on the molecular mechanisms of heart failure, cardiomyopathies and myocarditis in particular, looking at the interplay between inflammatory cells, fibroblasts and cardiomyocytes. Unraveled the key role of structural and non-structural matrix proteins, including matrix metalloproteinases, collagens and matri-cellular proteins, in mediating cardiac inflammation, fibrosis and dysfunction.
- Professor of Cardiomyopathies within the Netherlands Heart Institute (2009-), the Maastricht University Hospital (2009-), and Professor of Matrix Biology and Inflammation at the University of Leuven (2010-). Conducted research for preclinical (50 %) and clinical (50 %) work as a cardiologist, resulted in increasing funding's, a growing lab, and related extensive national and international collaborative network.

Prof.dr. Stephane Heymans is a Cardiologist and Research Scientist since 2003 focusing on the molecular mechanisms of heart failure, cardiomyopathies and myocarditis in particular, looking at the interplay between inflammatory cells, fibroblasts and cardiomyocytes. Dr. Stephane Heymans established a completely new area of clinical work and research to investigate the yet unknown role of inflammation in cardiac diseases, including non-ischemic cardiomyopathies, diastolic dysfunction, myocarditis and pericarditis and their use as therapeutic and biomarkers. He is Professor of Cardiomyopathies at the Maastricht University Hospital (2009-), and Professor of Matrix Biology and Inflammation at the University of Leuven (2010-). Acknowledged for developing a clinical programme, cohort and biobank on non-ischemic cardiomyopathies (diastolic dysfunction, dilated cardiomyopathies and myocarditis) (over 1200 patients with >17 yrs follow-up) which is now being "used" as a top-profiling clinical programme within the centre of excellence initiatives of the University together with the hospital in Maastricht. This Cardiomyopathy care programme includes the involvement of immunologist, virologists, pathologists and geneticians.

The sudden death of young adults due to myocarditis and genetic cardiomyopathies was the main trigger for his cardiomyopathy research line, supported by both Dr Dekker Fellowship (2003), Dutch Heart Foundation, Junior Staff Member, and the prestigious NWO-VIDI grant (2009). Utilized translational projects to collect patient data and cardiac samples in metabolic risk-induced HFPEF (FP7-MEDIA 2011 and FP7-Homage 2013), toxic (FP7-Hecatos 2013) and viral CMP (VIDI and FP7-Homage). His work has also been supported by the Dutch Heart Foundation, Dr. E. Dekker junior staff member research position in 2003., project grants (2006, 2007, 2008, CVONs: 2013, 2015, 2017). In Belgium, where he is a Professor of Matrix Biology and Inflammation, he has got numerous FWO Research grants (2000, 2007, 2009, 2010, 2016, 2017, 2019) attributed to PhD or post-doc projects, the latter ones in close collaboration with dr. E. Jones, also co-supervisor and appointed in his Maastrich group.
In 2018-2020, he has been chair of the Basic Science Section and part the Executive committee of the board of the Heart Failure Association of the ESC, chair of the Working Group of Myocardial Function of the ESC (2015-2018), and chair of the Committee on Translational Research of the HFA/ESC (2014-2018). His work was recognized by the

Outstanding Achievement Award of the European Society of Cardiology, for Basic Cardiovascular research (2015); the Leon Dumont Investigator Award of the Belgian Society of Cardiology, European Cardiovascular Research Award (2013).
Dr. Stephane Heymans has authored since 1999 many peer reviewed journals. His publications reflect his spirit of translating his clinical work on cardiomyopathies to the bench, and *vice versa*.

1. Hazebroek MR, Moors S, Dennert R, van den Wijngaard A, Krapels I, Hoos M, Verdonschot J, Merken JJ, de Vries B, Wolffs PF, Crijns HJ, Brunner-La Rocca HP, Heymans S. Prognostic relevance of gene-environment interactions in dilated cardiomyopathy patients: applying the MOGES classification. J. Am. Col. Card (JACC): 2015; Sep 22;66(12):1313-23. (https://pubmed.ncbi.nlm.nih.gov/26383716/)
   - In this landmark paper, we evaluate, using the Maastricht CMP Cohort, the prognostic relevance of gene-environment interactions in dilated cardiomyopathy patients by applying the MOGES classification
2. A novel 72-kDa leukocyte-derived osteoglycin enhances the activation of toll-like receptor 4 and exacerbates cardiac inflammation during viral myocarditis. Rienks M, Papageorgiou A,Verhesen W, Carai P, Summer G, Westermann D, Heymans S. Cell Mol Life Sci. 2016 Nov 23. https://pubmed.ncbi.nlm.nih.gov/27878326/
   - In human and murine viral myocarditis, we reveal a central role of 72-kDa leukocyte-derived osteoglycin that by activating the toll-like receptor 4 exacerbates cardiac inflammation during viral myocarditis.
3. Immunosuppressive Therapy Improves Both Short- and Long-Term Prognosis in Patients With Virus-Negative Nonfulminant Inflammatory Cardiomyopathy. Merken J, Hazebroek M, Van Paassen P, Verdonschot J, Van Empel V, Knackstedt C, Abdul Hamid M, Seiler M, Kolb J, Hoermann P, Ensinger C, Brunner-La Rocca HP, Poelzl G, Heymans S. Circ Heart Fail. 2018 Feb;11(2). (https://pubmed.ncbi.nlm.nih.gov/29449368/)
   - In a subgroup of DCM patients with increased cardiac inflammation and auto-immuen pathology, we demonstrate that immunosuppressive therapy improves both short- and long-term prognosis.
4. Mutations in LZTR1 drive human disease by dysregulating RAS ubiquitination. Steklov M, Pandolfi S, Baietti MF, Batiuk A, Carai P, Najm P, Zhang M, Jang H, Renzi F, Cai Y, Abbasi Asbagh L, Pastor T, De Troyer M, Simicek M, Radaelli E, Brems H, Legius E, Tavernier J, Gevaert K, Impens F, Messiaen L, Nussinov R, Heymans S, Eyckerman S, Sablina AA. Science. 2018 Dec 7;362(6419):1177-1182. (https://pubmed.ncbi.nlm.nih.gov/30442762/)
   - Here, a mutation in an inflammation related mitochondrial gene (LZTR1) is an important underlying mechanism for increased cardiac inflammation, fibrosis, hypertrophy and dysfunction.
5. Titin cardiomyopathy leads to altered mitochondrial energetics, increased fibrosis and long-term life-threatening arrhythmias. Verdonschot JAJ, Hazebroek MR, Derks KWJ, Barandiarán Aizpurua A, Merken JJ, Wang P, Bierau J, van den Wijngaard A, Schalla SM, Abdul Hamid MA, van Bilsen M, van Empel VPM, Knackstedt C, Brunner-La Rocca HP, Brunner HG, Krapels IPC, Heymans SRB. Eur Heart J. 2018 Mar 7;39(10):864-873.
   - This paper identifies specific inflammation and mitochondria related pathways in TTNtv cardiomyopathy patients, making them prone to increased cardiac fibrosis and arrhythmias. (https://pubmed.ncbi.nlm.nih.gov/29377983/)
6. Investigator initiated Clinical Trial: Intravenous Immunoglobulin (IVIg) for Parvovirus B19(PVB19) Mediated Cardiomyopathy (NCT00892112).
   - Investigator (Heymans) driven clinical trial initiated by Stephane Heymans, double blinded randomized placebo-controlled trial, ended in 2019. (https://clinicaltrials.gov/ct2/show/NCT00892112?term=Heymans&cond=Cardiomyopathy&cntry=NL&draw=2&rank=2)
7. Phenotypic clustering of dilated cardiomyopathy patients highlights important pathophysiological differences. Verdonschot JAJ, Merlo M, Dominguez F, Wang P, Henkens MTHM, Adriaens ME, Hazebroek MR, Masè M, Escobar LE, Cobas-Paz R, Derks KWJ, van den Wijngaard A, Krapels IPC, Brunner HG, Sinagra G, Garcia-Pavia P, Heymans SRB. Eur Heart J. 2020 Nov 6:ehaa841. (https://pubmed.ncbi.nlm.nih.gov/33156912/)
   - The present study identified four different DCM phenogroups associated with significant differences in clinical presentation, underlying molecular profiles related to inflammation, paving the way for a more personalized treatment approach based on immunomodulatory therapy, as being studied in the current project..