

# Cardiac fibrotic models



**Dr Gabriela Kania**

**Center of Experimental Rheumatology**

**Department of Rheumatology**

**University Hospital in Zurich, Switzerland**

A broad range of pathologic cardiac conditions is associated with myocardial tissue remodelling and fibrosis. Cardiac fibrosis represents a serious clinical problem. Progressive cardiac fibrosis has been recognized to cause life threatening arrhythmias. Development of novel treatment strategies is currently limited by the lack of the relevant experimental models in a human genetic context. Improvement of life-saving therapeutic strategies and new medications requires extensive scientific efforts to understand the pathophysiology of pro-arrhythmogenic fibrosis, which is currently poorly understood.

In experimental research, we studied cardiac fibrogenesis and alteration in the conduction system leading to cardiac arrhythmias in mouse model with gold-standard and novel functional and molecular methods. Likewise, we identified a novel key stromal cellular source of pathological myofibroblasts and indicated the overall role of systemic inflammation in fatal changes in the conduction system. Although mouse

models are helpful for research by reflecting complexity of the living organism, they lack the human genetic context. Development of induced pluripotent stem cell (iPSC) technology allowed for generation of human iPSC-derived cardiomyocytes, which have been successfully applied for congenital and drug-induced arrhythmic heart disease modelling *in vitro*. Human iPSC-derived cardiomyocytes together with cardiac fibroblasts have been also used to fabricate threedimensional cardiac microtissues (also called organoids). Such cardiac microtissues show structure with well-developed myofibrils and recapitulate cardiac functionality including responsiveness to electrical stimulation. Using human cardiac microtissues, we successfully established *in vitro* model of cardiac fibrosis. This novel *in vitro* technology represents an animal-free, cost-effective, high-throughput model that may be a highly attractive alternative to study fibrotic and arrhythmic processes in hearts.

# Curriculum Vitae

Dr Gabriela Kania

## Education:

- 1998** MSc, Faculty of Biology and Earth Sciences of the Jagiellonian University in Krakow/Poland
- 2001** PhD, Department of Animal Reproduction, National Institute of Animal Production in Balice/Krakow/Poland.
- 2009** Lecturer, Institute of Physiology, University of Zurich/Switzerland
- 2013** Habilitation, Faculty of Medicine, University of Zurich/Switzerland

## Staff Positions:

- 1998 - 2002** PhD student position and a research assistant position in the National Research Institute of Animal Production, Department of Animal Reproduction, Balice/Krakow, Poland (Head: Prof. Zdzislaw Smorag)
- 2002 - 2005** Post-doc position at the In Vitro Differentiation Group, IPK Gatersleben, Germany (Head: Prof. Anna M. Wobus)
- 2005 - 2009** Post-doc position in Experimental Critical Care Medicine Group, University Hospital Basel, Switzerland (Head: Prof. Dr. Urs Eriksson)
- 2009 - 2012** Independent research associate in Cardioimmunology (Head: Prof. Dr. Urs Eriksson) in Cardiovascular Research Department headed by Prof. Dr. Thomas F. Lüscher, Institute of Physiology, University of Zurich, Switzerland
- 2012 - 2013** Deputy group leader in Cardioimmunology (Head: Prof. Urs Eriksson) in Cardiovascular Research Department headed by Prof. Dr. Thomas F. Lüscher, Institute of Physiology, University of Zurich, Switzerland
- 2013-now** Group leader in Center of Experimental Rheumatology, Department of Rheumatology (Head: Prof. Dr. Oliver Distler), University Hospital Zurich, Bio-Technopark Schlieren, Switzerland

## Institutional responsibilities:

Leading own research group, directing research projects, managing research groups, organizing the funding, teaching, biosafety officer, organization of animal licenses and contact with Veterinary Office.

### Approved research projects\_grant funding:

2009	Swiss Heart Foundation, main applicant
2010-2012	Marie Heim-Vögtlin grant from Swiss National Science Foundation, main applicant PMPDP3_129013
2010	Olga Mayenfisch Stiftung, main applicant
2010-2013	Swiss National Science Foundation, co-applicant 32003B_130771
2010	Cardiovascular Biology Prize of the Swiss Society of Cardiology
2010	Hartmann Müller Stiftung, main applicant
2011	Holcim Foundation, main applicant
2013	Hartmann Müller Stiftung, main applicant
2013	Swiss Heart Foundation, main applicant
2014-2017	Swiss National Science Foundation, main applicant 310030_152876/1
2015	Bayer, Grant4Target, main applicant
2015	Kunt und Senta Hermann Stiftung, main applicant
2016	Hermann Klaus Stiftung, main applicant
2016	Forschungskredit UZH, supervisor
2016	Helmut Horten Stiftung, main applicant
2016	Eglli Stiftung, main applicant
2016	Baugarten Stiftung, main applicant
2017	Hartmann Müller Stiftung, main applicant
2017	Novartis Stiftung, main applicant
2017-2021	Swiss National Science Foundation, main applicant 310030_175663
2017	Swiss Heart Foundation, main applicant
2018	Swiss Life Jubiläumsstiftung, main applicant

### Teaching activities (summary information):

2009-2013	Teaching assistant during courses for students at the Institute of Physiology, University of Zurich, Switzerland
2011	Summer School 2011 for students (SFB-Transregio 19) Robert Koch Institute Berlin, Germany
2012	SmArt Symposium for SmArt fellows within FP7 project: Vascular Progenitors in Biology and Medicine; Fribourg, Switzerland
2014-now	Teaching in: Master Human Biology course: BME303; Molecular Methods for Autoimmune Diseases (4561,WBAT1429); Molecular methods training course (2922, RHE0S030) at the University Hospital Zurich/University of Zurich

**Active memberships in scientific societies, fellowships in renowned academies:**

**Membership:** Member of Zurich Center for Integrative Human Physiology (ZIHP), Swiss Stem Cell Network, Life Sciences Switzerland LS2

**Grant application reviewer:** European Commission within Horizon 2020 , National Science Center in Poland

**Editing:** Lead Guest Editor of the Special Issue Stem Cells International 2011:Nov 30; Member of the Editorial Board of “Stem Cell

Studies”, Member of the Editorial Board of “European Heart Journal”

**Manuscript reviewer:** “European Heart Journal”, “Circulation”, “Circulation Research”, “Annals of the Rheumatic Diseases “, “Current Cardiology Reviews”, “Transgenic Research”, “Journal of Inflammation”, “Stem Cell Studies”, “Cells Tissues Organs”, “Stem Cells international”, “The International Journal of Biochemistry & Cell Biology”, “Plos One”

**Prizes, awards, fellowships:**

2009 Swiss National Foundation Marie Heim-Vögtlin subsidy for Women in Science

2010 Cardiovascular Biology Prize of the Swiss Society of Cardiology 2010

2010 European Heart Journal Elite Reviewer Award

2011 European Heart Journal Elite Reviewer Award

**List of Publications within last five years (The citation according to Google Scholar):**

**Citations: All: 3038 Since 2014: 1057**

**h-index: All: 23 Since 2014: 17**

**i10-index: All: 31 Since 2014: 22**

1. Kozlova A., Pachera E., Maurer B., Jüngel A., Distler J.H.W., Kania G\*#, Distler O. MicroRNA-125b Regulates Fibroblast Apoptosis and Proliferation in Systemic Sclerosis. *Arthritis & Rheumatology* in press

2. Kania G.\*, Rudnik M., Distler O. Involvement of the myeloid cell compartment on fibrogenesis in systemic sclerosis. *Nature Reviews Rheumatology* in press

3. Blyszczuk P., Müller-Edenborn B., Valenta T., Osto E., Stellato M., Behnke S., Glatz K., Basler K., Lüscher TF., Distler O., Eriksson U., Kania G\*. TGF- $\beta$ -dependent Wnt secretion controls myofibroblast formation and myocardial fibrosis progression in experimental autoimmune myocarditis. *European Heart Journal*. 2017 May 7;38(18):1413-1425

4. Müller-Edenborn B., Kania G., Osto E., Jakob P., Beck-Schimmer B., Blyszczuk P., Eriksson U. Lidocaine Enhances Contractile Function of Ischemic Myocardial Regions in Mouse Model of Sustained Myocardial Ischemia. *Plos One*. 2016 May 3;11(5):e0154699.
5. Thelemann C., Haller S., Blyszczuk P., Kania G., Rosa M., Eriksson U., Rotman S., Reith W., Acha-Orbea H. Absence of nonhematopoietic MHC class II expression protects mice from experimental autoimmune myocarditis. *Eur J Immunol*. 2016 March.
6. Kania G., Siegert S., Behnke S., Prados-Rosales R., Casadevall A., Lüscher TF, Luther SA, Kopf M., Eriksson U., Blyszczuk P. Innate signalling promotes formation of regulatory nitric oxide-producing dendritic cells limiting T cell expansion in experimental autoimmune myocarditis. *Circulation* 2013 Jun 11;127(23):2285-94.
7. Blyszczuk P., Behnke S., Lüscher TF., Eriksson U., \*Kania G. GM-CSF turns heart-infiltrating progenitors into functional dendritic cells in inflammatory cardiomyopathy. *Biochim Biophys Acta-Mol Cell Res* 2013 Apr;1833(4):934-44.
8. Blyszczuk P., Berthonneche C., Behnke S., Glönkler M, Moch H., Pedrazzini T., Lüscher TF., Eriksson U., \*Kania G. Nitric oxide synthase 2 is required for conversion of inflammatory pro-fibrotic CD133+ progenitors into F4/80+ macrophages in experimental autoimmune myocarditis. *Cardiovascular Res*. 2013 Feb 1;97(2):219-29.
9. Speer T., Rohrer L., P Blyszczuk P., Shroff R., Kuschnerus K., Kränkel N., Kania G., Zewinger S., Martin T., Akhmedov A., Shi Y., Perisa D., Winnik S., Müller MF., Wernicke G., Jung A., Gutteck U., Deanfield J., von Eckardstein A., Lüscher TF., Fliser D., Bahlmann F., and Landmesser U. Abnormal High-Density Lipoprotein Induces Endothelial Dysfunction via Activation of Toll-Like Receptor-2. *Immunity* 2013 Mar 5 [Epub ahead of print].
10. Van Heeswijk R., De Blois J., Kania G., Gonzales C., Blyszczuk P., Stuber M., Eriksson U., Schwitter J. Selective *in-vivo* visualization of immune-cell infiltration in a mouse model of autoimmune myocarditis by fluorine-19 cardiac magnetic resonance. *Circulation CV imaging* 2013 Mar 1;6(2):277-84.