

Maturation of human cardiomyocytes using advanced systems for *in vitro* heart tissue culture



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Animal models, although very useful are often far from mimicking human physiology. On the other hand, classical cell cultures lack the *in vivo* environment complexity. FDA and EMA both have noted the problems with currently used models concerning drug development and evaluation processes. Since few years an intensive institutional support to develop Advanced Cell/Tissue Culture models is observed. According to published reports, these models should be obligatory employed in drug development as early as 2025.

Here, we have developed a micro-flow-based system for increased maturation and environmental control of human iPSC-derived cardiomyocytes. In this system iPSC-derived CMs show superior morphology, metabolism and physiology over static cultures. Additionally, we have developed a controlled environment with oxygen on-demand regulation that could be used to mimic heart diseases. This could be further developed into more advanced system and is currently used in basic cardiology research.

Curriculum Vitae

Dr Tomasz Kolanowski

Tomasz Kolanowski (PhD) specializes in tissue engineering and stem cell biology. He has graduated from University of Life Science in Poznan in field of Biotechnology and simultaneously Bioinformatics from Adam Mickiewicz University (both in 2010) and since that time focused on regenerative medicine. During his PhD he was a principal investigator in the project concerning derivation of human iPSC-derived cardiomyocytes (2012-2016). His PhD thesis concerned evaluation epigenetic mechanisms of spatio-temporal changes in chromatin architecture in subpopulations of human myoblasts, which aimed to predict their regenerative potential. After completion of the PhD in 2014, he moved to Germany (2015). His international experience include stays in: Leeds, UK; Goettingen, Germany and finally in Dresden, Germany. During his stay in the Institute of Pharmacology and Toxicology (Dresden) he developed two different human advanced cardiac tissue models: The Engineered Heart Tissue and Heart Microphysiological System.

Currently, he is employed as Assistant Professor in the Institute of Human Genetics, PAS, Poznan. He authored a total of 19 publications in impacted journals, H = 8, total citation number 104 (w/o self-citation). He was awarded with several prestigious scholarships including: Start (FNP), Etiuda (NCN) and Kulczyk family Foundation Scholarship. He is a member of Polish and European Society of Cardiology, International Society for Stem Cell Research and a board member of PAS Commission for Biotechnology located in Poznan. Additionally, he is an elected member of the COST action BIONECA: Biomaterials and Advanced Physical techniques for regenerative cardiology and neurology.

Job Experience

Assistant Professor in stem cell biology

11.2018 – to date

Department of Molecular Pathology, Institute of Human Genetics, Polish Academy of Sciences, Poznan, Poland

- Establishing the Stem Cell Laboratory for disease modelling using iPSCs-derived cardiomyocytes
- Project writing and organization of the group financing

Post-doctoral scientist in advanced cell culture models

03.2016 – 09.2018

Stem Cell Research and Regenerative Pharmacology and Toxicology Group, Institute of Pharmacology and Toxicology, MTZ, University Clinic, TU-Dresden, Germany

- Establishing Engineered Heart Tissue models for disease modelling using iPSCs-derived cardiomyocytes and fibroblasts – performing drug response curves, 2 projects ongoing
- Development of oxygen and fluidics controlled micro-physiological system with video-based imaging system, collaboration with Fraunhofer IWS (Dresden, Germany)

Post-doctoral visiting fellow in disease modelling

09.2015 – 03.2016

Stem Cell Unit, Cardiology and Pneumology Department; Medical University Gottingen, Germany

- CRISPR/Cas system gene correction in Vici syndrome patient cells
- Extensive culture of cardiomyocytes and their characterization

Post-doctoral position, scientific project manager

07.2014 – 09.2015

Department of Reproductive Biology and Stem Cells, Institute of Human Genetics, PAS, Poland

- Managing of the multitasking group (6 technical/scientific staff members) in project concerning robotic screening of iPS-derived cells for increased efficiency of CMs differentiation protocol,
- Extensive experience in flow cytometry, establishing flow cytometry analyses

Trainer/Coaching in “Flow cytometry in mammalian cell research” workshop

12.2014

Centre for Bio-Medical Education, Poznań, Poland

- 2-day-long workshop, lectures and active training sessions (group and one-to-one) including: flow cytometry basics, assays for cell preparation, compensation in flow cytometry, cell sorting
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Research fellow in human stem cells

09.2010 – 06.2014

Department of Reproductive Biology and Stem Cells, Institute of Human Genetics, PAS, Poland

- Human stem cells culture, molecular analyses, physiological assays, mitochondrial analyses
- 3D Image analyses, SQL database handling, script writing (real-time PCR, immunofluorescence data handling)
- Extensive experience (7 years, including studies) with animal model (mouse and rat), including advanced microsurgery procedures (heart infarction by LAD ligation, in situ heart fixation procedures) and basic handling

Visiting Student in Erasmus Placement Programme (3months)

07.2009 – 09.2009

Academic Unit of Anesthesia, Malignant Hyperthermia Unit, University of Leeds, United Kingdom

- Participation in NIH-financed project for development of malignant hyperthermia screening tests
- Development of bioinformatic tools for qPCR analysis & handling of malignant hyperthermia patients database

Education

PhD in medical sciences (medical biology); graduated with honors

09.2010 – 06.2014

Department of Reproductive Biology and Stem Cells, Institute of Human Genetics, PAS, Poland

- PhD Thesis: Changes of nuclear architecture and transcriptome during differentiation process of human stem cells of myogenic origin

Postgraduate studies - Strategic Marketing on Pharmaceutical Market

09.2012 – 06.2013

Poznań University of Economics and Business, Poland

Master in Biotechnology (Engineer course included); graduated with honors
Poznań University of Life Sciences, Poland

09.2005 – 06.2010

Bachelor in Bioinformatics; graduated with honors
Adam Mickiewicz University, Poznań, Poland

09.2007 – 06.2010

Scholarships / Achievements

- Awarded for the outstanding oral presentation at the XXIII Symposium of the Experimental Cardiology Section of the Polish Cardiac Society 2018
- START Scholarship for Outstanding Young Polish Researchers; FNP 2015
- Polish Academy of Sciences Award for PhD Students for publication in medical sciences field 2015
- Scholarship holder within EU co-financed project "Scholarship for PhD students specializing in strategic fields for Wielkopolska's development" – Wielkopolska Local Government, Poland 2012 - 2013
- Participation in EU financed project "Wielkopolska Engineer in European Research Area" – scholarship, trainings and practices; SPIWIN Poznan, Poland 2012
- Young scientist travel stipend - Ascona Workshop on Cardiomyocyte Biology, Switzerland 2012
- Scholarship for scientific achievements - Ministry of Higher Education and Science (3x). 2008 - 2011
- Fellowship of Kulczyk Family Foundation for the achievements in science 2009 / 2010
- Awarded in "Studencki Nobel" competition for the distinguished students in Poland 2009

Publications:

A total of 21 publications in impacted journals, H = 8, total cit number 104 (w/o self cit); 2 manuscripts in publication, further 3 in preparation, to be published in 2019. A list of selected publications from the last 5 years is available below.

1. The impact of in vitro cell culture duration on the maturation of human cardiomyocytes derived from induced pluripotent stem cells of myogenic origin. Lewandowski J, Rozwadowska N, Kolanowski TJ, Malcher A, Zimna A, Rugowska A, Fiedorowicz K, Łabędź W, Kubaszewski Ł, Chojnacka K, Bednarek-Rajewska K, Majewski P, Kurpisz M; Cell Transplant. 2018 Jul;27(7):1047-1067,

2. SPIN1 is pro-oncogenic whereas its repressor PUM1 and SPIN3, SPIN4 paralogues are anti-oncogenic in human seminoma Janecki DM, Sajek M, Kotecki M, Smialek MJ, Ginter-Matuszewska B, Spik A, Kolanowski T, Riko Kitazawa R, Kurpisz M, Jaruzelska J; Oncotarget. 2018 Aug 21;9(65):32466-32477,

3. Biological and Pro-Angiogenic Properties of Genetically Modified Human Primary Myoblasts Overexpressing Placental Growth Factor in In Vitro and In Vivo Studies. Zimna A, Wiernicki B, Kolanowski T, Rozwadowska N, Malcher A, Labedz W, Trzeciak T, Chojnacka K, Bednarek-Rajewska K, Majewski P, Kurpisz M. Arch Immunol Ther Exp (Warsz). 2018 Apr;66(2):145-159,

4. Microfluidic system for enhanced cardiac tissue formation. Busek M*, Kolanowski T*, Grünzner S, Steinfelder C, Guan K, Sonntag F. Curr D in Biomed Eng, 2017 3(2), pp. 367-370. *equal contribution,

5. Making human cardiomyocytes up to date: Derivation, maturation state and perspectives. Kolanowski TJ, Antos CL, Guan K. *Int J Cardiol.* 2017 Aug 15;241:379-386,
6. Safety, feasibility and effectiveness of first in-human administration of muscle-derived stem/progenitor cells modified with connexin-43 gene for treatment of advanced chronic heart failure. Gwizdala A, Rozwadowska N, Kolanowski TJ, Malcher A, Cieplucha A, Perek B, Seniuk W, Straburzynska-Migaj E, Oko-Sarnowska Z, Cholewinski W, Michalak M, Grajek S, Kurpisz M. *Eur J Heart Fail.* 2017 Jan;19(1):148-157,
7. Techniques for the induction of human pluripotent stem cell differentiation towards cardiomyocytes. Lewandowski J, Kolanowski TJ, Kurpisz M. *J Tissue Eng Regen Med.* 2016 Jan 17,
8. Human myoblast transplantation in mice infarcted heart alters the expression profile of cardiac genes associated with left ventricle remodeling. Wiernicki B, Rozwadowska N, Malcher A, Kolanowski T, Zimna A, Rugowska A, Kurpisz M. *Int J Cardiol.* 2016 Jan 1;202:710-21,
9. Implantation of autologous muscle-derived stem cells in treatment of fecal incontinence: results of an experimental pilot study. Romaniszyn M, Rozwadowska N, Malcher A, Kolanowski T, Walega P, Kurpisz M. *Tech Coloproctol.* 2015 Nov;19(11):685-96. Erratum in: *Tech Coloproctol.* 2015 Nov;19(11):697,
10. Can apoptosis and necrosis coexist in ejaculated human spermatozoa during in vitro semen bacterial infection? Fraczek M, Hryhorowicz M, Gaczarzewicz D, Szumala-Kakol A, Kolanowski TJ, Beutin L, Kurpisz M. *J Assist Reprod Genet.* 2015 May;32(5):771-9,
11. In vitro and in vivo characteristics of connexin 43-modified human skeletal myoblasts for future clinical applications. Kolanowski TJ, Rozwadowska N, Malcher A, Szymczyk E, Kasprzak JD, Mietkiewski T, Kurpisz M. *Int J Cardiol.* 2014 Apr 15;173(1):55-64,
12. Potential biomarkers of nonobstructive azoospermia identified in microarray gene expression analysis. Malcher A, Rozwadowska N, Stokowy T, Kolanowski T, Jedrzejczak P, Zietkowiak W, Kurpisz M. *Fertil Steril.* 2013; 100(6): 1686–1694.e7,
13. Characterization of nuclear architecture alterations during in vitro differentiation of human stem cells of myogenic origin. N Rozwadowska, Kolanowski T, Wiland E, Siatkowski M, Pawlak P, Malcher A, Mietkiewski T, Olszewska M and Kurpisz M. *PLoS One.* 2013 Sep 3;8(9):e73231.