BIOGRAPHICAL SKETCH

PERSONAL INFORMATION

NAME	Francisco Westermeier
NATIONALITY	Chilean
OFFICE	Institute of Biomedical Science FH Joanneum | University of Applied Sciences Eggenberger Allee 11, Graz 8020, Austria
PHONE	+43 316 5453-6687
E-MAIL	francisco.westermeier@fh-joanneum.at
WEBSITE	Francisco Westermeier´s profile

ACADEMIC EDUCATION

2009-2012	PhD in Physiological Sciences, Universidad Católica de Chile
2008-2009	MSc in Biological Sciences, Universidad Católica de Chile
2000-2007	BSc in Biochemistry, Universidad Austral de Chile

PROFESSIONAL CAREER

2024-present	Guest Lecturer, Institute of Biomedical Sciences, FH Campus Vienna, Austria
2022-present	Senior Lecturer, Institute of Biomedical Sciences, FH Joanneum, Graz, Austria
2021-present	Associate Researcher, Universidad Bernardo O´Higgins, Chile
2020-2002	Lecturer, Institute of Biomedical Sciences, FH Joanneum, Graz, Austria
2018-2020	Researcher, Institute of Biomedical Sciences, FH Joanneum, Graz, Austria
2013-2016	Lecturer, Fac. Pharmacy, Universidad San Sebastián, Chile
2013-2016	Postdoc, Fac. Medicine (Prof. S. Lavandero), Universidad de Chile
2012-2013	Postdoc, Fac. Medicine (Prof. L. Sobrevia), Universidad Católica de Chile

AWARDS & HONOURS

2024-present	Deputy Editor – Cardiovascular Diabetology
2023-present	Scientific Advisor – Bayer AG, Germany
2023-present	Scientific Advisor, ME/CFS Research Foundation, Germany
2020-present	External expert for the European Commission on the topic of ME/CFS
2020-present	Scientific Advisor – Österreichischen Gesellschaft für ME/CFS (CFS-Hilfe), Austria
2020-present	Member, Austrian Physiological Society
2020-present	Member, Chilean Physiological Society
2019	Short Term Scientific Mission (COST) London School of Hygiene and Tropical Medicine, UK
2018-2021	Member, Management Committee EUROMENE, Austria representative
2018	Award, UK ME/CFS Biobank, London

RESEARCH FUNDING

Principal Investigator

2021-2022	The Solve ME/CFS Initiative (USA)
2019-2021	ME Research UK
2013-2016	The National Fund for Scientific and Technological Development (Chile)

PEER-REVIEW ACTIVITIES

Associate Editor

2021-2023	Cardiovascular Diabetology

Associate Editor

2021-present	Frontiers in Cardiovascular Endocrinology

Guest Associate Editor

Frontiers in Vascular Physiology; Frontiers in Infectious Diseases – Surveillance, Prevention and Treatment; Frontiers in Infectious Diseases: Epidemiology and Prevention.

Solicited Reviewer

Peer Review Journals

Molecular and Cellular Neuroscience; Scientific Reports; Cellular and Molecular Life Sciences; Molecular Neurobiology; BBA-Molecular Basis of Disease; Molecular Aspects of Medicine; PLOS One; Mediators of Inflammation; Journal of Cellular Physiology; Journal of Diabetes Research; Frontiers in Pharmacology; Biomed Research International; Cell Death and Disease; Vascular Pharmacology; Cardiovascular Diabetology; Frontiers in Cardiovascular Endocrinology.

Research Funding Agencies
The Solve ME/CFS Initiative (USA); ME Research UK; The National Fund for Scientific and Technological Development (Chile); Netherlands Organization for Health Research and Development (ZonMw) (Netherlands).

CONTRIBUTION TO SCIENCE

(I) *Cardiovascular and endocrine abnormalities in ME/CFS*

Context: Since 2018 to date, I have been leading a line of research focused on myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS). ***Background***: ME/CFS is a complex multisystemic disease that affects more women than men and is characterized by persistent and debilitating fatigue sharing several similarities with the post-acute sequelae of COVID-19 - also known as "Long COVID". Post-exertional malaise (PEM) - defined as the worsening of symptoms after (minimal) physical or even mental exertion - is becoming widely accepted as a hallmark feature of the ME/CFS diagnosis. Despite this evidence, studies evaluating the underlying mechanisms associated with these cardiovascular and endocrine abnormalities are limited. ***Aims*:** We aim to provide new pathomechanisms to better explain the cardiovascular and endocrine abnormalities in ME/CFS. ***Central findings*:** We recently reported the upregulation of microRNAS (miRs) associated with endothelial dysfunction (ED) in plasma samples from ME/CFS patients. Through several bioinformatic analyses, we also propose that pathways related to oxidative stress and oxygen regulation may also be altered in ME/CFS and associated with PEM (Blauensteiner et al., 2021*). Consistent with clinical evidence of ED, we have also shown that plasma from affected individuals reduces the ability of endothelial cells (ECs) to produce nitric oxide (NO) *in vitro* (Bertinat et al., 2022*). From an endocrinological perspective, we recently provided new evidence reporting altered steroid hormone (SH) levels in ME/CFS stratified by sex and disease severity (Pipper et al., 2023* / Accepted; Journal of Endocrinological Investigation). ***Contribution*:** We propose that a combination of clinical evaluation of endothelial function along with the detection of circulating miRs reported to decrease the production of NO, might allow a more sensitive characterization of ED. On the other hand, our findings not only suggest the potential value of including SH in future studies aimed at improving stratification in ME/CFS, but also provide new perspectives to explore the clinical relevance of these SH-related differences within specific patient subgroups. ***Ongoing activities*:** Currently, our research group is focused on investigating whether oxidative stress and impaired arginine metabolism might be associated with reduced NO production and concomitant cardiovascular abnormalities in ME/CFS.

(*) *Corresponding author*: F Westermeier

(II) *Renal and pancreatic insulin signaling in diabetes*

***Context*:** From 2017 to present, I have maintained a collaborative interest in diabetes with a focus on identifying potential targets for pharmacological intervention at the (a) renal and (b) pancreatic levels.

Background (a)*:** The kidney is an insulin-sensitive organ involved in glucose homeostasis. Interestingly, the inorganic salt sodium tungstate (NaW) has been shown to exert insulin-mimetic and immunomodulatory activities in diabetic animal models. Although NaW has been widely used over the past two decades, neither its mechanism of action nor its side effects on renal function have been fully elucidated. ***Aims*:** To study the immunologic and metabolic effects of NaW on renal function. ***Central findings: We showed that NaW stimulates the secretion of pro- and anti-inflammatory cytokines in human kidney cells *in vitro* (Bertinat R, Westermeier F, *et al.* 2017) and abnormal glycogen accumulation in renal proximal tubules of diabetic IRS2 knockout mice (Bertinat R, Westermeier F, *et al.* 2018a). ***Contribution*:** Although several preclinical studies have shown the beneficial effects of NaW, our findings provide new evidence that sheds light on the adverse/unknown effects of NaW on renal function (Bertinat R, Westermeier F, *et al.* 2018b)

***Background (b)*:** The pancreatic islets of Langerhans, composed mainly of glucagon-producing α-cells and insulin-producing β-cells, are critical for glucose homeostasis. Insulin and glucagon modulate blood glucose levels in opposite directions in health, but a combined decrease in insulin secretion with increased glucagon secretion contributes to hyperglycemia in diabetes. Despite this bi-hormonal dysregulation, most studies have focused on insulin secretion and much less is known about glucagon secretion. ***Aim*:** To study α-cell metabolism and glucagon secretion in the human and murine pancreas in response to different metabolic states. ***Central findings*:** We showed that phosphoenolpyruvate carboxykinase (PCK1) is expressed in murine and human pancreatic α-cells. Furthermore, PCK1 transcription is induced by fasting and diabetes in rat pancreas (Westermeier *et al*., 2020). **Contribution:** To our knowledge, this study provided the first evidence that PCK1 is expressed in pancreatic α-cells in murine models and humans. These findings not only reinforced that PCK1 may be an interesting target to explore pancreatic α-cell metabolism, but also provided new alternatives to improve insulin secretion as a counterregulatory mechanism (Westermeier *et al*., 2019).

(III) *Role of insulin/eNOS/NO axis in cardiovascular function*

***Context*:** During my postdoctoral training (2013-2016), I collaborated on two Ph.D. theses (a & b) in which the effect of the insulin/eNOS/NO axis on cardiovascular function was an essential element to be investigated.

***Background (a)*:** Insulin regulates many aspects of cardiomyocyte physiology, including Akt-dependent glucose transport and mitochondrial dynamics. Nicotinamide adenine dinucleotide (NAD^+) also promotes insulin signaling by activating Akt in cardiomyocytes. On the other hand, FK866 (NAD^+ synthesis inhibitor) has been proposed as a treatment for inflammatory diseases (*e.g.*, autoimmune encephalitis) based on its ability to reduce inflammation. However, despite these promising findings, the potential risk of using FK866 on cardiomyocytes remained largely unexplored. ***Aim*:** To evaluate whether FK866-induced NAD^+ depletion negatively affects the mitochondrial metabolism in cultured neonatal rat cardiomyocytes (NRCs) in response to insulin. ***Central findings*:** FK866 reduces mitochondrial metabolism and the adaptive response of NRCs to insulin (Oyarzún AP, Westermeier F, *et al*., 2015). ***Contribution*:** This study highlighted the importance of NAD^+-induced insulin

signaling on mitochondrial function in ARCs. In addition, although these findings were observed *in vitro*, they called into question the safety of FK866 as a therapy, particularly in patients with cardiovascular disease.
***Background (b)*:** In ECs, insulin/eNOS/NO signaling plays a key role in cardioprotection. Dexmedetomidine (Dex) is an analgesic and sedative molecule that has been reported to induce cardioprotective effects. However, the role of the eNOS/NO axis in Dex-induced cardioprotection was unclear. ***Aim*:** To determine whether Dex-induced cardioprotection was associated with activation of the endothelial eNOS/NO axis. ***Central findings*:** Dex activated eNOS and induced NO production in ECs. Interestingly, Dex promoted cardioprotection only in adult rat cardiomyocytes (ARCs) co-cultured with ECs, suggesting that Dex requires the endothelium to reduce cardiomyocyte death (Riquelme JA, Westermeier F, *et al.* 2016). ***Contribution*:** From an integrative point of view, this work showed for the first time that Dex protects the myocardium through an eNOS/NO-dependent mechanism and indirectly via ECs. In addition, it highlighted the pharmacological relevance of targeting the cardiac endothelium to improve cardiac function.

(IV) *Defective insulin signaling and endothelial dysfunction in gestational diabetes mellitus*
***Context*:** During my Ph.D. (2008-2012), I was interested in identifying the molecular mechanisms associated with defective insulin signaling and endothelial dysfunction in gestational diabetes mellitus (GDM). ***Background*:** Insulin promotes endothelial function by activating endothelial nitric oxide synthase (eNOS), which generates the vasodilator nitric oxide (NO). Compelling evidence links GDM with impaired placental insulin signaling and endothelial dysfunction. However, the underlying mechanisms by which endothelial insulin signaling is altered in GDM pregnancies had not been fully elucidated. ***Aim*:** To investigate whether insulin receptor isoforms A (IR-A) and/or B (IR-B) were involved in the downregulation of eNOS in endothelial cells (ECs) from GDM pregnancies. ***Central findings*:** We observed *in vitro* that reduced eNOS activity and NO production were associated with upregulation of IR-A in ECs from GDM pregnancies. Interestingly, we also reported that insulin-induced vasodilation was reduced by ZM-241385, an adenosine receptor 2_A ($A_{2A}R$) antagonist. (Westermeier *et al*., 2011). Later, we moved a step further by showing that activation of the IR-A/p44/42^{mapk} axis is associated with reduced uptake of adenosine, an endogenous nucleoside well described to induce vasodilation via $A_{2A}R$. (Westermeier *et al*., 2015). ***Contribution*:** These studies provided new insights into IR-A and IR-B insulin signaling in GDM, suggesting that reduced insulin sensitivity could be pharmacologically restored by activating $A_{2A}R$.

KEYNOTE SPEAKER

09/2023	Medical University of Vienna, *ME/CFS Symposium und Vernetzungstreffen*
05/2023	Charité – Universitätsmedizin Berlin, *2nd International ME/CFS Meeting*
05/2022	Medical University of Vienna, *CCCFS Symposium*

CITATION METRICS (*)

- ORCID: https://orcid.org/0000-0002-4476-4198
- Pubmed: Full list of #publications=44
- Google Scholar: #citations=1524; #h-index=22

(*) Information updated on March 1st, 2024

CURRENT TEACHING ACTIVITIES
FH Joanneum | University of Applied Sciences
Department of Health Studies

(A) Bachelor's Degree / Biomedical Science
Courses: Scientific English; Physiology and biophysics.

(B) Bachelor's Degree / Radiography
Courses: Introduction to medical English; English in health management; English in health education.

(C) Master's degree / Mass Spectrometry and Molecular Analysis
Courses: Molecular cell biology and genetics; Personalized medicine; Scientific writing and dissemination; Molecular and genetic engineering methods; Molecular diagnostics I; Master thesis seminar.