

CURRICULUM VITAE

Josef Martin Penninger

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CURRENT POSITIONS

since 2018	Director, Life Sciences Institute	University of British Columbia
since 2018	Professor, Department of Medical Genetics	University of British Columbia
since 2018	Canada 150 Research Chair in Functional Genetics	University of British Columbia
since 2011	Guest Professor	Medical University of Vienna
since 2004	Professor of Genetics	University of Vienna
since 2004	Adjunct Full Professor in Immunology	University of Toronto

EDUCATION

2008	Leadership course, Harvard Kennedy School of Government, USA
1994	Post-doctorate, Immunology, Ontario Cancer Institute, Canada
1990	Doctorate, MD, Medicine, University of Innsbruck, Austria
1986-1990	Doctoral Thesis in Immunology as part of Medical School: "Phenotypical and functional analysis of intra-thymic nurse (TNC)-lymphocytes." Institute for General and Experimental Pathology (Prof. Dr. G. Wick), University of Innsbruck, Medical School
1982-1990	University of Innsbruck, Medical School, Austria; graduated as Dr. med. Univ.

EMPLOYMENT HISTORY

2002-2018	Founding Director, Institute of Molecular Biotechnology of the Austrian Academy of Sciences (IMBA), Vienna, Austria
2002-2004	Full Professor, Departments of Immunology and Medical Biophysics, University of Toronto, Canada
1994-2003	Associate Scientist, The Ontario Cancer Institute, Dept. of Molecular and Cellular Biology, Princess Margaret Hospital, Toronto, Canada
1999-2002	Associate Professor, Departments of Immunology and Medical Biophysics, University of Toronto, Canada
1997	Associate Professor, Department of Experimental and General Pathology, University of Innsbruck, Austria
1994-2002	Principal Investigator, Amgen Institute, 620 University Avenue, Toronto, Canada
1994-1999	Assistant Professor, Departments of Immunology and Medical Biophysics, University of Toronto, Canada
1990-1994	Postdoctoral fellow, The Ontario Cancer Institute, Princess Margaret Hospital, Toronto, Canada

AWARDS AND HONORS (SELECTED)

2020	Chosen #30 by OOOM 100: The Most Inspiring People in the World
2019	Honorary Professor, Qingdao University, China

2018	Canada 150 Research Chair in Functional Genetics
2018	Austria Order of Merit for Arts and Sciences
2017	CEE Innovation Award (AtoS Austria)
2015	Among the 400 most influential Thought Leaders in the world (#11 in german speaking countries http://www.thoughtleaders.world/en/).
2014	Wittgenstein Prize (highest Austrian Science Award)
2009	Medal of The Australian Society for Medical Research (ASMR)
2009	ESCI Award by the European Society for Clinical Investigation
2008	Karl Landsteiner prize of the Austrian Society of Immunology and Allergology
2008	Among 1000 most important Austrian immigrant/emigrants in Politics, arts, sports, philosophy, business or music from 1900-2008
2008	Carus Prize of the City of Schweinfurt
2007	Ernst Jung Prize for Medicine
2006	Descartes Prize (the highest EU research prize)
2005	Designation of the asteroid 48801 as Penninger

ELECTED MEMBERSHIPS (SELECTED)

2015	Elected Member – European Academy of Sciences and Arts
2012	Elected AAAS Fellow for “efforts on behalf of the advancement of science or its applications are scientifically or socially distinguished”
2010	Elected member – European Academy for Tumor Immunology (EATI)
2009	Elected member – European Research Institute for Integrated Cellular Pathology (ERI – ICP)
2009	Elected to the Academy of Europe (Academia Europaea)
2008	Elected as EMBO member
2007	Elected as the youngest full member to the Austrian Academy of Sciences
2004	Elected To the Deutsche Akademie Der Naturforscher Leopoldina
2001	Honorary member of the Golden Key International Honor Society

PARTICIPATION IN SCIENTIFIC COMMITTEES

since 2019	President of the Scientific Committee of the Toulouse University Hospital, c/o Faculté de Médecine, 37 Allées Jules Guesde, 31000 Toulouse, France
since 2019	Member of the Scientific Advisory Board of the Lupus Research Alliance, 275 Madison Avenue, 10th floor, New York, NY 10016
since 2017	Member of the Hilife Scientific Council, Hilife Helsinki Institute of Life Science, University of Helsinki, Yliopistonkatu 4, 00100 Helsinki, Finland
since 2013	Member of the Research Committee of the Mount Sinai Hospital, 600 University Avenue, Toronto, Canada

RECENT GRANT SUPPORT

I have held competitive grants since 1995 in Canada and since 2003 in Austria and the European Union, including a C150 Canada Research Chair, EU Excellence grant, and ERC Advanced grants. Below are selected recent grants:

Current grant support:

2020 – 2025	John R. Evans Leaders Fund (CFI) , “Hapscreen-RD: A platform for large-scale screening of human haploid cells for rare disease research” (CAD 1,996,647)
2020 – 2021	COVID-19 Rapid Research Funding Opportunity (CIHR) , “Mechanistic studies on ACE2 as a rational therapy for COVID-19” (CAD 578,090)
2020 – 2022	COVID-19 Rapid Response Grant (CIHR) , “Molecular and cellular therapies

- against COVID-19 using angiotensin-converting enzyme 2 (ACE2)" (CAD 1,000,000)
- 2020 – 2023 **UK-Canada Diabetes Partnership Initiative: UK-Canada Diabetes Research Team Grants (CIHR)**, "Bridging the gap to translation by understanding and preventing diabetic vascular complications using human organoid culture (MRC NPI: David Andrew Long)" (CAD 449,090)
- 2020 – 2024 **Innovative Medicines Initiative**, "Modern approaches for developing antivirals against SARS-CoV-2" (EUR 1,100,000)
- 2020 – 2025 **Canadian Institutes of Health Research Project Grant**, "Investigating the role of the BH4 pathway in Parkinson's Disease (PD)" (CAD 868,275)
- 2019 – 2021 **UBC Faculty of Medicine, Barbara Opperman Kidney Research Fund**, "Generating a vascularized kidney organoid for diabetic vasculopathy" (CAD 150,000)
- 2018 – 2025 **Canada 150 Research Chairs Program: Canada 150 Research Chair in Functional Genetics** (CAD 7,000,000)
- 2015 – 2021 **Wittgenstein Prize**, FWF Austrian Science Fund (EUR 1,500,000)

Completed grants:

- 2020 – 2021 **International Joint Research Project (Medical Research Institute of TMDU)**, "Establishment of a mouse sarcopenia model due to MKK7-deficiency" (JPY 500,000)
- 2014 – 2019 **Advanced European Research Council (ERC) grant**, "'Yeast' genetics in mammalian cells to identify and validate fundamental mechanisms of physiology and pathophysiology" (EUR 2,500,000)
- 2015 – 2018 **ERA-Net Infectious Diseases – Austria Science Fund (FWF)**, "Lethal Virus Infection in Haploid Stem Cells" (EUR 300,000)
- 2012 – 2018 **Innovator Award of the US Department of Defense**; "Novel approaches to breast cancer prevention and inhibition of metastases" (USD 7,400,000)

RECENT INVITED AND KEYNOTE LECTURES AND PRESENTATIONS

- (2020) ACE2 – from cardiovascular research to the heart of a pandemic. Dr. J. David Grimes Lecture at Research Day, Ottawa Hospital Research Institute (online due to COVID-19). Nov 19. Keynote.
- (2020) Engineered human tissues for COVID-19 research. Till & McCulloch Meetings (TMM) 2020 Virtual Conference (online due to COVID-19). Oct 26 – 29. Plenary Lecture.
- (2020) ACE2 – from discovery to COVID-19. Seminar at the University of Toronto Mississauga (online due to COVID-19). Oct 23. Invited.
- (2020) Organoids to study COVID19 infections. EUROoCS conference (online due to COVID-19). July 8. Keynote.
- (2020) Potential therapeutic strategies to prevent and conquer COVID-19. Digital Novel Coronavirus Investment Forum. Sachs Forum (Switzerland). Online due to COVID-19. July 8. Panelist.
- (2020) COVID-19 – the global challenge. MCI Management Center Innsbruck – International Hochschule GmbH, Austria. June 8. Distinguished guest – live talk.
- (2020) A Race Against the Clock: COVID-19 Vaccine and Treatment R&D in Canada – one of the featured presenters on a virtual Panel for Research Canada, Parliamentarians, and esteemed guests. May 21 and June 15.
- (2020) ACE2 – a rational frontline therapy for COVID-19. 2020 European Congress of Radiology (online due to COVID-19), Austria. March 12. Free livestream online lecture.
- (2019) Life Sciences Today. President's Concert Series - Sounds and Science: Vienna meets Vancouver. November 30, Vancouver BC, Canada. Keynote.
- (2019) Molecular control of T cell activation. 47th annual meeting of the Austrian Society of Allergology and Immunology (ÖGAI 2019) November 21 – 23, Graz, Austria. Invited.
- (2019) Tissue Engineering to understand diabetes patho-Physiology (in German). Salzburg Congress 2019 (Europasaal), Salzburg, Austria. Keynote.
- (2019) The Dream of Eternal Life – top science and biotech entrepreneurs. Tyrolean Economic

Forum, November 5 – 7, Innsbruck, Austria. Invited.

(2019) Human blood vessel engineering. BC Regenerative Medicine Cascadia Corridor Research Symposium, October 24 – 25, Victoria, BC, Canada. Invited.

(2019) Biomedicine and the Future of Health, a conversation moderated by Karin Pollack. Vienna Humanities Festival 2019: Hope and Despair, September 26 – 29, Vienna, Austria. Invited.

(2019) From haploid stem cells to blood vessel engineering. Annual meeting of the Anatomical Society (Anatomische Gesellschaft), September 25 – 27, Wurzburg, Germany. Keynote.

(2019) RANKL and RANK: Bone and Beyond. 58th annual meeting of the European Society for Paediatric Endocrinology (ESPE), September 19 – 21, Vienna, Austria. Keynote.

(2019) RANK Ligand: the key regulator of bone loss in aging. 1st Scientific Committee meeting of INSPIRE project of Toulouse Gerontopole, September 9 – 10, Toulouse, France. Invited.

(2019) The role of science in the age of artificial intelligence. 40th Ars Electronica Festival - Out of the Box: the midlife crisis of the digital revolution. September 5 – 9, Postcity Linz, Austria. Invited.

(2019) From haploid stem cells to blood vessel engineering. From the Laboratory to the Clinic: Generating new therapeutic targets for unmet needs conference, September 3 – 6, Trinity College, Oxford, United Kingdom. Invited.

(2019) Human blood vessel organoids as a model of diabetic vasculopathy (Zoom session). Hudson Institute of Medical Research, Melbourne, Australia. Invited.

(2019) Preventive healthcare and technology session at the Healthy Longevity: Future and Potential for Europe 2030 roundtable meeting, June 17-18, 2019, Vaduz, Liechtenstein. Invited.

(2019) From Haploid Stem Cells to Blood Vessel Engineering. Max Planck Institute for Biology of Ageing (MPI AGE), Cologne, Germany. Invited.

(2019) BH4 – a critical new metabolite for T cell proliferation. 17th annual meeting of the Association for Cancer Immunotherapy (CIMT), May 21 -23, 2019, Mainz, Germany. Keynote.

(2019) From Haploid Stem Cells to Blood Vessel Engineering. BC Regenerative Medicine Spring Symposium, UBC, Vancouver, BC Canada. Invited.

(2019) Molecular control of bone loss. Invention of Age: 14th Common Austrian-German Geriatric Congress, 59th Congress of the Austrian Society for Geriatrics and Gerontology, April 25 – 27, 2019, University of Vienna, Vienna, Austria. Keynote.

(2019) From haploid stem cells to blood vessel engineering. Department of Molecular Medicine and Medical Biotechnology, University of Napoli Federico II Medical School, Naples Italy. Invited.

(2019) Cancer immunology – cbl-b and beyond. Department of Molecular Medicine and Medical Biotechnology, University of Napoli Federico II Medical School, Naples Italy. Invited.

(2019) RANKL – regulation of bone loss and breast cancer. Department of Molecular Medicine and Medical Biotechnology, University of Napoli Federico II Medical School, Naples Italy. Invited.

(2019) From haploid stem cells to blood vessel engineering. Department of Molecular Medicine and Medical Biotechnology, University of Napoli Federico II Medical School, Naples, Italy. Invited.

(2019) Interview. Stem Cell Podcast (moderated by Daylon James, Asst Professor of Stem Cell Biology in the Center for Reproductive Medicine at Weill Cornell Medicine). Invited.

(2019) From haploid stem cells to human blood vessel engineering. Developmental and Stem Cell Biology Special Seminar, Hospital for Sick Children, University of Toronto, Toronto, Canada. Invited.

MOST SIGNIFICANT SCIENTIFIC CONTRIBUTIONS

Our basic approach is to genetically manipulate and change genes in mice and to determine the effects of these mutations in development of the whole organism and in diseases. From these mutations we are trying to establish basic principles of development and basic mechanisms of disease pathogenesis.

Total lifetime publications: 730; **Total Times Cited:** 81,994; **Web of Science H-index** 137.

For complete citations and citation metrics please see: <https://publons.com/researcher/2618826/josef-m-penninger/> or <http://orcid.org/0000-0002-8194-3777>

Below I snapshot my most significant contributions. On all the listed contributions I am the principal investigator who coordinated the research and came up with the ideas.

RANK/RANKL: My collective work on RANK/RANKL unlocked key mechanisms underlying osteoclast development and bone loss and revealed a crucial role for RANK/RANKL in bone metastasis in various cancers and the development of BRCA1-driven breast cancer. These discoveries contributed to the development of Denosumab, a RANKL antagonist, approved as osteoporosis and bone loss treatment in cancer. An international clinical trial to test whether blocking RANKL with Denosumab could prevent breast cancer in BRCA1 mutation carriers is currently underway. Recently, we also demonstrated that RANK plays a critical role in the rewiring of the thymus by pregnancy hormones to maintain Treg production in order to prevent miscarriage and gestational diabetes.

1. Paolino M *et al.* RANK links thymic regulatory T cells to fetal loss and gestational diabetes in pregnancy. *Nature*. 2021; 589(7842):442-7.
2. Sigl V, *et al.* RANKL/RANK control Brca1 mutation-driven mammary tumors. *Cell Research*. 2016; 26(7): 761-774.
3. Schramek D, *et al.* Osteoclast differentiation factor RANKL controls development of progesterin driven mammary cancer. *Nature*. 2010; 468(7320):98-102.
4. Hanada R, *et al.* Central control of fever and female body temperature by RANKL/RANK. *Nature*. 2009; 462 (7272):505-9.
5. Jones DH, *et al.* Regulation of cancer cell migration and bone metastasis by RANKL. *Nature*. 2006; 440(7084):692-6.
6. Wada T, *et al.* The molecular scaffold Gab2 is a crucial component of RANK signaling and osteoclastogenesis. *Nature Medicine* 2005; 11(4):394-9.
7. Teng Y, *et al.* Functional human T-cell immunity and osteoprotegerin ligand control alveolar bone destruction in periodontal infection. *J Clin Invest*. 2000; 106(6): R59-67
8. Fata J, *et al.* The osteoclast differentiation factor osteoprotegerin-ligand is essential for mammary gland development. *Cell*. 2000 29; 103 (1):41-50.
9. Kong Y, *et al.* Activated T cells regulate bone loss and joint destruction in adjuvant arthritis through osteoprotegerin ligand. *Nature*. 1999; 402(6759):304-9.
10. Kong Y, *et al.* OPGL is a key regulator of osteoclastogenesis, lymphocyte development and lymph-node organogenesis. *Nature*. 1999; 397(6717):315-23.

3D Human Blood Vessel Organoids: My lab recently developed self-organizing 3D human blood vessel organoids from ES cells. These, organoids faithfully recapitulate the structure and function of human blood vessels and are amenable systems for modelling and identifying the regulators of diabetic vasculopathy, a disease affecting hundreds of millions of people globally.

1. Wimmer R *et al.* Generation of blood vessel organoids from human pluripotent stem cells. *Nature Protocols*. 2019; 14: 3082-3100.
2. Wimmer R *et al.* Human blood vessel organoids as a model of diabetic vasculopathy. *Nature*. 2019; 565(7740): 505-510.

Haploid Embryonic Stem (ES) Cells: My lab generated first haploid ES cells and systems for whole genome mutagenesis. We can introduce 50-70 million mutations/day allowing for genome wide screens, and have developed a bank of > 100000 haploid ES cell clones where every single gene is reparably mutated; allowing direct clone-to-clone comparisons. To empower reproducible research, we have made these systems freely available to the scientific community via <https://www.haplobank.at/e-commerce/control/main>

1. Elling U, *et al.* Derivation and maintenance of mouse haploid embryonic stem cells. *Nature Protocols*. 2019; 14(7): 1991-2014.
2. Elling U, *et al.* A reversible haploid murine embryonic stem cell biobank resource for functional genomics. *Nature*. 2017; 550(7674):114-118
3. Elling U, *et al.* Forward and reverse genetics through derivation of haploid mouse embryonic stem cells. *Cell Stem Cell*. 2011; 9(6):563-74

Glycoproteomics Technology Platform: My lab has developed a new technology platform for **glycoproteomics**. > 50% of human proteins are glycosylated, altering their activities in many biological processes; yet, identification and functional validation of complex glycoproteins remains largely unexplored. Our quantitative approach identifies intact glycopeptides, allowing us to infer complex glycan structures and directly map them to sites within the associated proteins at the proteome scale.

1. Stadlmann J, *et al.* Analysis of PNGase FResistant N-Glycopeptides Using SugarQb for Proteome Discoverer 2.1 Reveals Cryptic Substrate Specificities. *Proteomics*. 2018; 18(13): e1700436
2. Stadlmann J, *et al.* Comparative glycoproteomics of stem cells identifies new players in ricin toxicity. *Nature*. 2017; 549(7673): 538-542.
3. Taubenschmid J, *et al.* A vital sugar code for ricin toxicity. *Cell Research*, 2017; 27 (11):1351-1364.

Cancer Immunotherapy and T Cell Biology: I am a trained immunologist and my lab has made several discoveries in T cell biology. My key contributions to cancer immunotherapy set the molecular groundwork for the currently transformative immune checkpoint therapies.

1. Uribealago I, *et al.* (2019). Apelin inhibition prevents resistance and metastasis associated with anti-angiogenic therapy. *EMBO Molecular Medicine*. 2019; 11(8):e9266
2. Cronin S, *et al.* The metabolite BH4 controls T cell proliferation in autoimmunity and cancer. *Nature*. 2018; 563(7732): 564-568.
3. Paolino M, *et al.* The E3 ligase Cbl-b and TAM receptors regulate cancer metastasis via natural killer cells. *Nature*. 2014; 507(7493):508-512.
4. Griffiths E, *et al.* Defective T cell proliferation, in vivo immune responses, and TCR-induced integrin-mediated adhesion in the absence of the adapter protein Fyb/Slap130. *Science*. 2001; 293, 2260-2263.
5. Bachmaier K, *et al.* Negative regulation of lymphocyte activation and autoimmunity by the molecular adaptor Cbl-b. *Nature*. 2000; 403(6766):211-216.
6. Sasaki T, *et al.* Function of PI3Kgamma in thymocyte development, T cell activation, and neutrophil migration. *Science*. 2000; 287(5455):1040-1046.
7. Fischer K, *et al.* The Proto-Oncoprotein Vav regulates antigen receptor oligomerization and cytoskeletal rearrangements in T Cells. *Curr. Biol*. 1998; 554-562.

Molecular control of blood pressure and heart functions

1. Monteil V, *et al.* Inhibition of SARS-CoV-2 Infections in Engineered Human Tissues Using Clinical-Grade Soluble Human ACE2. *Cell*. 2020; 181(4):905-13.
2. Haubner B, *et al.* Functional recovery of a human neonatal heart after severe Myocardial Infarction. *Circ Res*. 2016; 118(2):216-21.
3. Haubner, B, *et al.* Complete cardiac regeneration in a mouse model of myocardial infarction. *Aging*. 2012; 4, 966-977.
4. Hashimoto T, *et al.* ACE2 links amino acid malnutrition to microbial ecology and intestinal inflammation. *Nature*. 2012; 487(7408):477-81.
5. Neely GG, *et al.* A global in vivo *Drosophila* RNAi screen identifies NOT3 as a conserved regulator of heart function. *Cell*. 2010; 141(1):142-53.

6. Imai Y, *et al.* Identification of oxidative stress and Toll like receptor 4 signaling as a key pathway of acute lung injury. *Cell*. 2008; 133, 235-249.
7. Imai Y., *et al.* The SARS-coronavirus receptor ACE2 protects from severe acute lung failure. *Nature*. 2005; 436, 112-116.
8. Kuba K, *et al.* A critical role of angiotensin converting enzyme 2 (ACE2) in SARS pathogenesis. *Nature Medicine*. 2005; 11, 875-879.
9. Crackower M, *et al.* Angiotensin-converting enzyme 2 is an essential regulator of heart function. *Nature*. 2002; 417(6891):822-828.
10. Crackower M, *et al.* Regulation of myocardial contractility and cell size by distinct PI3K-PTEN signaling pathways. *Cell*. 2002; 110(6):737-49.

RESEARCH TRAINING AND SUPERVISORY EXPERIENCE

I have supervised 17 PhDs, 53 Postdocs and 11 Masters Students. Many are PIs at internationally recognized research institutions or University Professors. Some examples: Daniel Schramek (Univ. of Toronto); Magda Paolino (Karolinska Inst., Stockholm); Reiko Hanada and Toshi Hanada (Oita Univ., Japan); Vanja Nagy (LBI, Vienna); Manu Rangachari (CHUL, Quebec); Greg Neely (Univ. of Sydney); Mike Crackower (Ventus Therapeutics); Uli Elling (IMBA, Vienna); Shuan Rao (Nonfang Hospital, China); Takehiko Sasaki, Hiroshi Nishina, Tomoki Nakashima (Tokyo Medical and Dental Univ., Japan); Keiji Kuba (Akita Univ., Japan); Yumiko Imai (Osaka Univ., Japan); Yun Kong (Seoul National Univ., Korea); Urs Ericsson (GZO Wetzikon Hospital, Zurich); Kurt Bachmaier (Univ. of Illinois); Andrew Pospisilik and Connie Krawczyk (Van Andel Research Inst., Grand Rapids); Johannes Stadlman (BOKU, Vienna)

Current list of trainees (UBC and IMBA):

Master's Students

2019/9	Meilin An (in progress, UBC)
2019/9	Sebastian Dawo (in progress, UBC)
2019/9	Nicolas Werschler (in progress, UBC) -won prize in Engineering in Scrubs (CAD 12,000) -British Columbia Graduate Scholarship (CAD 15,000)
2020/4	Marion Horrer (in progress, IMBA)
2020/9	Sahra Tasdelen (in progress, IMBA)
2020/11	Irma Sakic (in progress, IMBA)
2020/11	Emi Miyakoda (in progress, IMBA)

PhD Students

2020/9	Jesse Fox (in progress, UBC)
2016/4	David Hoffman (in progress, IMBA)
2016/9	Carlos Gomez Diaz (in progress, IMBA)
2019/10	Gustav Jonsson (in progress, IMBA)
2020/12	Kirill Salewskij (in progress, IMBA)

Postdoctoral Fellows

2019/9	Jun Seong Lee (in progress, UBC)
2020/4	Ania Bogoslawski (in progress, UBC)
2020/4	Hirofumi Omori (in progress, UBC)
2020/5	Omar Hasan Ali (in progress, UBC)
2020/5	Jun Wang (in progress, UBC)
2020/10	Jie Jiao (in progress, UBC)
2012/5	Domagoj Cikes (in progress, IMBA)
2015/11	Masahiro Onji (in progress, IMBA)
2018/3	Bianca Gapp (in progress, IMBA)
2019/5	Stefan Mereiter (in progress, IMBA)

2020/10 Simon Licht-Mayer (in progress, IMBA)

Research Associates

2011/4 Shane Cronin (now Staff Scientist, IMBA)

2015/4 Astrid Hagelkruys (IMBA)