CURRICULUM VITAE

Josef Penninger

CURRENT POSITIONS

Since 2023 **Scientific Director, Helmholtz Centre for Infection Research**

Braunschweig, Germany

Since 2023 **Professor in Precision Medicine**

Medical University of Vienna, Austria

Since 2018 **Professor, Department of Medical Genetics**

University of British Columbia, Canada

Since 2018 **Canada 150 Research Chair in Functional Genetics**

University of British Columbia, Canada

Since 2004 **Adjunct Professor in Immunology (Status-only, at the rank of Full Professor)**

University of Toronto, Canada

EDUCATION

2024 **Doctorate**, PhD, Medical Science, Tokyo Medical and Dental University, Japan

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

2018-2023 **Director, Life Sciences Institute**

University of British Columbia, Canada

2004-2018 **Honorary Professor in Genetics**

University of Vienna, Austria

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

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)

2021 Allen Distinguished Investigator

2020 Austrian of the Year, International Success category

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 https://www.nachrichten.at/)

2014 Wittgenstein Prize (highest Austrian Science Award)

2012 Innovator Award of the US Department of Defense (USD 7,400,000)

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

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 life time publications: 784; Total Times Cited: 94,686;

Web of Science H-index 149.

Numbers updated on 20 March 2024. For complete citations and citation metrics please see: https://www.webofscience.com/wos/author/record/48812 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.

ACE2:

This research began with my lab providing the first genetic proof that ACE2 is a negative regulator of the renin-angiotensin system, and redefining the molecular control of heart functions. We then went on to show that ACE2 is the key receptor for SARS infections in vivo, and how SARS infections and ACE2 control lung injury. Subsequently we showed a role for ACE2 in the dietary control of intestinal inflammation, highlighted on the cover of Nature, and that a homologue of ACE2, collectrin, controls amino acid transporters in the kidney. In 2020, these pioneering findings became critical and ACE2 became the most researched molecule globally as the cellular receptor for SARS-CoV-2. We published a breakthrough paper demonstrating that a drug based on human recombinant soluble (hrs)ACE2 (APN01) can inhibit replication of SARS-CoV-2 by 1000 to 5000-fold in cell lines and human blood vessel and kidney organoids. This drug is now being tested for acute lung injury in humans and early data in a study describing compassionate use of APN01 showed promising results. I am also part of the Long COVID Web, a pan-Canadian network of leading researchers and experts investigating post-COVID condition.

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. Monteil V, et al. Human soluble ACE2 improves the effect of remdesivir in SARS-CoV-2 infection. EMBO Mol Med. 2021;13(1):e13426.
3. Zoufaly A, et al. Human recombinant soluble ACE2 in severe COVID-19. Lancet Respir Med. 2020;8(11):1154-1158.
4. Capraz T, et al. Structure-guided glycol-engineering of ACE2 for improved potency as soluble SARS-CoV-2 decoy receptor. Elife. 2021;10:e73641. doi: 10.7554/eLife.73641.
5. Garreta E, et al., A diabetic milieu increases ACE2 expression and cellular susceptibility to SARS-CoV-2 infections in human organoids and patient cells. Cell Metab. 2022;S1550-4131(22)00136-X. doi: 10.1016/j.cmet.2022.04.009.
6. Garreta E, et al., Protocol for SARS-CoV-2 infection of kidney organoids derived from human pluripotent stem cells. STAR Protocols. 2022; 34(6):857-873.e9.
7. Shoemaker RH, et al. Development of an aerosol intervention for COVID-19 disease: Tolerability of soluble ACE2 (APN01) administered via nebulizer. PLoS One. 2022; 17(7):e0271066.
8. Hashimoto T, et al. ACE2 links amino acid malnutrition to microbial ecology and intestinal inflammation. Nature. 2012; 487(7408):477-81.

9. Danilczyk U, et al. Essential role for collectrin in renal amino acid transport. Nature. 2006;444(7122):1088-91.
10. 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.
11. Imai Y., et al. The SARS-coronavirus receptor ACE2 protects from severe acute lung failure. Nature. 2005; 436, 112-116.
12. Kuba K, et al. A critical role of angiotensin converting enzyme 2 (ACE2) in SARS pathogenesis. Nature Medicine. 2005; 11, 875-879.
13. Crackower M, et al. Angiotensin-converting enzyme 2 is an essential regulator of heart function. Nature. 2002; 417(6891):822-828.

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 progestin 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; 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

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 F-Resistant 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 oxicity. Nature. 2017; 549(7673): 538-542.
3. Taubenschmid J, et al. A vital sugar code for ricin toxicity. Cell Research, 2017; 27(11):1351-64.

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. Uribesalgo 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.

Ten most important publications:

1. Kong YY, Yoshida H, Sarosi I, Tan HL, Timms E, Capparelli C, Morony S, Oliveira-dos-Santos AJ, Van G, Itie A, Khoo W, Wakeham A, Dunstan CR, Lacey DL, Mak TW, Boyle WJ, **Penninger JM**. OPGL is a key regulator of osteoclastogenesis, lymphocyte development and lymph-node organogenesis. Nature. 1999 Jan 28;397(6717):315-23. *(2428 citations, Publons)* https://www.nature.com/articles/16852
2. Kong YY, Feige U, Sarosi I, Bolon B, Tafuri A, Morony S, Capparelli C, Li J, Elliott R, McCabe S, Wong T, Campagnuolo G, Moran E, Bogoch ER, Van G, Nguyen LT, Ohashi PS, Lacey DL, Fish E, Boyle WJ, **Penninger JM**. Activated T cells regulate bone loss and joint destruction in adjuvant arthritis through osteoprotegerin ligand. Nature. 1999 Nov 18;402(6759):304-9. *(1415 citations, Publons)* https://www.nature.com/articles/35005552
3. Fata JE, Kong YY, Li J, Sasaki T, Irie-Sasaki J, Moorehead RA, Elliott R, Scully S, Voura EB, Lacey DL, Boyle WJ, Khokha R, **Penninger JM**. The osteoclast differentiation factor osteoprotegerin-ligand is essential for mammary gland development. Cell. 2000 Sep 29;103(1):41-50. *(532 citations, Publons)* https://www.cell.com/fulltext/S0092-8674(00)00103-3
4. Crackower MA, Sarao R, Oudit GY, Yagil C, Kozieradzki I, Scanga SE, Oliveira-dos-Santos AJ, da Costa J, Zhang L, Pei Y, Scholey J, Ferrario CM, Manoukian AS, Chappell MC, Backx PH, Yagil Y, **Penninger JM**. Angiotensin-converting enzyme 2 is an essential regulator of heart function. Nature. 2002 Jun 20;417(6891):822-8. *(1087 citations, Publons)* https://www.nature.com/articles/nature00786

5. Kuba K, Imai Y, Rao S, Gao H, Guo F, Guan B, Huan Y, Yang P, Zhang Y, Deng W, Bao L, Zhang B, Liu G, Wang Z, Chappell M, Liu Y, Zheng D, Leibbrandt A, Wada T, Slutsky AS, Liu D, Qin C, Jiang C, **Penninger JM**. A crucial role of angiotensin converting enzyme 2 (ACE2) in SARS coronavirus-induced lung injury. Nat Med. 2005 Aug;11(8):875-9. *(1530 citations, Publons)* https://www.nature.com/articles/nm1267
6. Imai Y, Kuba K, Rao S, Huan Y, Guo F, Guan B, Yang P, Sarao R, Wada T, Leong-Poi H, Crackower MA, Fukamizu A, Hui CC, Hein L, Uhlig S, Slutsky AS, Jiang C, **Penninger JM**. Angiotensin-converting enzyme 2 protects from severe acute lung failure. Nature. 2005 Jul 7;436(7047):112-6. *(1257 citations, Publons)* https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7094998/
7. Wimmer RA, Leopoldi A, Aichinger M, Wick N, Hantusch B, Novatchkova M, Taubenschmid J, Hämmerle M, Esk C, Bagley JA, Lindenhofer D, Chen G, Boehm M, Agu CA, Yang F, Fu B, Zuber J, Knoblich JA, Kerjaschki D, **Penninger JM**. Human blood vessel organoids as a model of diabetic vasculopathy. Nature. 2019 Jan;565(7740):505-510. *(149 citations, Publons)* https://www.nature.com/articles/s41586-018-0858-8
8. Cronin SJF, Seehus C, Weidinger A, Talbot S, Reissig S, Seifert M, Pierson Y, McNeill E, Longhi MS, Turnes BL, Kreslavsky T, Kogler M, Hoffmann D, Ticevic M, da Luz Scheffer D, Tortola L, Cikes D, Jais A, Rangachari M, Rao S, Paolino M, Novatchkova M, Aichinger M, Barrett L, Latremoliere A, Wirnsberger G, Lametschwandtner G, Busslinger M, Zicha S, Latini A, Robson SC, Waisman A, Andrews N, Costigan M, Channon KM, Weiss G, Kozlov AV, Tebbe M, Johnsson K, Woolf CJ, **Penninger JM**. The metabolite BH4 controls T cell proliferation in autoimmunity and cancer. Nature. 2018 Nov;563(7732):564-568. *(63 citations, Publons)* https://www.nature.com/articles/s41586-018-0701-2
9. Stadlmann J, Taubenschmid J, Wenzel D, Gattinger A, Dürnberger G, Dusberger F, Elling U, Mach L, Mechtler K, **Penninger JM**. Comparative glycoproteomics of stem cells identifies new players in ricin toxicity. Nature. 2017 Sep 28;549(7673):538-542. *(51 citations, Publons)* https://www.nature.com/articles/s41586-018-0701-2
10. Elling U, Wimmer RA, Leibbrandt A, Burkard T, Michlits G, Leopoldi A, Micheler T, Abdeen D, Zhuk S, Aspalter IM, Handl C, Liebergesell J, Hubmann M, Husa AM, Kinzer M, Schuller N, Wetzel E, van de Loo N, Martinez JAZ, Estoppey D, Riedl R, Yang F, Fu B, Dechat T, Ivics Z, Agu CA, Bell O, Blaas D, Gerhardt H, Hoepfner D, Stark A, **Penninger JM**. A reversible haploid mouse embryonic stem cell biobank resource for functional genomics. Nature. 2017 Oct 5;550(7674):114-118. *(31 citations, Publons)* https://www.nature.com/articles/nature24027