

### PERSONAL INFORMATION

Ralf Reinhard Tonjes

### WORK EXPERIENCE

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- August 1986-April 1988 **Postdoc, scientist**  
Fraunhofer-Institute for Toxicology and Aerosol-Research, Division of Cell Biology, Hannover (Germany)  
Research on liver specific regulation of genes in mutant and transgenic mice.
- May 1988-July 1988 **Technical Product Manager**  
PROCTER & GAMBLE, Brussels (Belgium)  
Department of Product security; Consumer security; Dermatological safety of napkins based on acrylate technology.
- August 1988-June 1991 **Scientist, Deputy Head of Division of Cell Biology**  
Fraunhofer-Institute for Toxicology and Aerosol-Research, Division of Cell Biology, Hannover (Germany)  
Research on liver specific regulation of genes in mutant and transgenic mice. Analyses of oncogenesis.
- July 1991-December 2002 **Scientist, Head of section 6/2**  
Paul-Ehrlich-Institut, Langen (Germany)  
Genetically engineered vaccines
- January 2003-June 2006 **Scientist, Head of section 6/4**  
Paul-Ehrlich-Institut, Langen (Germany)  
Xenogeneic Cell Therapeutics
- July 2006- Present **Scientist, Head of section 6/4**  
Paul-Ehrlich-Institut, Langen (Germany)  
Non-vital Tissue Preparations, Xenogeneic Cell Therapeutics

### EDUCATION AND TRAINING

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- October 1977-March 1978 **Graduation, 1st Semester**  
University of Bremen (Germany)  
Biology, German, and Pedagogics.
- April 1978-May 1983 **Graduation, 1st State exam**  
Philipps-University of Marburg (Germany)  
Biology, German, Sports and Pedagogics.
- June 1983-July 1986 **PhD thesis, Dr. rer. nat.**  
Philipps-University of Marburg (Germany)  
Molecular biology, biochemistry and evolution of histone genes and histones.
- May 1990-May 1991 **Sabbatical**  
Rockefeller University, Molecular Cell Biology Laboratory, New York (United States)  
Research on liver specific regulation of genes in mutant mice.
- January 2001-April 2002 **Habilitation (Privatdozent), Venia legendi in Biochemistry**  
Goethe University of Frankfurt/Main (Germany)  
Molecular genetics and functional analyses of human and porcine endogenous retroviruses. Lectures and practical courses for students in Biochemistry at Goethe University, Frankfurt.
- May 2002- Present **Adjunct Professor in Biochemistry**  
Goethe University of Frankfurt/Main (Germany)  
Lectures and practical courses for students in Biochemistry at Goethe University, Frankfurt.

- Expertise** Evaluations of medicinal products including genetically engineered vaccines, human tissue preparations and xenogeneic cell therapeutics. Scientific Focus: 1) Mutant mice, genetically modified mice, pigs and genetically modified pigs for studies in developmental biology, microbiology, virology and xenotransplantation. 2) Molecular characterization of human and animal (murine, simian, ovine, porcine) endogenous retroviruses and analyses of biological relevance for human diseases, e.g. Diabetes type 1 (IDDM). 3) Analyses of (genetically modified) cell therapy and tissue engineering products (autologous, allogeneic, xenogeneic). 4) Analyses of gene expression profiles (transcriptome) as well as microbiological (microbiome) and virological (virome) burden of pig cells and tissues.
- Publications** Since 2008: Godehardt AW, Tönjes RR (2020) Xenotransplantation of Decellularized Pig Heart valves - Regulatory Aspects in Europe. *Xenotransplantation*: DOI: 10.1111/xen.12609 Reichart B, Längin M, Radan J, Mokolke M, Buttgerit I, Ying J, Fresch AK, Mayr T, Issl L, Buchholz S, Michel S, Ellgass R, Mihalj M, Egerer S, Baehr A, Kessler B, Kemter E, Kurome M, Zakhartchenko V, Steen S, Sjöberg T, Paskevicius A, Krüger L, Fiebig U, Denner J, Godehardt AW, Tönjes RR, Milusev A, Sfriso R, Rieben R, Walz C, Kirchner T, Ayares D, Lampe K, Schönmann U, Hagl C, Wolf E, Klymiuk N, Abicht J-M, Brenner P (2020) Pig-to-non-human primate heart transplantation: the final step toward clinical xenotransplantation? *The Journal of Heart and Lung Transplantation*: doi.org/10.1016/j.healun.2020.05.004 Godehardt AW, Ramm R, Gulich B, Tönjes RR, Hilfiker A (2019) Decellularized pig pulmonary heart valves - Depletion of nucleic acids measured by proviral PERV pol. *Xenotransplantation*: DOI: 10.1111/xen.12565 Godehardt AW, Fischer N, Rauch P, Gulich B, Boller K, Church GM, Tönjes RR (2019) Characterization of porcine endogenous retrovirus particles released by the CRISPR/Cas9 inactivated cell line PK15 clone 15. *Xenotransplantation*: DOI: 10.1111/xen.12563 Hawthorne WJ, Cowan PJ, Bühler LH, Yi S, Bottino R, Pierson RN, Ahn C, Azimzadeh A, Cozzi E, Gianello P, Lakey JRT, Luo M, Miyagawa S, Mohiuddin MM, Park CG, Schuurman HJ, Scobie L, Sykes M, Tector J, Tönjes RR, Wolf E, Nuñez JR, Wang W (2019): Third WHO Global Consultation on Regulatory Requirements for Xenotransplantation Clinical Trials, Changsha, Hunan, China December 12-14, 2018: "The 2018 Changsha Communiqué" The 10-Year Anniversary of The International Consultation on Xenotransplantation. *Xenotransplantation* 26: e12513. Godehardt AW, Petkov S, Gulich B, Fischer N, Niemann H, Tönjes RR (2018): Comparative gene expression profiling of pig-derived iPSC-like cells: Effects of induced pluripotency on expression of porcine endogenous retrovirus (PERV). *Xenotransplantation* 25: e12429. Tönjes RR (2018): Nonviral pathogens: Identification, relevance, and prevention for xenotransplantation. *Xenotransplantation*: doi.org/10.1111/xen.12413 Denner J, Godehardt AW, Tönjes RR (2018): Infektionsrisiken und mikrobiologische Sicherheit. In: Jochen Sautermeister (Hrsg.), *Tierische Organe in menschlichen Körpern. Biomedizinische, kulturwissenschaftliche, theologische und ethische Zugänge zur Xenotransplantation*. Paderborn: mentis. S. 45-63, ISBN 978-3-95743-011-3 Cooper DKC, Cowan P, Fishman JA, Hering BJ, Mohiuddin MM, Pierson RN 3rd, Sachs DH, Schuurman HJ, Dennis JU, Tönjes RR (2017): Miscellaneous. *Xenotransplantation* 24: 12365. Cozzi E, Tönjes RR, Gianello P, Bühler LH, Rayat GR, Matsumoto S, Park CG, Kwon I, Wang W, O'Connell P, Jessamine S, Elliott RB, Kobayashi T, Hering BJ (2016): First update of the International Xenotransplantation Association consensus statement on conditions for undertaking clinical trials of porcine islet products in type 1 diabetes - Chapter 1: update on national regulatory frameworks pertinent to clinical islet xenotransplantation. *Xenotransplantation* 23: 14-24. Denner J, Tönjes RR, Takeuchi Y, Fishman J, Scobie L (2016): First update of the International Xenotransplantation Association consensus statement on conditions for undertaking clinical trials of porcine islet products in type 1 diabetes - Chapter 5: recipient monitoring and response plan for preventing disease transmission. *Xenotransplantation* 23: 53-59. Godehardt AW, Rodrigues Costa M, Tönjes RR (2015): Review on porcine endogenous retrovirus detection assays-impact on quality and safety of xenotransplants. *Xenotransplantation* 22: 95-101. Godehardt AW, Schilling-Leiß D, Sanzenbacher R, Tönjes RR (2015): Xenogene Zelltherapeutika : Behandlung von Typ 1 Diabetes mittels porciner Pankreasinseln und -inselzellen. *Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz* 58: 1281-1288. Godehardt AW, Tönjes RR (2015): Transcriptome analysis for comprehensive profiling of quality and safety of pig cells. *Symposium on Xenotransplantation. Xenotransplantation* 22: 161. Tönjes RR, Hergert P: Germany: Regulation of Tissues and Tissue Banking - A Special Case. In: Phillips GO (Hrsg.), *Legal Basis of Global Tissue Banking: A Proactive Clinical Perspective*. Singapore: World Scientific Publishing Co. Pte. Ltd., 2015. S. 211-226 ISBN 987-9814663434. Reichart B, Niemann H, Chavakis T, Denner J, Jaeckel E, Ludwig B, Marckmann G, Schnieke A, Schwinzer R, Seissler J, Tönjes RR, Klymiuk N, Wolf E, Bornstein SR (2015): Xenotransplantation of porcine islet cells as a potential option for the treatment of type 1 diabetes in the future. *Horm Metab Res* 47: 31-35. Tönjes RR, Godehardt AW (2015): Impact of PERV infection

on the pig transcriptome. *Xenotransplantation* 22 (Issue Supplement S1): S8-S9. Bhat RK, Rudnick W, Antony JM, Maingat F, Ellestad KK, Wheatley BM, Tönjes RR, Power C (2014): Human Endogenous Retrovirus-K(II) Envelope Induction Protects Neurons during HIV/AIDS. *PLoS One* 9: e97984. Costa MR, Fischer N, Gulich B, Tönjes RR (2014): Comparison of porcine endogenous retroviruses infectious potential in supernatants of producer cells and in cocultures. *Xenotransplantation* 21: 162-173. Schilling-Leiß D, Witt F, Tönjes RR (2014): Bericht zur Meldung nach § 8d Transplantationsgesetz (TPG) für die Jahre 2009 bis 2011. *Bundesgesundheitsbl - Gesundheitsforsch - Gesundheitsschutz* 57: 111-127. Tönjes RR (2013) Safe Transplantation. *Lifeline. Medical research for healthy lives International Innovations* 1/2013: 82-83. Denner J, Tönjes RR (2013) Berlin Symposium on Xenotransplantation. July 13, 2012, Robert Koch Institute, Berlin, in association with the 24th International Congress of the Transplantation Society (TTS), July 15-19, 2012 at the ICC in Berlin. *Xenotransplantation* 20: 39-64. Denner J, Tönjes RR (2012) Infection Barriers to Successful Xenotransplantation Focusing on Porcine Endogenous Retroviruses. *Clinical Microbiology Reviews* 25(2): 318-343. Denner J, Tönjes RR (2012) Berlin Symposium on Xenotransplantation, German DFG-Transregio Research Group Xenotransplantation (FOR 535) together with the 14th Minisymposium Xenotransplantation of the German Working Group Xenotransplantation (DAX), June 9-10, 2011, Robert Koch Institute, Berlin. *Xenotransplantation* 19: 2-22. Kaulitz D, Mihica D, Dorna D, Rodrigues Costa M, Petersen B, Niemann H, Tönjes RR, Denner J (2011). Development of sensitive methods for detection of porcine endogenous retrovirus-C (PERV-C) in the genome of pigs. *Journal Virological Methods* 175: 6065. Denner J, Tönjes RR (2011) Berlin Symposium on Xenotransplantation, German DFG-Transregio Research Group Xenotransplantation together with the 13th Minisymposium Xenotransplantation of the German Working Group Xenotransplantation (DAX), June 3-4, 2010, Robert Koch Institute, Berlin. *Xenotransplantation* 18(1): 56-72. Dörrschuck E, Fischer N, Bravo IB, Hanschmann K-M, Kuiper H, Spötter A, Möller R, Cichutek K, Münk C, Tönjes RR (2011) Restriction of Porcine Endogenous Retrovirus by Porcine APOBEC3 Cytidine Deaminases. *J. Virol.* 85(8): 3842-3857. Cover photograph in *Journal of Virology* 85(17). Kaulitz D, Mihica D, Plesker R, Geissler A, Tönjes RR, Denner J (2011) Absence of infection in pigs inoculated with high-titre recombinant PERV-A/C. *Archives of Virology* 156: 707-710. Meije Y, Tönjes RR, Fishman JA (2010) Retroviral Restriction Factors and Infectious Risk in Xenotransplantation. *American Journal of Transplantation* 10(7): 1511-1516. Denner J, Tönjes RR. (2010) International Symposium on Xenotransplantation, DFG-Transregio Research Group Xenotransplantation and 12th Minisymposium Xenotransplantation of the German Working Group Xenotransplantation (DAX), Berlin, June 3-5, 2009. *Xenotransplantation* 17: 94-120. Jungmann A, Tönjes RR (2008) Retrotransposition - another obstacle for xenotransplantation? *Transplantation Proceedings* 40(2): 596-597. Dörrschuck E, Münk C, Tönjes RR (2008) APOBEC3 proteins and porcine endogenous retroviruses. *Transplantation Proceedings* 40(4): 959-961. Schilling-Leiß D, Godehardt AW, Scherer J, Cichutek K, Tönjes RR (2008). Authorization Procedures for Classical Tissue Preparations according to Section 21a German Medicinal Products Act (Arzneimittelgesetz; AMG). *Genehmigungsverfahren für klassische Gewebezubereitungen gemäß § 21a Arzneimittelgesetz (AMG)*. *Transfus Med Hemother* 35(6): 453-462. Boller K, Schönfeld K, Lischer S, Fischer N, Hofmann A, Kurth R, Tönjes RR (2008) Human endogenous retrovirus HERV-K113 is capable of producing intact viral particles. *J. Gen. Virol.* 89: 567-572.

**Projects** DFG SFB TRC 127, Collaborative Research Centre, Biology of xenogeneic cell, tissue and organ transplantation - from bench to bedside: Due to COVID-19 pandemic review process delayed, grant extended 01.07.2020 31.12.2020. DFG SFB TRC 127, Collaborative Research Centre, Biology of xenogeneic cell, tissue and organ transplantation - from bench to bedside, 01.07.2016 30.06.2020. DFG SFB/Transregio 127, Collaborative Research Centre, Biologie der xenogenen Zell- und Organtransplantation vom Labor in die Klinik, 01.07.2012 30.06.2016. DFG Transregio Research Unit FOR 535 Xenotransplantation, 2004-2007; 2007-2010 (1st Renewal); 2010-2012 (2nd Renewal). BMBF Programme "Tissue Engineering", Feasibility study / Accompanying research Definition von Qualitäts- und Sicherheitsanforderungen an humane Stammzellen im Rahmen des Tissue Engineering (TE), 2005-2007. EU QLK2-CT-2002-70785 Xenodiagnostics, 2002-2004. EU QLK2-1999-40210 Xenotransplantation Exploratory Award, 1999. BMG Ressortforschung Xenotransplantation, 1999-2002. EU CRAFT BMH4-98-9579 Development of ultrasensitive diagnostic assays for the detection of genetic disorders, infections and for monitoring the therapeutic success, 1998-1999. DFG Research Project Pa 261/7-1 Entgiftung und hepatische Genkontrolle, 1991-1993.

**Memberships** Membership in Scientific Societies: Gesellschaft für Biochemie und Molekularbiologie (GBM); Deutsche Transplantationsgesellschaft (DTG); The Transplantation Society (TTS). Member of Editorial Board of "Xenotransplantation". Reviewer for numerous Scientific Journals. Foundation of the Deutsche Arbeitsgemeinschaft Xenotransplantation (DAX), 20 February 1998 at

Paul-Ehrlich-Institut, Langen, Germany. Shared leadership with Dr. Joachim Denner, Robert Koch-Institut, Berlin, Germany. Organisation of DAX Minisymposia and Symposia "Xenotransplantation", Paul-Ehrlich-Institut, Langen, and Robert Koch-Institut, Berlin, 1998-2013.

#### Other Relevant Information

German Expert and Representative at the European Commission (EC), Directorate D Health systems and products, Competent Authorities on Substances of Human Origin Expert Group (CASoHO). German Expert and Representative for Tissues and Cells at the European Directorate for the Quality of Medicines & HealthCare (EDQM), European Committee on Organ Transplantation (CD-P-TO). Member of permanent Working Group "Richtlinie zur Entnahme und Übertragung von menschlichen Keimzellen im Rahmen der assistierten Reproduktion" at German Medical Association (Bundesärztekammer, BÄK), Berlin. Since 2019 Member of permanent Working Group "Umschriebene Fortschreibung der Richtlinie zur Gewinnung von Spenderhornhäuten und zum Führen einer Augenhornhautbank" at German Medical Association (Bundesärztekammer, BÄK), Berlin. Since 2019 World Health Organization (WHO). Third WHO Global Consultation on Regulatory Requirements for Xenotransplantation Clinical Trials. Organized in collaboration with the International Xenotransplantation Association. Representative of the European Medicines Agency, Changsha, China, 12-14 December 2018 Member of Working Group "Umschriebene Fortschreibung der Richtlinie zur Gewinnung von Spenderhornhäuten und zum Führen einer Augenhornhautbank" at German Medical Association (Bundesärztekammer, BÄK), Berlin, 2016-2017. Member of Working Group "Richtlinie zur Entnahme und Übertragung von menschlichen Keimzellen im Rahmen der assistierten Reproduktion" at German Medical Association (Bundesärztekammer, BÄK), Berlin, 2015-2017. Member of Working Group "Richtlinie zur Gewinnung von Spenderhornhäuten und zum Führen einer Augenhornhautbank" at German Medical Association (Bundesärztekammer, BÄK), Berlin, 2009-2014. World Health Organization (WHO). Second Global Consultation on Regulatory Requirements for Clinical Trials of Xenotransplantation. Organized in collaboration with the International Xenotransplantation Association and the Transplantation Society. Geneva, Switzerland, 17-19 October 2011. Chairman of the Consultation: Ralf R. Tönjes, Germany. Member of Working Group on Guideline "Xenogeneic Cell-Based Medicinal Products" at European Agency for the Evaluation of Medicinal Products (EMA), London; Date for coming into operation, January 2010. World Health Organization (WHO). First Global Consultation on Regulatory Requirements for Clinical Trials of Xenotransplantation. Organized in collaboration with the Ministry of Health of China, the International Xenotransplantation Association and the University of Central-South China. Changsha, China, 19-21 November 2008. Coordinator of world-wide WHO network for monitoring, control and diagnostics of Xenotransplantations, since January 2007. World Health Organization (WHO). Advisory Consultation on Xenotransplantation; Clinical Procedures (CPR/EHT); Representative of Germany and of the European Agency for the Evaluation of Medicinal Products (EMA), Geneva, Switzerland, 18-20 April 2005. Member of Working Group "Xenogeneic cell therapy" at European Agency for the Evaluation of Medicinal Products (EMA), London; Drafting of a Points-to-Consider-Document, Date for coming into operation, June 2004. Member of the Steering and Expert Group for the Preparation of a Workshop by the Organisation For Economic Cooperation And Development (OECD) "Biotechnology for Infectious Diseases", Lisboa, Portugal, 07-09 October 2002. Panel Discussant representing Germany. Cooperation as invited expert for the Federal Republic of Germany, Conference of the Food and Drug Administration (FDA) Subcommittee Xenotransplantation 3-4 June 1999, Bethesda, MD, USA.