## BIOGRAPHICAL SKETCH

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NAME: **Schatzl, Hermann M.**

eRA COMMONS USER NAME (credential, e.g., agency login):

POSITION TITLE: Professor, Prion Biology and Immunology; Associate Dean, Research

EDUCATION/TRAINING *(Begin with baccalaureate or other initial professional education, such as nursing, include postdoctoral training and residency training if applicable. Add/delete rows as necessary.)*

| INSTITUTION AND LOCATION | DEGREE *(if applicable)* | Completion Date MM/YYYY | FIELD OF STUDY |
|---|---|---|---|
| Ludwig Maximilian University Munich, Germany | M.D. | 06/91 | Medicine |
| Ludwig Maximilian University of Munich (LMU) | Dr. med. (Ph.D.) | 10/91 | Retrovirology/Virology |
| Max von Pettenkofer-Institute, LMU Munich | Postdoctoral training | 1991-1992 | Virology |
| University of California at San Francisco, U.S.A. | Postdoctoral training | 1993-1995 | Prion Research, Neurology |
| Ludwig Maximilian University of Munich, Germany | Residency training | 1995-2001 | Med. Microbiology, Virology & Infectiology |

### A. Personal Statement

My experience covers human, animal and environmental health, as a tenured professor at faculties of human medicine (Germany), agriculture (USA), and now veterinary medicine (Canada). My work over 30 years studied infectious diseases, including human retroviruses, HIV, hepatitis viruses, SARS-CoV and prions. Over the past 25 years my work focused on the cellular and molecular biology of prion diseases. My laboratory has consistently produced high-quality outcomes in the field of infectology and prion disease biology and used this for devising anti-prion strategies. Trained by S.B. Prusiner (Nobel Prize 1997), I have established my own laboratory at the University of Munich, Germany, in 1995. From 2002 to 2010, I was Head of the Clinical Virology Unit at the Technical University of Munich. In 2010, I was appointed Wyoming Endowed Excellence Chair in Prion Biology, and in 2013, I joined the University of Calgary and set up the Calgary Prion Research Unit. I have trained >120 students and researchers in my laboratory, 9 of them having now faculty/junior faculty positions. I have published >120 research articles, >30 reviews and book chapters and 3 textbooks (Molecular Virology, Molekulare Virologie), and acquired >$25,000,000 of external funding for my lab. My laboratory pioneered active immunization against prion disease, characterized the impact of autophagy in prion infection, and contributed new cell models for studying prion and prion-like propagation. I participated in grant review activities worldwide and was co-host of the international conference Prion2019 (450 participants) in Edmonton, Canada. Most recently, I co-organized 2 virtual workshops on One Health & chronic wasting disease (CWD), attracting >230 participants from Canada, USA, Norway, Sweden, Germany, Italy and Spain. I lead the Calgary Prion Research Unit and I am Associate Dean Research, Faculty of Veterinary Medicine. I was founding member of the Canadian-German CWD macaque consortium that studies the zoonotic potential of CWD by inoculation into *Cynomolgus* macaques since 2008. My laboratory passaged macaque CWD into various rodent hosts, providing the first experimental evidence that CWD can orally infect old-world monkeys, considered a relevant non-human primate model. We also showed that it is feasible to interfere in prion infection by inducing self-antibodies against the normal prion protein ($PrP^C$) by active vaccination. Our recent results showed that our vaccine extends survival time to CWD in transgenic mouse models by up to 70%. Testing this strategy in the appropriate small and large animal models is the next logical step.

- **Schatzl,** H.M. Prion protein dimers useful for vaccination. Patent protection filed in 2001 and approved for EU countries in 2006 and USA in 2008 (**US Patent** 7387886).

- **Schatzl**, Abdulrahman, Zukiwski, Gilch, Proniuk. Compositions and methods for reducing prion levels. Patent issued 2018 (WO2017151687A1, US9974771B2).
- Abdulrahman, B.A., Abdelaziz, D.H., **Schatzl**, H.M. (2018). Autophagy regulates exosomal release of prions in neuronal cells. *JBC* 293, 8956-68. *Faculty1000prime recommended*.
- Abdelaziz, D., Thapa, S., Brandon, J., Maybee, J., Vankuppeveld, L., McCorkell, R., **Schatzl**, H.M. (2018). Recombinant prion protein vaccination of transgenic elk PrP mice and reindeer overcomes self-tolerance and protects mice against chronic wasting disease. *JBC* 293, 19812-22.

## B. Positions and Honors

### Positions and Employment

1995-2002 Assistant Professor, Max von Pettenkofer-Institute for Virology, University of Munich, Germany
1997-2002 Group Leader and Principal Investigator, Gene Center Munich, Germany
2002-2010 Professor of Clinical Virology (with tenure) and Head of Clinical Virology Section, Technical University of Munich, Germany
2006-2007 Director (interim) of the Institute of Virology, Technical University of Munich, Germany
2010-2013 Wyoming Endowed Excellence Chair in Prion Biology, University of Wyoming, Laramie, U.S.A.
2013- Professor of Prion Biology & Immunology, University of Calgary, Canada
2013-2019 Adjunct Professor, University of Wyoming, Departments of Vet. Sciences and Molecular Biology
2014-2019 Director (scientific), Prion-Virology Animal Facility, University of Calgary, Canada
2015- Head, Calgary Prion Research Unit, University of Calgary, Canada
2017-2023 Associate Dean, Research, Faculty of Veterinary Medicine, University of Calgary, Canada

### Other Experience and Professional Memberships

**Advisory and Review Committees and Boards**

1995- International and national advisory board and review board activity; e.g. Canada (CIHR), U.S.A (NIH), U.K. (MRC, MAFF, BBSRC, DH), Germany (BMBF, DFG), France (ANR), Italy (Telethon), Switzerland (SNF), Austria, South Africa, India, Australia and Israel (GIF)
2002-2008 Elected Member Scientific Advisory Board, German TSE-Platform
2003- Annual Prion Conference Organizing Committee (2003, 2005 and 2020) and International Advisory Committee (e.g. 2009, 2010, 2012, 2013, 2014, 2015, 2016, 2018)
2005-2010 Member MRC New Therapies Scrutiny Group, U.K.
2009-2015 MRC member of visiting Subcommittee; Quinquennial Review MRC Prion Unit, London, U.K.
2010- NIH study section/special emphasis panel ad hoc referee: CNBT, BDCN, CMBG, CMND, CDIN, ZRG1 panels (e.g. ZNS1 SRB-T (35), ZNS1 SRB-H 12; ZRG1 IDIB-D (90))
2011- Editorial board member of ‘Prion’, 'bio-protocol' and ‘Scientific Reports’
2019 Co-Host International Prion2019 Conference (Edmonton, Alberta, Canada)

### Honors

1991 Thesis Award 'summa cum laude', University of Munich, Germany
1992 'Henry Kaplan Award', Modern Trends in Human Leukemia X, Wilsede, Germany
1995 Stipend Ciba Foundation, London, U.K.
1996 Stipend 2nd Annual German American Frontiers of Science Symposium, U.S.A.
1997 1st Prize for scientific presentation Research Festival Munich, Germany
2008 Japanese Health Science Foundation Award; keynote speaker 'Prion 2008 Japan'
2012 WWAMI Lecture (elected) for 2011-2012 Science of Medicine Lecture series (UoWash)
2019 Outstanding Achievement in Graduate Supervision, Teaching award of Faculty of Veterinary Medicine (one per year)

## C. Contributions to Science

*Publication metrics: total >130; h-index: 44; citations: >15,200 (Google Scholar), names of trainees underlined. Over 30 reviews and book chapters, 3 textbooks (Molecular Virology, Molekulare Virologie; Springer)*

### 1) Characterizing roles and impact of autophagy in prion infection

Our work resulted in the first mechanistic descriptions of the role of autophagy in prion infection. We showed that chemical induction of autophagy induces clearance of prions in vitro and in vivo, which can be used as a therapeutic strategy. We also showed that the autophagy machinery has a role in prion propagation, and that autophagy regulates the exosomal release of prions in neuronal cells.

a. Ertmer, A., Gilch, S., Yun, S.-W., Flechsig, E., Klebl, B., Stein-Gerlach, M., Klein, M.A., **Schätzl**, H.M. (2004). The tyrosine kinase inhibitor STI571 induces cellular clearance of $PrP^{Sc}$ in prion-infected cells. *JBC* 279: 41918-27.
b. Ertmer, A., Huber, V., Gilch, S., Erfle, V., Yoshimori, T., Duyster, J., Elsässer, H.P., **Schätzl**, H.M. (2007). The anticancer drug imatinib induces cellular autophagy. *Leukemia* 21, 936-42.
c. Aguib, Y., Heiseke, A., Gilch, S., Riemer, C., Baier, M., **Schätzl**, H.M., Ertmer, A. (2009). Autophagy induction by trehalose counter-acts cellular prion infection. *Autophagy* 5, 361-69.
d. Abdulrahman, B.A., Abdelaziz, D.H., **Schatzl**, H.M. (2018). Autophagy regulates exosomal release of prions in neuronal cells. *JBC* 293, 8956-68. *Faculty1000prime recommended*.

**2) Pioneering active immunization strategies against prion disease, including CWD**
My laboratory pioneered active immunization against prion disease. We showed that it is feasible to interfere in prion infection by inducing self-antibodies against $PrP^{c}$ by active vaccination. We overcame self-tolerance by using β-sheeted multimeric rPrP as immunogen and induced humoral and cellular responses against PrP without adverse side effects. Our vaccine extends survival time to CWD in transgenic mouse models by 70%.

a. **Schatzl**, H.M. Prion protein dimers useful for vaccination. Patent protection filed in 2001 and approved for EU countries in 2006 and USA in 2008 (US Patent 7387886).
b. Gilch, S., Wopfner, F., Renner-Müller, I., Kremmer, E., Bauer, C., Wolf, E., Brem, G., Groschup, M. & **Schätzl**, H.M. (2003). Polyclonal anti-PrP auto-antibodies induced with dimeric PrP interfere efficiently with $PrP^{Sc}$ propagation in prion-infected cells. *JBC* 278, 18524-31.
c. Kaiser-Schulz, G., Heit, A., Quintanilla-Martinez, L., Hammerschmidt, F., Hess, S., Jennen, L., Rezaei, H., Wagner, H., **Schätzl**, H.M. (2007). PLGA microsphere co-encapsulated recombinant tandem PrP with CpG-ODN breaks self-tolerance to PrP in wt mice and induces CD4 and CD8 T cell responses*. J. Immunology* 179, 2797-07.
d. Abdelaziz, D., Thapa, S., Brandon, J., Maybee, J., Vankuppeveld, L., McCorkell, R., **Schatzl**, H.M. (2018). Recombinant prion protein vaccination of transgenic elk PrP mice and reindeer overcomes self-tolerance and protects mice against chronic wasting disease. *JBC* 293, 19812-22.

**3) Modulation of protein quality control pathways as novel intervention strategy in prion disease**
We pioneered interference in prion propagation by manipulation of cellular quality control mechanisms. We showed that protein quality control mechanisms in the secretory pathway can directly influence prion conversion by determining on the quality of conversion substrates. These studies provided mechanistic insights into basic molecular mechanisms relevant for neurodegenerative diseases.

a. Gilch, S., Winklhofer, K. F., Groschup, M. H., Nunziante, M., Lucassen, R., Spielhaupter, C., Muranyi, W., Riesner, D., Tatzelt, J., **Schätzl,** H.M. (2001). Intracellular re-routing of prion protein prevents propagation of $PrP^{Sc}$ and delays onset of prion disease. *EMBO J*. 20, 3957-66.
b. Nunziante, M., Ackermann, K., Dietrich, K., Wolf, H., Gadtke, L., Gilch, S., Vorberg, I., Groschup, M., **Schätzl**, H.M. (2011). Proteasomal Dysfunction and ER stress enhance trafficking of prion protein aggregates through the secretory pathway and increase accumulation of $PrP^{Sc}$. *JBC* 286, 33942-53. *F1000 must read*.
c. Thapa, S., Abdulrahman, B., Abdelaziz, D., Lu, L., Ben Aissa, M., **Schatzl**, H.M. (2018). Overexpression of quality control proteins reduces prion conversion in prion-infected cells. *JBC* 293, 16069-82. *F1000 recommended*.
d. Thapa, S., Abdelaziz, D., Abdulrahman, B., **Schatzl**, H.M. (2020). Sephin1 reduces prion infection in prion-infected cells and animal model. *Mol. Neurobiol*. 57, 2206-19.

**4) New cell models for studying prion infection and prion-like propagation**
We established new cell line models for prion disease, including gene-edited cells for CWD prion propagation. We demonstrated that cytosolic protein aggregates (yeast Sup35 prion domain NM) behave as infectious entities in mammalian cells. These data have implications for understanding prion-like phenomena associated with human diseases and for the growing number of amyloidogenic proteins discovered in mammals.

a. **Schätzl**, H., Laszlo, L., Holtzman, D.M., Weiner, R.I., Mobley, W. & Prusiner, S.B. (1997). A hypothalamic neuronal cell line persistently infected with scrapie prions exhibits apoptosis. *J. Virol.* 71, 8821-31.
b. Hofmann, J.P., Denner, P., Nussbaum-Krammer, C., Kuhn, P.H., Suhre, M.H., Scheibel, T., Lichtenthaler, S.F., **Schatzl**, H.M., Bano, D., Vorberg, I.M. (2013). Cell-to-cell propagation of infectious cytosolic protein aggregates. *PNAS* 110, 5951-56. *Featured PNAS (In This Issue), Cell (Leading Edge)*.

c. Walia, R., Ho, C.C., Lee, C., Gilch, S., **Schatzl**, H.M. (2019). Gene-edited murine cell lines for propagation of chronic wasting disease prions. *Sci. Rep*. 9(1):11151.
d. Tahir, W., Abdulrahman, B., Abdelaziz, D.H., Thapa, S., Walia, R., **Schätzl**, H.M. (2020). An astrocyte cell line that differentially propagates murine prions. *JBC* 295, 11572-83. *Recommended in Faculty Opinion.*

**5) Molecular and medical virology**

My group studied a variety of viruses under BSL2 and 3 conditions, including HTLV-1/STLV-1, HIV, HBV, norovirus, and SARS-CoV. This included studying the molecular biology of viral infections, establishing diagnostic approaches, and defining prophylactic and therapeutic targets.

a. Jilg, W., Sieger, E., Zachoval, R. & **Schätzl**, H. (1995). Individuals with antibodies against hepatitis B core antigen as the only serological marker for hepatitis B infection: high percentage of carriers of hepatitis B and C virus. *J. Hepatol*., 23, 14-20.
b. Voevodin, A., Samilchuk, E. **Schätzl**, H., Boeri, E. & Franchini, G. (1996). Interspecies transmission of macaque Simian T-cell Leukemia/Lymphoma Virus type I (STLV-I) in baboons resulted in the outbreak of malignant lymphoma. *J. Virol*., 70, 1633-39.
c. Hoffmann, D., Seebach, J., Cosma, A., Goebel, F.D., Strimmer, K., **Schätzl**, H.M. & Erfle, V. (2008). Therapeutic vaccination reduces HIV sequence variability. *FASEB J*. 22, 437-44.
d. Schneider, M., Ackermann, K., Stuart, M., Wex, C., Protzer, U., **Schätzl**, H.M., Gilch, S. (2012). Severe acute respiratory syndrome coronavirus replication is severely impaired by MG132 due to proteasome-independent inhibition of m-Calpain. *J. Virol*. 86, 10112-22.

**Complete List of Published Work in my Bibliography:**
https://www.ncbi.nlm.nih.gov/myncbi/hermann.schatzl.1/bibliography/public/

## D. Additional Information: Research Support and/or Scholastic Performance

### Ongoing Research Support

NIH R01 (1R01 NS121016-01) Schatzl (PI) 06/01/2021 to 05/31/2026
*Redefining the zoonotic potential of chronic wasting disease*
The goal of this project is to redefine the zoonotic potential of CWD by characterizing the biological properties of CWD prions emerging upon experimental transmission into macaques, for obtaining important information on how CWD could manifest in humans.
Role: lead-PI

NIH R01 (1R01 NS121016-01A1) Mathiason (PI) 07/01/2021 to 06/30/2026
*Chronic Wasting Disease vaccines*
The goal of project is to determine the efficacy, safety and ability of prototype CWD vaccines, alone or additive in combination to protect against chronic wasting disease infection
Role: co-applicant/subawardee

Alberta Environment and Parks Gilch & Schatzl (PIs) 04/01/2021 to 03/31/2023
*Oral vaccination strategies to mitigate transmission of chronic wasting disease*
The goal is to evaluate an oral vaccination strategy, which will be effective in reducing the spread of CWD.
Role: lead-PI

CFI 2020 INNOVATION FUND Kubes/McCoy (PIs) 07/01/2021 to 06/30/2026
*Wild Microbiome and Immunity Centre*
The goal of this infrastructure grant is to create the Wild Microbiome and Immunity Center (WiMIC) at the University of Calgary.
Role: Co-applicant/Principal user

CFI 2020 INNOVATION FUND Westaway/Woodside (PIs) 07/01/2021 to 06/30/2026
*Protein Misfolding Scientific Exploration" (ProMiSE) Team: Infrastructure*
The goal of this infrastructure grant is to foster research and method development, spanning atomic and molecular detail of protein misfolding to animal work and therapy development.
Role: Co-applicant/Principal user

Alberta Innovates/Alberta Prion Research Institute Westaway, Schatzl (PIs) 05/01/2016 to 03/31/2022
*Support of biological testing for prions and toxic misfolded proteins at the Universities of Alberta and Calgary*
The goal of this project is to consolidate activities and to support animal, cell culture and protein templating reaction studies that form a foundation for research into prions and prion-like diseases.
Role: Co-PI

Genome Canada/Genome Alberta McKenzie, Wishart (PIs) 10/01/2016 to 09/30/2021
*Systems biology and molecular ecology of Chronic Wasting Disease*
The goal of this study is to inform CWD biology, generate tools to detect disease and guide management strategies, using genomics and metabolomics approaches.
Role: Co-applicant

Natural Sciences and Engineering Research Council (NSERC) Schatzl (PI) 04/01/2020 to 03/31/2025
*Chronic wasting disease vaccine: inducing autoantibodies for interfering in CWD infection and prion shedding*
The goal of this study is to optimize CWD vaccine candidates.
Role: PI

Margret-Gunn Endowment University of Calgary Schatzl (PI) 07/01/2020 to 06/30/2022
*Developing a vaccine against chronic wasting disease in caribou*
The goal of this study is to develop prototype vaccines against CWD in caribou, using knock-in mouse models expressing wild-type and polymorphic caribou PrP alleles.
Role: PI

Alberta Innovates/Alberta Prion Research Institute Schatzl (PI) 04/01/2019 to 09/31/2021
*Novel cell culture models for studying old and new prions*
The goal of this project is to establish new cell culture-based tools for studying known and novel prions, including camel prions.
Role: PI

**Completed Research Support (recent)**

Alberta Innovates/Alberta Prion Research Institute Schatzl (PI) 03/01/2016 to 06/31/2021
*Final proof for presence or absence of prion infectivity and conversion activity in incubating macaques inoculated orally with CWD prions*
The goal of this study is to detect or exclude prion infection in CWD-inoculated macaques, to help assessing the hazard of zoonotic CWD transmission to humans.
Role: PI

Alberta Innovates/Alberta Prion Research Institute Gilch (PI) 04/01/2017 to 06/31/2021
*Expanding the use of cellulose ethers for treatment of prion and prion-like disorders*
The goal of this project is to test the potential application of compounds called cellulose ethers as inhibitors of the formation of misshaped proteins that cause inherited human prion disease, CWD or AD, and to combine different compounds for treatment to improve the therapeutic outcome.
Role: Co-applicant

Alberta Innovates/Alberta Prion Research Institute Schatzl (PI) 04/01/2017 to 06/31/2021
*Hsp110: a new therapeutic target in prion disease*
The goal of this study is to test whether Hsp110 is capable of disaggregating $PrP^{Sc}$ aggregates and represents a cellular modifier of prion infection.
Role: PI

NIH R01 NS076853-01A1 PI: Schatzl (year 1); Jarvis (years 2-5) 07/01/2013 to 06/30/2018
*Elucidating the cellular mechanisms of prion propagation and clearance for devising new targets for intervention in prion disease*
The goal of this project is to study the cellular and molecular biology of prion infections and to use gained understanding for delineating novel targets for intervention.
Role: PI Year 1, Subaward Principal Investigator Years 2-5