

## CURRICULUM VITAE

### Priv. Doz. Dr. Dr. Christian Michael Grimm

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#### **QUALIFICATION SUMMARY:**

- Extensive international research experience both in academic and industrial research settings
- PhD and postdoctoral training in molecular biology, cell biology, pharmacology, and physiology (e.g. in the areas of pain, inner ear biology, and metabolic diseases); target focus: ion channels
- Habilitation in Pharmacology LMU München
- Current affiliation: Pharmacy/Pharmacology Department, LMU München, Germany
- Past affiliations: Pfizer Ltd Global R&D, UK; Stanford University, Palo Alto, CA, USA; Harvard University, Boston, MA, USA; Freie Universität Berlin, Germany; Bayer AG, Bayer Health Care, Leverkusen, Germany
- >30 publications in international peer-reviewed journals such as Nature Communications, Chem. & Biol. (Cell Press), EMBO Journal, Science, JBC (Journal of Biological Chemistry), Traffic, and PNAS (Proceedings of the National Academy of Sciences of the USA)
- Member of the Collaborative Research Center (SFB/Transregio) 152; funded by the German (DFG) and Bavarian (BFS) Research Foundations and the Fritz-Thyssen Foundation

#### **PROFESSIONAL EXPERIENCE AND KEY ACHIEVEMENTS:**

- 01/2015 - Ludwig-Maximilians-Universität (LMU) München, Germany**  
**SFB (CRC) 152 Group Leader, Privatdozent (Pharmacology and Physiology)**  
Department of Pharmacy - Center for Drug Research and Center for Integrated Protein Science Munich (CIPSM)
- 02/2015** *Short term research stay: Université de Genève, Switzerland* (Laboratory of Prof. Dr. Jean Gruenberg, funded by the Fritz-Thyssen Foundation and the SFB (CRC) 152)
- 01/2015** **Habilitation** in Pharmacology, **LMU München**
- 12/2011 - 01/2015** **Ludwig-Maximilians-Universität (LMU) München, Germany**  
**Group Leader (Pharmacology and Physiology)**  
Department of Pharmacy - Center for Drug Research and Center for Integrated Protein Science Munich (CIPSM) (Director: Prof. Dr. Martin Biel)
- Work on mucolipins (TRPML channels) and TPCs (Two-pore channels), and their functions in the endolysosomal system
  - Discovered that TPC2 interacts with syntaxins and that loss of TPC2 leads to hepatic cholesterol accumulation and hypercholesterolemia (published in **Nature Commun.**, 2014)
  - Discovered novel small molecule activators of TRPML1 that rescue the function of mutations responsible for mucopolipidosis type IV (published in **Nature Commun.**, 2014)
  - Discovered that TRPML1 interacts with TMEM163 to control intracellular zinc levels (published in **Traffic**, 2014)
  - Co-discovered that inhibition of TPCs interferes with Ebola virus trafficking and disease development (published in **Science**, 2015)
  - Acquired extramural funding: DFG (GR-4315/1-1, "Einzelantrag") and Bavarian Research Foundation (DOK154-13)

- 09/2009 - 06/2011**      **Pfizer Ltd Global R&D, Sandwich Laboratories, United Kingdom**  
**Principal Scientist / Group Leader, Pain Research Unit, Discovery Biology** (Director: Dr. Stephen Phillips, now UCB Belgium)
- Contributed key pharmacology data and mechanistic understanding of ion channel targets to support progression of candidate small molecules for the treatment of (neuropathic) pain
  - Member of 'new target team' to explore additional sensory disorders and to identify potential novel drug targets
  - Exploratory work on various cation channels (e.g. TRPV1, TRPA1, Nav1.7, K2P)
  - Discovered the molecular determinant of voltage dependent proton activation and potentiation of TRPV1 (published in **EMBO J.**, 2011) and explored pharmacological aspects of TRPV1 species differences (published in **JBC**, 2011)
- 10/2005 - 09/2009:**      **Stanford University School of Medicine, Stanford, CA, USA**  
**Postdoctoral Research Fellow, Neuroscience/ENT**  
Departments of Otolaryngology - Head and Neck Surgery and Molecular & Cellular Physiology (Prof. Dr. Stefan Heller, PhD)
- Focus on ion channels in inner ear function and physiology
  - Discovered mechanism leading to deafness in mice carrying mutations in the *trpm3* gene (published in **PNAS**, 2007 and **JBC**, 2009)
  - Generated *trpm3* knockout mouse model
  - Identified first small molecule synthetic agonists of TRPML1, TRPML2, and TRPML3 channels using HTS methods (in cooperation with Scripps Institute FL, USA), published in **Chem. & Biol.**, 2010 and **JBC**, 2012)
- 11/2004 - 09/2005:**      **Harvard University School of Medicine, Boston, MA, USA**  
**Postdoctoral Research Fellow, Neuroscience/ENT**  
Department of Otolaryngology and Program in Neuroscience, Massachusetts Eye & Ear Infirmary (Prof. Dr. Stefan Heller, PhD)
- Discovered PACSIN proteins as novel interaction partners of TRPV4 (published in **JBC**, 2006)
- 09/2004:**      **Dr. rer. nat. (PhD, summa cum laude) Freie Universität (FU) Berlin**  
•Thesis title: *Molecular and functional characterization of the melastatin-related TRP cation channel TRPM3*  
<http://www.logos-verlag.de/cgi-bin/buch/isbn/0706>  
•**Ernst Reuter Award 2005**, Freie Universität Berlin  
(best doctoral thesis in the Departments of Biology, Chemistry and Pharmaceutical Sciences of the Freie Universität Berlin in 2004)
- 01/2001 - 10/2004:**      **Freie Universität (FU) Berlin Medical School, Germany**  
**Graduate student in Molecular Biology/Pharmacology**  
Department of Pharmacology, (Prof. Dr. Günter Schultz, MD and PD Dr. Christian Harteneck, PhD)
- Functionally characterized novel ion channel (TRPM3, published in **JBC**, 2003 and **Mol. Pharmacol.**, 2005)
- 05/2000 – 10/2000:**      *Industrial Research Placement: Bayer AG, Bayer Health Care,*  
Pharmaceutical R&D, Leverkusen, Germany (Dr. Peter Kurka, PhD)
- 10/1995 - 12/2000:**      **Julius-Maximilians-Universität Würzburg, Germany**  
**Undergraduate studies** (German State Examination, equivalent to M.Sc.) in **Pharmaceutical Sciences**

## ADDITIONAL ACADEMIC DEGREES:

- 11/2011: **Dr. phil. (PhD, magna cum laude) History/Philosophy/Theory of Science**, University of Kassel and Max-Planck-Institute for the History of Science, Berlin, Germany (Prof. Dr. Dr. Kristian Köchy and Prof. Dr. Dr. Hans-Jörg Rheinberger) <http://www.logos-verlag.de/cgi-bin/buch/isbn/3049>
- 10/2006: **Master of Arts (M.A.), European Philosophy**

## PUBLICATIONS

### Peer-reviewed scientific articles

- Müller, C., Binder, U., Maurer, E., **Grimm, C.**, Giera, M., Bracher, F. (2015) Fungal sterol C22-desaturase is not an antimycotic target as shown by selective inhibitors and testing on clinical isolates. *Steroids*. 2015 Sep;101:1-6. doi: 10.1016/j.steroids.2015.05.004. Epub 2015 May 27
- Ruas, M., Davis, L.C., Chen, C.-C., Morgan, A.J., Chuang, K.-T., Walseth, T.F., **Grimm, C.**, Garnham, C., Powell, T., Biel, M., Wahl-Schott, C., Parrington, J., Galione, A. (2015) Endogenous TPCs are essential for NAADP-induced Ca<sup>2+</sup> signaling. *EMBO J.*, 34:1743-58
- Sakurai, Y., Kolokoltsov, A.A., Chen, C.-C., Tidwell, M.W., Bauta, W.E., Klugbauer, N., **Grimm, C.**, Wahl-Schott, C., Biel, M., Davey, R.A. (2015) Two pore channels control Ebolavirus host cell entry and are drug targets for disease treatment, *Science*, 347:995-8
- **Grimm, C.**, Holdt, L.M., Chen, C.-C., Hassan, S., Müller, C., Jörs, S., Cuny, H., Kissing, S., Schröder, B., Butz, E., Northoff, B., Castonguay, J., Luber, C.A., Moser, M., Spahn, S., Lüllmann-Rauch, R., Fendel, C., Klugbauer, N., Griesbeck, O., Haas, A., Mann, M., Bracher, F., Teupser, D., Saftig, P., Biel, M., Wahl-Schott, C. (2014) High susceptibility to fatty liver disease in two-pore channel 2-deficient mice. *Nature Commun.*, 5:4699. doi: 10.1038/ncomms5699
- Cuajungco, M.P., Basilio, L.C., Silva, J., Hart, T., Tringali, J., Chen, C.-C., Biel, M., **Grimm, C.**# (2014) Cellular zinc levels are modulated by TRPML1-TMEM163 interaction. *Traffic*, doi: 10.1111/tra.12205. [Epub ahead of print]
- Chen, C.-C., Keller, M., Hess, M., Schiffmann, R., Urban, N., Wolfgardt, A., Schaefer, M., Bracher, F., Biel, M., Wahl-Schott, C., **Grimm, C.**# (2014) A small molecule restores function to TRPML1 mutant isoforms responsible for mucopolidosis type IV. *Nature Commun.*, 5:4681. doi: 10.1038/ncomms5681
- Gao, Z., **Grimm, C.**, Becker, L., Ricci, A.J., Heller, S. (2013) A novel ion channel formed by interaction of TRPML3 with TRPV5. *PLoS ONE*, 8:e58174
- **Grimm, C.**#, Jörs, S., Gao, Z., Obukhov, A.G., Heller, S. (2012b) Constitutive activity of TRPML2 and TRPML3 channels versus activation by low extracellular sodium and small molecules. *J. Biol. Chem.*, 287: 22701-22708
- Papakosta, M., Haythornthwaite, A., Cao, L., Stevens, E.B., Burgess, G., Russell, R., Cox, P., Phillips, S.C., **Grimm, C.**# (2011) The chimeric approach reveals that differences in the TRPV1 pore domain determine species-specific sensitivity to block of heat activation. *J. Biol. Chem.*, 286:39663-39672
- Aneiros, E., Cao, L., Papakosta, M., Stevens, E.B., Phillips, S.C., **Grimm, C.**# (2011) Biophysical and molecular basis of TRPV1 proton gating. *EMBO J.*, 30:994-1002
- Jörs, S.\* , **Grimm, C.**\* , Becker, L., Heller, S. (2010) Genetic inactivation of Trpml3 does not lead to hearing and vestibular impairment in mice. *PLoS ONE*, 5:e14317
- Lee, K.P.\* , Nair, A.\* , **Grimm, C.**\* , van Zeeland, F., Heller, S., Bindels, R.J.M., Hoenderop, G.J. (2010) A helix-breaking mutation in the epithelial Ca<sup>2+</sup> channel TRPV5 leads to reduced Ca<sup>2+</sup> dependent inactivation. *Cell Calcium*, 48:275-287
- Hoffmann, A.\* , **Grimm, C.**\* , Kraft, R., Goldbaum, O., Wrede, A., Nolte, C., Hanisch, U.K., Richter-Landsberg, C., Brück, W., Kettenmann, H., Harteneck, C. (2010) TRPM3 is expressed in sphingosine-responsive myelinating oligodendrocytes. *J. Neurochem.*, 114:654-665
- **Grimm, C.**\* , Jörs, S.\* , Saldanha, S.A.\* , Obukhov, A.G., Pan, B., Oshima, K., Cuajungco, M.P., Chase, P., Hodder, P., Heller, S. (2010) Small molecule activators of TRPML3. *Chem. & Biol. (Cell Press)*, 17:135-148
- Samie, M.A., **Grimm, C.**, Evans, J.A., Curcio-Morelli, C., Heller, S., Slauchaupt, S.A., Cuajungco, M.P. (2009) The tissue-specific expression of TRPML2 (Mcoln-2) gene is influenced by the presence of TRPML1. *Eur. J. Physiol.*, 459:79-91
- **Grimm, C.**\* , Jörs, S.\* , Heller, S. (2009) Life and death of sensory hair cells expressing constitutively active TRPML3. *J. Biol. Chem.*, 284:13823-13831
- D'hoedt, D., Owsianik, G., Prenen, J., Cuajungco, M.P., **Grimm, C.**, Heller, S., Voets, T., Nilius, B. (2008) Stimulus-specific modulation of the cation channel TRPV4 by PACSIN 3. *J. Biol. Chem.*, 283:6272-6280

- **Grimm, C.**, Cuajungco, M.P., van Aken, A.F.J., Schnee, M., Jörs, S., Kros, C.J., Ricci, A.J., Heller, S. (2007) A helix-breaking mutation in TRPML3 leads to constitutive activity underlying deafness in the varitint-waddler mouse. *PNAS*, 104:19583-19588
- Senn, P., Oshima, K., Teo, D., **Grimm, C.**, Heller, S. (2007) Robust postmortem survival of murine vestibular and cochlear stem cells. *JARO*, 8:194-204
- Oshima, K., **Grimm, C.**, Corrales, E., Senn, P., Martinez Monedero, R., Géléoc, G.S.G., Edge, A., Holt, J.R., Heller, S. (2007) Differential distribution of stem cells in the auditory and vestibular organs of the inner ear. *JARO*, 8:18-31
- Cuajungco, M.P.\*, **Grimm, C.\***, Oshima, K., D'hoedt, D., Nilius, B., Mensenkamp, A.R., Bindels, R.J.M., Plomann, M., Heller, S. (2006) PACSINS bind to the TRPV4 cation channel: PACSIN 3 modulates the subcellular localization of TRPV4. *J. Biol. Chem.*, 281:18753-18762
- Kraft, R., **Grimm, C.**, Frenzel, H., Harteneck, C. (2006) Inhibition of TRPM2 cation channels by N-(p-aminocinnamoyl)anthranilic acid. *Br. J. Pharmacol.*, 148:264-273
- **Grimm, C.\***, Kraft, R.\*, Schultz, G., Harteneck, C. (2005) Activation of the melastatin-related cation channel TRPM3 by D-erythro-sphingosine. *Mol. Pharmacol.*, 67:798-805
- Xu, S.Z., Zeng, F., Boulay, G., **Grimm, C.**, Harteneck, C., Beech, D.J. (2005) Block of TRPC5 channels by 2-aminoethoxydiphenyl borate: differential, extracellular and voltage-dependent effect. *Br. J. Pharmacol.*, 145:405-414
- Kraft, R., **Grimm, C.**, Grosse, K., Hoffmann, A., Sauerbruch, S., Kettenmann, H., Schultz, G., Harteneck, C. (2004) Hydrogen peroxide and ADP-ribose induce TRPM2-mediated calcium influx and cation currents in microglia. *Am. J. Physiol. Cell Physiol.*, 286:C129-137
- **Grimm, C.\***, Kraft, R.\*, Sauerbruch, S., Schultz, G., Harteneck, C. (2003) Molecular and functional characterization of the melastatin-related cation channel TRPM3. *J. Biol. Chem.*, 278:21493-21501

\* authors contributed equally; # corresponding or shared corresponding author

#### Reviews (Peer-reviewed)

- **Grimm, C.#**, Hassan, S., Wahl-Schott, C., Biel, M. (2012a) Role of TRPML and two-pore channels in endolysosomal cation homeostasis. *J. Pharmacol. Exp. Ther. (Perspectives in Pharmacology)*, 342:236-244
- **Grimm, C.#**, de Groot, M., Aneiros, E. (2011) Dissecting TRPV1: lessons to be learned? *CHANNELS*, 5:201-204
- Cuajungco, M.P., **Grimm, C.**, Heller, S. (2007) TRP channels as candidates for hearing and balance abnormalities in vertebrates. *Biochem. Biophys. Acta*, 1772:1022-1027

#### Books and book chapter

- **Grimm, C.#**, Barthmes, M., and Wahl-Schott, C. (2014) *TRPML3*, in: Nilius, B. and Flockerzi, V., *Mammalian Transient Receptor Potential (TRP) cation channels, The Handbook of Experimental Pharmacology (HEP)*, Springer Publishing, 222:659-674
- **Grimm, C.#** and Cuajungco, M.P. (2014) *Mucopolidosis type IV and TRPML channels*, in: Koschak, A. and Weiss, N., *Pathologies of Calcium Channels*, Springer Publishing, pp. 365-379
- Saldanha, S.A., **Grimm, C.**, Allais, C., Smith, E., Ouizem, S., Mercer, B.A., Roush, W.R., Heller, S., Hodder, P. (2013) *Identification of Selective Agonists of the Transient Receptor Potential Channels 3 (TRPML3)*. Probe Reports from the NIH Molecular Libraries Program [Internet]. Bethesda (MD): National Center for Biotechnology Information (US); 2010-2012 Mar 21 [updated 2013 Sep 03].
- Saldanha, S.A., **Grimm, C.**, Mercer, B.A., Choi, J.Y., Allais, C., Roush, W.R., Heller, S., and Hodder, P. (2011) *Campaign to Identify Agonists of Transient Receptor Potential Channels 3 and 2 (TRPML3 & TRPML2)*, Probe Reports from the NIH Molecular Libraries Program, Bethesda (MD): National Center for Biotechnology Information

# corresponding author

## **CONFERENCE PRESENTATIONS (first author only):**

- 2003:** •**44<sup>th</sup> spring conference of the DGPT** (German Society for Experimental and Clinical Pharmacology), **Mainz, Germany:**  
**Grimm, C.**, Grosse, K., Kraft, R., Hoffmann, A., Sauerbruch, S., Lache, W., Kettenmann, H., Schultz, G., Harteneck, C., TRPM2 is exclusively expressed in tissue macrophages. Naunyn-Schmiedeberg's Arch. Pharmacol., 367 (Suppl.), R65, Poster presentation
- 2004:** •**45<sup>th</sup> spring conference of the DGPT, Mainz, Germany:**  
**Grimm, C.**, Kraft, R., Schultz, G., Harteneck, C., Regulation of TRPM3 activity. Naunyn-Schmiedeberg's Arch. Pharmacol., 369 (Suppl.), R61, Oral presentation
- 2007:** •**37<sup>th</sup> annual meeting of the Society for Neuroscience (SfN), San Diego, CA, USA:**  
**Grimm, C.**, Korne, C.J., Cuajungco, M., Schnee, M., Atiba-Davies, M., Jörs, S., van Aken, A.F.J., Marcotti, W., Goodyear, R., Bryant, J.E., Richardson, G., Ricci, A., Noben-Trauth, K, and Heller, S., Impaired hair cell mechano-transduction and a constitutively active cation channel resulting from a TRPML3 helix-breaking mutation in varitint-waddler mice, Poster presentation
- 2008:** •**Janelia Farm Research Campus, Howard Hughes Medical Institute, Ashburn, VA, USA:**  
Force-Gated Ion Channels: From Structure to Sensation  
**Grimm, C.**, Cuajungco, M., van Aken, A.F.J., Schnee, M, Jörs, S., Korne, C.J., Ricci, A., and Heller, S., A helix-breaking mutation in TRPML3 leads to constitutive activity underlying deafness in the varitint-waddler mouse, Poster presentation
- 2009:** •**Ion channels as therapeutic targets, Novartis, Horsham, UK:**  
**Grimm, C.**, Saldanha, S. A., Oshima, K., Jörs, S., Hodder, P. S., and Heller, S., High-throughput screening for agonists of TRPML3 and TRPN1, two sensory hair cell cation channels of unknown function, Poster presentation
- 2009:** •**7<sup>th</sup> Molecular Biology of Hearing and Deafness Conference, Boston, MA, USA:**  
**Grimm, C.**, Jörs, S., Saldanha, S.A., Oshima, K., Hodder, P.S., and Heller, S., High-throughput screening for agonists of TRPML3, Poster presentation
- 2010:** •**TRP 2010 meeting, Katholieke Universiteit Leuven, Belgium:**  
**Grimm, C.**, Cao, L., Aneiros, E., Papakosta, M., Stevens, E., and Philipps, S.C., Acidic pH activation and potentiation of human TRPV1 involve key amino acid in transmembrane domain 6, Poster presentation
- 2010:** •**40<sup>th</sup> annual meeting of the Society for Neuroscience (SfN), San Diego, CA, USA:**  
**Grimm, C.**, Cao, L., Aneiros, E., Papakosta, M., Stevens, E., and Philipps, S.C., Aromatic key residue in transmembrane domain 6 determines proton activation and potentiation of human TRPV1, Poster presentation
- 2011:** •**Targets & Tools: Ion channels (Informa Conference), Berlin, Germany:**  
**Grimm, C.**, Cao, L., Aneiros, E., Papakosta, M., Stevens, E., and Philipps, S.C., Molecular determinants of TRPV1 heat and proton activation, Invited talk
- 2013:** •**1<sup>st</sup> Conference of the ML IV Foundation, New York Medical College, NY, USA:**  
**Grimm, C.**, TRPML protein function and potential therapeutic avenues, Invited talk
- 2013:** •**LMU Undergraduate Research Conference on Molecular Sciences, Wildbad Kreuth, Germany:**  
**Grimm, C.**, Circling mice and blind men: molecular and functional aspects of endolysosomal cation channels, Invited talk
- 2014:** •**LMU and University of Tübingen Summer School, Frauenchiemsee Monastery, Germany:**  
**Grimm, C.**, High susceptibility to fatty liver disease in two-pore channel 2 deficient mice, Invited talk
- 2014:** •**SFB/CRC 152 TRiPs to Homeostasis, Kick-off meeting, Mont St. Odile, France:**  
**Grimm, C.**, Role of TRPML channels in endolysosomal cation homeostasis, Oral presentation