Irene Tiemann-Boege

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EDUCATION

2015	*Venia docendi* (Habilitation) in Molecular Genetics, **Johannes Kepler University**, Linz, Austria
2003	Ph.D. in Molecular Biology, **University of Southern California**, Los Angeles, USA
1999	M.Sc. in Zoology, **Texas Tech University**, Lubbock, USA
1997	B.Sc. and M.Sc. in Biology--*summa cum laude*, **Universidad de las Américas**, Mexico

RESEARCH EXPERIENCE

2015 -	Associate Professor and Senior Group Leader of Single Molecule Genetics, Institute of Biophysics, Johannes Kepler University, Austria
2010-2015	Assistant Professor and Group Leader of Single Molecule Genetics, Institute of Biophysics, Johannes Kepler University, Austria
2009-2010	Lise Meitner Fellow, Institute of Biophysics, Johannes Kepler University, Austria;
2007-2008	Senior Research Associate, Department of Oncology, University of Cambridge, UK
2003-2007	Postdoctoral Research Associate, Department of Molecular and Computational Biology, University of Southern California, USA
1999-2003	Research Assistant, Department of Molecular and Computational Biology, University of Southern California, USA
1997-1999	Research Assistant, Department of Zoology, Texas Tech University, USA

Career Breaks
2004 and 2008 maternity leaves for children Lea and Lukas

MAIN AREAS OF RESEARCH

Tyrosine kinase receptors, Recombination hotspots, DNA sequence evolution, mutational processes, driver mutations, ultrasensitive rare variant or mutation detection; digital PCR, ultra-sensitive sequencing, single mutation analysis, functional protein characterization

RESEARCH ACHIEVEMENTS

- *Sequence-Function characterization of membrane proteins*: We have discovered a series of mutations in

different receptor tyrosine kinases (RTK). These are of particular importance since they correlate with tumorigenesis, mosaic disease, and congenital disorders. We have focused on *FGFR3* and *Erbb2* and discovered with deep-sequencing evidence for positive selection in mutations accumulating in the male germline (**Salazar et al., 2022**). We have characterized the clonal expansion of these mutants in sperm and dissected testis (**Moura et al submitted**) and are characterizing the function and activation of these receptors with biophysical methods (**Hartl et al accepted**).

- *Mutagenesis in driver genes:* We showed with several different molecular assays that the germline of older males is a repository of mutations linked to congenital disorders **(Tiemann-Boege et al. PNAS 2002; Wyrobyk et al PNAS 2006; Qin et al. PloS Biol 2007; Shinde et al. Hum Mol Genet 2013)**. Our work on the paternal age effect was the first to accurately quantify new mutations in human sperm DNA **(Tiemann-Boege et al. PNAS 2002)**. Currently, we are screening the frequency of *de novo* mutations in sperm of old and young donors in selected driver genes, and have discovered unreported substitutions expanding in the male germline (**Salazar et al, 2022**). We also observe a high number of de novo venets explained by a selective advantage of the driver mutation prior the maturation of the male germline **(Moura et al, submitted)**.
- *Sequence evolution and recombination hotspots*: We demonstrated by pooled-sperm typing that recombination in humans is concentrated in narrow regions, known as hotspots (**Tiemann-Boege et al PloS Genetics 2006**). As a principal investigator, my group showed in an unconventional work that a high number of *de novo* mutations accumulate in crossovers, which are counteracted by GC biased gene conversion, explaining the rapid evolution of hotspots **(Arbeithuber et al. PNAS 2015)**. My group also discovered that heterologies in microsatellites affect their transmission and evolution at recombination hotspots, in a process that leads to a genome-wide enrichment of short poly-As in hotspots **(Heissl et al. LSA 2019)**.
- *Protein binding*: My group has also developed important assays to characterize with diverse biophysical methods the binding of PRDM9. With these assays (e.g. SPR and FCS), my group showed that PRDM9 interacts with the DNA for many hours **(Striedner et al. Chromosome Res 2017)** and that the PRDM9 Zn finger domain binds to only one DNA target within a trimer **(Schwarz et al. LSA. 2019).**
- *Development of technologies to count rare events*: We have developed several single molecule-based approaches to measure mutations at very low levels **(Tiemann-Boege et al. PNAS 2002; Boulanger et al. PloS One 2012),** such as the digital emulsion PCR technology **(Tiemann-Boege et al Anal Chem 2009).** My team has explored potential technical caveats and considerable improvements of ultra-sensitive mutation detection methods **(Arbeithuber et al. DNA Res 2016)**, and developed ultra-sensitive sequencing protocols with NGS to detect rare mutations **(Salazar et al., 2022),** including the bioinformatics tools (**Povysil et al NARGB 2021**).

10 SELECTED PUBLICATIONS

1. *Salazar R, Arbeithuber B, Ivankovic M, Heinzl M, Moura S, Hartl I, Mair T, Lahnsteiner A,* Ebner T, Shebl O, Pröll J*, **Tiemann-Boege I**. (2022)* Discovery of an unusually high number of de novo mutations in sperm of older men using duplex sequencing. Genome Res 32(3):499-511. doi: 10.1101/gr.275695.121. Epub 2022 Feb 24.
2. *Povysil G, Heinzl M, Salazar Pereira R,* Stoler N, Nekrutenko A, ***Tiemann-Boege I***. (2021) Increased yields of duplex sequencing data by a series of quality control tools. NAR Genomics and Bioinformatics, 3-1
3. *Schwarz T, Striedner Y*, Haase K, Kemptner J, Zeppezauer N, Hermann P, **Tiemann-Boege I**. (2019) PRDM9 forms a trimer by interactions within the zinc finger array. Life Sci Alliance. 2019 Jul 15;2(4). pii: e201800291. doi: 10.26508/lsa.201800291
4. *Heissl A*, Betancourt AJ, Hermann P, Povysil G, Arbeithuber B, Futschik A, Ebner T, **Tiemann-Boege I**. (2019) The impact of poly-A microsatellite heterologies in meiotic recombination. Life Sci Alliance. 2019 Apr 25;2(2). pii: e201900364. doi: 10.26508/lsa.201900364
5. **Tiemann-Boege I,** *Schwarz T, Striedner Y, Heissl A.* (2017) Philos Trans R Soc Lond B Biol Sci. 19;372(1736). pii: 20160462. doi: 10.1098/rstb.2016.0462.

6. *Striedner Y., Schwarz T.*, Welte T., Futschik A., Rant U, and **Tiemann-Boege I**. (2017). Chromosome Research *doi: 10.1007/s10577-017-9552-1*
7. *Arbeithuber B*, Betancourt AJ, Ebner T, **Tiemann-Boege** I. (2015) Proc Natl Acad Sci U S A. 112(7):2109-14.
8. Shinde DN*, *Elmer DP**, Calabrese P, Boulanger J, Arnheim N, **Tiemann-Boege** I (2013) Hum Mol Genet 22: 4117-4126.
9. **Tiemann-Boege I**, Calabrese P, Cochran DM, Sokol R, Arnheim N (2006). PLoS Genet 2: e70
10. **Tiemann-Boege I**, Navidi W, Grewal R, Cohn D, Eskenazi B, Wyrobek AJ, Arnheim N (2002). Proc Natl Acad Sci U S A 99: 14952-14957

ADDITIONAL RESEARCH ACHIEVEMENTS

- 2016 Pilgerstorferpreis awarded by the Upper Austrian medical society for outstanding scientific achievements
- 2015 Upper Austrian researcher of the year; Landespreis Oberösterreichische Forscherinnen
- 2015 Regional award from the state of Upper Austria for Outstanding Research and Collaborative Effort (Winner in the category of Arts and Science)

Selected Invited talks at Conferences:

Embriologenforum Austria (2022); Society of Molecular Biology and Evolution (2022) European Society of Human Genetics (2019), Gothenburg, Sweden; European Society for Evolutionary Biology (2017), Groningen, Neatherlands; EMBO Meeting (2016), Mannheim, Germany; Embriologenforum Austria (2016); The Human Mutation Meeting, Leipzig (2015)

Editorial/reviewer duties

- Editor of the Springer Series Methods in Molecular Biology, "Methods in Haplotyping"
- Invited editor for Plos Genetics
- *Ad hoc* reviewer for journals Genome Research, American Journal of Human Genetics, Plos Genetics, Plant Cell, Analytical Chemistry, European Journal of Human Genetics, Genetics, and Genome Research, Nature Communications
- *Ad hoc* reviewer for funding agencies: European Research Council (ERC), Welcome Trust Investigator Awards, Czech Science Foundation, Vidi Program, Netherlands.

Funded Research Projects:

2022-2026	SFB Meiosis (FWF the Austrian Science Fund); Co-PI of 9 PIs (~400,000 per PI)
2020-2020	Linz Institute of Technology (LIT); JKU Covid-19 Testing. Principal Investigator: €43,000
2019 – 2022	Interreg, European Research Grant with Budweis, CZ (REGGEN: ATCZ207) €781,445;
2018-2022	DK NanoCell, University of Linz; Co-PI (~€150,000 per PI)
2018-2022	FWF the Austrian Science Fund (P30867-B26). Age related mutagenesis of driver genes in the male germline. Principal Investigator. €405,342
2017-2019	Linz Institute of Technology (LIT). Seed research grant. Discovery of New mutations using ultra-sensitive sequencing. Principal Investigator. €196,728
2014-2018	FWF the Austrian Science Fund (P27698). Binding properties of PRDM9. Principal Investigator. €349,000
2013-2017	FWF the Austrian Science Fund (P25525). Higher mutations in older men. Principal Investigator. €317,000
2011-2015	FWF the Austrian Science Fund (P23811-B12). Mutagenic recombination. Principal Investigator. €306,000