

**Dr. S. Hombach-Klonisch**

Associate Professor

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Publications:

<http://www.ncbi.nlm.nih.gov/pubmed/?term=Hombach-Klonisch+S>**Education**

2004

***Habilitation***

Anatomy and Reproductive Biology, Martin-Luther University Halle-Wittenberg, Germany (Mentor: Prof. Bernd Fischer, Head of Anatomy and Cell Biology, University Halle-Wittenberg, Germany)

2003

***Specialty in Anatomy***

- Medical Association of Saxony-Anhalt, Germany: “Fachärztin fuer Anatomie”
- Anatomical Society, Germany: “Fachanatomin”

1994

***Promotion – PhD equivalent***

Pathophysiology, Justus-Liebig-University Giessen, Germany

(Supervisor: Prof. Werner Seeger, Director of the University Medical Clinic, Justus-Liebig-University Giessen, Germany)

1991

***MD.***

Justus-Liebig-University Giessen, Germany

**Academic Experience**

2012- present ***Associate Professor (tenured)***, Dept. of Human Anatomy and Cell Science (tenured), Faculty of Health Sciences, College of Medicine, University of Manitoba, Winnipeg, Canada; Section Head Gross Anatomy.

2007-2012 ***Assistant Professor (tenure track)***, Dept. of Human Anatomy and Cell Science, University of Manitoba, Faculty of Medicine, Winnipeg, Canada; Section Head Gross Anatomy; ***Assistant Professor***, Dept. of Obstetrics, Gynecology & Reproductive Sciences, University of Manitoba, Faculty of Medicine, Winnipeg, Canada.

2004-2007 ***Assistant Professor (contingent)***, Dept. of Human Anatomy and Cell Science, University of Manitoba, Faculty of Medicine, Winnipeg, Canada

- 2000-2004 **Assistant Professor equivalent**, Dept. of Anatomy and Cell Biology, Martin-Luther University Halle-Wittenberg, Faculty of Medicine, Halle, Germany
- 1998-2000 **Postdoctoral Fellow**, Dept. of Anatomy and Cell Biology, Martin-Luther University Halle-Wittenberg, Faculty of Medicine, Halle, Germany

### Awards and Distinctions

- 2018 **Teaching Award for Best Small Group Teaching** by the Manitoba Medical Student Association (MMSA)
- 2009 **Murray L. Barr Young Investigator Award**  
The Canadian Association for Anatomy, Neurobiology, and Cell Biology (CAANCB)
- 2002 **Merck European Thyroid von Basedow Research Prize (Award)**  
German Endocrine Society (DGE; Deutsche Gesellschaft fuer Endokrinologie)
- 1998-2000 **Postdoctoral Fellowship (Award)**, Province of Saxony-Anhalt, Germany

### Research Activity

My research is focussed on investigating the cellular and molecular mechanisms of tumor cell invasion/metastasis and chemoresistance in cancers of the breast, thyroid and brain. I am particularly interested in studying the pathways that are involved in driving phenotypic and nuclear cancer cell plasticity in response to environmental challenges as these are key to cancer cell survival and treatment failures. In my lab, we are utilizing human cancer cell lines, patient-derived primary cancer cells and animal models for intracranial xenografting and in-vivo bioluminescence imaging. We use state-of-the-art fluorescence microscopy to monitor cellular protein interactions, DNA damage and 3D nuclear telomere changes in single cell analysis. Ongoing research projects study the nuclear function of the chromatin-remodeling protein and stem cell factor HMGA2 in DNA damage sensing/repair and telomere stability in promoting cancer cell chemoresistance and tumor cell survival and how these nuclear functions of HMGA2 promote cancer cell invasion, metastasis and tumor recurrences.

My lab is also investigating the tumor-promoting role of novel ligands of the transmembrane G protein-coupled receptor RXFP1 in brain and breast cancer models. We study the molecular signaling pathways and target molecules induced by RXFP1 activation which promote tissue invasion and survival of brain tumor (stem-like) cells. Our goal is to develop specific inhibitors to block RXFP1 function in human brain cancer cells.

I am a member of the Brain Tumor Research Alliance Manitoba (BTRAM) [[http://umanitoba.ca/faculties/health\\_sciences/medicine/units/anatomy/8723.html](http://umanitoba.ca/faculties/health_sciences/medicine/units/anatomy/8723.html)] and have close collaborations with the neurosurgeons, pathologists and medical oncologist members of BTRAM. I am also a member of the Breast Cancer Group at the University of Manitoba. My lab is actively involved in the brain tumor cell repository for glioblastoma (GB) tumors and the collection of liquid biopsies from brain cancer patients.

I have recently established an in-vivo breast cancer brain metastasis model using ultrasound-guided left ventricular injections of triple-negative breast cancer cells to investigate the molecular mechanisms of early metastasis formation in the brain. My research on primary and metastatic brain tumors combines

aspects of the brain-specific parenchymal environment and the interaction with brain-derived or metastatic tumor cells.

My research is funded by local, provincial and national funding agencies, including Natural Science and Engineering Research Council of Canada (NSERC), Canadian Breast Cancer Foundation (CBCF), the Cancer Research Society/Canadian Institute of Health partnership (CRS-CIHR), and the Breast Cancer Society of Canada (BCSC).

**Total publications: 84**; peer-reviewed 63 original and 16 review articles, 5 refereed chapters in books or proceedings. Publications in past 5 years: 29; **H-index 30** (based on Google Scholar)

<https://www.ncbi.nlm.nih.gov/pubmed/?term=Hombach-Klonisch+S>

### **Teaching and Mentoring Activity**

My teaching responsibilities encompass lectures, tutorials and laboratory sessions in gross anatomy, neuroanatomy, and histology to undergraduate and graduate students and to postgraduate trainees in different streams of the health professions.

I am supervising research graduate students, undergraduate summer students, BSc Med students, co-op students and MITACS-funded undergraduates and I serve as academic advisor for numerous Masters and PhD students at the University of Manitoba and as teaching mentor for young faculty and instructors in the Department of Human Anatomy and Cell Science.

In my position as Section Head Gross Anatomy I am responsible for the cadaveric gross anatomy program of the department and oversee the gross anatomy teaching involvement within the Rady Faculty of Health Sciences and outside the University.

**Research collaborations [national and international]** outside of the University of Manitoba

**Dr. Paul Fowler**, *Chair in Translational Medical Sciences*, Institute of Medical Sciences, School of Medicine, Medical Sciences & Nutrition, University of Aberdeen, Scotland

Maternal influence on human thyroid gland development and function

**Dr. Girish Shah**, Department of Molecular Biology, Medical Biochemistry and Pathology, Faculty of Medicine, Laval University in Quebec:

Effect of PARP deficiency on UV-induced skin cancer development in mice

**Dr. Tara Beattie**, Arnie Charbonneau Cancer Institute, University of Calgary, Alberta

Telomere maintenance mechanisms in cancer cells

**Dr. Brian Wilson**, Biology, Acadia University, Wolfville, NS:

Rodent brain slice cultures as ex-vivo models to investigate cancer cell invasion into the brain.

**Dr. William Wong**, Physiology, John's Hopkins, Baltimore, MD:

C1q-tumor necrosis factor related peptides (CTRPs) as ligands of the G-protein-coupled receptor RXFP1 in cancer cells.

**Dr. Claudius Mueller**, Center for Applied Proteomics and Molecular Medicine, George Mason University, Manassas, Virginia:

A new formalin-free fixative for pathology assessment: immune- and hybridization techniques on bone metastatic tissues.

**Publications – peer reviewed (2013-2019)**

1. Blanchard AA, Ma X, Wang N, **Hombach-Klonisch S**, Penner C, Ozturk A, Klonisch T, Pitz M, Murphy L, Leygue E, Myal Y. Claudin 1 is highly up regulated by PKC in MCF7 human breast cancer cells and correlates positively with PKC $\epsilon$  in patient biopsies. *Transl Oncol*. 2019 Jan 15;12(3):561-575.
2. **Hombach-Klonisch S**, Kalantari F, Medapati MR, Natarajan S, Krishnan SN, Kumar-Kanojia A, Thanasupawat T, Begum F, Xu FY, Hatch GM, Los M, Klonisch T. HMGA2 as a functional antagonist of PARP1 inhibitors in tumor cells. *Mol Oncol*. 2018 Oct 5. doi: 10.1002/1878-0261.12390.
3. Wu J, Kumar-Kanojia A, **Hombach-Klonisch S**, Klonisch T and Lin F. A radial microfluidic platform for higher throughput chemotaxis studies with individual gradient control. *Lab on a Chip*, 2018, **18**, 3855 – 3864.
4. **Hombach-Klonisch S**, Mehrpour M, Shojaei S, Harlos C, Pitz M, Hamai A, Siemianowicz K, Likus W, Wiechec E, Toyota BD, Hoshyar R, Seyfoory A, Sepehri Z, Ande SR, Khadem F, Akbari M, Gorman A, Samali A, Klonisch T, Ghavami S. “Glioblastoma and Chemoresistance to Alkylating Agents: Involvement of Apoptosis, Autophagy, and Unfolded Protein Response”. *Pharmacol Ther*. 2018 Apr;184:13-41. doi: 10.1016/j.pharmthera.2017.10.017.
5. Shojaei S, Alizadeh J, Thliveris J, Koleini N, Kardami E, Hatch GM, Xu F, **Hombach-Klonisch S**, Klonisch T, Ghavami S. Statins: a new approach to combat temozolomide resistance in glioblastoma. *J Investig Med* 2018;0:1–5. doi:10.1136/jim-2018-000874
6. Filis P, **Hombach-Klonisch S**, Ayotte P, Nagrath N, Soffientini U, Klonisch T, O’Shaughnessy P, Fowler P. Maternal smoking and high BMI disrupt thyroid gland development. *BMC Med*. 2018 Oct 23;16(1):194. doi: 10.1186/s12916-018-1183-7.
7. Mueller C, Gambarotti M, Benini S, Picci P, Righi A, Stevanin M, **Hombach-Klonisch S**, Henderson D, Liotta L, and Espina V. Unlocking bone for proteomic analysis and FISH [Paper #18-0034-TRR], *Lab Investigation*, 2018
8. Thanasupawat T, Glogowska A, Burg M, Krcek J, Beiko J, Pitz M, Zhang GJ, **Hombach-Klonisch S**, Klonisch T. C1q1TNF-related peptide 8 (CTRP8) promotes temozolomide resistance in human glioblastoma. *Mol Oncol*. 2018 Jun 27. doi: 10.1002/1878-0261.12349.
9. Alizadeh J, Glogowska A, Thliveris J, Kalantari F, Shojaei S, **Hombach-Klonisch S**, Klonisch T, Ghavami S. Autophagy modulates transforming growth factor beta 1 induced epithelial-to-mesenchymal transition in non-small cell lung cancer cells. *Biochim Biophys Acta*. 2018 May;1865(5):749-768. doi: 10.1016/j.bbamcr.2018.02.007.
10. Thanasupawat T, Natarajan S, Rommel A, Glogowska A, Bergen H, Krcek J, Pitz M, Beiko J, Krawitz S, Verma IM, Ghavami S, Klonisch T, **Hombach-Klonisch S**. Dovitinib enhances temozolomide efficacy in glioblastoma cells. *Mol Oncol*. 2017 Aug;11(8):1078-1098. doi: 10.1002/1878-0261.12076. Epub 2017 Jun 5.
11. Alizadeh J, Zeki AA, Mirzaei N, Tewary S, Rezaei Moghadam A, Glogowska A, Nagakannan P, Eftekharpour E, Wiechec E, Gordon JW, Xu FU, Field JT, Yoneda KY, Kenyon NJ, Hashemi M, Hatch GM, **Hombach-Klonisch S**, Klonisch T, Ghavami S. Mevalonate Cascade Inhibition by Simvastatin Induces the Intrinsic Apoptosis Pathway via Depletion of Isoprenoids in Tumor Cells. *Sci Rep*. 2017 Mar 27;7:44841. doi: 10.1038/srep44841.

12. Hammond E, Shu E, Sawchuk K, Myal Y, Raouf A, Klonisch T, **Hombach-Klonisch S**, Leygue E, Kung S, Safneck S, Mowat M, Xu W, Murphy L, Pitz M. Population-based analysis of breast cancer treatment by intrinsic sub-type in Manitoba, Canada. *Cancer Epidemiology*, 2016 Dec;45:82-90.
13. Sun Z, Worden M, Thliveris JA, **Hombach-Klonisch S**, Klonisch T, van Lierop J, Hegmann T, Miller DW. Biodistribution of negatively charged iron oxide nanoparticles (IONPs) in mice and enhanced brain delivery using lysophosphatidic acid (LPA). *Nanomedicine* 2016 Apr 25. pii: S1549-9634(16)30036-3. doi: 10.1016/j.nano.2016.04.008. [Epub ahead of print]
14. Natarajan S, Begum F, Gim J, Wark L, Henderson D, Davie JR, **Hombach-Klonisch S**, Klonisch T. High Mobility Group A2 protects cancer cells against telomere dysfunction. *Oncotarget*. 2016 Mar 15;7(11):12761-82. doi: 10.18632/oncotarget.6938.
15. Klonisch T, Glogowska A, Thanasupawat T, Burg M, Krcek J, Pitz M, Jaggupilli A, Chelikani P, Wong GW, **Hombach-Klonisch S**. Structural commonality of C1q Tumor Necrosis Factor-related proteins and their potential to activate RXFP1 signaling pathways in cancer cells. *Br J Pharmacol*. 2017 May;174(10):1025-1033
16. Medapati MR, Dahlmann M, Ghavami S, Pathak KA, Lucman L, Klonisch T, Hoang-Vu C, Stein U, **Hombach-Klonisch S**. RAGE mediates the pro-migratory response of extracellular S100A4 in human thyroid cancer cells. *Thyroid*. 2015 May;25(5):514-27.
17. Thanasupawat T\*, Bergen H\*, **Hombach-Klonisch S\***, Krcek J, Ghavami S, Del Bigio M, Krawitz S, Stelmack G, Halayko A, McDougall M, Meier M, Stetefeld J, Klonisch T. Platinum (IV) coiled coil nanotubes selectively kill human glioblastoma cells. *Nanomedicine*. 2015 May;11(4):913-25. *\*authors contributed equally*
18. Thanasupawat T, Glogowska A, Burg M, Wong GW, Hoang-Vu C, **Hombach-Klonisch S**, Klonisch T. RXFP1 is Targeted by Complement C1q Tumor Necrosis Factor-Related Factor 8 in Brain Cancer. *Front Endocrinol (Lausanne)*. 2015 Aug 13;6:127. doi: 10.3389/fendo.2015.00127. eCollection 2015. Review.
19. Evans NP, Bellingham M, Sharpe RM, Cotinot C, Rhind SM, Kyle C, Erhard H, **Hombach-Klonisch S**, Lind PM and Fowler PA. Reproduction Symposium: does grazing on biosolids-treated pasture pose a pathophysiological risk associated with increased exposure to endocrine disrupting compounds? *J Anim Sci*. 2014 Aug;92(8):3185-98.
20. **Hombach-Klonisch S**, Natarajan S, Thanasupawat T, Medapati MR, Pathak A, Ghavami S, Klonisch T. Mechanisms of therapeutic resistance in cancer (stem) cells with emphasis on thyroid cancer cells. *Front Endocrinol (Lausanne)*. 2014 Mar 25;5:37. eCollection 2014. Review.
21. Hochman J, Unger B, Kraut J, **Hombach-Klonisch S**. Gesture-Controlled Interactive Three Dimensional Anatomy: A Novel Teaching Tool in Neurotology. *J Otolaryngol Head Neck Surg*. 2014 Oct 7;43(1):38.
22. Ho J, Wiebe C, Gibson IW, **Hombach-Klonisch S**, Gao A, Rigatto C, Karpinski M, Storsley L, Nickerson PW, Rush DN. Elevated urinary CCL2: Cr at 6 months is associated with renal allograft interstitial fibrosis and inflammation at 24 months. *Transplantation*, 2014 Mar 18.
23. Wark L, Danescu A, Natarajan S, Zhu XG, Cheng S-Y, **Hombach-Klonisch S**, Mai S, Klonisch T. Three-dimensional (3D) telomere dynamics in follicular thyroid cancer. *Thyroid*. 2014 Feb;24(2):296-304.
24. Glogowska A, Kunanuvat U, Stetefeld J, Patel TR, Thanasupawat T, Krcek J, Weber E, Wong GW, Del Bigio M, Hoang-Vu C, **Hombach-Klonisch S\***, Klonisch T\*. C1q-tumor necrosis factor-related protein 8 (CTRP8) is a novel ligand of relaxin receptor RXFP1 in human brain cancer cells. *J Pathol*. 2013 Dec;231(4):466-79.

25. Danescu A, Herrero Gonzalez S, Di Cristofano A, Mai S, Hombach-Klonisch S. Three-dimensional (3D) Nuclear Telomere Architecture Changes during Endometrial Carcinoma Development. *Genes, Chromosomes and Cancer* 2013 Aug;52(8):716-32..
26. Natarajan S, Hombach-Klonisch S, Dröge P, Klonisch T. HMGA2 inhibits apoptosis through interaction with ATR-CHK1 signaling complex in human cancer cells. *Neoplasia* 2013 Mar;15(3):263-80.
27. Hombach-Klonisch S, Danescu A, Begum F, Amezaga MR, Rhind SM, Sharpe RM, Evans N, Bellingham M, Cotinot C, Mandon-Pepin B, Fowler PA and Klonisch T. "Periconceptional changes in maternal exposure to sewage sludge chemicals disturbs fetal thyroid gland development in sheep". *Mol Cell Endocrinol.* 2013 Mar 10;367(1-2):98-108.
28. Thanasupawat T, Hammje K, Adham I, Ghia J-E, Del Bigio M, Krcek J, Hoang-Vu C, Klonisch T, Hombach-Klonisch S. INSL5 is a novel marker for human enteroendocrine cells of the large intestine and neuroendocrine tumours. *Oncol Rep.* 2013 Jan;29(1):149-54.
29. Chowdhury B, Hemming R, Hombach-Klonisch S, Flamion B, Triggs-Raine B. Murine hyaluronidase 2 deficiency results in extracellular hyaluronan accumulation and severe cardio-pulmonary dysfunction. *J Biol Chem.* 2013 Jan 4;288(1):520-8