

Curriculum Vitae

Ingmar Blümcke, M.D.



Present Position Full Professor and Director

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Date of Birth March 4th, 1965

Medical studies: Medical Faculty, Christian-Albrechts-University Kiel, Germany

Doctoral Thesis (MD): June, 10th, 1991 at the Dept. of Anatomy (University of Kiel)
Title: The distribution of the calcium-binding protein parvalbumin in the visual cortex of human and old world monkeys: a comparative immunohistochemical study (Blümcke et al., 1990, J Comp Neurol. 301: 417-32).

Current employment

since May, 1st, 2002 Full Professor of Neuropathology (tenure) at the Univ. Erlangen-Nürnberg, Germany and Director of the Department of Neuropathology, Univ. Hospital Erlangen

2014 – present Consultant, Epilepsy Center, Cleveland Clinic Foundation, OH, USA

A handwritten signature in blue ink, appearing to read 'I. Blümcke'. The signature is fluid and cursive, with a long horizontal stroke at the end.

Erlangen, September 20th, 2022

Positions and Employment

1991-1994	Post-Doctorate at the Institute of Histology, Univ. Fribourg, Switzerland (Chair: Prof. Dr. M.R. Celio)
1994-1996	Helmholtz fellowship (BMBF) at the Dept. of Neuropathology, Univ. Bonn, Germany (Chair: Prof. Dr. O.D. Wiestler)
1996-1999	Resident at the Dept. of Neuropathology, Univ. Bonn, Germany (Chair: Prof. Dr. O.D. Wiestler)
Dec. 12 th , 1999	Neuropathology board examination, Ärztekammer Nordrhein, Germany
1/2000-4/2002	Consultant of Neuropathology, Univ. Bonn, Germany (Chair: Prof. Dr. O.D. Wiestler)
Oct, 25 th , 2000	Venia Legendi for Neuropathology, Univ. Bonn, Germany
since May, 1 st , 2002	Full Professor of Neuropathology (tenure) at the Univ. Erlangen-Nürnberg, Germany and Director of the Department of Neuropathology, Univ. Hospital Erlangen
2014 – present	Consultant, Epilepsy Center, Cleveland Clinic Foundation, OH, USA

Committees/ editorial roles:

2007 - 2011	Advisory Board, German “Epilepsy Surgery” Working Group
2008 - present	Editorial Board of Acta Neuropathologica, Epileptic Disorders
2009 - 2015	Editorial Board of Epilepsia
2009 - 2017	Chair, ILAE Task Force for Neuropathology
2012 - 2020	Executive committee of the German Society against Epilepsy
2013 - 2017	Chair, ILAE Commission for Diagnostic Methods
2010 - present	Associate Editor of Epileptic Disorders
2003 - present	Chair, German Neuropathology Reference Center for epilepsy surgery
2006 - present	Chair, European Epilepsy Brain Bank
2017 - 2021	Executive committee of ILAE Europe
2017 - present	Chair, ILAE Education Council
2019 – present	Executive committee of ILAE

Grant Review Experience

2000 - present	German Research Council
2002 – present	Sander Foundation, Germany
2007 – present	University College London, UK
2011 – present	BONFOR, University Bonn, Germany

Ad Hoc reviewer for Forum: University Bochum-Germany, Forum: University Rostock-Germany, APART-Austria, Jubiläumsfond-Austria, Welcome Trust-UK, Medical Research Council-UK, Brain Tumor Charity-UK, Epilepsy Research-UK, ERC EU-Belgium, Academy of Finland, Monash University Melbourne-Australia, Fondation Francaise Pour La Recherche Sur L'Epilepsie-France, ZonMw-The Netherlands.

Ad hoc reviewer for as many scientific journals

Honors and Awards

1994	Helmholtz-Fellowship (German Research Council)
2011	Alfred-Hauptmann Prize of the German Epilepsy Society
2015	Ambassador of Epilepsy Award (ILAE/IBE)
2018	Dorothy Russell Medal of the British Society for Neuropathology

Contribution to Science

1. My early scientific work centered on neuroanatomical studies of primate neocortex and the subpopulation of GABAergic neurons characterized by calcium-binding proteins, e.g. Parvalbumin, Calbindin and Calretinin. Today, these studies have been reproduced and CaBPs are applied widely as selective neuronal marker proteins.

- a) **Blümcke I**, Hof PR, Morrison JH, Celio MR. Distribution of parvalbumin immunoreactivity in the visual cortex of Old World monkeys and humans. J. Comp. Neurol. 1990; 301: 417-32. PMID 2262599
- b) Schwaller B, Buchwald P, **Blümcke I**, Celio MR, Hunziker W. Characterization of a polyclonal antiserum against the purified human recombinant calcium binding protein calretinin. Cell Calcium 1993; 14: 639-48. PMID 8242719
- c) Andressen C, **Blümcke I**, Celio MR. Calcium-binding proteins: selective markers of nerve cells. Cell Tissue Res. 1993; 271: 181-208. PMID 8453652
- d) **Blümcke I**, Beck H, Nitsch R, Eickhoff C, Scheffler B, Celio MR, Schramm J, Elger CE, Wolf HK, Wiestler OD. Preservation of calretinin-immunoreactive neurons in the hippocampus of epilepsy patients with Ammon's horn sclerosis. J. Neuropathol. Exp. Neurol. 1996; 55: 329-41. PMID 8786391

2. With my advancing expertise in neuropathology of epileptic human brain specimens, I tried to understand functional consequences as a result from focal brain lesions, i.e. altered memory performance in the human hippocampus related to various patterns of segmental neuronal cell loss. Our studies have confirmed previous animal data that acquisition of new memories largely depend to the patient's capability in generating new hippocampal neurons.

- a) Grunwald T, Beck H, Lehnertz K, **Blümcke I**, Pezer N, Kurthen M, Fernandez G, Van Roost D, Heinze HJ, Kutas M, Elger CE. Evidence relating human verbal memory to hippocampal N-methyl-D- aspartate receptors. Proc. Natl. Acad. Sci. USA 1999; 96:12085-9 PMID 10518580

- b) Coras R, Siebzehnrubl FA, Pauli E, Huttner HB, Njunting M, Kobow K, Villmann C, Hahnen E, Neuhuber W, Weigel D, Buchfelder M, Stefan H, Beck H, Steindler DA & **Blümcke I**. Low proliferation and differentiation capacities of adult hippocampal stem cells correlate with memory dysfunction in humans. *Brain* 2010; 133(11):3359-72. PMID 20719879
- c) Coras R, Pauli E, Li J, Schwarz M, Rössler K, Buchfelder M, Hamer H, Stefan H, **Blümcke I**. Differential influence of hippocampal subfields to memory formation: insights from patients with temporal lobe epilepsy. *Brain* 2014; 137(Pt 7):1945-57. PMID 24817139
- d) Marschallinger J, Schäffner I, Klein B, Gelfert R, Rivera FJ, Illes S, Grassner L, Janssen M, Rotheneichner P, Schmuckermair C, Coras R, Boccazzi M, Chishty M, Lagler FB, Renic M, Bauer HC, Singewald N, **Blümcke I**, Bogdahn U, Couillard-Despres S, Lie DC, Abbracchio MP, Aigner L. Structural and functional rejuvenation of the aged brain by an approved anti-asthmatic drug. *Nat Commun.* 2015; 6:8466. PMID 26506265

3. This work has widely contributed to the international rejuvenation of neuropathology in the area of epileptology and the recognition that reliable histopathology diagnosis build the best available foundation for patient stratification in human brain tissue research. The ILAE has appointed me as chair of the Neuropathology Task Force in 2009 and 2013 to deliver international consensus classification schemes for epilepsy-associated brain lesions. Today, these classification schemes are widely accepted in clinical practice and were also used in many translational research studies.

- a) **Blümcke I**, Thom M, Aronica E, Armstrong DD, Vinters HV, Palmini A, Jacques TS, Avanzini G, Barkovich AJ, Battaglia G, Becker A, Cepeda C, Cendes F, Colombo N, Crino P, Cross JH, Delalande O, Dubeau F, Duncan JS, Guerrini R, Kahane P, Mathern GW, Najm I, Özkara C, Raybaud C, Represa A, Roper SN, Salamon N, Schulze-Bonhage A, Tassi L, Vezzani A, Spreafico R (2011) The clinico-pathological spectrum of Focal Cortical Dysplasias: a consensus classification proposed by an ad hoc Task Force of the ILAE Diagnostic Methods Commission. *Epilepsia* 52(1):158-174
- b) **Blümcke I**, Thom M, Aronica E, Armstrong DD, Bartolomei F, Bernasconi A, Bernasconi N, Bien CG, Cendes F, Coras R, Cross JH, Jacques TS, Kahane P, Mathern GW, Miyata H, Moshé SL, Oz B, Özkara C, Perucca E, Sisodiya S, Wiebe S, Spreafico R (2013) International Consensus Classification of Hippocampal Sclerosis in Temporal Lobe Epilepsy: A Task Force Report from the ILAE Commission on Diagnostic Methods. *Epilepsia* 54(7):1315-29
- c) **Blümcke I**, Aronica E, Becker A, Capper D, Coras R, Honavar M, Jacques TS, Kobow K, Miyata H, Mühlebner A, Pimentel J, Söylemezoğlu F, Thom M. Low-grade epilepsy-associated neuroepithelial tumours - the 2016 WHO classification. *Nat Rev Neurol.* 2016 Dec;12(12):732-740.
- d) **Blümcke I**, Aronica E, Miyata H, Sarnat HB, Thom M, Roessler K, Rydenhag B, Jehi L, Krsek P, Wiebe S, Spreafico R. International recommendation for a comprehensive neuropathologic workup of epilepsy surgery brain tissue: A consensus Task Force report from the ILAE Commission on Diagnostic Methods. *Epilepsia.* 2016 Mar;57(3):348-58.

4. My ongoing interest in clinical neuropathology focus on the integration of phenotype-genotype studies for international classification schemes when recognizing the broad spectrum of epileptogenic brain lesions.

- a) Jabari S, Kobow K, Pieper T, Hartlieb T, Kudernatsch M, Polster T, Bien CG, Kalbhenn T, Simon M, Hamer H, Rössler K, Feucht M, Mühlebner A, Najm I, Peixoto-Santos JE, Gil-Nagel A, Delgado RT, Aledo-Serrano A, Hou Y, Coras R, von Deimling A, **Blümcke I**.

- DNA methylation-based classification of malformations of cortical development in the human brain. *Acta Neuropathol.* 2022 Jan;143(1):93-104. PMID: 34797422.
- b) Holthausen H, Coras R, Tang Y, Bai L, Wang I, Pieper T, Kudernatsch M, Hartlieb T, Staudt M, Winkler P, Hofer W, Jabari S, Kobow K, **Blümcke I**. Multilobar unilateral hypoplasia with emphasis on the posterior quadrant and severe epilepsy in children with FCD ILAE Type 1A. *Epilepsia.* 2022 Jan;63(1):42-60. PMID: 34741301
- c) Bonduelle T, Hartlieb T, Baldassari S, Sim NS, Kim SH, Kang HC, Kobow K, Coras R, Chipaux M, Dorfmueller G, Adle-Biassette H, Aronica E, Lee JH, **Blümcke I**, Baulac S. Frequent SLC35A2 brain mosaicism in mild malformation of cortical development with oligodendroglial hyperplasia in epilepsy (MOGHE). *Acta Neuropathol Commun.* 2021 Jan 6;9(1):3. PMID: 33407896
- d) **Blümcke I**, Coras R, Busch RM, Morita-Sherman M, Lal D, Prayson R, Cendes F, Lopes-Cendes I, Rogerio F, Almeida VS, Rocha CS, Sim NS, Lee JH, Kim SH, Baulac S, Baldassari S, Adle-Biassette H, Walsh CA, Bizzotto S, Doan RN, Morillo KS, Aronica E, Mühlebner A, Becker A, Cienfuegos J, Garbelli R, Giannini C, Honavar M, Jacques TS, Thom M, Mahadevan A, Miyata H, Niehusmann P, Sarnat HB, Söylemezoglu F, Najm I. Toward a better definition of focal cortical dysplasia: An iterative histopathological and genetic agreement trial. *Epilepsia.* 2021 Jun;62(6):1416-1428. PMID: 33949696
- e) Kobow K, Ziemann M, Kaipananickal H, Khurana I, Mühlebner A, Feucht M, Hainfellner JA, Czech T, Aronica E, Pieper T, Holthausen H, Kudernatsch M, Hamer H, Kasper BS, Rössler K, Conti V, Guerrini R, Coras R, **Blümcke I**, El-Osta A, Kaspi A. Genomic DNA methylation distinguishes subtypes of human focal cortical dysplasia. *Epilepsia* 2019 Jun;60(6):1091-1103 PMID 31074842

5. My expertise in histopathology review of surgical human brain specimens and the establishment of an unprecedented European Epilepsy Brain Bank results in an active engagement in international research consortia, which gathered vivid momentum. Human brain tissue with neuropathologically well documented lesions is instrumental to approve scientific hypothesis obtained from experimental animal models but also to translate into current diagnostic schemes and novel treatment options.

- a) **Blümcke I**, Spreafico R, Haaker G, Coras R, Kobow K, Bien CG, Pfäfflin M, Elger CE, Widman G, Schramm J, Becker A, Braun KP, Leijten FS, Baayen JC, Aronica E, Chassoux F, Hamer HM, Stefan H, Rössler K, Thom M, Walker MC, Sisodiya SM, Duncan JS, MyEvoy AW, Pieper T, Holthausen H, Kudernatsch M, Meencke HJ, Kahane P, Schulze-Bonhage A, Zentner J, Heiland DH, Urbach H, Steinhoff BJ, Bast T, Tassi L, Lo Russo G, Özkara C, Oz B, Krsek P, Vogelgesang S, Runge U, Lerche H, Weber Y, Honavar M, Pimentel J, Arzimanoglou A, Ulate Campos A, Noachtar S, Hartl E, Schijns O, Guerrini R, Barba C, Jacques TS, Cross JH, Feucht M, Mühlebner A, Grunwald T, Trinka E, Winkler PA, Gil-Nagel A, Toledano Delgado R, Mayer T, Lutz M, Zountsas B, Garganis K, Rosenow F, Hermsen A, Von Oertzen TJ, Diepgen TL, Avanzini G. (2017) Histopathological findings in brain tissue obtained from epilepsy surgery. *New England Journal of Medicine* 2017 Oct 26;377(17):1648-1656. PMID 29069555
- b) Lamberink, H. J., Otte, W., **Blümcke, I.** & Braun, K. P. J. (2020) Seizure outcome and use of antiepileptic drugs after epilepsy surgery according to histopathological diagnosis: a retrospective multi-centre cohort study. *The Lancet Neurology* Sep;19(9):748-757. PMID: 32822635
- c) Capper D, Jones DTW, Sill M, Hovestadt V, Schrimpf D, Sturm D, Koelsche C, Sahm F, Chavez L, Reuss DE, Kratz A, Wefers AK, Huang K, Pajtler KW, Schweizer L, Stichel D, Olar A, Engel NW, Lindenberg K, Harter PN, Braczynski AK, Plate KH, Dohmen H, Garvalov BK, Coras R, Hölsken A, Hewer E, Bewerunge-Hudler M, Schick M, Fischer R,

- Beschorner R, Schittenhelm J, Staszewski O, Wani K, Varlet P, Pages M, Temming P, Lohmann D, Selt F, Witt H, Milde T, Witt O, Aronica E, Giangaspero F, Rushing E, Scheurlen W, Geisenberger C, Rodriguez FJ, Becker A, Preusser M, Haberler C, Bjerkvig R, Cryan J, Farrell M, Deckert M, Hench J, Frank S, Serrano J, Kannan K, Tsirigos A, Brück W, Hofer S, Brehmer S, Seiz-Rosenhagen M, Hänggi D, Hans V, Rozsnoki S, Hansford JR, Kohlhof P, Kristensen BW, Lechner M, Lopes B, Mawrin C, Ketter R, Kulozik A, Khatib Z, Heppner F, Koch A, Jouvet A, Keohane C, Mühleisen H, Mueller W, Pohl U, Prinz M, Benner A, Zapatka M, Gottardo NG, Driever PH, Kramm CM, Müller HL, Rutkowski S, von Hoff K, Frühwald MC, Gnekow A, Fleischhack G, Tippelt S, Calaminus G, Monoranu CM, Perry A, Jones C, Jacques TS, Radlwimmer B, Gessi M, Pietsch T, Schramm J, Schackert G, Westphal M, Reifenberger G, Wesseling P, Weller M, Collins VP, **Blümcke I**, Bendszus M, Debus J, Huang A, Jabado N, Northcott PA, Paulus W, Gajjar A, Robinson GW, Taylor MD, Jaunmuktane Z, Ryzhova M, Platten M, Unterberg A, Wick W, Karajannis MA, Mittelbronn M, Acker T, Hartmann C, Aldape K, Schüller U, Buslei R, Lichter P, Kool M, Herold-Mende C, Ellison DW, Hasselblatt M, Snuderl M, Brandner S, Korshunov A, von Deimling A, Pfister SM. DNA methylation-based classification of central nervous system tumours. *Nature*. 2018 Mar 22;555(7697):469-474. PMID 29539639
- d) Di Liberto G, Pantelyushin S, Kreutzfeldt M, Page N, Musardo S, Coras R, Steinbach K, Vincenti I, Klimek B, Lingner T, Salinas G, Lin-Marq N, Staszewski O, Costa Jordão MJ, Wagner I, Egervari K, Mack M, Bellone C, **Blümcke I**, Prinz M, Pinschewer DD, Merkler D. Neurons under T Cell Attack Coordinate Phagocyte-Mediated Synaptic Stripping. *Cell*. 2018 Oct 4;175(2):458-471. PMID 30173917
- e) D'Gama AM, Woodworth MB, Hossain AA, Bizzotto S, Hatem NE, LaCoursiere CM, Najm I, Ying Z, Yang E, Barkovich AJ, Kwiatkowski DJ, Vinters HV, Madsen JR, Mathern GW, **Blümcke I**, Poduri A, Walsh CA. Somatic Mutations Activating the mTOR Pathway in Dorsal Telencephalic Progenitors Cause a Continuum of Cortical Dysplasias. *Cell Rep*. 2017 Dec 26;21(13):3754-3766. PMID 29281825

Complete List of Published Work in

http://scholar.google.de/citations?hl=de&user=uUKmWIAAAAAAJ&view_op=list_works

449 Publications listed (Clarivate Web-of-Science)

20,034 times cited (Clarivate Web-of-Science)

h-index: 76 (Clarivate Web-of-Science)

Research Support and/or Scholastic Performance

European Reference Networks GA# 769051

03/01/2017-02/28/2021

Establish local standards and expertise for tissue harvest, handling and distribution across participating European epilepsy centers. Adapt the existing virtual neuropathology database to EpiCARE environment by connecting the existing virtual neuropathology database. Further promote the European Epilepsy Brain Bank for standardized tissue preservation/biobanking, histopathological tissue diagnostics and advanced molecular-genetic analysis.

Role: PI (WP6)

NIH R01 NS097719-01A1 (Dr. Jehi)**04/01/2017-3/31/2022**

A Nomogram to Predict Seizure Outcomes after Resective Epilepsy Surgery

The major goals of this project are to develop a nomogram to predict seizure outcomes following epilepsy surgery using clinical, EEG, neuroimaging, and histopathological data. This is the grant proposal that is concerned with this JIT request.

Role: Consultant

German Research Council (DFG) BL 421/4-1**06/01/2019 – 05/31/2022**

A collaborative project of the Univ. Hospital Erlangen, Univ. of Cologne, and Cleveland Clinic Epilepsy Center to assess the genomic burden of risk factors in focal epilepsy from almost 1000 retrospectively collected human brain samples of the Erlangen and Cleveland Clinic biorepositories.

Role: PI

NIH R01 NS109439 (Dr. Wang)**1/15/19 – 12/31/23**

This project aims to develop a quantitative MRI protocol specific for epilepsy patients, which could provide more sensitive and specific measures of brain structure, thereby improving focal cortical dysplasia (FCD) detection and subtyping.

Role: Consultant



Prof. Dr. Ingmar Blümcke

Erlangen, September 2022